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Key Lecture





Genitourinary Syndrome of Menopause: current treatment options in breast

Genitourinary Syndrome of Menopause: current treatment options in breast cancer survivors

Camil Castelo-Branco (ES)

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Breast cancer survivors (BCS) usually receive treatments which lead to persistent oestrogen suppression, which may cause atrophic vaginitis in a large proportion of these women. The most effective treatments for vulvovaginal atrophy (VVA) are based on local oestrogen therapy. However, these treatments are restricted in BCS due to the controversy over their use in women who had hormone-dependent tumours. Therefore, it is common to find untreated symptoms that affect sexual function and quality of life in BCS, thereby leading to the discontinuation of anti-oestrogenic treatments.

In BCS, GSM is the leading cause of sexual dysfunction and severely limits the quality of life of these patients. First-line treatment in BCS presenting mild-moderate VVA is always the use of non-hormonal therapies, which according to the data analyzed, seem to be safe but present limited efficacy and short-term effects. In cases of VVA in BCS refractory to non-hormonal treatment or presenting moderate-severe clinical VVA, the use of local oestrogen therapy is considered and has been demonstrated as being the most effective treatment. Only vaginal oestrogen administration is approved for BCS and always with the use of the lowest possible dose and with consensus between the oncology team and the patient including evaluation of the risks and benefits of the use of these treatments. There is disagreement regarding local oestrogen therapies, and thus, there is controversy as to the safety of these treatments. Some studies suggest a possible increase of serum oestrogen levels that may entail an increased risk of BC recurrence. Finally, new lines of treatment such as vaginal laser, SERMs (Ospemifene) and vaginal androgens or prasterone seem to be effective. Clinical studies assessing their safety in terms of evaluation of elevation in serum estradiol levels or relapse are still lacking in BCS.



Meet the Experts





Operative hysteroscopy in adverse uterine bleeding

Symptomatic submucous fibroids

Stefano Luisi (IT)

University of Siena, Italy

Hysteroscopic myomectomy is now the standard uterus-sparing surgical procedure for treating submucous fibroids. The most common investigative techniques for pre-surgical evaluation are office hysteroscopy, TVS-transvaginal ultrasound and sonohysterography. Above all office hysteroscopy gives information about the presence of the submucous fibroid, the assessment of the intracavitary component of the mass, its localization, its relationship with the uterine structures, the aspect of the endometrium and, not least, the presence of possible associated intracavitary pathologies. New systems of classification have been proposed in order to predict the feasibility and complexity of an hysteroscopic approach. Hysteroscopic myomectomy technique options mostly depend on type and location of the fibroid within the endometrial cavity of the fibroid. Resectoscopic slicing still represents the standard technique to treat this kind of myoma; an innovative device, called IUM, has been proposed and it may become a valid alternative to the traditional transcervical resectoscopic myomectomy. One-step myomectomy remains the most auspicious procedure and the “cold loop” myomectomy seems to represent the best option since it allows a safe and complete removal of fibroids in just one surgical procedure, respecting the surrounding healthy myometrium and reducing the risk of operative (bleeding, perforation) and long term complication (IUA and uterine rupture).



Operative hysteroscopy in adverse uterine bleeding

Endometrial pathologies

Andrea Giannini (IT)

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Context

Abnormal uterine bleeding is defined as uterine bleeding that is abnormal in duration or timing. It affects 14-25% of women of reproductive age. Most of the causes of abnormal uterine bleeding (AUB) are benign; however, it is also the most common symptom of endometrial hyperplasia (EH), endometrial polyps, and endometrial carcinoma (EC).

Objective

This presentation aims to improve knowledge about incidence and presentation of AUB in healthy women of different ages or in presence of specific risk factors and about the use of hysteroscopy in this clinical scenario.

Methods and main outcomes

The counseling of patients with AUB in perimenopause and postmenopausal periods should be exhaustive regarding the fact that, although the incidence of endometrial cancer increases after menopause, 10% of it occurs before menopause. Atypical endometrial hyperplasia is associated with a concurrent carcinoma in up to 50% of the first step to identify structural abnormalities is transvaginal sonography (TVS), because the measurement of the thickness of the endometrium is important to stratify the risk and plan next diagnostic steps if required.

Results

Thickness of the endometrium has to be less than 5 mm in postmenopausal women and less than 15 mm during the pre and perimenopausal women, however age and personal risk factors play an important role in the choice of different diagnostic approaches to AUB and the possible use of hysteroscopy as diagnostic tools. Ultrasonography, hysteroscopy, and endometrial sampling, alone or in combination are sufficient for the diagnosis of AUB in most women, even undergoing menopausal hormonal therapy with a continuous or sequential regimen based on atrophy or proliferative tissue. Indeed, hysteroscopy allows the detection and the characterization of polyps, myomas or adenomyosis, and endometrial pathologies.

Conclusions

The identification of endometrial cancer or precancerous endometrial pathologies in women could be based on a the structured evaluation of the endometrium and the possibility to perform direct and precise biopsies with hysteroscopy using different techniques and tools. There are also additional tests which can be carried out during the assessment. Additional exams include: laboratory tests with a full blood count and iron studies. Pregnancy testing and thyroid screening may also be appropriate for the general evaluation of patients with AUB before or after hysteroscopy.



Estrogens contribute to reduce the severity of Covid 19 infections

Understanding the mechanisms responsible for sex-related differences in innate and adaptive immunity during viral infectious diseases

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Severe forms of COVID-19 are more common in men than in women in all countries examined so far. It has been proposed that the sex bias in COVID-19 severity might be related to a relative deficiency in innate-immunity to viruses in males compared to females.

Toll-like receptor 7 (TLR7), encoded by an X-linked gene, is key to the innate defense against RNA viruses, including SARS-CoV-2, and the TLR7-driven innate and adaptive B cell immunity to RNA viruses are stronger and of better quality in females compared to males. TLR7 deficiency due to loss-of-function variants has been identified in patients with severe COVID-19, and are associated with suppressed production of type I interferons (IFN-I) by plasmacytoid dendritic cells (pDCs).

Thus, TLR7 and pDCs are essential for protective type I IFN immunity against SARS-CoV-2 in the respiratory tract. Remarkably, the capacity of female pDCs to produce higher levels of IFN-I, compared to those of males, is one immune characteristic that robustly distinguishes the two sexes.

I will discuss the findings supporting the notion that both estrogen-signaling and/or X-linked genetic factors independently contribute to the female predominance in pDC innate functions, and present recent development on the analysis of the sex differences in TLR7-driven interferogenesis across ages.



Round Table - Talk Show





COVID-19 and women's health

COVID-19 and stillbirth in Italy

Fabio Facchinetti (IT), Cristina Salerno (IT), Valeria Donno (IT), Beatrice Melis (IT), Daniela Menichini (IT), Francesca Monari (IT)

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WHO declared SARS-CoV-2 infection as a pandemic in March 2020. The aim of this study is to compare SB occurrence and its features during pandemic period (March to December 2020) with the ones in the same period, in the previous 6 years, in Emilia Romagna region, Italy.

This study collected SB information by the Surveillance System, active since 2014. Each case was audited in a multidisciplinary meeting to evaluate the causes of SB according to ReCoDe classification, and the quality of care by using CESDI grade (grades 2 and 3 refer to substandard care = different management might/would have made a difference to outcome). SB was defined according to WHO recommendations (≥ 22 weeks or ≥ 500 g when gestational was unknown). The numbers of birth per years were obtained by birth certificates (CedAP).

During pandemic, there were 89 SB out of 25,225 births (3.52/1000) compared with the previous 6 years when SB rate ranged from 3.00 (83/27,625) in 2018 to 3.55 (91/26,493) in 2019. No cases of SB was detected in pregnant women affected by SARS-CoV-2 infection.

Maternal age, years of education, country of origin, gestational weight gain and smoking did not change, while an increased number of SB was recorded in multiparous women (OR 1.62; 95% CI: 1.02-2.55). The proportion of preterm births was not substantially different between pandemic period compared to the previous period (OR 1.34; 95% CI: 0.81-2.23). At multivariate analysis, a higher risk of SB was found in overweight mothers, in those at 22+0-24+6 weeks and in SGA infants.

There were not significant changes in the frequency of SB causes, compared to the previous period, although a trend toward an increase of the placental abruption cases (OR 1.72; 95% CIC 0.96-3.09). Cases with grade 2 or 3 during pandemic was 6%, similar to the reference period (10%). No significantly changes occurred in the number of obstetric evaluations as well as in the number of ultrasounds exams.

Globally, SARS-CoV-2 pandemic did not substantially influence SB incidence and pregnancy care. The pandemic restrictions might have affected the access of women at risk to pregnancy services, especially in the first half of gestation, with subsequent low detection rate of SGA.



COVID-19 and women's health

COVID-19 and menstruation

Jacqueline A. Maybin (UK)

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Abnormal uterine bleeding (AUB) is a debilitating symptom that affects up to one in three women at some point in their reproductive lives. There are many anecdotal reports of experiencing AUB during the COVID-19 pandemic. This may have a significant negative effect on individual quality of life and have wider negative economic impacts on healthcare services and society.

This session will define typical and problematic menstrual bleeding before exploring the potential association between COVID-19 and AUB, including possible causal mechanisms. Effects of the pandemic, acute COVID-19, Long COVID and COVID-19 vaccination will be addressed. Conversely, the impact of the menstrual cycle on COVID-19 symptoms will be reviewed. The current available evidence will be discussed throughout and gaps in our current knowledge and understanding will be signposted, highlighting specific priority areas for future research.

The aim of the presentation is to provide medical professionals with the evidence base to inform their clinical consultations and empower them to advocate for the inclusion of menstrual symptoms in future research.



Symposia





How to improve fertility treatments

Controlled ovarian stimulation in IVF/ICSI: positive modulation of aromatase inhibitors (AOI) on follicular and luteal phase function

Sven Skouby (DK)

Clinical Medicine University of Copenhagen, Denmark

Infertility is defined as the inability of conception after one year of regular sexual activity without using any contraception methods. Controlled ovarian stimulation (COS) might be required to improve ovulatory problems. One of the medications used is clomiphene citrate (CC), which leads to successful ovulation rates in most cases (up to 90%). Despite the high ovulation rates the pregnancy rates are still disappointing.

The aromatase inhibitors (AOI), which have letrozole as its main representative, have been increasingly used over the past years. Letrozole reduces circulating estrogens by preventing aromatization of androgens. A study presented in 2005 in ARSM showed that letrozole use was associated with a high risk of malformations in the newborns. Studies subsequently published showed no increase. Letrozole is also an established adjuvant in ovarian stimulation for fertility preservation in breast cancer patients. It's general use in COS for IVF is limited. However, there is growing interest in its potential value as an adjuvant to gonadotropins via limiting the supra-physiological rise in estrogen. Furthermore, it may improve response to gonadotropins in those women with reduced ovarian reserve.

The presentation will focus on the functional endocrine changes with original data during COS with letrozole intervention.



How to improve fertility treatments

Luteal phase in frozen embryo transfer cycles

Pedro N. Barri (ES), Manuel Alvarez (ES), Iñaki González (ES), Nikolaos Polyzos (ES), Buenaventura Coroleu (ES)
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The ratio between FET/IVF has spectacularly increased in the last years mainly thanks to the pursuit of an ovarian hyperstimulation syndrome free clinic and the development of preimplantation genetic testing (PGT). There is currently a big concern regarding the endometrial preparation for FET, especially in relation to serum P4 levels around the time of embryo transfer.

Several studies have described impaired pregnancy outcomes in those patients with low P4 levels around the time of FET, considering 10 ng/ml as one of the most accepted reference values. To date, no prospective study has been designed to compare the reproductive outcomes between patients with adequate P4 the day previous to euploid FET and those with low, but restored P4 levels on the transfer day after iLPS through daily Psc started on the day previous to FET.

A prospective observational study was conducted at a university-affiliated fertility centre between November 2018 and January 2020 in patients undergoing PGT for aneuploidies (PGT-A) IVF cycles and a subsequent FET under hormone replacement treatment (HRT). A total of 574 cycles (453 patients) were analysed: 348 cycles (leading to 342 euploid FET) with adequate P4 on the day previous to FET, and 226 cycles (leading to 220 euploid FET) under iLPS after low P4 on the previous day to FET, but restored P4 levels on the transfer day.

Patients with low serum P4 the day prior to euploid FET can benefit from the addition of daily subcutaneous P4 injections (Psc), when started the day prior to FET, and achieve similar reproductive outcomes compared to those with initial adequate P4 levels.



The patient needs oriented contraception

Emergency contraception revisited

Ali Abdullah M H Kubba (UK)

London Bridge Hospital London, United Kingdom

Everybody (nearly) needs it sometime.

Emergency contraception (EC) is an essential element of contraceptive care. In parts of the world where access to contraception is poor or among risk taking population such as adolescents it could be a life saver.

Women (and their partners) need clear information:

- EC works
- there are oral and intrauterine options
- the sooner it is accessed the better

Access remains a challenge and a barrier due to lack of knowledge and myths and misconceptions among HCPs and the population.

All scientific evidence supports OTC availability. Medical regulators in some countries need educating that EC is not an abortifacient.

Safeguarding is essential where a vulnerable person requests EC.

Contraceptive technologies are getting better, we now have more effective EC pills and always recognized that the copper IUD is the most effective EC method. Hormonal IUDs may also work but more evidence is required.

All these points will be explored in my presentation.



The patient needs oriented contraception

LARC focused counselling and impact on unintended pregnancy

Kristina Gemzell-Danielsson (SE)

Karolinska University Hospital, Stockholm, Sweden

Background

There are no consistent recommendations or models on how to provide effective contraceptive counselling involving informed decision making.

Aim

To evaluate the effect of structured contraceptive counselling on the uptake of long-acting reversible contraceptives (LARCs) and pregnancy rates.

Methods

A cluster randomised controlled trial conducted at abortion, youth and maternal health clinics in Stockholm, Sweden. Clinics were randomised to intervention, implementing a study-specific intervention package designed for structured contraceptive counselling, or control providing routine counselling. Eligible participants were sexually active women aged ≥ 18 years without a wish for pregnancy seeking contraceptive counselling. The primary outcome was choice of LARCs at first visit. Secondary outcomes were LARC initiation at 3 months and pregnancy rates at 12 months.

Results

Study period: September 2017 to May 2020. Analyses including 1,338 subjects showed that more participants in the intervention group compared with the control group chose LARCs, LARC initiation was higher in the intervention group compared with the control group and at the abortion clinics, the pregnancy rate was significantly lower at 12 months in the intervention group compared with the control group.

Conclusions

Structured contraceptive counselling increased LARC uptake in all clinics and significantly reduced unintended pregnancy rates.



The patient needs oriented contraception

Impaired peak bone mass in hormonal contraception – reality or myth?

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For years, it was believed that hormonal contraception (HC) was safe and did guarantee bone health in all users. This is still true for healthy post-adolescent women >30 years of age and for perimenopausal women where low-dose preparations containing 15-20 EE are still capable of protecting bone as do older pills delivering 30-35µg EE/day. Combined oral contraception (COC) may prevent the physiological bone loss that occurs in women >40 years of age and possibly increase BMD in the perimenopause.

However, evidence shows today this is not the case for some subgroups of HC users. In adolescents ($\leq 18-20$ years), the strongly anti-gonadotropic progestins used in COCs containing 15-20µg EE over-suppress the hypothalamic-pituitary-ovarian axis and reduce profoundly endogenous E2 production. As a consequence, 15-20µg EE do not guarantee the necessary oestrogen activity for the acquirement of a normal peak bone mass (PMB) as do 30µg EE COCs. For the same reason, in adolescents, depot-medroxyprogesterone acetate (DMPA) administration may reduce PBM, particularly when given early after menarche.

Furthermore, there is strong evidence from longitudinal data that DMPA affects significantly BMD in adult current users. However, the BMD decrease appears to be at least partially reversible in adult and in adolescent women.

This evidence leads to the following recommendations:

1. In adolescents, 30-35µg EE COCs are safe for the acquisition of a PMB.
2. In contrast, 15-20µg EE COCs should not be used in young women until stable ovulatory cycles are reached.
3. DMPA should be avoided in adolescents before PMB is acquired. Initiation of DMPA within the first 3 years after menarche is of particular concern. DMPA should remain a reserve medication where no alternative is possible.
4. For all other HC methods, good evidence is missing in adolescent girls and it is not known if their use is safe in young women before PBM is completed.



Menopause: the latest news and recommendations

Hormone-dependent cancer: lessons from the breast with a message in the endometrium and the ovary

Antonio Cano (ES), Ester Ortiz (ES)

Service of Obstetrics and Gynecology, Hospital Universitario Dr Peset, Valencia, Spain

Clinical studies with both contraceptives and menopausal hormone therapy have confirmed the link of progestogens with breast cancer. Progression in the molecular details of progestogens action on the breast has unraveled that the system composed of one cytokine, the ligand of the receptor activator of nuclear factor- κ B ligand (RANKL) and its receptor RANK, is sensitive to progestogens. RANKL/RANK have been shown to play a role in increasing the malignant susceptibility of breast epithelial cells. The awareness of this mechanistic link has expanded clinical interest, so that RANKL/RANK have emerged as a biomarker of tumor differentiation. The implications in clinical practice are being considered in what forms a breakthrough in current oncological research.

The mediation of the pro-mitotic action of progestogens on breast by RANK/RANKL raises questions on whether the system is involved in the diametrically opposed actions of progestogens in the endometrium. The anti-proliferative effect of progestogen on endometrial epithelium is well known, although the molecular basis is not totally clear. RANK and RANKL are expressed in normal endometrium and, as for breast cancer, the system behaves as markers of the malignant potential of endometrial tumors. There is some incipient molecular work partly describing the action of progestogens on the cellular pathways involving RANK in endometrium.

The intricacies of the links between breast and genital tumors also relate with ovarian cancer. An additional feature is that the ovary shares a tumor susceptibility status associated with high penetrance genes, like BRCA1/2, although little is known about the molecular background of the link. It is of interest that the pharmacologic inhibition of RANKL seems to interfere some preneoplastic lesions conditioned by mutated BRCA1 in mouse models. In consistence with those findings, RANK/RANKL has been recently found to be expressed in the ovary, and the expression is increased in ovarian cancer. This is particularly notorious in BRCA1/2 mutated tumors and, as for endometrial cancer, it seems inversely related with reduced progression free and overall survival.



Menopause: the latest news and recommendations

Connective tissue turnover with the menopause and in response to HRT

Mark P. Brincat (MT)

Department of Obstetrics & Gynecology, Mater Dei Hospital, Msida, Malta

Interest in connective tissue turnover started indirectly with the realisation in the early 1940's but possibly decades before that older women were sustaining many more long bone fractures that were attributed to Osteoporosis than men were. It was soon realised that the loss of Osteoporosis was a main factor in contributing to the rapid bone loss in women, that was occurring after the menopause.

Similar changes were found to be taking place in skin dermal collagen, blood vessel media as measured primarily in the carotid artery and later in vertebral discs and also some suggest that connective tissue was also declining in articulated joints.

There were significant differences in the above symptoms when compared to premenopausal women. These were moreover significant differences in all the above parameter when women who were not on HRT were compared to those who were on HRT. This seemed to be dose dependable.

The losses in connective tissue could not only be prevented, but in certain cases, there was evidence of connective tissue lost, being replaced with HRT.



Menopause: the latest news and recommendations

MHT: why to start, how to manage

Andrea R. Genazzani (IT)

Division of Obstetrics and Gynecology, Department of Clinical and Experimental Medicine, University of Pisa, Italy

Context

Menopausal symptoms can be very distressing and considerably affect a woman's personal and social life. It is becoming more and more evident that leaving bothersome symptoms untreated in midlife women may lead to altered quality of life, reduced work productivity and possibly overall impaired health.

Objective

Hormone therapy (HT) for the relief of menopausal symptoms has been the object of much controversy over the past two decades. At the beginning of the century, a shadow was cast on this treatment due to the concern for cardiovascular, cerebrovascular risks, and breast cancer from a large randomized placebo-controlled trial.

Methods and main outcomes

Findings of a subanalysis of the trial data, extended follow-up studies, along with other more modern clinical trials and observational studies, have provided new evidence on the effects of HT.

Results

Menopausal symptoms can be very overwhelming for women. Over the years, many pharmacotherapeutic options have been tested, and others are still being developed. Hormone therapy is the most efficient therapy for managing vasomotor symptoms and related disturbances. The term HT comprises estrogens and progestogens, androgens, tibolone, the tissue-selective estrogen complex (TSEC), a combination of bazedoxifene and conjugated estrogens, and the selective estrogen receptor modulators, such as ospemifene. Estrogens and progestogens and androgens may differ significantly for chemical structure and can be delivered through different routes, thereby displaying various pharmacological and clinical properties. Tibolone, TSEC and SERM also exhibit unique pharmacodynamics that can be exploited to obtain distinctive therapeutic effects. For women with contraindications to HT, such as breast cancer, endometrial cancer, cardiovascular disease, a non-hormonal approach can be considered. Non-hormonal options fall mainly into the selective serotonin reuptake inhibitor (SSRI) and selective noradrenergic reuptake inhibitor (SNRI), GABA-analogue drug classes.

Conclusions

Current research is focusing on neurokinin receptor antagonists for the non-hormonal management of hot flashes. Physicians must have in-depth knowledge of the pharmacology of compounds to tailor therapy to the individual patient's characteristics and needs.



Menopause: the latest news and recommendations

POI: IMS latest recommendations

Nick Panay (UK)

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This is a summary of the 2020 International Menopause Society POI White paper recommendations, which will be presented in full at the European Society of Gynecology 2021 meeting:

Demographics / etiology / pathophysiology of POI

- Terminology and diagnostic criteria should be standardised to avoid confusion about diagnosis.
- Full understanding of etiology / pathophysiology will facilitate efficient diagnosis and management, e.g. global registry/biobank.
- Global, ethnic and cultural variations in prevalence, presentation require clarification.

Diagnosis of POI

- Personal e.g. menstrual health and family history are very important in making the diagnosis.
- The diagnosis should not be made on the basis of only one FSH level.
- AMH testing is only required if there is diagnostic uncertainty.
- A baseline DEXA scan should be offered to all women diagnosed with POI.

Management of POI

- Management of women with POI should ideally be multidisciplinary and include patient advocacy groups.
- Lifestyle, diet exercise should be optimised.
- Hormone replacement at least until average age of menopause - first line unless contraindicated or if rejected by woman after counselling.
- There are few data for the benefits and risks of CAMS and non-hormonal bone sparing agents in POI.
- Replacement can be with COC initially if contraception is required or because of personal preference, but in the long term HT is recommended to optimise bone and metabolic health.

Key Research priorities in POI

- Global POI registry collaboration / expansion / biobanking.
- Further determination of etiologies of POI, especially genetic.
- Discovery of reliable biomarkers for predicting POI.
- Impact of hormonal interventions e.g. HT v COC, types of HT/COC on:
 - QOL
 - Psychological/psychosexual aspects
 - Bone, cardiovascular and cognitive health.
- Role of androgen supplementation for QOL, cardiovascular, bone, cognitive health and fertility.
- Differential impact and management of iatrogenic and spontaneous POI.
- POI as part of an aging syndrome versus aging following POI due to hormone deficiency.
- Confirmation of efficacy and safety of fertility enhancing techniques.
- Further clarification of role and division potential of human oogonial stem cells.



Screening in early pregnancy

Maternal infections: revisiting the need for screening in early pregnancy

Yves Ville (FR)

EA Fetus, Paris Descartes Université, Université de Paris, Paris, France; Assistance Publique-Hôpitaux de Paris, Hôpital Necker Enfants-Malade, Maternité, Paris, France

The decision to implement screening for infections during pregnancy depends upon epidemiological, economic, therapeutic and test performance criteria. It therefore varies with public health priorities from country to country. When screening is implemented, the first trimester has become the best time slot to build individual care pathways in this field. This is most relevant for evaluating the risk of embryonic consequences, planning diagnostic testing, initiating primary or secondary prevention and optimising the accuracy of ultrasound follow-up. This lecture will be a critical appraisal of epidemiological data and current international screening recommendations for infections in pregnancy

Among all infections posing a threat to the pregnancy, Cytomegalovirus has become the new rubella and unlike the former maternal symptomatology is not helpful, immunity is only partly protective and there is no vaccine to date. It is the main cause of non-genetic sensori-neurological handicap in children. Congenital cytomegalovirus infection is an important health problem for the individual and the community. Although it could derive from both primary and nonprimary maternal infection, the prospective risk of congenital infection in seronegative pregnant women is 4 times than that of immune women.

Maternal serology is the only reliable screening tool in pregnancy that would identify up to 50% of all congenital cytomegalovirus infections, by yielding positive immunoglobulin M and immunoglobulin G and low immunoglobulin G avidity in approximately 0.5% of the population at 11 to 14 weeks. The exceptionally high risk for young parous seronegative women planning a second pregnancy makes a compelling case for offering serologic screening as soon as pregnancy is planned or diagnosed and by the end of the first trimester. The 11- to 14-week consultation has become an unmissable one worldwide and would represent the most practical compromise if only 1 sample can be taken. Valaciclovir that can be safely used in the early fetal period decreases vertical transmission by 70% and should be implemented as early as possible after maternal infection. Facilities for diagnosis and treatment are available in high- and middle-income countries through laboratory and fetal medicine networks. Amniocentesis with amplification of the viral DNA by polymerase chain reaction in the amniotic fluid is a reliable diagnostic test but chorionic villi sampled by chorionic villus sampling could achieve the same performance 2 months earlier. Fetal imaging of a known infected fetus yields a negative predictive value on symptoms at birth and congenital handicap of between 95% and 99%, and prenatal treatment of infected fetuses decreases the occurrence of symptoms at birth and at 2 years of age.



Screening in early pregnancy

First trimester screening for pregnancy complications

Pavel Calda (CZ)

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First trimester pregnancy assessment at 11-13weeks' gestation is used for estimation of gestational age, diagnosis of multiple pregnancy and chorionicity, screening for fetal aneuploidy, risk assessment of preterm preeclampsia and diagnosis of fetal morphological anomalies.

Recently, preeclampsia risk screening allows prophylactic administration of aspirin with substantial reduction of preeclampsia occurrence before 34 weeks of pregnancy, and reduction of preterm birth with all unwanted consequences. First trimester screening developed to sophisticated discipline, allowing to distinguish between low and high risk pregnancies.

Thanks to FTS it is possible to invest resources and energy to those who really need it.



Polycystic Ovary Syndrome: from genetic aspects to therapy

PCOS: metabolic dysfunction and its short- and long-term implications

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At an early age the most common reasons for women diagnosed with PCOS to consult a doctor are irregular bleeding and infertility. Diagnosis is based on cycle abnormalities, polycystic ovaries and hyperandrogenemia. Subtle sign of metabolic dysfunction can often be observed, even at an early age. Bleeding problems can often be addressed adequately by hormonal interventions. Prognosis for infertility with ovulation induction followed by IVF is usually excellent with high cumulative (singleton) pregnancy rates up to 80%. However, pregnancy complications are clearly increased, and perinatal outcomes are compromised. Gestational diabetes represents the most common pregnancy complication in women with PCOS and the clinical benefit of preventive strategies - such as the use of insulin sensitizing drugs - remain uncertain. Recent studies also provide evidence of subtle but distinct cardiometabolic abnormalities in male and female PCOS offspring, even at a young age.

When women with PCOS get older, menstrual cycle patterns often normalize and fertility potential may even be restored. However, metabolic abnormalities aggravate, and type 2 diabetes, dyslipidemia or hypertension can often be observed. Many studies confirm the presence of subclinical cardiovascular disease (i.e. abnormal intima media thickness and flow mediated dilatation) in women with PCOS between 40 and 50 years of age. Surprisingly, despite overwhelming evidence suggesting increased risk for developing cardiovascular disease in later life in these women, most studies so far failed to demonstrate an increased incidence of cardiovascular events such as myocardial infarction, stroke or death. Moreover, large sample size population based studies recently demonstrated that elevated androgen levels after menopause is not associated with increased cardiovascular risk. The presence of - as yet unknown - protective factors may be hypothesized.

PCOS - a condition occurring in 10-15% of all women - has become a disease condition broadly recognized as having major implications for quality of life throughout the life cycle. In the past, gynecologists focused only on reproductive dysfunction in these women, but at present many other specialties are getting involved. We need multi-disciplinary approaches for proper care of women with PCOS including preventive strategies at different phases of life.



Polycystic Ovary Syndrome: from genetic aspects to therapy

Integrative approach to PCOS: trick and tips

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PCOS is a very frequent endocrine disease characterized at least by 2 out of 3 of the Rotterdam criteria, that are anovulation/oligomenorrhea, hyperandrogenism, polycystic ovarian morphology. However, in these recent years, a new issue has been added to the syndrome, that is the dimetabolic aspect related to the insulin resistance (IR) and the compensatory hyperinsulinemia that are frequently, though not always, related to overweight/obesity.

At present most of the clinicians try to face and solve IR prescribing insulin sensitizers, such as metformin, to subjects with PCOS and IR but in many cases this treatment is not well tolerated especially at high dosages. Recently new integrative strategies have been developed to overcome this problem, finding a more natural way to face the issue of hyperinsulinemia and IR. In fact the use of inositols, i.e. MYO-inositol (MYO) & D-chiro inositol (DCI), have been demonstrated to be helpful to the syndrome, being however essential the knowledge of the anamnestic history of the patient. MYO is usually converted by an epimerase into DCI. Such epimerase is however less expressed in patients with familiar diabetes or suffering for diabetes thus determining an unbalancing between the biological actions of MYO and DCI. This impairment is potentially a serious issue since 50-65% of PCOS patients have familiar diabetes and are overweight/obese.

In addition, also an imbalance in alpha lipoic acid (ALA) synthesis has been reported in the same group of PCOS subjects due to a mitochondrial impairment of expression/function of LASY (lipoic acid synthase) enzyme.

Moreover, recent studies reported that PCOS shows also a pro-inflammatory state mainly sustained by an impairment of the endogenous anti-oxidant system. In fact recent studies clearly demonstrated that the integrative approach using canitines, L-arginine (L-Arg) and N-acetyl cystein (NAC) greatly improve the hyperinsulinemic state reducing IR acting on the pro-inflammation.

As for what above described, new treatments, mainly integrative, are now available to face the complex genetic and/or epigenetic impairments that PCOS shows. Theoretically, inositols, ALA, L-Arg and NAC are the new strategic integrations that might be associated with a correct life style, being this last essential.

In conclusion, the real relevant aspect is to have specific insights and advices so that to better choose what might be the more appropriate integrative approach for PCOS.



Polycystic Ovary Syndrome: from genetic aspects to therapy

What about the PCOS phenotypes

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Polycystic ovary syndrome (PCOS) is a disease comprising all periods of woman's life, starting from the foetal periods until menopause. Taking into account many options, we recommend identification of PCOS women in the aspect of ovulation dominant disturbances, hyperandrogenism and metabolic problems, which prevail both in pubescence and menopausal periods. Taking into account phenotypes adopted in ESE consensus, metabolic, hyperandrogenic and reproductive phenotypes should be considered. Metabolic phenotype is predominant and metabolic disturbances accompany abdominal obesity, however also this phenotype was recognised in women with metabolic obesity and normal weight. This phenotype associated with insulin resistance and dyslipidemia. In hyperandrogenic phenotype, biochemical and/or clinical hyperandrogenism symptoms are dominant. In reproductive phenotype, irregular (rare) menstruation with disturbed ovulation or no ovulation and secondary amenorrhea are dominant problems. According to PCOS phenotypes personalised therapy is recommended.



Impacts of endometriosis and adenomyosis on women's health and fertility: strategies and therapies

Infertility and adenomyosis: the mechanisms

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Adenomyosis is a benign uterine disorder in which endometrial glands and stroma are pathologically demonstrated in the uterine myometrium. Although it has always been considered the classic condition of multiparous women over 40 years old who have pain and heavy menstrual bleeding, adenomyosis is increasingly identified in young women with infertility and reproductive failure, by using imaging techniques such as transvaginal ultrasound and magnetic resonance. Approximately 25% of infertile women, especially those who have had recurrent pregnancy loss and implantation failure, those requiring IVF, and those with concomitant endometriosis. Among women under fertility treatments, rates of implantation, clinical pregnancy per cycle and embryo transfer, ongoing pregnancy, and live-birth rate were significantly reduced, whereas miscarriage rate was increased.

In infertile women with adenomyosis, eutopic endometrium shows a wide variety of molecular alterations, causing an altered receptivity. This includes altered sex steroid hormone pathway, increased inflammatory markers and oxidative stress, reduced expression of implantation markers, lack of expression of adhesion molecules, and altered function of the gene for embryonic development (HOXA 10 gene), causing an impairment of implantation.

Abnormal uterotubal transport seems to be another important mechanism leading to infertility and is due to anatomical distortion of the uterine cavity but also to disturbed uterine peristalsis and sperm transport. The inner myometrium and, in particular, the junctional zone, present with dysfunctional hyperperistalsis and increased intrauterine pressure. In addition, in the presence of adenomyosis, ultrastructural myometrial abnormalities cause a disturbance in normal myocyte contractility. All these endometrial and myometrial mechanisms seem to contribute to the impact of adenomyosis on fertility.



Adolescent gynecology

Kisspeptin role in puberty process and puberty disorders

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Puberty is defined as a gradual biological process characterized by several hormonal changes that allows an individual to become sexually mature and acquire the reproductive ability.

The reproductive system is governed by hypothalamic-pituitary ovarian axis. Puberty onset is related to an increase of gonadotropin-releasing hormone (GnRH).

Kisspeptin is a neuropeptide encoded by kisspeptin gene (KISS1) and located in different brain regions mainly in hypothalamus (arcuate nucleus and preoptic area). Kisspeptin is regarded as the main positive regulator of GnRH pulsatile release. Kisspeptin acts through GPR54 receptor (Kisspeptin receptor). Scientific evidences suggest that hypothalamic kisspeptin neurons play a critical role in controlling puberty onset via GnRH stimulation.

Clinical studies revealed that inactivating mutations of the GPR54 gene and mutation of Kisspeptin gene caused the impairment of pubertal maturation and reproductive function (hypogonadotropic hypogonadism). Activating kisspeptin receptor gene mutation as a cause of precocious puberty also has been described. Further studies on kisspeptin are required to fully elucidate underlying mechanisms of pubertal onset and puberty disorders in humans. Additionally possible studies on kisspeptin agonists and antagonists for the potential treatment of puberty disorders should be considered.



Progestogens, progestins or natural progesterone: why all the confusion in pregnancy maintenance?
(organized by PREIS School Academy)

Potential benefits with progesterone and related progestins in late pregnancy maintenance (PTB)

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Progesterone plays an important role in maintaining pregnancy thanks to suppressive actions on the immune system and lymphocyte proliferation and activity. Uterine smooth muscle activity is suppressed by progesterone ensuring maintenance of pregnancy. In mammalian species onset of labour accompanied by decreased progesterone levels in peripheral blood. This mechanism has not been described in humans.

We hypothesize, that the cervical ripening is caused by progesterone antagonists leading to cervical shortening. The use of vaginal progesterone, due to meta-analyses, reduces the risk of preterm birth before 34 weeks and composite adverse neonatal outcome in women with a singleton pregnancy and short cervix <25mm. In low risk singleton women without a history of PTB, cervical length measurements may be of value to identify women at risk for preterm birth. When a midtrimester measurement of the cervix of 25 mm is detected, women can be offered treatment with vaginal progesterone 200 mg. Screening for short cervical length in midtrimester in a low risk population makes the use of vaginal progesterone cost-effective.

Women with one or more PTB in their history, should be offered routine progesterone starting at 16 weeks of gestation until 36 weeks. In addition, serial cervical length screening is indicated between 16 and 24 weeks of gestation.



Scientific Society Symposia





New data and approach of current problems

(organized by SELFAGO - Société Européenne de Langue Franco-Allemande de Gynécologie-Obstétrique)

Chronic pelvic pain syndrome and its multidisciplinary management

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The understanding of the pathophysiological mechanisms of chronic pain has evolved in recent years. This evolution is established for example in the fields of neurology, rheumatology, orthopedics, oncology.

When pain is chronic in the female pelvis, the scientific and medical awareness of the complexity of these situation seems less developed.

The gynecologist and the general practitioner are the specialists the most often consulted in this context. Pelvic pain leads the patient as well as the primary care physicians to a gynecological origin.

Among the gynecological etiologies endometriosis, adenomyosis and uterine fibroids will be the most frequent.

However, pelvic pain in female patients is not necessarily related to the female genital organs. Occasional, permanent, diffuse or localized pelvic heavy feeling or dyspareunia may be related to other etiologies. Among these etiologies, irritable bowel syndrome, interstitial cystitis, pelvic congestion or adhesions have been described. These syndromes can have an inflammatory but also vascular or infectious origin.

An inflammatory process can be caused by endocrinological, rheumatological, psychological and nutritional disorders.

Vascular disorders such as the Nutcracker syndrome or the Cockett syndrome represent recently described complex pathologies.

A history of pelvic infection or of abdomino-pelvic surgery can create adhesions causing chronic pain.

Likewise, it might be possible that the patient demands an advice in a context of vulvodynia. It can be discussed if the chronic pelvic pain syndrome should include this entity, also.

Without wishing to claim an exhaustive list of the etiologies of pelvic pain in female patients, it is obvious that this subject can no longer - apart from clinically clear contexts - be limited to treatment by a single caregiver. The multiplicity of etiologies of chronic pelvic pain is linked to often severe, frustrating and persistent symptoms which have an adverse impact on the quality of life. The patient may have a long medical « journey » and, without an answer to her question, turns to different doctors - often again gynecologists. Today, in view of the awareness of the complexity of this clinical frequent situation and also without forgetting its economic impact, the doctors are brought to explore this syndrome in a multidisciplinary context. Only a global approach will have a positive effect on the patients' quality of life.



New data and approach of current problems

(organized by SELFAGO - Société Européenne de Langue Franco-Allemande de Gynécologie-Obstétrique)

Itch and hitch-Lichen sclerosus is the chameleon of the vulvar disorders

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Context

Lichen sclerosus (LS) of the vulva is an inflammatory disease with an estimated prevalence of 1.7% in the general female population. Many studies are based on the clinical suspicion of LS without histological confirmation. But symptoms are often unspecific and clinical presentation may vary. This results in delayed diagnosis and represents a challenge for the physician.

Objective

Aim of this study was to determine the correlation of clinical suspicion of LS with the histological findings.

Methods

We performed a subanalysis of data collected during a drug trial comparing various treatments in patients with vulvar LS.

Patient(s)

For the study 105 women with a clinical suspicion of LS were screened by experts in our specialized consultation for vulvar disorders.

Intervention(s)

During the screening visit we recorded symptoms with questionnaires and collected clinical findings in colposcopy. A cold cut biopsy was performed.

Main outcome measure(s): Symptoms, clinical findings and histological results were correlated.

Result(s)

We screened 105 patients with a strong clinical suspicion of Lichen sclerosus but only in 30 (28.6%) patients the diagnosis was histological confirmed. Clinical findings did not match histological results in 75 cases. The main differential diagnoses were: Lichen simplex chronicus n=20, eczema n=17 and mechanical irritation in 12 patients.

Regarding the principal symptoms itching, burning and dyspareunia and their severity we were unable to find a statistical significant difference between the patients with histological proven lichen sclerosus and those with above mentioned vulvar disorders. Clinical findings were more evident in patients with proven LS. In those we found statistically significant more severe objective signs. They had more often hyperkeratosis (36.7% vs. 9.3%, respectively p 0.003), adhesions/synechiae (36.7% vs. 18.7%, respectively p 0.01) and atrophy (50% vs. 17.3%, respectively p 0.001).

Conclusions

Diagnosis of Lichen sclerosus remains a challenge even for trained experts. Symptoms may be similar to other vulvar disorders whereas severe clinical findings as hyperkeratosis and synechiae seem to be more specific clinical findings for lichen sclerosus. Biopsy is essential to determine further treatment patients with LS should be informed about the chronic course of the disease and have colposcopy on a regular basis because of the increased risk of squamous cell carcinoma.



New data and approach of current problems

(organized by SELFAGO - Société Européenne de Langue Franco-Allemande de Gynécologie-Obstétrique)

Cervical cancer during pregnancy

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Context

Cervical cancer is one of the most common malignancies in pregnancy, with an estimated incidence of 1 to 10 cases per 10,000 births. It is the third most common cancer during pregnancy after breast cancer and lymphoma. Most patients are diagnosed at an early stage of disease and during the second trimester of the pregnancy. Stage for stage, the course of disease and prognosis of cervical cancer in pregnant patients are similar to those of nonpregnant patients. The management of the cervical cancer during pregnancy depends of four criteria: tumour stage and size, nodal status, term of pregnancy and histological subtype.

Objective

To outline the issues between pregnancy and treatment of cervical cancer to ensure the best maternal prognosis while maintaining the pregnancy without compromising the child's future.

Methods

Review of the literature.

Patient(s)

Women with a diagnosed cervical cancer during pregnancy.

Intervention(s)

None.

Main outcome measure(s)

The ESMO clinical guidelines recommend in FIGO stage IB2 to IVB to treat with a neoadjuvant chemotherapy with platinum-based chemotherapy with or without paclitaxel for the second trimester. Carboplatin is now preferred over cisplatin due to the risk of ototoxicity in children after cisplatin exposition. The maternal toxicity is lower too with carboplatin. During the first trimester, a close monitoring is need to delay the treatment after 14 weeks if the patient wishes to preserve the pregnancy. In the third trimester, the treatment can be delay until after the delivery. A caesarean section has to be perform to avoid vaginal dissemination and the incision of the uterus must be corporeal to avoid abdominal dissemination.

Result(s)

The use of chemotherapy during pregnancy is largely described in the literature, its efficacy combined with good neonatal tolerance, and maternal tolerance make use reasonable for this type of clinical situation.

Conclusions

The majority of studies do not suggest a difference in the oncologic prognosis of women with invasive cervical cancer diagnosed during pregnancy compared with nonpregnant women with invasive cervical cancer when adjusted for stage; however, data are limited. The most important thing is to make the right diagnosis and to take care of these patients very quickly in centres specialised in gynaecological oncology. The best treatment options have to be discussed with the patient and a very precise treatment plan will be established.



New data and approach of current problems

(organized by SELFAGO - Société Européenne de Langue Franco-Allemande de Gynécologie-Obstétrique)

Management of HPV associated lesions during pregnancy

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The prevalence of Human Papillomavirus (HPV) infection during pregnancy is unknown, but probably higher than in general population, due to a diminished HPV clearance in the first and second trimester and an increased viral replication at the beginning of the pregnancy.

Depending on age, high risk HPV infections are found in 22,8% of 24 to 25 years old women and in 6,2% of women older than 30 years. Cervical dysplasia is found in 0,6-10/1000 of pregnant women. Vulvar condyloma as a manifestation of a low-risk HPV infection are observed in about 1% of all women.

Mother-to-child HPV transmission is discussed by different ways: antenatal transmission through transplacental transmission or ascending infection, perinatal transmission through an infected birth canal or postnatal transmission. The overall risk for neonatal HPV infection is estimated at 6,5%.

In pregnancy, the indications for colposcopy and targeted biopsies remain unchanged comparing to non-pregnant women but anatomic changes in pregnancy can cause difficulties in colposcopic evaluation and biopsy can be complicated by bleedings.

Conization is not indicated for preinvasive lesions during pregnancy, but active surveillance must be ensured every 3 months.

Diagnosis and therapy of cervical cancer in pregnancy needs individual and interdisciplinary decisions.

Condyloma during pregnancy can be treated by trichloroacetic acid or surgery, primary cesarean section is not indicated except in vaginal obstruction.

Conclusion

HPV associated lesions are frequently seen during pregnancy, the incidence is correlated with maternal age. Precise diagnosis including colposcopy and targeted biopsy is necessary to avoid cervical damage by unnecessary surgical interventions on the one hand and the evolution of invasive lesions on the other hand.



New data and approach of current problems

(organized by SELFAGO - Société Européenne de Langue Franco-Allemande de Gynécologie-Obstétrique)

BRCA-P: international prevention trial in women with BRCA1 germline mutation

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Purpose

The birth year-dependent onset of breast cancer in BRCA1 and 2 mutation carriers suggests a risk-modifying role for reproductive and life style factors. We therefore examined possible associations between these factors and age at diagnosis.

Patients and methods

Individual reproductive and life style factors were identified in 197 Austrian BRCA 1 and 2 mutation carriers who had developed breast cancer. Cox regression analysis and log-Rank testing were used to estimate the effect of potential risk factors on the onset of breast cancer.

Results

Nulliparous BRCA mutation carriers developed breast cancer at a younger age than those who had delivered (36.4 vs 40.9; $p=0.001$). Similarly, smokers and women who had used oral contraceptives experienced an earlier breast cancer onset (39.0 vs. 41.4; $p=0.05$ and 39.3 vs. 44.9; $p=0.0001$, respectively). In multivariate analysis oral contraceptive use (HR:1.7; $p=0.006$) and birth cohort ($<$ vs ≥ 1965 HR:4.5; $p=0.001$) were associated with an earlier breast cancer onset, while previous pregnancies led to a delay (HR:0.2; $p=0.04$). Mutation carriers born ≥ 1965 were less likely to have experienced pregnancies and more likely to have used oral contraceptives, and consequently developed breast cancer at an earlier age (median age: 42 vs 58; $p<0.0001$ log Rank test).

Conclusion

We here demonstrate that in BRCA1 and 2 mutation carriers the birth cohort-associated differences in the onset of breast cancer are profound and influenced by reproductive factors such as the number of pregnancies and the use of oral contraceptives.



Sponsored Key Lecture





Clinical evidence for successful treatment of vulvovaginal atrophy symptoms with a non-hormonal oil-in-water cream (sponsored by Dr. August Wolff)

Clinical evidence for successful treatment of vulvovaginal atrophy symptoms with a non-hormonal oil-in-water cream

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Objective

Genitourinary Syndrome of Menopause (GSM) is a silent epidemic, with a prevalence as high as 50% in postmenopausal women and 63% in women treated for breast cancer. According to the North American Menopause Society (NAMS), the initial goal of treatment with hormone-free products is to relieve subjective symptoms (vaginal dryness, itching, burning, pain independent of sexual intercourse). All these symptoms are interrelated with vulvovaginal dryness (VVD).

Methods

Three clinical studies (n=280) have been evaluated to assess the efficacy and safety of an oil-in-water emulsion (hormone-free moisturizing vaginal cream, VMC) used to relieve symptoms of vulvovaginal atrophy (VVA). The efficacy of VMC has been compared with that of a hormone-free water-based gel and an estriol cream (0.1%) and has been tested in post-menopausal women as well as in women treated for breast cancer.

Main outcome measures

The cumulative subjective symptom score of the respective treatments, as well as individual subjective symptoms, dyspareunia score and objective signs (thinning of the vaginal epithelium, redness, petechiae and discharge). Two of the studies assessed impairment of daily life due to VVD symptoms.

Results

Firstly, in a 4-week study (n=92) the improvement of subjective symptoms and objective signs was significantly greater after treatment with VMC compared to the hormone-free gel. VMC confirmed its statistical superiority over gel. Secondly, both VMC and an estriol cream (0.1%) improved all subjective symptoms in a 6-week study of 151 postmenopausal women suffering from VVD symptoms ($p<0.001$). VMC confirmed its non-inferiority compared to estriol cream. In addition, dyspareunia and impairment of daily life scores significantly improved with both treatments ($p<0.001$). Thirdly, in a 4-week study with 117 women treated for breast cancer and suffering from VVD, all subjective symptoms and dyspareunia improved significantly ($p<0.0001$). At the end of treatment, all patients were free of petechial haemorrhages ($p<0.0001$). The severity of objective findings improved significantly compared to baseline values ($p<0.0001$).

Conclusions

The emollient properties of VMC, which provide moisturising and soothing lipids to the dry and sensitive skin of the vagina and vulva, appear to significantly benefit the relief of subjective symptoms, as well as dyspareunia and, ultimately, impairment of daily life due to these symptoms.



Sponsored Symposia





Time to look behind the mask in oral contraception
(sponsored by Gedeon Richter and Mithra Pharmaceuticals)

Time to reflect on 60 years since the first oral contraceptive was made available

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While thousands of medicinal products have been developed over the years, only one deserves to be referred to as ‘the pill’. Launched in the 1960s, the first oral contraceptive pill – Anovlar in Europe and Enovid-10 in the United States – transformed the lives of women and their families. Women had control over their own bodies to plan their families and develop professional careers, bringing freedom and empowerment to women over the last 60 years. Pioneering work initially by Ludwig Haberlandt (1921), known as ‘grandfather of the pill’, followed by Carl Djerassi and Russell Marker (1930s), Gregory Pincus, Margaret Sanger, Katherine Dexter McCormick and John Rock (1950s), provided major contributions to the discovery and development of the first oral contraceptive.

Worldwide, oral contraceptives are among the most popular reversible methods of family planning. In Europe, combined oral contraceptives (COCs) are the most commonly used method, used by approximately one-third of contraceptors. Although the mechanism of action of COCs essentially remained the same over 60 years, COCs evolved to improve safety and meet the needs of women. The gradual lowering of ethinylestradiol (EE) content resulted in lower risks of venous thromboembolism (VTE); the introduction of 17 β -estradiol (E2) and newer progestogens gave women additional choices along with improved non-contraceptive benefits (Practice Committee of the American Society for Reproductive Medicine, 2017).

Pill regimens that shorten the hormone-free interval or allow continuous pill-taking sit alongside the classical 21-day active treatment/7-day hormonal-free interval regimen. These modifications have reduced menstrual bleeding and pain, offering users the convenience to choose when they bleed (Mansour et al. 2011, Christin-Maitre et al. 2011). But poor pill compliance contributes to the number of unintended pregnancies occurring each year, which may result in substantial health problems. Other concerns may be related to the development of rare but serious side effects, including VTE or breast cancer (Brynhildsen, 2014), or fear for health issues related to the product, such as acne, weight gain (Gupta, 2000), breast tenderness, nausea and mood disorders (Grossman Barr, 2010), which may lead to dissatisfaction and subsequent product discontinuation. These concerns underline women’s unmet need for a reliable and easy-to-use method that complements their lifestyles without compromise.

Hence, it is not only time to reflect on the last 60 years since the first oral contraceptive was marketed, but time to reassess estrogens and better understand the current challenges in contraception.



Time to look behind the mask in oral contraception
(sponsored by Gedeon Richter and Mithra Pharmaceuticals)

Time to reassess estrogens: the real reason behind current challenges?

Jean-Michel Foidart (BE)

Estetra SPRL, an affiliate's company of Mithra Pharmaceuticals, Liège, Belgium; University of Liège, Liège, Belgium

Combined oral contraceptive (COC) pills evolved over time by various estrogen/progestin types and combinations. Ethinylestradiol (EE) is the primary estrogen used since the 1960s, primarily due to its half-life, oral bioavailability and high potency, allowing low doses to be effective. However, EE affects the vascular endothelium as well as liver protein synthesis related to the coagulation cascade, resulting in an increased risk of rare but serious venous thrombotic effects (Bitzer 2011, Hugon-Rodin et al. 2014, Farris et al. 2017). To minimize side effects and morbidity, EE doses in COCs were step-wisely reduced over time. Yet, low doses resulted in a less favourable bleeding profile, an undesired effect that often leads to product discontinuation (Archer et al. 2013, Gallo et al. 2013, Rosenberg et al. 1998).

More recently, COCs with natural estrogen derivatives, including estradiol (E2) and E2 valerate (E2V), were developed with the prospect to have less impact on hemostasis, lipid and carbohydrate metabolism, and thus a decreased cardiovascular risk compared to synthetic analogues. Although E2-containing COCs may have a better safety profile compared to EE-containing COCs, their bleeding profiles are less favourable (Mansour et al. 2011, Westhoff et al. 2012, Ahrendt et al. 2009). Thus, there is an unmet need for highly effective and safe COCs with a predictable bleeding profile.

Endogenous estrogens can be classified into adult (estrone [E1], E2) and fetal estrogens (estriol [E3], estetrol [E4]). E4 has four hydroxyl groups, making it structurally distinct from the others. E4 is produced by the human fetal liver, reaching maximum levels at the end of gestation. For clinical use, E4 is synthesized from a plant source. E4 is quickly absorbed after oral ingestion and has a prolonged half-life. Unlike other estrogens, E4 is not metabolized by cytochrome P450, but undergoes extensive phase 2 metabolism to form inactive sulfo- and glucurono-conjugates (Holinka et al. 2008, Visser et al. 2008a, Visser et al. 2008b).

E4 is considered the first Native Estrogen with Selective Tissue action (NEST): E4 binds and activates the nuclear ER α to induce gene transcription via coregulator recruitment in a way similar to other estrogens but different from selective estrogen receptor modulators, exerting estrogenic activity on the vagina, endometrium, bone and cardiovascular system. However, unlike other estrogens, E4 blocks the membrane ER α (Foidart et al. 2019, Arnal et al. 2017). Furthermore, E4 has a neutral impact on the liver (Mawet et al. 2015, Klufft et al. 2017, Doux fils et al. 2020, Klipping et al. 2021), and recent evidence from cell, animal and clinical studies suggests its low impact on normal and malignant breast tissue (Abot et al. 2014, Giretti et al. 2014, Gérard et al. 2015a, Gérard et al. 2015b, Liu et al. 2015, Genazzani et al. 2019, Yue et al. 2019, Visser et al. 2012, Singer et al. 2014, Creinin et al. 2021, Gemzell Danielsson et al. 2021). Altogether, these unique clinical features support the fact that the choice of estrogen in COCs matters.



Time to look behind the mask in oral contraception
(sponsored by Gedeon Richter and Mithra Pharmaceuticals)

Time to reveal a gamechanger: Drovelis

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Estetrol (E4) is an attractive candidate for use in combined oral contraceptives (COCs). Contraceptive efficacy and overall safety of E4 15 mg/drospirenone (DRSP) 3 mg was assessed in an open-label, 13-cycle, phase-3 trial conducted in a 24/4-day regimen in Europe/Russia (Gemzell-Danielsson et al. 2021). A parallel study was also conducted in North America (Creinin et al. 2021). Efficacy (Pearl Index [PI]) was assessed in subjects <35y; bleeding and safety outcomes were assessed in all subjects. The Europe/Russia trial included 1,577 enrollees (1,373 18-35y). The primary efficacy endpoint was determined according to the EMA definition (no other birth control methods used, regardless of intercourse). Five on-treatment pregnancies occurred, of which three were due to method failure, resulting in an overall PI of 0.44 (95% CI: 0.14-1.03) and method-failure PI of 0.26 (95% CI: 0.05-0.77). Scheduled bleeding occurred in 91.9–94.4% of participants per cycle. Unscheduled bleeding/spotting (B/S) episodes decreased from 23.5% in cycle 1 to <16% from cycle 6 onwards, and over all cycles, 71.8% of episodes were spotting-only. The percentage of subjects discontinuing treatment due to bleeding events was 3.4%. Only one case of deep venous thrombosis occurred, suggesting that the new combination E4 15 mg/DRSP 3 mg serves as an effective COC with a predictable bleeding pattern and favourable safety profile.

E4/DRSP had limited effects on sex hormone binding globulin, similar to ethinyl estradiol (EE) 30 µg/levonorgestrel (LNG) 150 µg, which is considered one of the safest COCs, while EE 20 µg/DRSP 3 mg led to a substantial increase. E4/DRSP had less pronounced effects than EE/LNG and EE/DRSP on procoagulant markers, fibrinolytic proteins plasminogen and tissue plasminogen activator, prothrombin fragment 1+2, and endogenous thrombin potential-based activated protein C resistance (Douxflis et al. 2020). E4/DRSP minimally changed lipid parameters and its effect on triglycerides was similar or less than EE/LNG or EE/DRSP (Klipping et al. 2021). Thus, E4/DRSP has limited impact on endocrine/metabolic parameters and a neutral hemostasis profile.

Together, these data demonstrate E4 15 mg/DRSP 3 mg (Drovelis) as a gamechanger in the contraceptive era. Large phase-4 studies are needed to confirm if this new COC is associated with an improved adverse event profile including a lower thrombosis risk.



Maternal DHA and choline for prenatal and postnatal child development
(sponsored by P&G Health)

Crucial nutrients during pregnancy and lactation: the rise of choline

Emma Derbyshire (UK)

Nutritional Insight, Surrey, United Kingdom

Any array of nutrients are needed for the health of both mother and child during pregnancy and lactation. Micronutrients play a central role in the structural and functional roles of the central nervous system. For example, nerve cell development, differentiation and migration are all thought to be facilitated and regulated by certain micronutrients. In particular, an adequate supply of folic acid, iron, iodine, calcium, copper, and choline, amongst others, have been regarded as being important for neurodevelopment in early life.

Choline is now beginning to catch the eye of Obstetricians and Gynecologists with the American Academy of Pediatrics and American Medical Association now reinforcing the importance of maternal choline intake during pregnancy and lactation. Choline is an 'essential' nutrient, with a growing body of evidence implying that choline supply during the first 1000 days of life could impact on normal brain development. The present presentation discusses the role(s) of crucial nutrients during pregnancy and lactation, with particular focus on choline.



Why 2 (hormones) if 1 is enough. The new estrogen free drospirenone only pill (sponsored by Exeltis)

Progestogens and VTE risk. From haemostatology to epidemiology

Sven Skouby (DK)

Clinical Medicine, University of Copenhagen, Denmark

Almost one half of all pregnancies are unplanned, making it important for patients to know about effective forms of contraception. Among the many hormonal preparations, the contraceptive pill is used most often. Heightened publicity about thrombosis risk have led to multidisciplinary discussions on the use. The overall relative risk of thrombosis in combined oral contraception users is four- to eightfold higher compared to 1-2 per 10,000 in reproductive-aged comparable women.

The thrombotic risk is affected by estrogen dose, type of gestagen, mechanism of delivery, and length of therapy. Since 2019 a gestagen-only pill with 4 mg of drospirenone has been approved in several countries worldwide. Drospirenone (DRSP) is a gestagen derived from spiro lactone and an analog of spironolactone, with anti-gonadotropic, anti-mineralocorticoid, and anti-androgenic properties.

With the drospirenone pill, there has been no evidence of venous thromboembolism (VTE) cases in the product's clinical development program (>20,000 cycles). Correspondingly, DRSP 4 mg was not associated with any significant change in the hemostatic balance. To day, medicine is taking an individualized approach, and contraception has to be individualized too. Risk factors for VTE, including obesity, age, and family/personal history, have to be assessed. In the future, the estrogen free gestagen only preparations should be considered more attractive for women in general and in women with VTE risk factors in particular.



Oral Presentations





(OP01) Obstetrics 1

How prenatal diagnosis of Harlequin ichthyosis can be missed?

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Context

Ichthyoses represent a heterogeneous spectrum of genodermatoses characterized by skin hyperkeratosis and desquamation of the epidermis. Harlequin ichthyosis (MIM: 242500) is the most severe form of this spectrum, inherited in an autosomal recessive manner. ABCA12 has been identified as the major disease-causing gene of this form of ichthyosis. Prenatal sonographic diagnosis is not frequently reported in literature.

Objective

Here, we describe a rare case report of a preterm birth of Harlequin ichthyosis with a prenatal missed diagnosis.

Observation

A 36-year-old female (gravida 4 and para 3) married to a non-consanguineous 40-year-old husband, from the south of Tunisia was referred for severe hydramnios in her fourth pregnancy on the third trimester. Two anterior prenatal examinations revealed a single live intrauterine gestation in cephalic presentation, with no significant abnormalities. Prenatal ultrasound at 34 weeks of gestation showed uncertain malformed fetus. Maternal gestational diabetes was excluded. Familial history record revealed three healthy children and no history of congenital anomalies in the family. The patient had medical induction for preterm rupture of membranes at 35 weeks of gestation. A female baby was delivered by urgent caesarean section for failed induction. The appearance of the neonate was remarkable with confirmed intrauterine growth restriction (2800 g) and polyhydramnios. In fact, facial anomalies included bilateral ectropion (eversion of the eyelids), eclabium (eversion of the lips), and a large, round, and wide-open mouth. The nose and ears were hypoplastic. The limbs were short and held in a fixed, flexed position. Medical genetic evaluation confirmed the diagnosis of Harlequin ichthyosis.

Conclusion

Harlequin ichthyosis seems to be extremely difficult to diagnose with imaging. Literature review showed that three-dimensional ultrasound applications is the best way to recognize facial morphology, and thus, greatly contributes to prenatal diagnoses of this syndrome. Imaging features are typically seen in late gestation in most of the cases. Severe hydramnios, intrauterine growth restriction and preterm birth associated to sonographic features may be helpful for diagnosis.



(OP01) Obstetrics 1

Breast cancer and pregnancy

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Breast cancer is common, and is currently considered the first cancer in women. In Tunisia, it accounts for about 30% of all female cancers.

The term “pregnancy-associated breast cancer” is used if this cancer is diagnosed during pregnancy and up to one year after giving birth. This association was considered for a long time to be of rapid evolution and unfavorable prognosis. Breast surgery during pregnancy is complicated due to the hypervascularization of the gland during this period.

Therefore, it imposes proper hemostasis and lymphostasis. The main effects of radiotherapy during the preimplantation period (from conception to 10 days) are represented by embryonic death and malformation risk during the embryonic phase (days 10-14 up to 8 weeks). When chemotherapy is administered in the first trimester, the rate of malformations is 14% to 19%, and the rate dropped to 1.3% when chemotherapy is introduced in the second or third trimester.

The literature reported a 3.8% of fetal malformations in his study. However ; A protocol based on Anthracyclins (up to 100 mg/m² but 50 mg/m² in most studies) appears to be prescribed without major materno-fetal consequences. Experience of maternity and neonatology center of tunis-tunisia; We report in this retrospective study a series of 25 patients with pregnancy-associated breast cancer (PABC) recorded over 10 years at the Tunis Maternity and Neonatal Center (TMNC).

In conclusion, it seems that the prognosis of breast cancer is not much aggravated by pregnancy itself as by the delay in diagnosis and management. Treatment should be started promptly during pregnancy.



(OP01) Obstetrics 1

Volume and placental quotient correlation with BMI and parity

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Objectives

To evaluate whether parity and BMI affect placental volume and placental quotient in the first trimester.

Material and methods

140 women undergoing first trimester screening were prospectively assessed using three-dimensional ultrasound in order to measure PV using the VOCAL software (Voluson E8, GE). The off-line analysis was performed by 4D View software and PV was calculated using VOCAL option (85°). Body mass index (BMI) was calculated (kg/m^2) and recorded. To assess parity influence on the placental volume patients were divided in two subgroups - there were 60 patients in nullipara and 80 in multipara subgroup. Spearman's correlation coefficient (ρ) was used to study the relationships between all the studied variables. $P < 0.05$ was considered statistically significant.

Results

The median PV in nullipara group was 73.88 mm^3 and 71.86 mm^3 in multipara group, therefore there were no statistically significant difference between two groups ($\rho=0.12$; $P=0.63$). The median PQ in nullipara group was 0.22 and 0.19 in multipara group, there were no significant difference between two groups ($P=0.53$).

On the average BMI was 23.7 (range: 17.1-43.1) kg/m^2 . BMI did not correlate with PV ($\rho=0.12$; $P=0.23$) or PQ ($\rho = 0.075$; $P=0.56$).

Conclusions

The results of our study suggest that placental volume does not correlate with parity of BMI. The limitation of current study was the small numbers of patients. Further studies are needed to evaluate the influence of parity and obesity on placental volume.



(OP01) Obstetrics 1

The value of radiant flow and 3D HD power Doppler flow ultrasound in detection of velloamentous insertion of umbilical cord

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Objectives

To analyse the application of radiant color flow and 3D HD flow in confirmation of velloamentous insertion of umbilical cord.

Methods

In a two year period we examined 5120 patients and analysed placental insertion and also insetion of umbilical cord. Examinations were performed on GE E10 with transabdominal probe RMC6 and GE E8 with transabdominal probe RAB6. Umbilical cord insertion was checked in color Doppler mode with radiant flow. When suspicious finding was detected, 3DHD power Doppler flow was applied in order to confirm velloamentous umbilical cord insertion. 3D volume was obtained in power Doppler mode, High2 resolution with sweep angle of 45 degrees. Futher analysis was performed in gloss body mode with color and monochrome reconstruction of umbilical vessels position.

Results

In the studied period we detected 5 patients with velloamentous insertion of umbilical cord. Velloamentous insertion was detected in two patients with singleton pregnancy in second trimester. Two of them had vasa praevia confirmed with 3D HD flow with vessels overlying internal cervical orifice and isthmic part of the uterus. Placental insertion was on the anterior wall and umbilical cord insertion on posterior wall of the uterus. Three patients had twin pregnancy with septal velloamentous insertion. All patients were followed up until delivery. Patients with vasa praevia and twin pregnancies with velloamentous insertion were delivered by caesarean section and umbilical cord insertion confirmed after extraction of the placenta.

Conclusion

Velloamentous umbilical cord insertion and vasa praevia can be screened by Radiant color flow and definite diagnosis can be confirmed in 3D HD power Doppler mode. In order to prevent obstetrical complications pregnancies with vasa praevia were terminated by caesarean section.



(OP01) Obstetrics 1

Progesterone receptor genetic variants in pregnant women and fetuses as possible predictors of spontaneous premature birth

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Context

Premature birth (PTB) is defined as a live birth before 37 weeks of gestation. Besides its association with mortality, there are both acute and chronic morbidities associated with PTB, including long-term sequelae such as cognitive and motor delays. One of the recognized risk factors for PTB is a maternal and/or fetal genetic predisposition. One of the main pathways involved in uterine quiescence is progesterone (P4) pathway. A number of single nucleotide polymorphisms (SNPs) have been described in human PGR.

Objective

To evaluate the roles of four selected genetic variations in fetal and maternal progesterone receptor gene (PGR) and to identify women who may have higher or lower odds for PTB compared to the general population.

Methods

A case-control study with two groups of pregnant women and two groups of newborns was performed. Venous blood samples were taken from pregnant women and blood from the umbilical cord of the newborns once after obtaining informed consent. Four described genetic variants of PGR (rs1042838, rs1042839, rs10895068, and rs1932836) were analyzed. Statistical analysis has been made

Patient(s)

The study was conducted between November, 2017 and January, 2021. The study enrolled two groups of pregnant women (109 women who delivered at term and 109 women who had a preterm delivery) and two groups of newborns (109 term and 109 preterm). None of the subjects were genetically related.

Result(s)

There was a statistically significant difference between cases and controls in the distribution of newborns' allele frequency of the minor C allele of the PGR SNP rs1942836 ($P=0.03$, Fisher's exact test) in favor of premature birth. A statistically significant difference between the frequency of the mothers' minor T allele of rs1042838 ($P=0.005$; Chi-squared test) and the mothers' minor T allele of rs1042839 ($P=0.005$; Chi-squared test) in favor of extremely premature birth has been found. There was a statistically significant difference between the frequency of the newborns' minor C allele of rs1942836 ($P=0.03$; Chi-squared Test) and newborns' heterozygotes CT genotype of rs1942836 ($P=0.03$; Fisher's exact Test) when comparing the control group and the early premature group.

Conclusions

Our study suggests that patients with selected genetic variants of the progesterone receptor gene (mothers SNP rs1042838 and rs1042839 and newborns SNP rs1942836) could have greater odds for premature birth compared to the general population.



(OP01) Obstetrics 1

Use of 3D endometrial spheroids and organoids to understand vertical transmission of COVID-19

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Introduction

The COVID-19 pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a public health emergency, which has resulted in more than 4 million deaths worldwide. The SARS-CoV-2 virus enters the host cells by binding to the angiotensin-converting enzyme 2 (ACE2) and facilitates its entry via transmembrane protease, serine 2 (TMPRSS2). Recent reports suggest that SARS-CoV-2 infection can cause pregnancy complications such as pre-term birth and miscarriages. Despite rapidly evolving research, little is known about the effects of SARS-CoV-2 infection in the endometrium and thus its effect on vertical transmission and pregnancy outcome remains inconclusive.

Objective

To understand the effects of SARS-CoV-2 infection on the endometrium and investigate the possibility of vertical transmission.

Methods

3D-cell culture models, endometrial spheroids (cell lines) and primary endometrial organoids were generated. Downstream methods including, RT-qPCR, immunofluorescence, western blotting and in silico analysis were employed to assess the machinery involved in SARS-CoV-2 transmission.

Results

Pseudo-bulk single cell RNA-seq data of human first trimester decidua was analyzed to understand the distribution of ACE2 and TMPRSS2 in different maternal cell populations. To verify these findings, endometrial spheroid and organoids model were established. Both entry receptors, ACE2 and TMPRSS2, were expressed in both models.

Conclusions

Our studies provide initial insights into the transmission route of SARS-CoV-2 and emphasize that endometrial spheroids and organoids could be better models to understand maternal pathologies of COVID-19.



(OP01) Obstetrics 1

Music is able to modulate autonomic nervous system activity in fetuses

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Context

Fetal Autonomic Nervous system Evaluation (FANTE) is a non-invasive tool able to evaluate the autonomic nervous system activity in fetus. Autonomic nervous system is a key-regulator of the fetal homeostasis during the prenatal and postnatal life and its modulation could be important to assess ANS maturation and development.

Objective

Primary endpoint was determining the effect of musical stimulation on fetal heart rate, and on six specific parameters linked to ANS activity, in particular heart rate variability (RRsd, ANNs, LPPsd, Ptot), sympathetic (LFn) and parasympathetic activity (CVI).

Method

All FANTE registrations were acquired using 12 derivations placed on the maternal abdomen. In every session, 5 min basal FANTE (bFANTE), 10 min stimulus FANTE (sFANTE), and 5 min post-stimulus FANTE (psFANTE) were registered. The musical stimulus was “Clair de lune” Debussy from London Symphony Orchestra, played through headphone on the mother abdomen at an average sound intensity of 50.8dB.

Population

Thirty women between the 32nd and 38th week with a singleton uncomplicated pregnancy were recruited in this study. A weekly FANTE registration was performed.

Results

No differences were observed between FHR during bFANTE, sFANTE and psFANTE.

Comparing bFANTE to sFANTE, a statistically significant increase in cardiac variability index were observed (RRsd: 20.3±6.2ms vs 28.33±5.9ms, p=0.010; ANNs: 11.18±6.1ms vs 28.33±5.9ms, p<0.001; LPPsd: 25.72±7.3ms vs 37.4±9.0ms, p=0.009; Ptot: 403±231.9ms² vs 624.2±253.9ms², p=0.009). Also parasympathetic activity index was modified by music stimulation (CVI: 2.34±0.4ms² vs 2.68±0.2ms², p=0.018). In all the parameters evaluated, the increase in ANS activity persisted during psFANTE registration. The sympathetic activity index remained stable during the sFANTE, and subsequently, significantly increased during psFANTE (LFn: 0.29±0.1 vs 0.20±0.1, p=0.009).

Conclusion

Music can influence the fetal basal activity of the autonomic nervous system, enhancing total cardiac variability and parasympathetic function. This response persists also after the termination of the stimulus. Even if music seems to not have an immediate effect on sympathetic function, a delayed reduction of sympathetic activation was observed.



(OP01) Obstetrics 1

Postpartum rehabilitation: the use of a mobile application to evaluate the adherence to Kegel exercises

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Context

Postpartum is a very important phase to avoid long-term pelvic floor problems. The application of new technologies (as mobile APPs) to achieve a correct rehabilitation is amazing.

Objective

To determine if the use of a mobile application can help patients to have a greater improvement in their muscular strength and a bigger adherence when doing Kegel exercises during postpartum rehabilitation.

Methods

Randomised prospective trial with intention to treat which includes 26 patients who had two or more risk factors of suffering of future pelvic floor disfunctions.

Patients

This patients were visited 40 days postpartum and their perineum muscular strength was evaluated using the Oxford vaginal testing. They were randomized in two groups.

Intervention

Our intervention was the use of a mobile application (Tät©). Patients perineum muscular strength was reevaluated by the same professional in a new visit 6 months after, who didn't know random.

Main Outcome Measures

The main variables of the study were: the initial perineal testing, the adherence to the rehabilitation programme, the increase in the perineum testing compared to the initial physical exploration and the diagnosis of pelvic floor pathology. A descriptive and comparative analysis of the pelvic floor results between both groups was done using an SPSS 17.0 programme.

Results

A significant statistical relation between using the mobile application and an improvement in the vaginal testing in one point or more was found. Patients who had used APP had a higher value at 73% (11/15). Patients who had not used APP had an improvement at 20% (2/10), $p < 0.05$. No significant statistical relation between using the mobile application and an improvement in the vaginal testing in two points or more was found.

Conclusions

From our results we can determine that the practise of Kegel exercises monitored by a mobile application during six months improves the Oxford vaginal testing in patients with risk factors to develop future pelvic floor disfunctions. This improvement indirectly helps to prevent future conditions such as urine or faecal incontinence or urogenital prolapses. Though the adherence to the exercises could not be evaluated a significant statistical relation was found between those patients who used the mobile application and an improvement in Oxford vaginal testing. It seems that this tool helps patients to do the exercises, improve the perineum strength and avoid future perineum floor disfunctions.



(OP01) Obstetrics 1

Chorioamnionitis-incidence, risk factor and maternal outcome a 3 years review Al Wakra Hospital Qatar

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Context

Clinical diagnosis of chorioamnionitis can be challenging, as its clinical presentation, can be shared with physiological changes in labor and increasing use of epidural analgesia. Knowing the risk factors can add to the diagnostic accuracy, as in all situation treatment needs to be initiated based on clinical diagnosis before the definite diagnosis can be made by culture and histopathology (HPE).

Objective

To know incidence of chorioamnionitis in all patients who presented to our department. To analyze and find most likely risk factors and maternal outcomes. To look for positive diagnostic markers and their association in our setting.

Design

Retrospective study, all patients from January 2016 to December 2018 treated for suspected clinical chorioamnionitis were included in study.

Method

172 cases (> 37 week) treated for clinical chorioamnionitis were identified through EMR. Mode of delivery, association with gestational age and parity, common risk factors, association of clinical presentation with laboratory markers and maternal complications, were studied.

Results

Total number of clinical chorioamnionitis cases identified were 172(1.03% of total deliveries (16,699 deliveries)).77% cases were in nulliparous as compared to average nulliparous woman (21%). 43% cases were identified at >40 weeks gestation. Rate of caesarean section (CS) was 44.76% and instrumental delivery rate was 22% as compared to 33% (CS rate) and 8% (instrumental delivery) in general population. Most common risk factors identified were premature rupture of membrane (49%), post-date pregnancies (42%) and induction of labor (31.4%). CRP was found to be high in > 95% of cases and CRP >50 was shown to be strongly correlating with positive placental HPE of chorioamnionitis. Blood culture was positive in 14% of cases and placental culture in 39% of cases. 80% of CS were primary CS and main indications being failure to progress (39%) and fetal distress (36.66%). PPH rate was as high as 19% in CS and 9.5% in vaginal delivery.

Conclusion

To overcome diagnostic challenges of chorioamnionitis, clinical manifestation, laboratory tests and risk factors all must be taken into consideration before starting the management in actual clinical scenario. Our review agrees with the literature in association of chorioamnionitis with adverse maternal outcome mainly increased operative delivery, primary caesarean section and PPH. High CRP value (>50) has shown 100% correlation with positive HPE.



(OP01) Obstetrics 1

One size does not fit all: diagnosis and treatment of pelvic floor trauma following spontaneous vaginal delivery - a tailored approach

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The miracle of childbirth is often clouded by the adverse effects on the soft tissue of the pelvic floor induced by passage of the fetus through the birth canal, which can ultimately have a significant impact on the quality of life of women.

The aim of this presentation is provide an illustration of the origins and consequences of maternal pelvic floor trauma on the structure and function of the urogenital system and to present a complex realistic approach to surgical management of pelvic floor defects.

An MRI derived 3-D model of the female pelvis with high-resolution images demonstrating key anatomical structures as are visualized during surgery will be utilized. The etiology of pelvic floor trauma during childbirth will be discussed and the biophysical principles underlying the mechanical strain and load on the soft tissues with passage of the fetal head during vaginal delivery will be addressed.

The operative method will be illustrated through a series of photo slides detailing intraoperative technique, identification and utilization of native tissue structures (fascia), suture placement and material as well as a general appreciation for the interconnectedness (tissue mapping) of the pelvic floor muscles, fascia, and paravaginal tissues in the anatomical restoration of the vaginal axis, length, and overall physiological function.

Lastly, the important role of postoperative physiotherapy and education of women in regaining pelvic floor function should not be underestimated and used concurrently with surgery to insure successful patient outcomes.



(OP01) Obstetrics 1

Screening pregnant women for suboptimal vitamin D levels

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Context

Approximately 1 in 5 of the UK population are vitamin D deficient. National guidance highlights pregnancy as a risk factor; however, vitamin D screening in pregnancy is not the norm in most hospital guidelines except in those most at risk. A maternity business case was made in October 2020 to screen all pregnant women for vitamin D status.

Objective

Compare whole population vs. at risk screening national guidance. Methods: Audit (W&C.NP.21.078) undertaken in a UK hospital setting. Patient data extracted via maternity-information-system (CMIS), vitamin D levels obtained via the picture-archiving-communication system (PACS). Data analysis via MS Excel.

Patients

1,312 women attending their antenatal booking appointment from 01/01/21-31/03/21, with 450(34.3%) selected randomly for auditing.

Interventions

Data collected: Visit-date, age, gestation, ethnicity, place-of-birth, booking Vitamin D levels and repeat if available. Analysis for vitamin D <50nmol/l [insufficient plus deficient status] and <25nmol/l [deficient status]. Ethnicity used as surrogate marker for 'high-risk' versus 'low-risk' status.

Results

447 (99%) pregnant women had their vitamin D levels checked. 250/447 (56%) had levels <50nmol/l and 74/447(17%) were deficient. Analysis of ethnicities of women with levels <50nmol/l (of 447) mainly identified those of 'Indian' background (135;30%), and 'other White background' (131;29%). The latter ethnicity is not considered high-risk based on current guidance. The country of origin for around 70% (92/131) of 'other White background' was Romanian. 53 (57%) had vitamin D levels <50nmol/l;10 had levels <25nmol/l. We have identified 'Romanian' pregnant women as a new group at risk of suboptimal vitamin D levels. Chirita-Emandi et al (2015) reported poor vitamin D levels in 59% of the Romanian population, with being older, female and winter period as risk factors. For those Romanian women now in the UK, our audit identifies a need for vitamin D assessment in pregnancy with supplementation for those with suboptimal levels.

Conclusion

Screening for vitamin D status should ideally be undertaken for all pregnant women. However, if screening is directed by risk stratification, this population needs to include Romanian women.



(OP02) Endometriosis, adenomyosis and fibroids

LIBERTY randomized withdrawal study: 2-year efficacy and safety of relugolix combination therapy in women with heavy menstrual bleeding associated with uterine fibroids

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Context

In the pivotal LIBERTY 1/2 trials and Long-Term Extension (LTE), once-daily relugolix combination therapy (Rel-CT: relugolix 40mg, estradiol 1mg, norethindrone acetate 0.5mg) reduced menstrual blood loss (MBL) volume, was well tolerated, with bone mineral density (BMD) preservation in women with uterine fibroids (UF) through 52 weeks (wks).

Objective

Evaluate the efficacy and safety of Rel-CT for up to 2 years.

Methods

Phase 3 LIBERTY randomized withdrawal study (RWS).

Patients

Women with UF-associated heavy menstrual bleeding (HMB) who completed the 24-wk LIBERTY 1/2 trials and the 28-wk LTE, and who met responder criteria (MBL volume <80 mL, $\geq 50\%$ reduction from pivotal study baseline at Wk 48 in LTE).

Interventions

Women were randomized 1:1 to Rel-CT or placebo (blinded) for up to 52 wks (total treatment period: 104 wks). Women who relapsed with HMB during the study (MBL ≥ 80 mL) received open-label Rel-CT.

Main outcome measures

Primary endpoint: % of women who maintained MBL <80 mL at Wk 76. Key secondary endpoints included: time to MBL volume ≥ 80 mL, % of women who maintained MBL of <80 mL through Wk 104 (over the 52-wk randomized treatment period), and % of women achieving/maintaining amenorrhea at Wk 76/end of treatment.

Results

Of 229 randomized women (Rel-CT: 115, placebo: 114), 228 were treated and 89 (77.4%) and 86 (75.4%) completed the RWS. At Wk 76, 78.4% of women on Rel-CT maintained MBL <80 mL vs 15.1% with placebo ($p < 0.0001$). Through Wk 104, 88.3% of women randomized to placebo at Wk 52 relapsed (median time to relapse: 5.9 wks); 87/89 women who relapsed and received open-label rescue Rel-CT responded (MBL <80 mL). At Wk 104, 69.8% of women on Rel-CT maintained MBL <80 mL vs 11.8% with placebo ($p < 0.0001$). The % of women who achieved/maintained amenorrhea was 57.4% vs 13.3% at Wk 76 and 58.3% vs 10.6% at Wk 104 for Rel-CT vs placebo, respectively (both $p < 0.0001$). Rel-CT was generally well tolerated; no new safety signals were detected, and the adverse event profile was consistent with that reported through 1 year. BMD remained stable in women on Rel-CT from Wk 52 to Wk 104; cumulative assessment showed that BMD was maintained through 2 years.

Conclusions

After 2 years of Rel-CT, there was evidence of effect durability in maintaining low MBL volume in women with symptomatic UF and of return of HMB in most women after treatment cessation, which improved upon Rel-CT re-treatment. Long-term Rel-CT was generally well tolerated.



(OP02) Endometriosis, adenomyosis and fibroids

Patients with endometriosis – medical care under COVID-19 conditions

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There is increasing concern that Corona could limit adequate medical care. The Scientific Endometriosis Research Foundation (SEF) therefore examined the situation of women with endometriosis in cooperation with the German IVF Register (D·I·R)[®] in 2020 under the COVID-19 special conditions.

On the one hand, certified endometriosis centres were asked via questionnaire for information on the care services for such patients in 2019 and 2020. On the other hand, the annual reports from IVF centres were evaluated regarding women with the mentioned main diagnosis of endometriosis.

The care services in the outpatient area remained the same during the study period. Looking for surgeries for those women, there was to state a reduction of 8% in 2020 compared to 2019. In reproductive medicine, there was an increase of 20% in ART treatment cycles, even more as compared with all ART treatment cycles in 2020.

We can conclude that in the field of reproductive medicine the medical care was not impaired by the COVID-19 conditions for patients with endometriosis. It remains to be seen whether the decline in endometriosis surgery under COVID-19 conditions will affect the severity of the disease in the future care.



(OP02) Endometriosis, adenomyosis and fibroids

Secondary umbilical endometriosis to non-gynecological surgery in a patient with primary dysmenorrhea a case report

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Context

Umbilical endometriosis is an unusual clinical presentation

Objective

Case report of a skin lesion of endometriosis in the umbilicus secondary to non-gynecological videolaparoscopic surgery (cholecystectomy) in a patient with primary dysmenorrhea with complete resolution of symptoms after surgical treatment. Demonstrate the diagnosis and surgical treatment of the lesion

Methods

Description of symptoms, surgical treatment and case follow up

Patient(s)

A 37-year-old female with a history of primary dysmenorrhea and infertility for 5 years, presenting with a brownish nodular lesion in the umbilicus with severe pain (8/8 on a visual analogue pain scale) and local bleeding during the menstrual period. She underwent laparoscopic cholecystectomy surgery 3 years before the onset of symptoms

Intervention

Diagnosis of umbilical scar endometriosis and pelvic endometriosis (left uterosacral ligament) was performed through history and physical examination. Pelvic magnetic resonance imaging (MRI) with protocol for endometriosis confirmed the diagnosis. Total excision of the umbilical lesion was performed through the abdominal route and, in the same surgical procedure, videolaparoscopic surgery for resection of the pelvic endometriosis of the left uterosacral ligament and systematic peritonectomy of the posterior compartment of the pelvis

Main outcome measure

The patient monitoring showed complete resolution of symptoms after surgical intervention

Result

The diagnosis and treatment was effective for the case

Conclusion

Secondary umbilical cutaneous endometriosis is uncommon, but it should be included in the differential diagnosis of lesions in this anatomical region in women with previous abdominal surgery and a clinical history compatible with endometriosis, which may be a marker for deep endometriosis in the pelvis. The concomitant surgical treatment of umbilical and pelvic disease with removal of the lesion of the uterosacral ligament and systematic peritonectomy of the posterior compartment of the pelvis proved to be effective for the resolution of painful symptoms



(OP02) Endometriosis, adenomyosis and fibroids

Leptin concentrations in endometriosis: a systematic review and meta-analysis

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Introduction

Endometriosis is an inflammatory condition, affecting mainly women of re-productive age. Leptin is a regulator of food intake and energy expenditure, posing pleiotropic actions, and regulating immunity and fertility. The aim of this study was to systematically review the literature regarding leptin concentrations in biological fluids and tissues of women with endometriosis, and to investigate and propose a possible role of leptin in the pathophysiology of endometriosis.

Materials and methods

A systematic search of the literature was conducted in two electronic databases (Medline, Cochrane) and grey literature for original research articles on humans, published in any language.

Results

Twenty-nine studies with 1,291 women with endometriosis and 1,664 controls were included in the systematic review. Peritoneal fluid and follicular fluid leptin concentrations were higher in endometriosis compared with control group [mean difference (MD) 7.10, 95% confidence interval (CI) 4.76 to 9.44 ng/ml, 18 studies], (MD 1.35, 95% CI: 0.54 to 2.17 ng/ml, 2 studies) respectively. No differences were evident in serum (MD 0.92, 95% CI: -0.84 to 2.68 ng/ml, 12 studies) or plasma (MD -0.95, 95% CI: -4.63 to 2.72 ng/ml, 3 studies) between the groups. No meta-analysis was conducted for ovarian tissue leptin (2 studies).

Conclusions

The meta-analysis provided evidence for increased leptin concentrations in both peritoneal fluid and follicular fluid of women with endometriosis compared with control; these differences were not present in the serum or plasma. The above results support a potential pathophysiologic role for leptin in the local microenvironment while declines its use as a blood diagnostic marker. Furthermore, we propose a possible role of leptin in the pathophysiology of endometriosis.



(OP02) Endometriosis, adenomyosis and fibroids

Impact on ovarian reserve and therapeutic efficacy of catheter-directed ethanol sclerotherapy for ovarian endometrioma with decreased ovarian reserve: a preliminary study

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Context

Catheter-directed ethanol sclerotherapy (CDS) is efficacious in patients with low anti-Müllerian hormone without adversely affecting the ovarian reserve.

Objective

To investigate the therapeutic efficacy of CDS and its effect on the ovarian reserve in patients with endometrioma with a decreased ovarian reserve.

Method

This is a retrospective study.

Patients

We evaluated 18 patients with ovarian endometriomas measuring ≥ 3 cm and a pre-procedural anti-Müllerian hormone (AMH) level below 2 ng/mL.

Interventions

An 8.5-F catheter was inserted either transabdominally or transvaginally into the endometrioma. Following the aspiration, sclerotherapy with 99% ethanol was conducted with subsequent 20-minute ethanol retention.

Main Outcome Measures

Ultrasonography was performed pre-procedurally and 6 months following CDS to evaluate any changes in cyst size and determine recurrence. The serum AMH levels, CA-125 levels, and the visual analog scale (VAS) scores were obtained to analyze the ovarian reserve and treatment efficacy pre-procedurally and 6 months after CDS.

Results

The mean cyst size decreased after CDS on 6 months' follow-up US ($p < .001$). All patients reported a decreased VAS score for dysmenorrhea ($p < .001$). The CA-125 level also decreased 6 months after CDS ($P = .001$). Meanwhile, the difference in serum AMH level before and after CDS was statistically insignificant ($p = .875$).

Conclusion

CDS was efficacious in reducing pain and serum CA-125 level in those patients who had low AMH without adversely affecting the ovarian reserve.



(OP02) Endometriosis, adenomyosis and fibroids

Effects of relugolix combination therapy on bone mineral density through 2 years in women with heavy menstrual bleeding associated with uterine fibroids

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Context

Relugolix combination therapy (Rel-CT; relugolix 40 mg, estradiol 1 mg, norethindrone acetate 0.5mg) is being investigated for the treatment of heavy menstrual bleeding (HMB) associated with uterine fibroids. The rationale for combination use is to mitigate anticipated hypoestrogenic effects with relugolix monotherapy, including bone loss. Rel-CT preserved bone mineral density (BMD) in the pivotal LIBERTY 1/2 trials and Long-Term Extension (LTE) study. In the LIBERTY randomized withdrawal study (RWS), Rel-CT maintained low menstrual blood loss (MBL) for up to 2 years.

Objective

Examine BMD changes up to 104 weeks (wks) of Rel-CT.

Methods

Phase 3 LIBERTY RWS.

Patients

Women who completed 24-wk LIBERTY 1/2 trials and 28-wk LTE, met responder criteria (MBL <80 mL, $\geq 50\%$ reduction from baseline to Wk 48 in LTE) and had BMD loss of <7% from pivotal study baseline.

Interventions

LIBERTY 1/2: 24 wks of Rel-CT, placebo, or relugolix monotherapy then Rel-CT (both for 12 wks), followed by open-label Rel-CT in the 28-wk LTE study. RWS: women were blindly randomized 1:1 to Rel-CT or placebo for up to 52 wks (total treatment period: 104 wks). Those who relapsed with HMB (MBL volume ≥ 80 mL) received open-label Rel-CT.

Main outcome measures

% change in BMD (Wks 52–104) at the lumbar spine (L1–L4), total hip, and femoral neck (assessed by dual-energy X-ray absorptiometry and analyzed by treatment group). Cumulative mean % change in BMD from pivotal study baseline was analyzed by pivotal treatment group.

Results

Of 229 randomized women, 228 were treated in the RWS (Rel-CT: 116, placebo: 112). At the lumbar spine, the least squares mean % change in BMD from Wk 52 to Wk 104 was 0.81% with Rel-CT vs 0.10% with placebo. Cumulatively, mean % change in BMD from pivotal study baseline to Wk 104 in women who received continuous Rel-CT (N=32) was 0.04%. In women who received placebo for 24 wks followed by Rel-CT for 80 wks (N=29), the mean % change in BMD from pivotal study baseline to Wk 104 was 0.45%. BMD initially declined in women who received relugolix monotherapy for 12 wks but stabilized after initiation of Rel-CT for 92 wks (N=21; mean % change in BMD from pivotal study baseline to Wk 104: -1.85%). BMD findings at the total hip and femoral neck were generally consistent with the lumbar spine.

Conclusions

BMD remained stable in women who received Rel-CT from Wks 52 to 104. Cumulative assessment showed that BMD was maintained through 2 years of treatment.



(OP02) Endometriosis, adenomyosis and fibroids

Adenomyosis in MIGS (new progressive vistas)

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Objective

Minimally invasive approach in the treatment of adenomyosis within the uterine & fertility-sparing surgery, mainly for focal adenomyosis in office-settings is safe and effective treatment. It can be performed in local analgesia (with or without a combination of analgesics) in selected patients in office-settings, thus avoiding the risks of general anaesthetic. Fertility preservation and/or quality-of-life improvement can be achieved.

Adenomyosis of the uterus is defined as the presence of endometrial tissue, including glands and stroma, situated at least 2.5 mm below the endometrial-myometrial junction and widely distributed within the myometrium layer of the uterus. Many women still have a desire to preserve the uterus, for which conservative and uterine-sparing procedures are increasingly used. Although medical management can be effective, similar to the management of uterine fibroids, its effect is often transient and rapid regrowth of adenomyosis and relapse of symptoms and signs always occur once the treatment is stopped. Therefore, other strategies should be selected.

Design

Case report.

Setting

Office-settings.

Methods

Our experience and results in office-settings with focal variants of adenomyosis (adenomyomatous cyst, adenomyoma and a rare variant - polypoid adenomyoma), often associated with pelvic pain, dysmenorrhea and infertility. The most common surgical treatment for adenomyosis is laparoscopic resection, but here we used the hysteroscopic approach, which may allow for an alternative minimally invasive surgical approach.

Result

The main results of a minimally invasive intrauterine approach are disappearance of metrorrhagia, dysmenorrhea, pelvic pain and outcome of pregnancy. Another very important factor is the identification of precancerous lesions.

Conclusions

The minimally invasive intrauterine approach for the treatment of adenomyosis in office-settings is an easy to use, safe procedure with excellent results. It is well suited in office-settings. It has positive outcomes and is an acceptable treatment option for selected patients at the same time in accordance with the need for expert experience with ultrasound diagnostics.



(OP02) Endometriosis, adenomyosis and fibroids

Molecular pathomechanisms underlying the progesterone receptor modulator Ulipristal acetate/progesterone treatment effects on uterine leiomyomas

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Context

Ulipristal acetate (UA), a selective progesterone receptor modulator, is used successfully for the treatment of symptomatic uterine leiomyomas (ULs). Increased P4 and nuclear progesterone receptors (PGR) expression has been suggested to regulate the proliferation, growth and the synthesis of the intercellular matrix of ULs. Little is known on the distinct pathomechanisms of UA action on ULs.

Objective

We studied the P4-induced activation of signaling cascades in ULs without or with the UA treatment. This further determined the P4/UA effects on the molecular pathomechanisms underlying the development and progression of ULs.

Methods

This laboratory-based study was carried out on slow-frozen and paraffin-fixed UL-patient tissue specimens with or without the UA treatment. Normal healthy patient myometrium served as control.

Patients

We evaluated a total number of n=250 women with ULs (n=100 UA-treated; non-treated n=150) and normal myometrium (n=100). Pre-operative UA therapy was with 5 mg/ day lasting for 3-months.

Intervention

Cultured primary cells from ULs and UL-explants were exposed to UA, P4, SMAD3 inhibitor, PGRMC1 inhibitor, TGFBR1/RII inhibitor, IL-6 inhibitor, VEGF inhibitor, VEGF, IL-6 and their combinations. All the PRs subtype expressions were characterized in ULs.

Main outcome measures

Signaling pathways activated by P4 in the absence and presence of UA in ULs regarding the ECM deposition in ULs and tumor growth were analyzed.

Results

Abundant expression of nuclear PGR and membrane PRs α , β , and Progesterone receptor membrane component 1 (PGRMC1) was found in ULs. UA treatment downregulated all the analyzed genes, except nuclear PGR. P4 treatment *in vitro* of ULs cells significantly stimulated, whereas UA at 1 μ M inhibited the cell viability. UA-treatment reversed the P4 effects. Both UA and P4 treatment activated the TGF β signaling pathway in ULs. Inhibition of TGF β receptors enhanced the effects of UA, whereas SMAD3 inhibitor strongly inhibited the P4 action in ULs. Moreover, UA inhibited the SMAD3 nuclear translocation. P4 upregulated significantly the expression of VEGF, IL-6, RhOA, and COL1A1 in ULs. Furthermore, SMAD3 inhibitor suppressed the P4-stimulated collagen release and enhanced the UA antagonist effects on ULs *in vitro*.

Conclusion

Our findings provide novel mechanistic insights into the action of P4/PRs through the TGF- β family signaling pathway regulation that promoted ULs growth, as well as upregulation of VEGF, IL-6, and RhOA.



(OP02) Endometriosis, adenomyosis and fibroids

Diagnosis and treatment of diaphragmatic endometriosis: results of an international patient survey

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Objective

To quantify the delays associated with the diagnosis and treatment of diaphragmatic endometriosis (DE) and to evaluate postoperative outcomes.

Method

An anonymous international patient survey was designed to collect data regarding demographics, duration and nature of DE symptoms, type of surgery and postoperative outcomes. 137 patients diagnosed with DE were invited to participate via endometriosis patient associations in 14 countries. Factors associated with postoperative outcomes were analysed using Mann-Whitney U and Fisher's exact tests (P-value < 0.05 was considered statistically significant).

Results

Data was available for 136 respondents (median age 34 years). The dominant reported symptom of DE was moderate-severe pain (upper abdomen 68%, chest 64%, shoulder 54%, upper back 44%, neck 40%), and preceded pelvic symptoms in 90 respondents (66%). Of 122 people who initially consulted a primary care physician, referral to a gynaecologist occurred after a median of five consultations (range 1-100). The median time between first primary care consultation and diagnosis of DE was two years (range 0-23). 31% of respondents were diagnosed later than one year after their first gynaecology consultation (range 1-13 years), and 30% required two or more laparoscopies before diagnosis. 116 patients underwent surgical treatment for DE (abdominal 93, thoracic 7, combined 16). Postoperative data was available for 113 respondents, and 65% reported significant improvement or complete resolution of DE symptoms. There was no significant difference in age (P=0.19), timing of diagnosis (P=0.59) or type of procedure (excision or ablation) (P=0.13) between respondents who did and did not experience symptomatic relief after surgery. 61% of respondents reported long-lasting symptomatic relief after a median of 1 year, whilst 39% reported ongoing moderate-severe pain or have undergone further surgery for recurrent symptoms.

Conclusions

Diagnosis of DE is often delayed due to general lack of awareness. Due to the limited sensitivity of non-invasive investigations and the restricted views of the diaphragm at laparoscopy, the diagnosis of DE requires a high index of suspicion and early involvement of surgeons trained in laparoscopic liver mobilisation. Recurrent symptoms are common following surgical treatment of DE, and due to its relatively low incidence, international collaborative studies are required to determine the long-term outcomes of this condition.



(OP02) Endometriosis, adenomyosis and fibroids

Multidisciplinary approach to uterine artery embolization: initial success and short-term results

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Context

Uterine artery embolization (UAE) for uterine fibroids (UF) is used to be a procedure performed without proper supervision and follow-up by gynaecologist, that possibly could lead to higher complications rate.

Objective

To describe one-year experience in uterine artery embolisation (UAE) for uterine fibroids (UF) as a multidisciplinary team.

Methods

Statistical analysis of follow-up results (complaints and the volumes of the uterus and the dominant UF) of patients who underwent UAE in Kyiv private clinic Verum Expert clinic.

Patient(s)

55 patients aged $39,5 \pm 1,79$ (21-50) underwent UAE for UF in the period of June 2020 to June 2021.

Intervention(s)

The indication for treatment was done by gynecologists based on patient history, clinical examination, and TV-US. Superselective UAE was performed by an experienced endovascular surgeon on Philips Allura Xper FD20 with Clarity IQ function. Patients were under supervision of gynaecologist during hospitalisation and under online follow-up. The TV-US was performed before UAE and 1, 3, 6 month after.

Main outcome measure(s)

Uterine fibroid size reduction, symptom relief, infection complications rate.

Result(s)

In 35 patients who returned for the TV-US 1 month after the UAE the reduction of the UF volume was $-29,21\% \pm 11,45$, uterine volume $-21,93\% \pm 9,42$. 24 patients were available for follow-up in 3 month after UAE - the reduction of the UF volume was $-34,57\% \pm 13,06$, uterine volume $-31,93\% \pm 14,49$. We obtained TV-US in 10 patients after 6 month after UAE - the reduction of the UF volume was $-63,22\% \pm 9,04$, uterine volume $-46,02\% \pm 10,11$.

The absence of blood flow in the UF was observed in all patients at first TV-US, and only 1 patient had blood flow in 2 of 5 UF at 3 months of follow-up.

In the follow-up period there was no increase of body temperature over 38°C in any of the patients. Migration of UF of 2-5 types occurred in 12 patients. Expulsion of UF developed in 6 patients, 2 of which required hysteroscopic resection of the UF, in 4 patients expulsion occurred spontaneously. 6 patients had vaginal discharge, which allowed us to judge the expulsion by sloughing.

Percent of symptom reduction in 1 month - 64% for abnormal uterine bleeding, 60% for pelvic pain.

Conclusions

Multidisciplinary approach to UAE has proven to be a successful strategy for good clinical outcomes for patients with UF.



(OP02) Endometriosis, adenomyosis and fibroids

Organoids from endometriosis: a powerful *in vitro* model for the endometriotic-pelvic crosstalk mechanisms

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Context

The pathogenesis of endometriosis remains largely unknown, mainly due to lack of authentic models. Organoids, a three-dimensional *in vitro* model, recapitulate critical molecular characteristics of tissues and present powerful tools to mimic disease process.

Objective

To establish an *in vitro* model of organoids and explore its roles for the endometriotic-pelvic crosstalk mechanisms.

Methods

Organoids were established from paired ectopic endometrium (ECT) and eutopic endometrium (EUT) using a chemically conditioned medium. Hematoxylin and Eosin staining, immunohistochemistry, immunofluorescence, confocal microscopy and RNA sequencing were performed.

Patient(s)

Twenty-four patients with III–IV staged ovarian endometrioma in Xiangya Hospital Central South University.

Intervention(s)

Organoids were treated by periodical estrogen followed by progesterone, and ECT organoids also knockdown of SERPINE2. ECT and EUT organoids were incubated with a lentivirus carrying luciferase and intraperitoneally injected into nude mice.

Main outcome measure(s)

The organoids characteristics were identified by endometrial markers (CK7, FOXA2, E-cadherin, ER α and PR), markers of cell polarity (phalloidine) and intercellular junction (β -catenin). The morphology and proliferation capacity (Ki67) were recorded after hormones treatment. The luciferase intensity, volumes and numbers of xenografts in pelvic were analyzed after 21 days.

Result(s)

Endometriosis-derived organoids capture endometrial epithelium phenotype and substantial proliferation. Different morphology distribution of ECT and EUT organoids were observed. The ECT organoids showed more hormone-sensitive. RNA sequencing found that differential expressed genes were mainly enriched in key pathways, including cell adhesion junction, ECM-receptor interaction, PI3K-Akt and Wnt signaling pathway. SERPINE2, ITGA11 and collagen I were higher expressed in both in ECT tissues and organoids. Knockdown of SERPINE2 in ECT organoids changed the proliferative capacity and morphology distribution. Xenografts prevailed in both graft volumes and numbers after injection of ECT organoids compared with EUT organoids.

Conclusions

Organoids from endometriosis capture disease nature, mimic endometriotic-pelvic crosstalk mechanisms of retrograde menstruation, and provide a powerful experimental and preclinical model for further researches on therapeutic targets.



(OP02) Endometriosis, adenomyosis and fibroids

Identifying common pathogenic features in deep endometriotic nodules and uterine adenomyosis

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Context

Although the notion of deep endometriotic nodules (DENs) and uterine adenomyosis (AD) sharing the same pathogenesis is becoming increasingly popular, their link is almost exclusively based on their similar symptoms, histological patterns and high rates of coexistence.

Objective

This study aimed to assess the relationship of DENs and AD, identifying potential common pathogenic features.

Methods

Histological study.

Patients

Women with DENs of the rectovaginal septum (n=13), AD (n=14), and control subjects (n=14).

Intervention

Collection of formalin-fixed paraffin-embedded tissue (endometrium and lesions).

Main outcome measures

Immunohistochemistry (IHC) for platelet marker CD41 and macrophage marker CD68 was conducted to determine the role of inflammatory cells. Levels of vascular endothelial growth factor (VEGF) were quantified, and total numbers of vessels, immunostained against CD31, were calculated to investigate the mechanism of angiogenesis. Double IHC for CD31 and alpha smooth muscle actin (α SMA) was performed to discern stable vessels. Picosirius red staining was carried out to assess fibrosis.

Results

- Platelet aggregation was significantly decreased in both lesion types compared to their corresponding endometrium and healthy.
- Macrophage numbers were higher in both DENs and AD lesions than in their corresponding endometrium and healthy.
- VEGF was downregulated in the stromal compartment of AD lesions compared to healthy endometrium.
- Microvessel density was higher in both DENs and AD lesions than in healthy endometrium.
- Rates of α SMA-surrounded vessels were lower in DENs and AD lesions compared to their corresponding endometrium and healthy.
- High rates of collagen accumulation, indicative of fibrosis, were detected in DENs and AD lesions, and were significantly higher than in their respective endometrium and healthy controls.

Conclusions

Increasing MRI and ultrasound data point to a link between DENs and AD. We now confirm this link at a histological level, having identified specific features shared by DENs and AD, namely macrophage-related inflammation and fibrosis. We found evidence of angiogenesis, with increased numbers of vessels in the lesions, but only few of them were positive for α SMA, suggesting the presence of immature vessels.

All in all, our findings pave the way for more rigorous research into the potential common origin of DENs and AD, and its clinical value in the management of these debilitating conditions.



(OP02) Endometriosis, adenomyosis and fibroids

Unexpected uterine sarcomas in myomectomies and hysterectomies carried out for benign indications and in a tertiary hospital

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Context

The proportion of unexpected sarcoma at the time of myomectomies and hysterectomy for presumed benign indication remains unclear

Objective

The objective of the study was to estimate the incidence of sarcoma among women undergoing myomectomies and hysterectomy for benign indication in a tertiary hospital between 2010 and 2020

Methods

Retrospective and observational study. We conducted a population-based study including all myomectomies and hysterectomies performed for benign indication in a tertiary hospital between January 1, 2010, and December, 2020.

Intervention

The records of women who underwent myomectomy or hysterectomy through laparoscopy, laparotomy or vaginal route for preoperatively benign pathology from January 2010 to December 2020 were reviewed and data were retrospectively analyzed.

Patients

1,251 women undergoing miomectomy or histerectomy for benign indications (971 histerectomies and 280 myomectomies).

Main outcome measure

Number and type of uterine sarcoma diagnosed after myomectomies and hysterectomies for benign indication.

Results

Fourteen patients were diagnosed of uterine sarcoma among 1251 myomectomies or histerectomies for benign indications. Seven patients had some ultrasound suspicious criteria of malignancy and seven were diagnosed of sarcoma incidentally in the histological study of surgical piece (0.56%). The mean age of the patients diagnosed of sarcoma was 54 years, 42% of the patients were menopausal and 28% of them were obese. Patients symptoms of women with sarcoma were: premenopausal abnormal bleeding (50%), postmenopausal bleeding (14%), pelvic pain (42%), palpable pelvic mass (54%), postpartum hemorrhage in one patient and hemoperitoneum in one other woman.

Histological diagnosis found were endometrial stromal sarcoma (57%), leiomyosarcoma (28%), sarcoma mixed Müllerian (7%) and unclassified sarcoma (7%). The stage I was the most frequent (64%). Adjuvant treatments (chemotherapy, radiotherapy or hormonotherapy) were used in 57% of cases. Two women died due to the disease within the 2 years after the diagnosis.

Conclusions

Uterine sarcomas are a heterogeneous group of tumors showing a range of preoperative sonographic aspects and clinical variety. The preoperative diagnosis of uterine sarcomas is not easy, neither ultrasound nor computer tomography, magnetic resonance imaging, nor PET-CT are able to identify patients with uterine sarcomas. The final diagnosis relies on the histopathologic examination after surgery.



(OP03) Menopause

Patient-Derived Xenograft (PDX) of endometrium: a promising model to assess endometrium safety of new menopausal hormone treatments

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Among menopause hormone treatments (MHT), estrogen-progestogen formulations are associated with the highest risk of breast cancer. Nevertheless, the use of a progestogen is necessary to protect the endometrium of non-hysterectomized women from hyperplasia and cancer induced by estrogens.

A better understanding of the estrogen receptor (ER) signaling in endometrium, upon estrogen-related treatments, is thus crucial to develop a new generation of MHT that could be safer for the endometrium and breast. Especially, the fine paracrine interactions occurring between epithelial and stromal cells of the endometrium is far to be fully understood in human tissue.

In this context, the aim of this work is to develop patient derived xenograft (PDX) of endometrium associated to cell sorting by flow cytometry, discriminating stromal and epithelial cells. This methodology allows to study the impact of MHT-related treatments on human tissue at cellular and molecular levels.



(OP03) Menopause

Erbium YAG SMOOTH[®] laser vs. conventional less invasive methods in the treatment of urinary incontinence in women

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The initial treatment for stress urinary incontinence (SUI) should include nonsurgical therapies. Surgical procedures are more likely to cure SUI but are associated with more adverse events. Less invasive operative mesh techniques are relatively effective, but are not immune to complications such as bleeding, bladder perforation, urethral injury, infection, and the retention requiring mesh resection. In patients for whom the risks of anesthesia and surgery are too high, a minimally invasive approach with shorter recovery times and lower implicated costs is recommended. In this sense, recent evidence supports laser treatment as an alternative and effective intervention for SUI. The association between SUI and collagen is well established. The expression levels of Type I and Type III collagen are significantly lower in patients with SUI. That is a possible explanation for the failure of many surgical procedures in urogynecology with a frequent recurrence of symptoms. Laser generated thermal energy effectively improves collagen structure and stimulates neocollagenesis.

Pelvic floor muscle training (PFMT) is the first line treatment for mild to moderate SUI, but patient's adherence and the success rate are quite low. Recent study indicate that non-ablative Er:YAG laser treatment for SUI is a simple, noninvasive, well tolerated procedure which may improve mild and moderate SUI comparable to PFMT.

Head to head studies showed that Er:YAG SMOOTH[®] therapy improve urinary incontinence in women as effectively as the tension-free vaginal tape (TVT) and transobturator tape (TOT) procedures. For patients with mixed urinary incontinence (MUI), some in the TVT and TOT groups showed exacerbation. However, all patients in the laser therapy group tended to improve.

Vaginal erbium laser (VEL) safely and effectively improve overactive bladder symptoms score (OABSS) compared to common pharmacotherapies, anticholinergics and β_3 -adrenoceptor agonists, however through a different mechanism. VEL improves blood flow in the bladder, urethra, and vaginal wall reducing OABSS without adverse effects typical for medication.

Comparative study showed that Er:YAG SMOOTH[®] deliver equal significant reduction in SUI, both in hysterectomized and non-hysterectomized patients.

However, long-term well-designed prospective studies are still required to disclose the effectiveness of laser in the treatment of urinary incontinence and genitourinary syndrome of menopause.



(OP03) Menopause

Pelvic floor dysfunction incidence immediately after instrumental vaginal delivery: a important focus of attention

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Context

Pelvic Floor Dysfunction (PFD) is a condition of high prevalence in our environment, about 30 to 40%. PFD is a multifactorial process that includes several risk factors, some of which are predictable or compensable. Instrumental delivery is one of the most common of these predisposing factors. We have a postpartum care program for women with highest risk of PFD, and this study is conducted to assess the need for continuity of this service.

Objective

Our main goal with this study is to know the real incidence of this PFD after instrumental delivery in our area.

Methods

Prospective Observational Unicentric Study between 1 January 2018 and 31 December 2020. Epidemiological, clinical, obstetrical and follow-up data are collected in an Access® database. Statistic parameters are then analysed with Stata® version 14.0.

Patients

We included patients who had an instrumental delivery with risk factors: overweight/obesity (BMI>25), time of second stage of delivery, neonatal weight > 4,000 g, neonatal cephalic perimeter >37cm o chronic maternal pneumologic affections.

Sample size

n=159.

Main outcome

Incidence of pelvic floor dysfunction: urinary incontinence, faecal incontinence, pelvic organ, prolapse and sexual dysfunction.

Measures

Descriptive analysis of all the variables included in the study will be done. Quantitative variables were summarized around a central parameter (mean) and dispersion measure (standard deviation) and dichotomic variable were described on number and percentage.

Results

In our study we have detected a 60 women with urinary incontinence (UI), it supposes at 37.73%. Most of them are stress UI 33 (20.75% of global, 55.00% of UI), 25(15.72% of global, 41.67% of UI) women present mixed UI and 2 women present urge UI (1.26% of global, 3.33% of UI). Results in means of quality of life on IU (ICIQ-SF) were 10.09(±3.80) in IU patients and 3.81(±1.48) globally.

Incidence on faecal incontinence (FI) was 11(6.9%). Mean of Wexner test is 10.25(±2.01) in this group. Incidence on pelvic organ prolapse was low 5(3.14%) and all cases presented first grade.

About sexual dysfunctions: our group presented dyspareunia in 23 cases (15.23%) and in 2(1.32%) women a total vaginal insensibility was appeared.

Globally in our study, 87 of 159 women presented some PFD. It was an incidence of 54.71%.

Conclusions

Elevate incidence confirms the need for a program to assess and improve their pelvic floor state immediately after instrumental vaginal delivery.



(OP03) Menopause

Genito-urinary syndrome in menopause: hormones and vaginal microbiome

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(In memoriam of Dr. Elia David)

How the changing nature of the vaginal microbiome throughout a woman's life is able to interfere on quality of life via the modifications of the anatomy and physiology of the vagina, the vulva and the low urinary system (bladder and urethra)?

What is the role of HRT on vaginal microbiota, is there a link between probiotic therapy and vaginal infection?

Vaginal microbiome evolution: Lactobacilli decrease along with menopause-related to hormonal and epithelium layers change.

Vaginal lactobacilli are strongly associated with vaginal health in menopause.

GSM (genito-urinary syndrome of menopause)-is related with diminished estrogen and androgen levels and ageing.

It associates: vulvovaginal atrophy (VVA) symptoms; impaired sexual function; and urinary and pelvic symptoms (UI/prolapse).

In contrast to vasomotor symptoms which usually improve over time, GSM is progressive without effective treatment.

There is a lack of clear correlation between the physical exam, the symptomatology and age at which GSM appears.

GSM is underdiagnosed despite the deterioration of QoL for the women affected.

It is necessary to encourage and to push patients to talk about the subject. They describe dryness, pain and/or urinary problems.

The dysbiosis's role is today better understood.

Infections as bacterial vaginosis, vulvo-vaginal candidosis, recurrent cystitis are related to this dysbiosis.

Treatments exist to restore the vaginal microbiota.

Low dose vaginal estrogens may prove effective.

We will discuss about the management of hormonal (HRT, vaginal estrogens, DHEA, SERM) or non hormonal (lubricants, moisturizers) treatments, advising lifestyle changes; the hyaluronic acid use, the place of probiotics, the pelvic floor therapy and the future techniques as Laser, Leds or Minileads.

No taboos are necessary, right questions have to be used.



(OP03) Menopause

Incidence of transvaginal Tension-free Vaginal Tape-Obturator (TVT-O®) surgical section due to complications after surgical treatment of Stress Urinary Incontinence (SUI)

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Context

Suburethral tapes have been widely adopted to treat stress urinary incontinence. Further resection of such tapes may be necessary in certain cases.

Objective

Study of the incidence of transvaginal Tension-free Vaginal Tape-Obturator (TVT-O®) section due to complications after anti-incontinence surgery, analysis of risk factors and evolution of symptoms after the section.

Methods

Retrospective observational study of patients undergoing anti-incontinence surgery for the correction of SUI or mixed urinary incontinence with predominance of SUI between 2007-2018. All patients were followed in the pelvic floor unit undergoing anamnesis, physical examination and urodynamic study. All of them underwent TVT-O® surgery. The follow-up was monthly, at 6 months and annually, and after this period by telephone control. The epidemiological, surgical and follow-up data of all patients were collected in an Access© database. A descriptive and comparative statistical analysis was performed using Stata©.

Patients

840 women undergoing anti-incontinence surgery between 2007 to 2018.

Mean outcome measure

The need for a surgical tape section for urinary retention ± recurrent cystitis.

Results

A total of 840 women with a mean age in the two groups of 58 ± 11 years ($p > 0.05$) were included. The incidence of tape section was 2.8% (24 cases). In the section group, early ($p < 0.05$) and late ($p < 0.05$) surgical complications appeared, such as urinary retention and recurrent cystitis. An increase in adverse effects (obstructive types) requiring surgical tape section was detected when TVT-O® and previous colpoplasty were performed concomitantly with an Odds Ratio (OR) of 2.29, representing 58% of cases requiring surgical tape section comparing to anti-incontinence surgery alone ($p < 0.05$). We didn't find any other relationship with other types of pelvic organ prolapse surgery ($p > 0.05$). We also found that number of days of post-intervention urinary catheter associated with need for surgical tape section ($p < 0.05$), being the average of 5 days in the section group.

During 12 months after surgical tape section, only 2 cases (8.3%) of recurrent SUI, 9 cases (37.5%) of IUU and one (4.17%) of IUM were found.

Conclusion

In our pelvic unit, the incidence of tape section was 2.8%, the main risk factor was the concomitant performance of anterior colpoplasty at the same time of TVT-O® and immediate postoperative urinary retention was associated to the need of tape section.



(OP03) Menopause

Evaluation of posterior tibial nerve electrostimulation in urgency incontinence in our Center: observational study

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Context

Urgency incontinence is defined as the intense urge to urinate followed by an involuntary loss of urine. Although there are many medical treatments available, such as anticholinergics and beta-adrenergics drugs, an alternative can be found in the use of the posterior tibial nerve electrostimulation (PTNS) to ease up the symptomatology.

Objective

The objective was to study the quality of life in women with urgency incontinence or urgent urination using PTNS treatment.

Methods

We performed an observational study with prospective data collection between January 2020 and April 2021. All patients were evaluated through a basic medical history and an ICIQ-SF test before and 3-6 months after the PTNS treatment.

Patients

A total of 37 patients were reviewed, with a mean age of 65 (between 31 and 88 years old) and a mean of 6 years in symptomatology (between 1 and 20 years). In 89.19% of cases, a previous treatment was used. The mean BMI was 31.4 (with an interval between 22.9 and 48.4). In 72.97% cases there was no pelvic prolapse, in 18.91% of cases an anterior prolapse was found and in 6 cases a posterior prolapse was observed. 5.41% of the studied women were nulliparous and 81.08% had 2 or more vaginal deliveries. A total of 4 women had a history of a forceps delivery.

Mean outcome measure

The main outcome measure was the difference in the ICIQ-SF score before and after the use of PTNS.

Results

The mean treatment months was 5.64 with an interval between 3 and 11 months. In 51.35% of the cases there was no difference in the ICIQ-SF value before and after PTNS treatment. The mean difference in ICIQ-SF value observed was 3.02, in a range between 0 and 16. A difference of 4 or more was seen in 35.13% of the cases. Non prolapse was found in 76.92% of the women that improved their ICIQ-SF value and in all of the patients with a total symptomatology resolution. Previous medical treatment with mirabegron, fesoterodine and propiverine and pelvic floor rehabilitation were used in patients with an important improvement in the ICIQ-SF value.

Conclusions

In conclusion, PTNS is a useful alternative to medical treatment with drugs in the urgency incontinence therapy and has no adverse effects. Results may variate due to adherence to treatment or delay in the symptomatology improvement.



(OP03) Menopause

HIFEM technology used for the treatment of pelvic floor dysfunctions in female population: preliminary data

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Objective

The aim is to introduce current possibilities of using HIFEM (High-Intensity Focused Electromagnetic Technology) in reconstructive and cosmetic gynecology, uro-gynecology & sexology and new views on their use together with current methods.

Methods

A group of women suffering with the most common issues such as urine incontinence (SUI, UUI, MUI, ISD), POP (pelvic organ prolapse), IL (introital laxity), VRS (vaginal relaxation syndrome), VA (vaginal atrophy), SD (sexual dysfunction) and Post-op patients, who would benefit from neuromuscular re-education were treated with HIFEM technology in the pelvic floor area. Ultrasound measurements of the pelvic area along with subject satisfaction were performed before and after the HIFEM procedure. The subjects were furthermore monitored by a physiotherapist focusing on the pelvic floor. The lecture will introduce data based on HIFEM application on the women's population since May 2020 and present the preliminary data of an ongoing prospective study.

Results

The results on a very wide group of patients with their ongoing follow-up are showing significant improvement in the treated conditions, along with high level of satisfaction. The treatments are showing a very fast onset of a significant positive effect, compared to the announced and expected time of the onset of the positive effect, as patients report improvements already after two to three sessions.

Conclusions

The non-invasive HIFEM technology for the treatment of wide group of pelvic organs and functional disorders together with psychological aspects is an easy to use and safe procedure with excellent results. It is well suited in-office procedure with positive outcomes and is an acceptable treatment option, which should be considered as a first choice prior to use of invasive techniques.



(OP03) Menopause

A Phase 3, randomized, placebo-controlled, 12-week, double-blind study, plus a non-controlled extension treatment period, to assess efficacy and safety of fezolinetant, a neurokinin-3 receptor antagonist, in women with moderate-to-severe vasomotor symptoms

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Objective

To evaluate the efficacy and safety of fezolinetant vs placebo on the frequency and severity of vasomotor symptoms (VMS) associated with menopause.

Methods

Double-blind, placebo-controlled, multicenter Phase 3 study; NCT04003142.

Patients

Women aged ≥ 40 -65 y with moderate-to-severe VMS (minimum average 7 hot flashes/day).

Interventions

Placebo, fezolinetant 30 mg or 45 mg once daily (1:1:1).

Main outcome measures

Mean change from baseline to week 4 and 12 in frequency and severity of moderate-to-severe VMS (co-primary efficacy endpoints); mean change from baseline to week 12 in Patient-reported Outcomes Measurement Information System Sleep Disturbance-Short Form 8b (PROMIS) Total Score, and effect on weekly mean change in frequency and severity of moderate and severe VMS (secondary endpoints); treatment-emergent adverse events (TEAEs; safety and tolerability).

Results

501 women were randomized and 500 took ≥ 1 dose (placebo n=167, fezolinetant 30 mg n=166, fezolinetant 45 mg n=167). Both fezolinetant doses were statistically significant compared with placebo. For VMS frequency, least squares (LS) mean reduction over placebo (SE) at week 4 was -1.82 (0.46), $p < 0.001$ for fezolinetant 30 mg and -2.55 (0.46), $p < 0.001$ for 45 mg. At week 12, these values were -1.86 (0.55), $p < 0.001$ for fezolinetant 30 mg and -2.53 (0.55), $p < 0.001$ for 45 mg. For VMS severity, reductions at week 4 were -0.15 (0.06), $p = 0.021$ for fezolinetant 30 mg and -0.29 (0.06), $p < 0.001$ for 45 mg, and at week 12 were -0.16 (0.08), $p = 0.049$ for fezolinetant 30 mg and -0.29 (0.08), $p < 0.001$ for 45 mg. Fezolinetant 45 mg, but not 30 mg, statistically significantly reduced the PROMIS total score vs placebo at week 12: LS mean difference (SE) -2.0 (0.7), $p = 0.007$ for fezolinetant 45 mg; -0.7 (0.7), $p = 0.381$ for 30 mg. Efficacy was evident by week 1 of treatment and maintained over the 12-week study period. TEAEs were reported by 40% (fezolinetant 30 mg), 36% (fezolinetant 45 mg) and 32% (placebo) of women. Headache was the most common TEAE in the fezolinetant groups: 3% (30 mg), 4% (45 mg) and 2% (placebo). Serious TEAEs were reported by 2% (30 mg), 1% (45 mg) and 0% (placebo) of women; there were no drug-related serious TEAEs.

Conclusions

Fezolinetant 30 mg and 45 mg once daily were efficacious for the treatment of moderate-to-severe VMS associated with menopause. Fezolinetant 45 mg improved patient-reported sleep and no safety signals of concern were apparent for either fezolinetant dose.



(OP03) Menopause

Estetrol and mammary gland: friends or foes?

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Hormonal treatments used to treat menopause symptoms increase the breast cancer risk. New formulations with a better benefit/risk profile are thus necessary. Estetrol (E4) is a native fetal estrogen that is currently approved for use as the estrogen component in a combined oral contraceptive. E4 is also being developed as a menopause treatment (MT) that abrogates hot flushes. E4 like the other estrogens activates the nuclear Estrogen Receptor alpha but antagonizes the membrane form of this receptor. This causes selective tissue actions, with limited impact on the normal and malignant breast.

Here, we show that doses of E4 that are neutral on breast cancer growth and lung metastasis dissemination enhance endometrial proliferation. A progestogen should thus be combined to E4 to prevent endometrial hyperplasia and cancer. Through *in vivo* observations and transcriptomic analyses, our work provides evidence that combining a progesterone (P) or Drospirenone (DRSP) with E4 is neutral on breast cancer growth and dissemination, with very limited transcriptional impact.

Our study provides new evidence that a therapeutic dose of E4 for MHT or COC, combined with P or DRSP may provide a better benefit/risk profile towards breast cancer risk compared to hormonal treatments currently available for patients.



(OP03) Menopause

Expression and distribution of protein kinase enzymes in the human vagina - A biochemical and immunohistochemical study

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Context

There is limited knowledge on the role of cyclic nucleotide (cyclic AMP/cyclic GMP)-binding enzymes in female genital tissues.

Objective

Cyclic AMP- and cyclic GMP-binding protein kinases (cAK, cGK) have been identified as important receptors for cyclic nucleotides in human tissues. A significance of protein kinases in the control of the function of the male and female reproductive tract has been suggested, however, up until today, only a few approaches have addressed these enzymes in female genital tissues. The present study aimed to investigate the expression of cAK and cGK in human vaginal tissue. The distribution of cAK(I) and cGK(I) in relation to the vasoactive intestinal polypeptide (VIP), calcitonin gene-related peptide (CGRP) and phosphodiesterase type 4 (PDE4) was also evaluated.

Methods

Cytosolic supernatants prepared from specimens of vaginal wall smooth muscle or epithelium were subjected to anion exchange chromatography and the activities of cAK and cGK(I) were measured. Western blot analyses were also commenced. In order to evaluate the distribution of cAK(I) and cGK(I) in relation to VIP, CGRP and PDE4, immunohistochemistry was conducted in sections of the human vaginal wall.

Patients/interventions

Specimens of the human vagina were obtained from 10 pre-menopausal female cadavers (age at the time of death: 16 - 42 years). Full wall preparations were taken from the lower mid portion of the vaginal tube.

Main outcome measures

To investigate in human vaginal tissue by means of biochemical and immunohistochemical methods the expression and distribution of cAK(I) and cGK(I).

Results

Activities representing cGK(I) and cAK(I) were resolved from the chromatography column. Staining specific for cAK(I alpha) was identified in both vascular and non-vascular vaginal smooth musculature, immunoreactivity for cGK(I beta) was observed in the smooth muscle and endothelium of small arteries interspersing the sections. cAK(I alpha)-positive vessels were found innervated by slender varicose nerve fibers presenting the expression of VIP and CGRP. These arteries also expressed PDE4.

Conclusion

Localization of cAK and cGK in close relation to key mediators of the cyclic AMP (PDE4, VIP) and cyclic GMP (CGRP) pathway indicate that both signaling systems may synergistically work together in human vaginal tissue.



(OP03) Menopause

Re-evaluation of the expression and distribution of isoenzymes of the Nitric Oxide Synthase (NOS) in the human vagina using the Tyramide Signal Amplification technique

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Context

There is evidence that responses mediated by nitric oxide (NO) and cyclic GMP are involved in smooth muscle relaxation in the female genital tract, for example, in the erectile tissue of the clitoris. An increase in cyclic GMP triggered by NO has been supposed to be involved in the regulation of vaginal blood flow as well as in the control of vaginal non-vascular smooth muscle.

Objective

Although a significance of the non-adrenergic, non-cholinergic (NANC) system, including the nitric oxide (NO)/cyclic GMP signaling, in the control of the female sexual response has been assumed, only very few studies have addressed the distribution of nitric oxide synthase (NOS) in human female genital tissues. The present study aimed to re-examine in the human vagina the localization of isoforms of NOS (endothelial NOS, neuronal NOS).

Methods

Vaginal tissue was obtained from 15 pre- or postmenopausal women. Using specific antibodies in combination with the Tyramide Signal Amplification (TSA) technique, the occurrence and distribution of eNOS, nNOS and synapsin was examined.

Patients/interventions

Human vaginal wall tissue was obtained from 15 female cadavers (seven menopausal, eight postmenopausal, aged 48 - 63 years) who had been subjected to forensic autopsies. Macroscopically normal tissue was excised from the mid to proximal portion of the vaginal tube.

Main outcome measures

To re-examine the localization of eNOS and nNOS in the human vagina by applying optimized fixation and staining protocols and the TSA technique in order to enhance the sensitivity of the cytochemical labeling procedure.

Results

Immunohistochemistry revealed a dense subepithelial meshwork of varicose nerve fibres characterized by the expression of synapsin. A subpopulation of these fibers presented immunoreactivity specific for nNOS. Interestingly, the cells of the epithelial layer also showed cytoplasmatic labeling for nNOS. Small arteries presenting signals for eNOS in their endothelial lining were found in close proximity to nNOS-positive nerve terminals. Signals related to nNOS were also observed in large nerve trunks.

Conclusion

The results are in support of the hypothesis that nerves utilizing NO play a role in the control of vaginal function. Our findings indicate that, in the human vagina, the NO signaling is rather involved in the control of blood flow than in the mechanism of vaginal non-vascular smooth muscle relaxation.



(OP03) Menopause

Human breast organoids: a promising model to assess breast safety of new menopausal hormone therapy formulations

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Estrogens are the most commonly used and the most powerful treatments to relieve climacteric-related symptoms, known to highly impact menopausal women's well-being. However, the use of menopausal hormone therapy (MHT) based on estrogen formulations remains controversial since it increases the risk to develop breast cancer, by promoting cell proliferation, migration and dissemination.

Developing new MHT generation which are safer for estrogen-sensitive tissues while remaining effective on climacteric symptoms is crucial. In that view, a better *in vitro* modeling of these organs is mandatory to assess the impact of new potential MHT formulations on estrogen-sensitive human tissues at cellular and molecular levels. Human breast organoid is a useful preclinical model to study the effects of drugs on the healthy human mammary gland. After dissection and culture with appropriate growth factors and cytokines, human breast tissue forms organoids that are composed of the different epithelial cell subtypes found in the human breast.

Following MHT-related treatments, beside immunohistochemistry analyses, cell sorting by flow cytometry allows to isolate each epithelial cell populations and to decipher the impact of those treatments at a molecular level.

This strategy is an opportunity to develop new MHTs which are safer for the breast, providing a better women's quality of life.



(OP04) Contraception

A longitudinal cohort study assessing the effectiveness of extended levonorgestrel-containing combined oral contraceptive use

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Context

The efficacy of Seasonique, a 91-day levonorgestrel-containing combined oral contraceptive (COCLNG) in preventing undesired pregnancies was evaluated in pivotal randomised clinical trials (RCT). However, its effectiveness in a real world setting is not known. In the context of the regulatory submission for market authorization of 91-day COCLNG in Europe, the European Medicines Agency requested a post-authorization safety study to assess the cardiovascular risk associated with 91-day COCLNG in routine clinical practice.

Objective

To evaluate the incidence of pregnancies among women exposed to Seasonique compare to women exposed to 28-day COCLNG.

Methods

The current study is a post hoc analysis of this large safety study, conducted using a United States (US) healthcare claims database (2006-2017). Patients (females) using Seasonique were propensity score (PS)-matched to those using 28-day COCLNG. Only episodes of pregnancies occurring during current use, defined by prescription dispensing dates, days supplied and a grace period, were included in the analysis. Incidence significance was calculated by Chisq. test.

Results

The study included 44,085 Seasonique users and 132,264 28-day COCLNG PS-matched comparators. There were 334 pregnancies (0.76%) among Seasonique users compared to 1,403 (1.06%) among 28-day COCLNG users ($P < 0.001$)

Conclusions

These findings suggest high effectiveness of the extended 91-day COCLNG compared to 28-day COCLNG in routine clinical practice.



(OP04) Contraception

The effect of estetrol/drospirenone on menstrual phase symptoms: results from the Europe/Russia phase 3 trial

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Context

Hormonal contraceptives have a neutral, negative, or positive impact on menstrual symptoms.

Objective

To describe the effect of estetrol (E4) 15 mg/drospirenone (DRSP) 3 mg on menstrual symptoms from a multicentre, open-label, phase 3 trial conducted in Europe and Russia.

Methods

Data from the Menstrual Distress Questionnaires (MDQs) that participants completed at enrolment (baseline) and end-of-treatment (EoT) for the premenstrual (4 days before menstruation), menstrual (most recent flow), and intermenstrual (remainder of the cycle) phases, respectively, were used. The MDQ measures symptoms in 8 domains: pain (6 symptoms); negative affect (8); water retention (4); autonomic reaction (4); impaired concentration (8); behavioural change (5); arousal (5); and control (6). Symptoms are scored on a 5-point scale (0=none to 4=present, severe). Maximum domain mean total scores range from 16 to 32.

Participants

Healthy women, 18-50 years, regular cycles.

Intervention

E4/DRSP in a 24/4-day regimen for up to 13 consecutive 28-day cycles.

Main outcome measures

Mean total domain scores change from baseline at EoT for each menstrual phase overall and for starters/switchers based on hormonal contraceptive use in the 3 months before enrolment.

Results

1,553 participants (606 starters; 947 switchers) received E4/DRSP. Across domains, baseline mean total scores were below 4, indicating that participants on average reported mild symptoms. Mean total score at baseline was highest for menstrual pain for all subjects (4.0). Mean pain domain score decreased from baseline to EoT (-0.4) for all subjects in the menstrual phase; in starters, this decrease was most prominent (-1.0). Mean negative affect domain score decreased from baseline to EoT for all participants in the premenstrual (-0.3) and menstrual (-0.4) phases; this decrease was most pronounced in starters (-1.0 in both phases). Mean water retention domain score increased in switchers (0.2, intermenstrual and premenstrual; 0.3, menstrual) and decreased in starters (0.2, intermenstrual; -0.6, premenstrual and menstrual). Changes were also observed for the autonomic reaction, concentration, behaviour, arousal, and control mean domain scores in all phases for all participants (range: -0.3 to 0.0), for switchers (-0.3 to 0.0), and for starters (-0.0 to -0.4).

Conclusion

Overall, menstrual symptoms remain mild in women switching to E4 15 mg/DRSP 3 mg. Menstrual pain and negative affect improved in starters.



(OP04) Contraception

Bleeding patterns with estetrol/drospirenone oral contraceptive by age, obesity status, and recent hormonal contraceptive use

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Context

Estetrol (E4) is a natural oestrogen produced by the human fetal liver. E4 combined with drospirenone (DRSP) demonstrated a high contraceptive efficacy and an excellent safety profile in two phase 3 trials performed in Europe/Russia and US/Canada.

Objective

To examine vaginal bleeding patterns by subgroups observed in the Europe/Russia trial.

Methods

A multi-centre, open-label, phase 3 trial. Participants kept a daily paper record of bleeding (requiring sanitary protection) and spotting (requiring no sanitary protection) and reported adverse events (AEs).

Participants

1,553 participants 18-50y with regular menstrual cycles and body mass index (BMI) 18-35 kg/m².

Interventions

E4 15 mg/DRSP 3 mg in a 24/4-day regimen for up to 13 cycles.

Main outcome measures

Proportion with unscheduled bleeding and/or spotting (B/S) episodes or absence of scheduled B/S per cycle (cycles 1-12). We analysed outcomes by age (18-25y [n=793], 26-35y [n=560] and 36-50y [n=200]), BMI (<30 kg/m² [n=1,464] and ≥30 kg/m² [n=89]), and hormonal contraceptive use in the 3 months before enrolment (starters [n=606] and switchers [n=947]).

Results

Unscheduled B/S episodes for the three age groups were 24.3%, 23.3% and 21.0% in cycle 1, respectively; 19.4%, 19.5% and 18.0% in cycle 2, respectively; and 13.4%, 13.0% and 11.6%, resp. in cycle 12. No scheduled B/S occurred in 5.0-8.2% of cycles among 18-25y, 6.1-8.5% of cycles among 26-35y, and 6.2-11.6% of cycles for 36-50y participants. For the two BMI groups, unscheduled B/S for users with BMI <30 kg/m² and ≥30 kg/m² occurred in 23.2% and 27.6% in cycle 1, respectively; 19.3% and 18.6% in cycle 2, respectively; and 13.1% and 11.9%, in cycle 12, respectively. No scheduled B/S occurred in 5.4-7.7% and 8.0-17.4% of cycles for users with BMI <30 kg/m² and ≥30 kg/m², respectively. Unscheduled B/S for starters and switchers was 29.3% and 19.7% in cycle 1, respectively; 16.6% and 20.9% in cycle 2, respectively; and 9.3% and 15.3% in cycle 12, respectively. No scheduled B/S occurred in 4.0-5.9% and 6.3-9.6% of cycles for starters and switchers, respectively. Fifty-three (3.4%) participants discontinued due to bleeding-related AEs.

Conclusion

Bleeding patterns with E4/DRSP appeared comparable for users of different ages, BMI and recent hormonal contraceptive use. Unscheduled B/S episodes decreased over time in all subgroups. Results for obese participants should be interpreted with caution due to the low numbers.



(OP04) Contraception

Contraceptive efficacy by age, smoking status and recent hormonal contraceptive use and safety of a new combined oral contraceptive containing estetrol/drospirenone

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Context

Estetrol (E4) is a natural oestrogen produced by the human fetal liver. Two pivotal phase 3 trials in Europe/Russia and US/Canada with E4 in combination with drospirenone (DRSP) demonstrated high contraceptive efficacy with a favourable bleeding profile.

Objective

To assess contraceptive efficacy of E4/DRSP in subgroups and overall safety in the Europe/Russia trial.

Methods

Multicenter, open-label, phase 3 trial.

Participants

18-50y with regular menstrual cycles and a body mass index (BMI) 18-35 kg/m².

Intervention

E4 15 mg/DRSP 3 mg in a 24/4-day regimen for up to 13 cycles.

Main outcome measures

Efficacy based on Pearl Index (PI) in at-risk cycles (with sexual intercourse and no other contraceptive method use). PI was assessed in the entire population, by age (18-25y, 26-35y and 36-50y), and for 18-35y participants based on smoking status and hormonal contraceptive use in the 3 months before enrolment (starters/switchers). We assessed if subgroups have a PI less than 3 times higher than the general population PI. Safety was assessed in the entire population and reported as treatment-related adverse events (AE) and serious AEs.

Results

1,553 participants were included in the efficacy and safety evaluation of which 1,353 were ≤ 35 y. Five on-treatment pregnancies occurred, for a PI of 0.47 (95% CI: 0.15-1.11). The PIs for 18-25y, 26-35y, and 36-50y groups were 0.50 (95% CI: 0.10-1.46, 3 pregnancies, 770 participants, 7,823 cycles), 0.44 (95% CI 0.05-1.60, 2 pregnancies, 543 participants, 5,869 cycles), and zero (95% CI: 0.00-2.22, 197 participants, 2,157 cycles), respectively. The PI for smokers was 1.04 (95% CI: 0.13-3.76, 2 pregnancies, 238 participants, 2,496 cycles) and non-smokers 0.35 (95% CI: 0.07-1.02, 3 pregnancies, 1,075 participants, 11,196 cycles). For starters, the PI was 0.25 (95% CI: 0.01-1.42, 1 pregnancy, 500 participants, 5,113 cycles). For switchers, the PI was 0.61 (95% CI: 0.17-1.55, 4 pregnancies, 813 participants, 8,579 cycles). Most common treatment-related AEs were metrorrhagia (5.0%), vaginal haemorrhage (4.3%) and acne (3.8%). Discontinuation due to treatment-related AEs was 9.1%. One SAE was reported, a venous thromboembolism, which resolved without sequelae.

Conclusion

E4/DRSP provides high contraceptive efficacy across different age groups, smokers/non-smokers and starters/switchers, with a PI in different subgroups ranging from zero to 1.04 compared to 0.47 for the total population. E4/DRSP has a favourable safety profile.



(OP04) Contraception

Risk of venous and arterial thromboembolism in users of nomegestrol acetate and 17 β -estradiol (NOMAC-E2) is not increased as compared to levonorgestrel-containing combined oral contraceptives - Final results from the PRO-E2 observational comparative safety and efficacy

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Context

Clinical experience with combined oral contraceptives (COCs) containing ethinyl estradiol (EE) suggests serious clinical outcomes are rare. One of the most serious outcomes associated with COC use is venous thromboembolism (VTE). Nomegestrol acetate (NOMAC) and a natural estrogen 17 β -estradiol (E2) were found to have less effects on parameters of hemostasis.

Objective

To assess and compare the risk of VTE and arterial thromboembolism (ATE) in NOMAC-E2 users with levonorgestrel-containing COC (COCLNG) users.

Methods

Between August 2014 and September 2019, a prospective study was conducted including 101,000 women from 12 countries in Europe, Australia, and Latin America. Women newly prescribed an eligible COC and not using a COC in the past 2 months were recruited by health care professionals during routine clinical practice. After submitting a signed consent, they were followed up via questionnaires at 6, 12, and 24 months and self-reported outcomes were validated via treating physicians. A non-inferiority design with an upper limit of the 95% confidence interval (CI) of 1.5 was used for the risk of VTE. Crude (HR_{crude}) and adjusted hazard ratios (HR_{adj}) were calculated. Statistical analyses were conducted using SAS 9.4.

Main outcome measure(s)

The main outcome was VTE, specifically deep venous thrombosis of the lower extremities (DVT) and pulmonary embolism (PE). Secondary outcomes included all VTE and ATE.

Results

A total of 101,498 women (49,598 NOMAC-E2 users and 51,900 COCLNG users) were enrolled and followed up for a maximum of 2 years. NOMAC-E2 users had a statistically significantly ($p < 0.0001$) higher mean age (31.0 years) than COCLNG users (29.3 years) but other baseline characteristics were similar between the cohorts. The main analysis comparing risk of DVT of the lower extremities and PE in NOMAC-E2 users versus COCLNG users yielded an HR_{adj} of 0.59 (95% CI: 0.25-1.35; adjusted for age, BMI, family history of VTE, and current duration of contraceptive use). The risk of all VTE and ATE was not higher in NOMAC-E2 users compared with COCLNG users.

Conclusion(s)

NOMAC-E2 use was not associated with a higher risk of VTE and ATE compared with COCLNG in a real-world setting, consistent with findings of previous studies investigating estradiol-containing COCs.



(OP04) Contraception

NOMAC-E2 is associated with a significantly lower risk of unintended pregnancy compared with levonorgestrel-containing combined oral contraceptives: final results on contraceptive effectiveness from the PRO-E2 observational comparative safety and efficacy

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Context

NOMAC-E2 is a monophasic combined oral contraceptive (COC) containing a fixed dose of nomegestrol acetate (2.5mg) and 17 β -estradiol (1.5mg), which is taken for 24 days followed by 4 days of placebo.

Objective

To assess and compare the risk of unintended pregnancy in NOMAC-E2 users with levonorgestrel-containing COC (COCLNG) users in clinical practice.

Methods

In this large, prospective, observational study, new users of NOMAC-E2 and COCLNG were recruited in 12 countries in Europe, Australia, and Latin America. Women were followed-up via questionnaires for up to 2 years and self-reported outcomes of interest were validated via treating physicians. Data on potential confounders, such as age and body mass index (BMI) were captured. Unintended pregnancy was measured by the Pearl Index, which calculates the number of contraceptive failures per 100 women-years (WY). Incidence rates, crude and adjusted hazard ratios (HRadj) were calculated.

Participants

Women were enrolled after the participating physician and the woman had determined that NOMAC-E2 or COCLNG use was appropriate. There were no specific medical inclusion/exclusion criteria and no age restrictions.

Outcome Measure

The main study outcome was venous thromboembolism. Contraceptive failure assessed as unintended pregnancy was one of the secondary endpoints.

Results

A total of 101,498 women (49,598 NOMAC-E2 and 51,900 COCLNG users) were enrolled and followed up. NOMAC-E2 users had a statistically significantly ($p < .0001$) higher mean age (31.0 years) than COCLNG users (29.3 years) but other baseline characteristics were similar between the cohorts. There were 64 unintended pregnancies in NOMAC-E2 users (0.15 per 100 WY; 95% CI, 0.11-0.19) and 200 in COCLNG users (0.41 per 100 WY; 95% CI, 0.35-0.47). The risk of unintended pregnancy was statistically significantly lower in the NOMAC-E2 cohort ($p < .0001$). The HRadj for unintended pregnancy comparing NOMAC-E2 vs COCLNG was 0.45 (95% CI, 0.34-0.60; adjusted for age, BMI, gravidity, COC user status 1, education level). Stratified analyses showed lower unintended pregnancy rates for NOMAC-E2 in younger women and those with lower educational level.

Conclusions

NOMAC-E2 showed a better effectiveness profile compared to COCLNG, consistent with its short hormone-free interval and the long half-life of NOMAC.



(OP04) Contraception

Gynaecological profile of 126 French women with venous thrombosis

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Context

Combined contraceptives (COC) are well-known venous thrombosis (VTE) risk factors. Recently, certain gynaecological pathologies appear to be risk factors for VTE as Polycystic Ovary Syndrome (PCOS) or endometriosis.

Objective

To assess the gynaecological profile of patients hospitalized for VTE and their contraceptive use at the time of VTE and now.

Methods

A retrospective monocentric study.

Patients

Women aged between 18 and 50 years old who were hospitalized at Saint Joseph Hospital, Paris, France, for a VTE from January 1, 2016 to December 31, 2020 were enrolled.

Interventions

None.

Main outcome measures

VTE characteristics, use of contraceptive at time of VTE and now, gynaecological and obstetrical characteristics were collected through the computerized patient record and completed by a phone call.

Results

126 patients were enrolled. At time of VTE, mean age was 39 years (± 8.1) and mean body mass index 31 kg/m^2 (± 8.7). 40 women (32%) had a deep venous thrombosis (DVT) only, 67 women (53%) had a pulmonary embolism, 4 women (3%) had a cerebral or splanchnic venous thrombosis. 38 women (30%) used a COC at time of VTE. Fourteen women (11.1%) had PCOS and eleven (8.7%) had endometriosis. Women with PCOS appeared to be younger at the time of VTE compared to non PCOS women (mean age $32 [\pm 6]$ and $40 [\pm 8]$ respectively). Among PCOS patients, 57% had DVT only and 5 (36%) were using COC at the time of VTE. 67 women (53%) had at least one pregnancy, 4 women (3%) had repeated miscarriages and 3 (2%) had a vascular pathology during pregnancy.

Regarding contraceptive use now, with a mean delay since the VTE of 2.6 years (± 1.5), 1 woman use a COC, 12 women (9.5%) use progestin only contraceptive and 35 (28%) use contraceptive without hormones. 68 women (54%) are not currently using contraceptive while they have partners without parental plans. Seventy-three women (58%) think that they were informed about hormonal contraindications after their VTE.

Conclusion

The gynaecological profile of patients who had VTE appears to differ according to the underlying gynaecological pathology, particularly for patients with PCOS who are younger at the time of their thrombosis. As these results were obtained on a small number of patients, a larger study is now necessary to a better understanding of VTE in young women. Information to women on contraceptive after a venous thrombosis need to be intensified and repeated over time.



(OP04) Contraception

Subjective sensations during menstruation after COVID-19 and vaccination: is the association real?

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Context

Recent studies find possible connection of menstrual function disorders with previous COVID-19 and vaccination against SARS-CoV-2.

Objective

To compare the severity of subjective sensations during menstruation in COVID-19 convalescents with those who were not ill and vaccinated with unvaccinated.

Methods

538 women were filled out the questionnaire posted at social networks.

Main outcome measures

The severity of menstrual pain measured with 10-points scale, duration and intensity of bleeding during the last menstruation and a year ago, the quantity of painkiller pills taken over the last month and on average per month a year ago.

Patients

The age of the respondents was 21 (19-24) years. 363 women were COVID-19 convalescents, 195 of them were PCR-positive in the acute period of the disease, 9 women were hospitalized. 163 women was vaccinated.

Results

The intensification of unpleasant sensations during menstruation was noted by 19.0% of COVID-19 convalescents and 10.9% of women who were not ill ($P<0.001$); 24.6% of respondents with positive PCR test results and 9.9% with unconfirmed COVID-19 ($P<0.001$); 55.6% of hospitalized and 18.3% of treated as outpatient ($P<0.02$). The dynamics of unpleasant sensations in vaccinated and non-vaccinated patients did not differ significantly.

Detailed assessment of the duration, intensity of menstrual bleeding and intensity of menstrual pain with 10-points scale find no significant differences between COVID-19 convalescents and those who were not ill. Women vaccinated against COVID-19 had significantly shorter duration of the last menstruation than unvaccinated (5.2 ± 1.4 and 5.6 ± 1.6 days, $p=0.043$).

Women hospitalized with COVID-19 had higher duration and intensity of the last menstrual bleeding (7.3 ± 2.9 and 5.5 ± 1.6 days, $p=0.023$ and 7.8 ± 1.2 to 6.2 ± 2.0 points, $p=0.013$), and number of painkillers taken over the last month, and monthly a year ago (a 5.4 ± 2.6 and 3.0 ± 5.1 tablets, $p=0.004$; 6.8 ± 5.4 3.5 ± 6.6 tablets, $p=0.012$) than treated as outpatients.

Conclusions

COVID-19 convalescents reported about intensification of unpleasant sensations during menstruation more often than those who were not ill. Despite this, detailed survey with the score assessment of the duration, intensity of menstrual bleeding and pain did not reveal a significant association of these parameters. There was no association of vaccination and the severity of unpleasant sensations during menstruation.



(OP04) Contraception

From thermometer to finger ring, basal body temperature measurement in the new era of FDA cleared digital contraception

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Context

Fertility awareness based methods (FABMs) of birth control traditionally involve manual basal body temperature (BBT) measurement. Advanced FABMs in the form of apps such as Natural Cycles, the first FDA cleared digital birth control, streamlines calculation of fertile days with little effort from the user however, the manual task of BBT measurement sublingually remains.

Objective

To improve the user experience, validation of a new continuous measurement device (CMD) for use with the Natural Cycles algorithm was necessary. Furthermore, an automated correction model applied to abnormal temperatures was explored.

Materials and methods

Users were also instructed to log alcohol consumption. Parameters measured by the CMD included distal body temperature, heart rate (HR) and movement. The day to day variability of the temperatures taken sublingually and with the CMD were calculated. CMD temperatures were also plotted as a function of HR, time and movement.

Patients

40 female active users and 3 male users simultaneously measured BBT sublingually and wore a CMD ring on their finger for a total of 5262 nights.

Interventions

Wearing CMD and taking sublingual BBT.

Main outcome measures

Temperature variation, correlation between HR and BBT.

Results

The variability for sublingual temperatures was higher than CMD. A correlation between BBT and HR existed with the HR spectrum being highly affected by alcohol consumption. Therefore, HR could be used to identify anomalous temperatures by exploiting the correlation to correct the temperature value.

Conclusions

The use of a CMD to collect data for use by the Natural Cycles algorithm reduces day to day variability in temperatures. Furthermore, development of the anomalous temperature correction model is revolutionary to digital fertility awareness based methods, reducing effort by the user further, potentially increasing satisfaction and thus compliance with the method. Contraceptive compliance and satisfaction are important factors when choosing birth control and its subsequent effectiveness. Use of continuous measurement and a correction model could help improve both compliance and satisfaction for users.



(OP04) Contraception

Overall and bleeding-related discontinuation rates of a new oral contraceptive containing 4 mg drospirenone only in a 24/4 regimen and comparison to 0.075 mg desogestrel

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Context

Progestin-only pills do not increase the risk of venous thromboembolism, stroke, and myocardial infarction but are associated with poor cycle control. A novel estrogen-free pill containing only drospirenone (DRSP) to improve bleeding patterns and tolerability and reduce discontinuation rates has been introduced into the market.

Objective

The present study aims to describe the improvement in the acceptability of this DRSP-only pill e.g., regarding the bleeding profile and the reduction in discontinuation rates due to unacceptable bleeding compared to desogestrel (DSG).

Methods

Double-blind, double-dummy prospective phase III study in healthy women aged 18 to 45 years evaluating a total of 858 women with 6691 DRSP and 332 women with 2487 DSG treatment cycles.

Results

Overall, 82 (9.6%) women in the DRSP group and 44 (13.3%) women in the DSG group experienced treatment-emergent adverse events (TEAEs) leading to premature termination of the trial meaning that 32% more women in the DRSP group finished the trial in comparison to the desogestrel group (based on the AUC of Kaplan Mayer Curves). Discontinuation rates due to abnormal bleeding were 3.7% for DRSP and 7.3% for DSG users. This is a 55,7% lower discontinuation rate in the DRSP group compared to the DSG group.

Conclusions

This report describes the improvement in acceptability and bleeding profile of women using the new DRSP-only oral contraceptive compared to DSG, providing a better quality of life and adherence to the contraceptive method as demonstrated by lower discontinuation rates of women using the estrogen-free DRSP-only pill.

EudraCT: 2011-002396-42.



(OP04) Contraception

Impact of the Coronavirus disease 2019 (COVID-19) pandemic on contraception use in 2020 and up to April 2021 in France

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Context

In 2020 and 2021, French authorities decided to impose restrictions such as lockdowns and curfews to limit COVID-19's spread. This may have had consequences on access to family planning services and on the use of contraceptives.

Objective

We aimed to assess the impact of COVID-19 pandemic from March 16th 2020 to April 30th 2021 in France on oral contraception, emergency contraception, levonorgestrel-intrauterine system (LNG-IUS), copper-intrauterine device (C-IUD) and contraceptive implant dispensations.

Methods

We conducted the first national register-based cross-sectional study on contraceptives use during COVID-19 pandemic. We analyzed data from 67 million French people in the National Health Insurance database (SNDS). This database provides anonymous detailed information on health insurance claims for 99% of the population living in France.

Main outcome measures

We examined all contraceptive dispensations in the SNDS in 2018, 2019, 2020 and 2021. We then calculated the expected use of contraceptives in 2020 and 2021 without the pandemic based on 2018 and 2019 usage, taking into account holidays and the annual trend. We assessed evolution of dispensations between observed and expected dispensations, by type of contraceptive and by class of ages (≤ 25 years old, $25 < \text{age} \leq 35$, > 35).

Results

A decrease of all contraceptive dispensations had been estimated during the pandemic period comparing to expectations: -2.0% for oral contraception (the less impacted contraceptive), -5.0% for emergency contraception, -9.5% for LNG-IUS, -8.6% for C-IUD, 16.4% for implant on the overall period (the most impacted). However, an increase of oral contraception dispensations had been observed during the first weeks of lockdowns. Last, dispensations concerning women younger than 25 years old were the most affected by the decrease.

Conclusions

We showed that dispensations of contraceptives in France had been deeply impacted by restrictions implemented to limit the COVID-19 pandemic, with different levels of decreases depending on the type of contraceptive and ages. Continued contraception monitoring in 2021 is essential to assess the impact of pandemic on the reproductive and sexual health in France.



(OP04) Contraception

Use of Intra-Uterine Devices in France in 2019 and 1 year after: a national register-based observational study

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Context

According to a national survey in 2016, 25.6% of French women taking medical contraception use an intra-uterine device. But utilization of Copper-Intrauterine devices (C-IUD) and Levonorgestrel-Intrauterine Systems (LNG-IUS) has never been studied separately and in real-life conditions on a nationwide cohort. Moreover, LNG-IUS is recommended in France as a second intention contraception and for specific gynecological history, but little is known about prescriber's compliance to this recommendation and about prescribing practices of LNG-IUS different dosages.

Objective

We aimed to describe the sociodemographic characteristics of C-IUD and LNG-IUS users and prescribers, to assess the association between the choice of type of intra-uterine contraceptive in 2019 and users' characteristics and the determinants of utilization of devices one year after.

Methods

We conducted a national register-based study using data from the French National Health Insurance database (SNDS). This database provides anonymous detailed information on health insurance claims for 99% of the population living in France.

Patients

We included all French women aged 13-49 years old who got an intra-uterine contraceptive dispensation in 2019.

Main outcome measures

We collected information about sociodemographic characteristics and medical and gynecological history of women at the time of the device dispensation, and indicators of utilization one year after.

Results

A total of 477,705 C-IUDs (user's mean age: 32.5 years) and 355,242 LNG-IUS (mean age: 36.4) had been dispensed in 2019. Having a LNG-IUS dispensation rather than a C-IUD dispensation is associated with older ages ($OR_{\geq 45} = 3.69$ [3.62-3.76]), a gynecologist's prescription ($OR = 1.10$ [1.08-1.11]), living in an area with the most deprived social index ($OR = 1.29$ [1.27-1.31]) and having a gynecological history (endometriosis, heavy menstrual bleeding, myoma/polyp) ($OR = 2.34$ [2.26-2.42]). The 1-year continuation rate of LNG-IUS and C-IUD was respectively 85.7% and 86.4%. C-IUD dispensation was associated with a higher chance of being still a device user one year after.

Conclusions

A high prevalence of intrauterine devices dispensations with high estimated continuation rates has been assessed in 2019. The choice of having a LNG-IUS or a C-IUD dispensation seems to correspond to two different patterns of French women. The LNG-IUS is likely to be prescribed according to French professional recommendations.



(OP04) Contraception

Contraceptive efficacy, safety and acceptability of a benzalkonium chloride spermicide in women aged 40 and over: a prospective international, open-label, multicentre study

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Context

Contraceptive needs change as women get older and methods that were not ideal at younger ages can become suitable. Barrier methods like spermicides may thus be adequate for women aged 40 and over seeking alternative to pills and devices or having infrequent sexual intercourses. However, to date, no spermicide has been evaluated for efficacy specifically in late reproductive age women.

Objective

Our study aimed to assess a benzalkonium chloride spermicide in women aged ≥ 40 .

Methods

A Phase IV, open-label, single-arm study was conducted in 7 private gynaecologist-obstetricians in France and 6 obstetrics and gynaecology clinics in Russia. The benzalkonium chloride spermicide tested was in the form of a cream (Pharmatex®).

Patients

All participants enrolled had to be fertile and sexually active women aged 40 and over and were instructed to systematically use the spermicide before each intercourse.

Intervention

After eligibility assessment, study visits took place at 2 and 6 months. At the end of the 6-month period, participants were given the option to continue to use the spermicide for further 6 months. A final visit was planned for these women at 12 months.

Main outcome measures

The primary endpoint was the contraceptive efficacy over up to 12 months of typical use (Pearl Index - PI). Main secondary endpoints were the PI over up to 6 months of typical use, 6 and 12 months of perfect use. Other key secondary endpoints were investigator's and woman's global treatment satisfaction, acceptability and safety outcomes.

Results

151 women (mean age: 45.9 years) were enrolled. The median monthly number of intercourses during the first 6 months ranged between 3 to 5. The spermicide was applied before 96.3% of the 5,895 intercourses. The typical-use PI over up to 12 months was 0 (no unintended pregnancy) in the full analysis set population ($n=151$, 1249.7 women-months at risk). The upper 95% confidence interval limit (2.88) was well below the hypothesis value of 22, corresponding to the accepted PI value for spermicides in France in the general population. More than 99% of satisfaction ratings were at least good, and 96.1% of women found the lubricating effect appropriate. No serious treatment-related adverse event was reported.

Conclusions

If these results are confirmed, benzalkonium chloride spermicide could be an effective, safe and well-accepted non-hormonal alternative in women ≥ 40 years seeking an 'on-demand' contraception.



(OP05) Adolescence, PCO, ethics

The role of the FMR-1 gene and the FMR-1 protein in the genesis of oligomenorrhea in adolescents

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Context

The search for new molecular biological markers for disease prediction long before it develops is currently relevant.

Objective

The purpose of the study is to improve the differential diagnosis of oligomenorrhea in adolescents based on the investigation of molecular genetic markers as predictive factors of ovarian dysfunction.

Methods

One of the objects of the study was the fragile X mental retardation-1 (FMR1) gene on the X chromosome and protein FMR1 (FMR1P). The determination of allele variants of FMR1 genes was carried out by PCR. In addition to the studies included in the standard of patient management with oligomenorrhea, the ELISA method defined the serum content of anti-ovarian antibodies, AMH, Inhibin-B.

Patient(s)

The study included 80 adolescent girls diagnosed primary and secondary oligomenorrhea.

Main outcome measure(s)

In retrospect, patients with oligomenorrhea were divided into 3 groups depending on the various heterozygous subgenotypes of the FMR1 gene: I group – heterozygous individuals with «het-norm / low» subgenotype - the number of CGG repeats of one allele within the normal range (26-34), and in the second allele - less than the lower limit of the norm (26); II group - heterozygous individuals with het-norm / high, whose number of CGG repeats of one allele - within the normal range, and in the second allele - exceeds the upper limit of standards (34); III group - unaffected individuals, the FMR1 gene contains 29 or 30 repeats of the sequence CGG.

Results and Conclusion

Based on the results of our study, we have identified the clinical heterogeneity of the cohort of patients with oligomenorrhea, caused by various heterozygous subgenotypes of the FMR1 gene, formulated the clinical-laboratory characteristic of each subgenotype and developed a personalized algorithm for examination and therapy of adolescents with oligomenorrhea.

1. Heterozygous low - characterized by an increased titer of autoantibodies to TPO and ovarian antigens, increased production of AMH, FMR1P, hyperandrogenism and small cystic ovarian transformation and can be considered as an autoimmune phenotype of polycystic ovary syndrome. The incidence according to our study was 25%;
2. Heterozygous high - characterized by an decreased level of FMR1P, inhibin B, AMH relative to age-related standards, with moderately elevated gonadotropins, which can be considered as the initial signs of POI. The incidence was 13.75%.



(OP05) Adolescence, PCO, ethics

Persistent amenorrhea in patients with anorexia nervosa after weight restoration - what is to be done?

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Context

Amenorrhea is a persistent feature of Anorexia Nervosa (AN). So far not identified prognostic criteria recovery menstrual cycle after weight gain.

Objectives

To develop a method of forecasting of menstrual cycle restoration at patients at a stage of AN reduction.

Patients and methods

Serum levels of leptin (L), BMI and L/BMI ratio were investigated in 20 healthy adolescents girls (control group) and in 89 AN diagnosed patients (I group) at the first visit, in 3 and 6 months. I group was divided on 2 subgroups depending on a disease outcome:

- A. 42 patients with persistent amenorrhea;
- B. 47 patients with restored menstrual cycle.

Results

Through 3 months from the beginning of treatment L levels in B group exceeded the similar indicator A group in 3,5 times and exceeded the basic levels in 6.3 times. No one of the research periods of L values and L/BMI ratio of A group did not come nearer to indicators of control group and were below values B group. Absence of the dynamics of leptin/BMI ratio within 3 months from a starting of treatment, despite BMI increase, can be used as a criterion of the adverse forecast of menstrual cycle restoration.

On the basis of a comparative analysis of the L levels in two subgroups through 3 months from the treatment beginning, using ROC analysis we estimate diagnostic Cut-off of L and L/BMI ratio for predicting the future course of the disease.

Conclusion

At proceeding amenorrhea and presence of the criteria defining the adverse forecast of menstrual function restoration, in 3 months from a starting of treatment at achievement by the patient of the set weight, necessity of replacement hormone therapy is proved.

With a positive forecast recovery of menstrual cycle in sexually active patients should be prescribed low-dose monophasic combined oral contraceptives (COC). Given the presence of folate deficiency in AN, shows the assignment of COCs with folic acid - Yaz Plus®. This medication may also be used to improve folate levels for women who choose to use birth control pills. Yaz Plus® (drospirenone + ethinylestradiol + calcii levomefolate) is also indicated for the treatment of symptoms of premenstrual dysphoric disorder (PMDD).



(OP05) Adolescence, PCO, ethics

Toward a sustainable humankind

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Objective

The size of the human population and its perpetual growth exacerbates a variety of environmental, healthcare, political, economic and social problems, from climate change, biodiversity loss, and environmental degradation to water scarcity, pandemic emergence, forced migration and widespread conflict. It is also a major obstacle to achieving the Sustainable Development Goals like (1) No poverty, (2) Zero hunger, (3) Good health and well-being. Bringing human population to sustainable numbers is a must in order to achieve sustainable development that supports humanity's continued existence on this planet.

Methods

This presentation is based on data from the United Nations (World Population Prospects), Population Reference Bureau (World Population Data Sheet), Alliance of World Scientists (World Scientists' Warning to Humanity) and other scientific literature on sustainable development and the environment.

Results

Human population increases by over 80 million people a year. This growth could be reduced, stopped and ultimately reversed by (1) greater focus and investments into family planning methods and services, i.e., achieving full availability of contraception to all women and couples wishing for it, (2) promotion of reproductive ethics on principle to small families worldwide (a maximum of two children per family, i.e., replacement level, and ideally less), (3) advocacy on delaying a woman's first child until her thirties (lengthening generations) as an effective measure against population momentum, and finally (4) providing optimal environmental education for both decision-makers and the public on how unsustainable human population risks humanity's future—and all planetary life.

Conclusions

Sustainable development is achievable but requires a sustainable human population. Healthcare providers in the field of gynaecology and obstetrics can lend strong support by embracing the aforementioned four tasks based on voluntary, never-coercive pro-family planning principles.



(OP05) Adolescence, PCO, ethics

One-child ethics as the only solution to our overpopulation crisis

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Objective

Since 1950, humanity has witnessed rapid population growth. This population expansion is the “up-stream” driver of numerous existential threats, from climate change, biodiversity loss, and environmental degradation to poverty, mass starvation, rampant disease, and widespread conflict.

Methods

This presentation is based on a critical analysis of the World Scientists’ Warning to Humanity and other scientific literature.

Results

If humanity wants to avoid these negative phenomena, population growth must be stopped and reversed. This presentation explores the hypothetical results of a voluntary, global agreement from 2020 that all families should have either two children or only one child, and compares them with current population projections, concluding that only universal one-child families could solve the problem. It further discusses the remarkable fact that a UN-projected fertility decrease, down from 2.4 in 2020 to below 2.0 by 2100, results in a steadily increasing population: 11.2 billion by 2100. This is because decreasing fertility is counterbalanced by a higher population base over time. Though a hypothetical decrease to two-child families would stop the global population from rising above 10 billion, it would take until 2480 to return to 2020-level population.

Conclusions

While it is not likely for even voluntary one-child ethics to be globally accepted or embraced in the foreseeable future, it should be widely circulated and promoted among gynecologists and other healthcare providers to emphasize that this is ultimately the only ethical solution to our population predicament.



(OP05) Adolescence, PCO, ethics

Characterisation of the lipid mediator profiles of PCOS patients

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Context

Polycystic Ovary Syndrome (PCOS) is an endocrinologic disorder that affects 5-15% of women in their reproductive age and is a frequent cause for infertility. Major symptoms include hyperandrogenism, ovulatory dysfunction, a characteristic multi-follicular morphology of the ovary, an elevated ratio of LH/FSH and often obesity and/or insulin resistance. PCOS also represents a state of chronic low-grade inflammation that is closely interlinked with the metabolic features.

Inflammatory processes consist of the acute inflammatory response and resolution processes, initiated concomitantly. "Classical" pro-inflammatory lipid mediators like prostaglandins (PG), leukotrienes (LT) or thromboxanes (TX) are derived from arachidonic acid (AA) and are crucial for the initial response. Resolution processes are driven by 4 families of so-called specialized pro-resolving mediators (SPMs): resolvins, maresins, lipoxins and protectins. SPM biosynthesis starts from the essential poly-unsaturated fatty acids DHA, DPA or EPA via certain hydroxylated intermediates.

Several chronic diseases have been attributed to insufficient resolution of inflammation and the benefit of SPM supplementation has been demonstrated. However, up to now there is no information on the role of SPMs in PCOS.

Objective

To establish lipid mediator profiles of PCOS patients compared to healthy women to identify differences in their resolutive and pro-inflammatory lipid parameters.

Methods

Blood samples were taken (20 ml) and analyzed by HPLC/MS-QQQ.

Patients

14 female patients (18-45 years) with a diagnosed PCOS according to Rotterdam criteria and 5 healthy women were recruited in one study centre in Germany.

Main outcome measure

Pro-inflammatory lipid mediators (PG, LT, TX) and their precursor AA; SPMs (Resolvins, Maresins, Protectins, Lipoxins), their precursors EPA, DHA, DPA and the metabolic intermediates (18-HEPE, 17-HDHA, 14-HDHA). Ratio [(sum of pro-inflammatory molecules)/sum of SPMs].

Results

The level of pro-inflammatory parameters in serum was significantly higher in PCOS patients. The ratio [(sum of pro-inflammatory molecules) / (sum of SPMs plus hydroxylated intermediates)] reflecting the inflammatory state was significantly lower in the group of healthy women.

Conclusion

There is a strong pro-inflammatory state in PCOS patients. Further research will clarify whether a supplementation with SPMs or their precursors may improve this state.



(OP05) Adolescence, PCO, ethics

Correlation between levels of homocysteine, anti-müllerian hormone and insulin resistance in PCOS patients with recurrent pregnancy loss

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Context

Correlation between levels of homocysteine, AMH and insulin resistance have become the main subject of interest nowadays in PCOS patients for predicting Recurrent Pregnancy Loss (RPL).

Objective

To determine the relationship between the levels of Homocysteine, AMH and insulin resistance in PCOS patients with recurrent pregnancy loss.

Methods and patients

80 Georgian young women (<30 years) with PCOS were involved in the prospective, open label study. The diagnosis of PCOS was based on the criteria of Rotterdam Consensus 2003. Patients were divided into two groups: Group I - 50 patients who experienced two or more spontaneous abortions during the first trimester (study group) and Group II - 30 patients with live births in anamnesis (control group). PCOS patients with RPL were divided into two subgroups based on HOMA-IR: subgroup A- patients with insulin resistance (n=28); subgroup B- patients without insulin resistance (n=22). All patients underwent hormonal and US investigation on day 2 to 3 of menstrual cycle. Data was analyzed using the statistical analysis programs SPSS 24.0 and Past 3.0.

Results

Average Hcy level ($11.5 \pm 2.24 \mu\text{mol/l}$), HOMA-IR and BMI in PCOS patients with RPL was significantly higher compared with PCOS patients and live births in anamnesis $p < 0.001$. Incidence of Hcy and IR in PCOS patients with RPL was 70% (n=35) and 56% (n=28) respectively, which was significantly higher when compared to the controls (HHcy-54.3%; IR- 9.4% $p < 0.001$). Average AMH level, LH, FSH, FT, T levels, AFC and Ov/V in PCOS patients with RPL with and without insulin resistance statistically did not differ significantly. In the group of PCOS with RPL statistically significant positive correlation between Hcy and HOMA-IR, BMI, AMH and FT levels was detected ($p < 0.001$).

Conclusions

Serum homocysteine level in PCOS patients with RPL was significantly higher than in PCOS patients with live births. Homocysteine level is correlated with the degree of obesity, BMI, insulin resistance status, AMH and androgen levels in PCOS patients with RPL.



(OP05) Adolescence, PCO, ethics

Obesity, PCOS and new therapeutic options

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Obesity and overweight is associated with multiple chronic, comorbid conditions; in addition, when fat is mainly accumulated in the abdominal belly, these co-morbidities seem to worsen.

Besides the well known metabolic consequences, several gynaecological abnormalities are described, many of them leading to female sub- or infertility. Polycystic Ovary Syndrome (PCOS) often occurs in the presence of fat excess and is metabolically characterized by visceral fat accumulation, insulin resistance and glucose intolerance and dyslipidemia.

PCOS pathophysiology is complex and remains largely unclear: besides a genetic predisposition, PCOS is characterized by a hormonal imbalance (increased androgens, ovarian dysfunction) and hypothalamic pituitary abnormalities.

According to recent analyses, obesity occurs in 60-80% of individuals with PCOS.

Management of PCOS starts with lifestyle intervention as first-line treatment for PCOS, in order to improve the metabolic dysfunction and normalize the hyperandrogenism.

Treatment options to improve fertility include ovulation induction agents, gonadotropins, laparoscopic ovarian surgery and bariatric surgery and anti-obesity medications. Not all of them are recognized as successful, some are 'off-label' in some countries and others are still considered an experimental therapy in women with PCOS for the purpose of improving fertility, with risk to benefit ratios currently too uncertain to advocate this as fertility therapy.

Weight loss improves clinical features and long-term metabolic health in women with PCOS: it lowers insulin levels and decreases insulin resistance, hormonal parameters, mainly androgens, are restored to normal, menstrual cyclicality, ovulation and fertility improved and risk factors for CVD and diabetes reduced. Androgen levels are reduced with weight loss in women with PCOS: testosterone and free androgen index reduced to near normal in 54% of women who achieved >5% weight loss in one of the studies reported.

Fertility outcomes (conception and live birth rate) is superior when weight loss reaches >10% of baseline weight. Also in women scheduled for IVF, cumulative live birth rates seem to benefit from weight loss among obese women.

Among the recent developed anti-obesity agents, glucagon like peptide- 1 receptor agonists (GLP-1 RA) seem to offer an interesting and challenging treatment option.

Cycle event rate was reported to perform better with SC exenatide, certainly in combination with metformin. Liraglutide, another GLP-1 RA, increases satiety and reduces hunger via neurons in the nucleus arcuatus: besides promising metabolic improvements, in PCOS liraglutide has effects on body composition as well. In a randomized trial, liraglutide improves ovarian hormonal function in PCOS women; with a mean weight loss of 5.2 kg from baseline, liraglutide treatment was associated with improved bleeding ratio compared to placebo treated women, decrease in free testosterone and a trend towards lower ovarian volume. Preconception intervention with low-dose liraglutide (1.2 mg) added to metformin aided in increasing pregnancy rate (PR) per embryo transfer and cumulative PRs in infertile women with obesity and PCOS; in another pilot study, liraglutide increase IVF pregnancy rates in obese PCOS women with poor response to first-line reproductive treatments.

In a challenging field of PCOS, novel approaches with existing and new developed GLP-1 receptor agonist may help to improve the specific and more general burden of women with PCOS.



(OP05) Adolescence, PCO, ethics

Evidence of PCOS in adolescents with type 2 diabetes

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Background

The obesity-related type 2 diabetes (T2DM) in children and adolescents has reached an epidemic level globally. Pediatric obesity is also associated with metabolic syndrome, hypertension, dyslipidemia, nonalcoholic fatty liver disease (NAFLD) and in females, polycystic ovarian syndrome (PCOS).

The diagnostic criteria for adolescent polycystic ovary syndrome (PCOS) is challenging as criteria include normal physiological events that occur during puberty such as acne, hirsutism and menstrual irregularities.

Aim

The aim of this study is to evaluate the documentation of PCOS in female teenagers diagnosed with T2DM. The diagnosis of T2DM was made based on clinical presentation, insulin and C-peptide levels and lack of autoimmune markers of type 1 diabetes.

Method

A retrospective chart review of female teenagers diagnosed with T2DM in a three-year period was performed. Prepubertal females were excluded.

Age, race, body mass index (BMI), blood pressure, Hemoglobin A1c, documentation of dyslipidemia, elevated liver enzymes and PCOS (medical history/ review of systems, androgen levels, or pelvic ultrasound).

Results

Twenty-six patients were initially diagnosed in a three-year-period. Average age of diagnosis was 16 years and 3 months (range 9 to 18 years). Sixty one percent of patients were Hispanics, 30% were African-Americans/Blacks.

Average HbA1c at diagnosis was 9.8%. Thirty four percent of the patients had hypertension at diagnosis but only 15% of them remained hypertensive and required therapy.

Dyslipidemia and elevated liver enzymes were seen in 56% and 78% of patients, respectively.

Almost 69% of females had a history of irregular menses but only 5% of had elevated testosterone levels. One patient was referred to adolescent gynecology for persistent menstrual irregularities.

Discussion

It is well known that adult PCOS/hyperandrogenism may have roots in the pediatric and adolescence period. Obesity, metabolic syndrome and T2DM have complex cause- effect relation with PCOS.

PCOS and T2D are both obesity-related conditions that share insulin resistance as an important pathogenic factor. PCOS is a well known high-risk of development of T2DM. Early diagnosis, management of PCOS along with T2DM, and other comorbidities of obesity should be emphasized.

Conclusion

Documenting PCOS features in obese teenagers with T2DM should be emphasized. We have used this data to improve our screen for PCOS in our patient population



(OP05) Adolescence, PCO, ethics

A systematic review and meta-analysis on associations of ER α and ER β gene polymorphisms with polycystic ovary syndrome

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Objective

While estrogen receptor genes (ER α and ER β) polymorphisms were long-time considered contributing substantially to the development of the disease. Controversial results existed in amounts of studies investigating the authentic association of ER α /ER β polymorphisms with the occurrence and progression of PCOS. To find potential correlations between ER α /ER β polymorphisms and PCOS risk, we conducted the first systematic review and meta-analysis to comprehensively summarize current studies in a large combined population.

Method

Eligible studies were retrieved from PubMed, MEDLINE, EMBASE, Cochrane Library, CBM, CNKI, WANFANG and VIP up to February 28, 2021 irrespective of language. The quality of studies was assessed using the Newcastle-Ottawa Scale (NOS) scoring system. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated to synthesize data in five genetic models: allele model, dominant model, recessive model, heterozygote model, homozygote model. Subgroup analyses were conducted by ethnicity. Heterogeneity and publication bias were also assessed. Egger's test was used to assess the publication bias and sensitivity analysis was performed to determine the robustness of the results.

Results

A total of 8 moderate or high-quality studies involving 1522 PCOS patients and 4198 controls were included in the quantitative analysis. No evidence demonstrated the association of ER α rs2234693 (OR=1.07 - 95% CI: 0.98-1.18; OR=1.17 95% CI: 0.96-1.42; OR=1.06 - 95% CI: 0.90-1.26; OR=1.13 - 95% CI: 0.96-1.32; OR=1.23 - 95% CI: 0.88-1.72), ER α rs9340799 (OR=0.99 - 95% CI: 0.69-1.43; OR=0.99 - 95% CI: 0.60-1.62; OR=1.05 - 95% CI: 0.71-1.56; OR=0.96 - 95% CI: 0.60-1.53; OR=1.05 - 95% CI: 0.60-1.84), or ER β rs4986938 (OR=1.06 - 95% CI: 0.81-1.38; OR=1.10 - 95% CI: 0.77-1.57; OR=1.08 - 95% CI: 0.87-1.35; OR=1.07 - 95% CI: 0.75-1.53; OR=1.10 - 95% CI: 0.87-1.40) polymorphisms and PCOS risk in five genetic models respectively. Stratified subgroup analyses showed ethnicity was the major source of heterogeneity. No publication bias ($p=0.238$) was found in all studies.

Conclusions

The rs2234693 and rs9340799 polymorphisms in ER α gene as well as rs4936938 polymorphism in ER β gene were not likely to be associated with individual PCOS susceptibility, even if ethnicity was taken into account. Meanwhile, more studies with elaborated clinical data were strongly required to perform subgroup analysis based on phenotypes.



(OP05) Adolescence, PCO, ethics

Newborns of PCOS women have higher AMH levels: a systematic review and meta-analysis

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Objective

There was long-existed controversial human evidence investigating the exposure to maternal PCOS state and subsequent alteration of neonatal ovarian functions. To find authentic correlation between maternal PCOS and neonatal ovarian functions, we conducted the first systematic review and meta-analysis to eliminate heterogeneity and evaluate AMH levels in neonates born to PCOS mothers compared with healthy mothers.

Methods

A search of the literature was conducted in the PubMed, MEDLINE, EMBASE and Cochrane Library for studies assessing AMH levels in newborns of PCOS and non-PCOS mothers. The quality of studies was assessed using the Newcastle-Ottawa Scale (NOS) scoring system. Standardized mean differences (SMDs) with 95% confidence intervals (CIs) were adopted to calculate the overall estimates with random-effects models. Subgroup analyses were performed to investigate the potential source of inconsistencies. Funnel plots and Egger's test were also used to assess the publication bias. Sensitivity analysis was performed to determine the robustness of the results.

Results

6 high-quality studies involving 846 participants were included. The pooled analysis found an increased AMH level in the umbilical cord blood of newborns at labor of PCOS mothers (SMD =0.62, 95% CI [0.28, 0.95]). Subgroup analyses revealed an elevation of AMH concentrations in female neonates (SMD=0.64, 95%CI=[0.14, 1.14]), neonates born to American and Asian PCOS mothers (SMD=0.81, 95%CI=[0.47, 1.16]; SMD=1.12, 95%CI=[0.79, 1.46], respectively). In addition, higher AMH levels were also found in studies diagnosed by the National Institute of Health (NIH) criteria (SMD=0.97; 95%CI=[0.74, 1.21]), maternal clinical/biochemical hyperandrogenism (SMD=0.66; 95%CI=[0.21, 1.11]), or maternal body mass index (BMI) >30 kg/m² (SMD=0.78; 95%CI=[0.39, 1.17]). Meta-regression analysis suggested that diagnostic criterion contributed mostly to the high heterogeneity (p<0.01). There was no publication bias and our results remained robust after sensitivity analysis.

Conclusion

In summary, the positive findings of this study suggested that AMH levels in neonates born to PCOS mothers were noticeably higher than those in neonates born to healthy controls. The conclusion we draw from the meta-analysis may bring favorable repercussions to female reproductive health and propel the study of pathogenesis and etiology of PCOS.



(OP06) Fertility

Endometrial expression of estrogen and progesterone receptors in women with different thickness of the endometrium

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Context

The receptivity of “thin” endometrium has not been sufficiently studied.

Objective

To study the endometrial expression of estrogen (ER) and progesterone (PR) receptors in women with different thickness of the endometrium.

Methods

Following methods were used: immunohistochemical (H-score ER, PR in the endometrium); chemiluminescent (estradiol (E2), progesterone (P) levels in peripheral blood.

Patients

There were main (I: 37 women with “thin” (<7 mm) endometrium), comparison (II: 58 patients with the endometrium ≥ 7 mm) (I, II: women with miscarriage, infertility in the anamnesis), control (III: 16 healthy women) groups (20-40 y.o.).

Interventions

On 6-8th day after ovulation we performed vacuum-aspiration endometrial biopsy, obtained peripheral blood.

Main outcome measures

H-score ER, PR expression (range 0-300) in endometrium samples.

Results

All women had ovulatory cycle ($P \geq 16,1$ nmol/l); normoestrogenemia (E2, pmol/l): 635.5 ± 40.2 (I) vs 752.4 ± 43.8 (II) vs 707.4 ± 66.1 (III) ($p > 0.05$).

In I and II groups respectively in 22% (Ia: n=8) and 45% (IIa: n=26) of women H-score count of endometrial ER, PR was found similar to healthy women (III) ($p > 0.05$ for all compared ER/PR indicators): in the glands – ER 91.2 ± 17.1 (Ia) vs 118.1 ± 6.4 (IIa) vs 113.7 ± 8.3 (III), PR 31.2 ± 16.5 (Ia) vs 25.7 ± 6.1 (IIa) vs 28.1 ± 2.4 (III); in the stroma – ER 118.7 ± 21.7 (Ia) vs 107.3 ± 8.6 (IIa) vs 80.6 ± 8.7 (III), PR – 243.7 ± 22.4 (Ia) vs 265.4 ± 8.6 (IIa) vs 285.1 ± 1.8 (III). 78% (n=29) (Ib) of women with “thin” endometrium in I group and 55% (n=32) (IIb) of women with normal endometrial thickness in II group had inadequate hormone-receptor endometrial status with significant differences ($p < 0.05$) in all indicators of ER/PR H-score in endometrial glands and stroma from those of healthy women (III), but without corresponding differences between subgroups Ib and IIb ($p > 0.05$) regardless of the thickness of the endometrium: in the glands – ER 203.8 ± 13.9 (Ib) vs 225.0 ± 11.7 (IIb), PR 234.5 ± 14.9 (Ib) vs 242.8 ± 13.3 (IIb); in the stroma – ER 162.4 ± 14.5 (Ib) vs 177.5 ± 14.1 (IIb), PR 268.6 ± 4.8 (Ib) vs 275.0 ± 4.5 (IIb).

Conclusions

In women with endometrium <7 mm normal hormone-receptor endometrial status was noted 2 times less often in women with a history of reproductive dysfunctions of unclear reason, compared with women with normal endometrial thickness; at the same time, the “thin” endometrium is not an absolute predictor of disorders of the hormone-receptor response in the endometrium.



(OP06) Fertility

Evaluating the efficacy of ovulation stimulation with Intrauterine Insemination (IUI) in women with diminished ovarian reserve compared to women with normal ovarian reserve

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Objective

This study aims to assess the efficacy of ovulation induction and intrauterine insemination in couples with diminished ovarian reserve.

Methods

We evaluated patients who were treated with ovarian stimulation and intrauterine insemination at a university-based infertility clinic between January 2012 and January 2018. Inclusion criteria were menstruating women aged 20-39 years and male age below 50 years. Study group included 153 cycles of 75 women with decreased ovarian reserve and 617 cycles of 287 women with normal ovarian reserve as controls. Four “ovarian reserve groups” were created according to AMH and female partner’s age. Group I involved women whose AMH levels equal or greater than 1.2 ng/ml and younger than 35 years, group II involved women whose AMH levels equal or greater than 1.2 ng/ml but older than 35 years. Group III involved women whose AMH levels are lower than 1.2 ng/ml and younger than 35 years, group IV involved women whose AMH levels lower than 1.2 ng/ml and age more than 35 years. The finding of a gestational sac on ultrasound was the primary outcome measure.

Results

The rate of pregnancy was similar in four ovarian reserve groups in terms of first, second, third plus fourth and total attempts of IUI cycles. Moreover, pregnancy rate, miscarriage rate and multiple pregnancy rate were similar in women with diminished ovarian reserve (groups III and IV) compared to women with normal ovarian reserve (groups I and II) and in women younger than 35 years (groups I and III) compared to women older than 35 years (groups III and IV). We have found no difference in terms of cumulative pregnancy rate among groups after four IUI cycles. Multivariate logistic regression analysis in entire cohort has revealed that infertility duration, postwash sperm count and follicle number greater than 11 mm on the day of hCG trigger were independent predictors of pregnancy ($p < 0.001$). Neither age nor AMH have predicted pregnancy after ovulation stimulation and IUI.

Conclusions

Ovulation stimulation and intrauterine insemination are equally effective in women with diminished ovarian reserve and in women with normal ovarian reserve in terms of pregnancy rate, multiple pregnancy rate and miscarriage rate per IUI cycle or cumulative pregnancy rate after 4 cycles of IUI.



(OP06) Fertility

Should endometrial polyps always be surgically managed? A retrospective study of 11 years in a tertiary hospital

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Introduction

The diagnosis of endometrial polyps is very frequent, being one of the most common diagnosis in gynecology.

The popularization of hysteroscopy has led to an increase in the number of diagnosed cases in the past years. The estimated prevalence of endometrial polyps ranges between 20 to 30% of the population, with an association with endometrial carcinoma between 0 to 4.8%.

Since it is a very frequent diagnosis, many times with no associated symptoms, there is no accepted guideline for the treatment for polyps, balancing between expectant management, clinical treatment or surgical removal.

Objetives

The goal of this study is to evaluate the malignant potential of the endometrial polyps, through an analysis of the cases of women submitted to polypectomy through histeroscopy in our service, during a period of 11 years.

Methods

Retrospective study of the clinical files of the women submitted to polypectomy through hysteroscopy, in Hospital Espírito Santo de Évora, between January 2008 and December 2019.

Results

Between January 2008 and December 2019, 1676 women were submitted to polypectomy through hysteroscopy. The histologic result of the extracted pieces was positive for malignancy in 2.3% of the cases, and revealed atypical hyperplasia in 0,9%.

Conclusion

Considering there is a low association between endometrial polyps and malignancy (2.3%), the treatment should be personalized, according to factors such as the presence of symptoms, age, personal and family history, taking into account the desire and consent of the patient.



(OP06) Fertility

Insulation of *Candida* spp. of the vaginal secretion in fertile age woman

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Context

Vulvovaginal candidiasis is a disease that affects about 75% of women throughout their lives. The indiscriminate use of antibiotics is associated with changes in the vaginal microbiome, leading to recurrent vulvovaginal candidiasis. In this context, it is necessary to search for new alternatives in the treatment of vaginal infections for its recolonization, such as probiotics. However, it's pivotal to comprehend the woman's vaginal microbiota and identify possible changes that may occur during fertile age.

Objective

This paperwork objective is to handle the isolation and observe the characterization of *Candida* spp., in women of fertile age, associating evidence and data, such as age and presence of lactobacilli in the vaginal microbiota.

Methods/Patients

Lactobacilli and *Candida* spp., were isolated from a sample of vaginal content from asymptomatic and symptomatic women, aged 18 to 55 years, during their routine consultations in a private gynaecological office in Brazil, in the period of February 5, 2021 to August 2, 2021. The sociodemographic data and all clinical information were collected during the patient's anamnesis clinical information. The study was approved by the Research Ethics Committee (CAAE- protocol number: 39638620.8000.5515).

Main outcome measures/Results

250 women were selected to participate in the research, in which 153 did not filled the necessary criteria to continue the study, due age, antibiotics, and probiotics usage, chemotherapy, or being in menopause. Therefore, the collected data of 97 patients were used. The age range of the patients was the following: 52.8% were between 18 and 28 years old, 40.2% were between 29 and 40 years old, and only 7.2% were between 41 and 55 years old.

The following were isolated from patient samples: 44 (45.4%) lactobacilli, 27 (27.8%) *Candida albicans*, 1 (1.03%) *Candida Krusei*, 1 (1.03%) *Candida Tropicallis* and 2 (2, 06%) patients colonized with *Candida albicans* and *Candida Tropicallis*.

Conclusions

The research concluded the observation study of *Candida* spp. and Lactobacilli isolation and characterization are important in the development of promising alternatives for biotechnological application, and in the new therapies for the vaginal microbiome reconstitution.



(OP06) Fertility

Improving the probability of successful *in-vitro* fertilisation through vaginal microbiome screening using Advanced Technique for Genetic Composition

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The relationship between the vaginal microbiome and the probability of a successful *in-vitro* fertilisation (IVF) have been well documented in the past few years. As the knowledge grows, the limits of untargeted analysis such as 16S-sequencing (16S) and Whole Genome Sequencing (WGS) is being reached. In order to deploy practical, reproducible and reliable vaginal microbiome analysis that can be included in the practice of reproductive medicine, new targeted analysis are needed.

We propose to use Advanced Testing for Genetic Composition (ATGC) to measure the vaginal microbiome in routine IVF. The goal of our analysis and study is to develop a model of diagnostic test that could establish a link between some pathogens in the vaginal microbiome and the success rates of IVF.

ATGC technology consists in cycling temperature capillary electrophoresis (CTCE) combined with bioinformatics and statistical modelling used to separate DNA molecules based on their physical properties. This technology linked to an specific target analysis will allow us to save time, money and reducing the risks associated with the biopsy currently used.

For this project, we use our maps of bacteria to establish our target analysis, develop our assay and implement it on our tests. A hundred vaginal samples selected from patients undergoing IVF already collected in the Centre Hospitalier Universitaire Vaudois (CHUV). We present the results of a benchmarking analysis against 16S (40 patient samples), and rtPCR (20 patient samples) panel analysis. As an intervention it would help developing specific treatments for woman under IVF. Using ATGC technology to analyse the microbiome of vaginal samples is a power tool to predict good results on reproductive treatments. It has been one of the unique technologies that showed better results in the latest studies in vaginal infections and with high level of accuracy to screen samples and predict reproductive outcomes. Because of those characteristics already demonstrated, those results are often associated with qualitative and quantitative measurements that allow us to better understand not only the presence of some microbes but also the relation between those based on the level of each one in that specific sample.

The model and latest results with ATGC analysis has demonstrated that it is possible to use this type of model and apply it to a complex map of bacteria to produce a usable treatment for the future field work of Reproductive Medicine.



(OP06) Fertility

Endometrial scratch injury before intrauterine insemination. Systematic review and meta-analysis

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Context

Endometrial scratch injury is a technique that induces an endometrial trauma with a Pipelle biopsy or a curette in order to induce an acute inflammatory process that releases growth factors and proinflammatory cytokines to improve implantation in women undergoing treatment with assisted reproduction technology.

Objective

To assess the impact of endometrial scratch injury on the outcomes of intrauterine insemination stimulated cycles.

Methods

A systematic literature search was conducted on the electronic databases PubMed and Web of Science with no date or language restriction. The key search terms included endometrial injury OR endometrial scratching AND intrauterine insemination OR fertility. Only randomized controlled trials were included.

Patients

Patients undergoing intrauterine stimulated cycles with gonadotropins.

Intervention

Endometrial injury during the course of intrauterine stimulated cycle or during the menstrual cycle preceding.

Main outcome measure

Clinical pregnancy rate.

Results

5 randomized controlled trials were included with a total of 913 patients. Endometrial scratch injury was associated with a higher clinical pregnancy rate (OR 2.3) with a p-value < 0.1.

Conclusions

Endometrial injury during the follicular phase or during the menstrual cycle preceding a intrauterine insemination improves clinical pregnancy rates.



(OP06) Fertility

Perspectives of young women with gynaecologic cancers on fertility and fertility preservation: a systematic review and metasynthesis

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Context

Standard treatment of gynaecologic cancers often requires the removal of some reproductive organs, making fertility preservation a complex challenge. Despite heightened oncofertility awareness, knowledge about fertility attitudes and decisions of young women with gynaecologic cancer is scarce.

Objective

This systematic review focused on knowledge, attitudes and decisions related to fertility, fertility preservation and parenthood among young women with gynaecologic cancers.

Methods

Peer-reviewed journals published in English were searched in PubMed, Web of Science and EMBASE from 1 January 2000 to 1 July 2020, using combinations of the phrases or keywords: “gynecologic cancer OR gynecologic neoplasm OR cervical cancer OR ovarian cancer OR endometrial cancer” AND “fertility OR reproductive issues OR childbearing OR pregnancy OR fertility preservation” AND “QOL OR attitudes OR decision OR decision making OR perspectives”. The inclusion criteria were studies with young adult patients of childbearing age, conducted exclusively with gynaecologic cancer patients or using a heterogeneous sample of different cancer diagnosis but with results presented for each cancer type. Also included was primary research reporting on childbearing, fertility, fertility preservation, pregnancy and parenthood attitudes/decisions after gynaecologic cancer from the woman’s perspective, as well as research on decisional conflict and regret regarding fertility decisions. Four authors (VG, MS, CT, GQ) extracted data into a template containing information for each study (study origin, aims, inclusion criteria, sample, study design, relevant measures/data collection and relevant findings) and evaluated the quality of each article using the Mixed Methods Appraisal Tool (MMAT) included in the review.

Results

Of the 1106 publications identified, 11 met the inclusion criteria, in addition to 2 publications retrieved manually. A total of 13 studies comprised the review. These studies showed that fertility and parenthood were important matters in patients’ lives. The majority of women valued fertility preservation procedures that could be perceived as a means to restore fertility. Additionally, a unique feature identified was that fertility preservation was seen also as a way to restore the femininity that women perceived to be lost or threatened during cancer treatment. Fertility counselling was found to be sub-optimal, with wide variability in rates of fertility counselling. Also, comparisons between gynaecologic cancers and other cancer types about fertility counselling rates were also inconclusive. This review also documents the potential negative impact of impaired fertility on patients’ mental health and QOL.

Conclusions

Multidisciplinary oncofertility programs that provide optimal fertility counselling should be included routinely in gynaecologic cancer care. Timely identification of patients at risk for mental distress and provision of psychosocial interventions are essential to reduce the likelihood of long-term distress. Large and robust multicentre studies that overcome methodological flaws in existing research, and also provide new insights regarding gynaecologic cancer patients’ attitudes and decision-making on fertility, fertility preservation options and alternative family building while taking into consideration cultural variables, are much needed.



(OP06) Fertility

How to detect bilateral tubal occlusion by hysteroscopic fluid shifts in the pouch of Douglas: a prospective cohort study

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Context

Hysteroscopy, as the gold standard for the evaluation of the uterine cavity, can be performed in in- and outpatient settings. The gold standard for tubal evaluation is the laparoscopic access with chromopertubation and requires general anesthesia. There have already been methods described in the literature how tubal patency can also be assessed by hysteroscopy. These include a technique using sonography to detect post-hysteroscopy shifts of fluid in the pouch of Douglas.

Purpose

This study was conducted to find out whether an increase in fluid in the pouch of Douglas after hysteroscopy would be reflective of tubal patency.

Methods

Prospective cohort study.

Patients

115 subfertile women undergoing laparoscopic and hysteroscopic surgery at the Medical University of Vienna were included into the study.

Interventions

A vaginal sonography was performed before and after the hysteroscopy to measure the amount of fluid in the pouch of Douglas. Subsequently, a laparoscopy with chromopertubation was performed.

Main outcome measures

Fluid in the pouch of Douglas and chromopertubation results.

Results

The laparoscopic chromopertubation showed bilateral tubal occlusion in 24.3% of women (28 women). 67.5% of patients (28/40 patients) with no fluid shift revealed bilateral tubal occlusion during laparoscopic chromopertubation ($p < 0.001$). 1.3% of patients (1/75 patients) who had a fluid shift also showed a bilateral tubal occlusion in laparoscopy (sensitivity of a present fluid shift for uni- or bilateral patency 85.1%, 95% CI: 81.7-99.9, specificity: 96.4%, 95% CI: 75.8-91.8). The risk for a false abnormal result (i.e. tubal patency despite the lack of a fluid shift) was increased by intracavitary abnormalities (odds ratio, OR, 0.038; $p = 0.030$) and adhesions covering at least one tube (OR 0.076; $p = 0.041$).

Conclusions

This method is a sensitive test for tubal occlusion when the fluid in the pouch of Douglas does not change after the hysteroscopy. If an increase in the fluid in the pouch of Douglas can be detected after conducting the hysteroscopy, particularly for patients with no fluid present prior to the hysteroscopy, this method is sensitive and specific for uni- or bilateral tubal patency.



(OP06) Fertility

Lack of total concordance in aneuploidy rates between fresh trophoctoderm samples and non-invasive screening in vitrified blastocysts

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Context

Thirty years after the first implementation of preimplantation genetic testing (PGT) for aneuploidy (PGT-A), there is still concern about the impact of the trophoctoderm (TE) biopsy on the embryo health. Two decades later, scientists are trying to find non-invasive approaches to obtain embryo DNA e.g. using the blastocoel fluid (BF) from the expanded blastocyst.

Objective

The aim was to evaluate whether the cell-free DNA (cfDNA) from vitrified blastocysts, previously biopsied, can serve as a confirmation of the results from classical PGT for aneuploidy screening (PGT-AS).

Methods

Total 56 embryos from 31 couples were donated for the analysis. The blastocysts were biopsied on day five and trophoctodermal (TE) samples were obtained for PGT-AS. All embryos were vitrified for the purpose of the testing. Only those embryos, which have been diagnosed as abnormal and/or chaotic were included in this study. A detailed patient consent form was signed from each couple. Four hours post warming and re-expanding, the blastocysts were collapsed by laser pulses in Calcium and Magnesium free medium. The blastocoel fluid (BF) expelled in the medium was given for chromosome retesting by WGA followed by next generation sequencing (NGS).

Main outcome measure(s)

In the current investigation, the success rate of cfDNA amplification of BF from vitrified blastocyst was 100% and this approach has a confirmative value of the results of classical PGT-AS and could also serve as a non-invasive method for aneuploidy detection in already vitrified preimplantation embryos.

Result(s)

Total concordance in aneuploidy detection between fresh TE and post-warmed BF was found in 50% (28 out of 56), partial concordance 32.2% (18 out of 56) and total lack of concordance in 10 of the analyzed samples (17.8%). All results confirmed previously given diagnosis of chromosomally abnormal status of embryos.

Conclusions

Despite the lack of total concordance in aneuploidy rates between fresh TE samples and cfDNA from BF of post warmed vitrified blastocysts, this approach could be used as a confirmation of the results of classical PGT-AS and also could serve as a non-invasive method for aneuploidy detection in already vitrified preimplantation embryos.



(OP06) Fertility

Fertility preservation decision making and treatment outcomes among transgender men

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Context

Patients undergoing gender reassignment therapies face high risk of infertility, due to effects of testosterone in suppressing ovulation and alter ovarian histology. The effects of hormonal therapy may be reversible, although its degree is unclear. Surgical procedures within gender reassignment procedures, such as hysterectomy and oophorectomy, will result in permanent infertility. To allow for biological parenting, transgender men should be offered the possibility to undergo fertility preservation (FP) to preserve their oocytes.

Objective

This study assesses motivations for undergoing FP and FP outcomes in a sample of transgender men referred for FP counseling in the Fertility Preservation Centre (FPC) of Coimbra Hospital and University Centre (CHUC).

Methods

Since 2018, 51 transgender men were referred for FP counselling in the FPC of Reproductive Medicine Unit at the CHUC. Motives for deciding for or declining FP were assessed. Results of FP procedures were examined.

Patient(s)

Patients are 51 transgender men counselled for fertility presentation. Of these, 11 (21.5%) undergone hormonal stimulation for oocyte collection and cryopreservation.

Intervention(s)

Fertility preservation counselling, Hormonal stimulation procedures and oocyte cryopreservation.

Main outcome measure(s)

Motives for FP, FP decision, Numbers of cryopreserved oocytes.

Result(s)

A total of 51 transgender men were referred for fertility preservation counselling. Of these, 25 (49%) had already started hormonal therapy. Of the total sample, 11 transgender men (21.5%) had already completed FP procedures. The main reasons for choosing to undergo FP were 1) the enhancement of genetic ties in parenting and 2) keeping this option open. The main reasons for not wanting to perform FP were 1) not valuing the biological ties in parenting; 2) fears related with the procedure; 3) not wanting to postpone gender reassignment procedures; and 4) envisioning difficulties in accomplishing parental roles using FP. Considering the 11 patients who completed the FP procedures, an average of 10 oocytes ($M=10.10$; $SD = 4.76$) were cryopreserved.

Conclusions

The discussion of FP options in transgender men is a key component in gender reassignment procedures and should be considered and discussed with patients as early as possible to enable informed and thoughtful decision making. Fertility preservation may contribute to allow for biological parenting in transgender men.



(OP06) Fertility

Hyaluronic acid during myomectomy and pregnancy rate in infertile women - double centric, non randomized, prospective clinical trial

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Objective

To determine the number of pregnancies reached in the first and the second year after laparoscopic or open myomectomy.

Study design

The doublecentric, not randomized, prospective clinical study cohort consisted of 358 women of reproductive age, desiring pregnancy, with symptomatic intramural uterine fibroids who underwent laparoscopic or open myomectomy with follow-up of 2.5 years after surgery. Early pregnancy and early pregnancy rate in the first year and the number of pregnancies in the second year after the procedure was evaluated - designated as late pregnancy and late pregnancy rate.

Results

No significant difference in the pregnancy rate were recorded in the course of throughout 2,5 years of follow-up in both groups. But significantly higher early pregnancy rate in laparoscopic myomectomy group compared to early pregnancy rate of open myomectomy group were observed (80,77% vs 62,5%) and significantly higher late pregnancy rate in open myomectomy group compared to late pregnancy rate of laparoscopic myomectomy group were observed (37,5% vs 19,23%).

Conclusion

Significantly higher early pregnancy rate in group after laparoscopic myomectomy compared to early pregnancy rate in group after open myomectomy were observed.



(OP06) Fertility

Psychotropic drugs-related male infertility: an underestimated reality

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Context

Various psychotropic medications have been implicated in the transient or permanent disturbance of reproduction in men. In the literature, studies of the effect of chronic exposure to some psychotropic drugs on sperm quality and male fertility reported divergent results. In addition, drug safety tests are generally performed on female animals to eliminate effects on fertility, pregnancy and the fetus.

Objective

The aim of this study is to analyze the effects of chronic exposure to psychotropic drugs on sperm quality and man fertility.

Methods

We conducted a retrospective study of the Cas-Témoins type. A review of the international literature was also collected to analyze the impact of psychotropic drugs in male reproduction.

Patients

A total of 70 patients were investigated for couple's infertility. 39 patients (Group G1) were treated with various psychotropic drugs for a period exceeding 12 months and 31 patients did not take any chronic drug (G2 control group).

Interventions

We excluded from the study all patients with azoospermia or any factor that could alter sperm parameters.

Main outcome measure(s)

For all patients, at least 2 sperm analysis have been investigated according to WHO guidelines.

Results

We noted a significant decrease in total mobility ($p=0.006$), progressive mobility ($p=0.02$) and sperm vitality ($p=0.03$) in G1 group patients. Hypospermia and necropermia were significantly more common in patients treated with psychotropic drugs ($p=0.04$, $p=0.04$ respectively). Sexual disorders such as decreased libido, erectile dysfunction and ejaculation were noted in 20.5% of patients. Improvements in ejaculate volume, numeration, mobility and vitality were noted in all patients who had modifications in psychotropic treatment. Spontaneous pregnancy was observed in two severe oligospermic patients after modification of the therapeutic protocol.

Conclusions

The majority of psychotropic drugs are involved in spermatogenesis alteration, sperm quality defects and sexual dysfunction. These effects are reversible and may be related to several intricate mechanisms including a direct gonadotoxic effect and endocrine disruption. These reprotoxic effects should be taken into account in any infertile patient taking chronic psychotropic treatment.



(OP06) Fertility

Artificial intelligence in Reproductive Medicine: clinical applications and perspectives

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Context

Artificial intelligence (AI) is performing an important role in different fields of medicine and is gradually converting medical practices in patient management. With growing progress in digital technologies and computing infrastructure, numerous applications in reproductive medicine and Assisted Reproductive Techniques (ART) have currently emerged.

Objective

In this review, we outline recent breakthroughs in AI technologies, their applications in the management of couple infertility and the challenges for further progress in assisted reproductive technology.

Methods

A non-systematic review of the literature was performed by screening PubMed up to July 2021.

Interventions

Using the search terms including “artificial intelligence”, “male infertility”, “female infertility”, “Reproduction” and “Assisted Reproductive Technology”.

Results and conclusions

New digital systems for semen analysis can offer potential applications in male infertility diagnosis, clinical decisions and medical research. Furthermore, artificial intelligence integration in ART is promising for selection of the best embryos with more developing potential and prediction of pregnancy outcomes.

AI algorithms may help physicians to more accurate diagnosis and individualized treatment of couple infertility. However, there are still many challenges on how this domain could be implemented in reproductive medicine.



(OP06) Fertility

Microbiota-related male and female infertility: an update

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Context

The commensal microbiota is a complex communities of microorganisms that including bacteria, fungi, viruses and parasites that play a fundamental role in the contrôle of human meta-organism homeostasia. In recent years, the microbiota has been considered as an important factor having adverse effects on human reproduction. Significant advances in microbiota research using DNA sequencing, metabolomics and proteomics provide insights into the involvement of microbiota in human infertility.

Objective

we provide an overview of the male and female reproductive system microbiome. We focus on the cause-effect mechanisms of human microbiota in couple reproductive health.

Personalized therapeutic approaches taking into account the microbiotic profile are discussed in some cases of couple infertility.

Methods

A non-systematic review of the literature was performed by screening PubMed up to July 2021.

Interventions

Using the search terms including “Microbiota”, “male infertility”, “female infertility”, “Reproduction” and “Assisted Reproductive Technology”.

Results and conclusions

Deleterious effects of an unfavorable microbiota have been implicated in the genesis of female infertility. In contrast, some microbiota such as probiotics could promote women reproduction both *in vivo* and *in vitro*, including embryo implantation. However, less is known about male microbiota and its influence on human reproduction. Recent studies have been carried out to explore the implication of reproductive tract microbiome on male fertility with debated results.



(OP06) Fertility

Extracellular vesicles derived from plasma and follicular fluid as biomarkers for Assisted Reproductive Techniques outcomes

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Context

Follicular fluid (FF) provides the microenvironment that supports oocyte development and comprises constituents of circulating plasma, products from theca, granulosa (GC) and cumulus cells (CC). The bidirectional communication between the gamete and adjacent somatic cells is critical for oocyte competence, fertilization and embryo development. The intercellular release and internalization of extracellular vesicles (EV) constitutes a mechanism of intrafollicular crosstalk. FF-EV are incorporated by GC and CC and modulate their physiological activity.

Objective

The main objective of this work was to assess if plasma and FF-EV are correlated with ART outcomes.

Methods

EV were isolated from FF and plasma through size exclusion chromatography (SEC) and ultracentrifugation (UC) and characterized regarding their surface protein markers and size.

Patients

FF and plasma samples were collected from women undergoing ART treatments in the Reproductive Medicine Unit at Coimbra University Hospitals.

Interventions

Women were subjected to an ovarian stimulation using both agonist and antagonist protocols with rFSH or hMG. Ovarian stimulation was monitored through ultrasound. When follicles reached a diameter larger than 18 mm, ovulation was induced with hCG and, 36h after, transvaginal ultrasound-guided follicles aspiration was performed.

Main outcome measures

The diameter and surface markers of EV were assessed and compared between FF and plasma samples. Results were correlated with ART outcomes such as oocyte/embryo quality, embryo development and pregnancy rate.

Results

The results confirm that both plasma and FF contain EV, and that those particles can be isolated through SEC and UC. Moreover, it was also observed in both biofluids that isolation through SEC provides a more purified EV population i.e. without protein contaminants. However, a preliminary analysis demonstrated no correlation between particle size and ART outcomes.

Conclusion

Understanding the correlation between FF-EV and ART outcomes may allow us to use those particles as non-invasive biomarkers for oocyte competence and, therefore, embryo development. This would be of great interest since FF is a discarded fluid in ART and EV isolation is relatively simple. Moreover, the discovery of plasma biomarkers is relevant since it is an easier to access biofluid. In the future, the study of other parameters such as EV number or content may highlight novel biomarkers for ART outcomes.



(OP06) Fertility

Hysteroscopy in patients with chronic endometritis: endometrium findings and clinical correlation

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Objective

The main objective was to determine the correlation between hysteroscopy findings and histological diagnosis in our center.

Methods

Retrospective observational study of patients who underwent hysteroscopy in office (n= 5535) in a tertiary Hospital between January 1, 2010, and December 31, 2020. In 65 patients chronic endometritis (EC) was diagnosed by histological findings (plasma cells). 5F hysteroscope was used. Local anesthesia was administered in 60% of the patients (paracervical with 2% Lidocaine). Targeted hysteroscopic biopsies were performed. We analyzed the age of presentation, clinical symptoms and treatments carried out.

Results

A total of 65 patients (1.17%) with histological findings (plasma cells) chronic endometritis was analyzed.

The mean age was 47 years (19-90), 22% of the patients were menopausal, 47% had a history of previous abortions.

The most frequent presentation was abnormal uterine bleeding (23%), only 7.6% had infertility.

The most frequent finding in the endometrium was proliferative (25%). Typical Hysteroscopic findings in chronic endometritis: micropolyposis, stromal edema or congestion, diffuse or focal hyperemia only was observed in 23%.

The patients were subjected to three possible treatments: removal of polyps, antibiotic treatment and expectant management.

Conclusions

The diagnosis of chronic endometritis requires hysteroscopic suspicion and a directed search by the pathologist for the specific findings of this entity. The histological correlation of the finding of micropolyposis in hysteroscopy was in 23% of the cases. Hysteroscopic findings alone aren't enough to correctly diagnose endometrial pathology and histological diagnosis remains the gold standard.



(OP07) Oncology and surgery

Uterine serous cystadenoma - a case report

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Context

Serous cystadenomas represent the most common type of ovarian neoplasm, and are also known to be associated with benign pathology of the pancreas. We present a rare case in which a serous cystadenoma is found to arise from the uterus.

Patient

A 52 year old woman presented to the gynaecology clinic for consideration of surgical management of a known 5.6 cm left-sided simple cyst. CA125 33. The patient was known to have previously had open right salpingectomy for an ectopic pregnancy. A six month follow-up ultrasound indicated that the simple cyst had increased in size to 6.9 cm, and surgical management was planned. Intraoperatively, normal ovaries were seen bilaterally, although the right ovary was noted to be adherent to the posterior aspect of the uterus. The right fallopian tube was noted to be absent, consistent with the patient's previous surgery, and the left fallopian tube and ovary appeared normal. An 8 cm cyst was noted to arise from the anterior wall of the uterus. Similar but smaller cysts were also noted arising from the posterior wall of the uterus. These cysts were excised and sent for analysis. Histological examination of the uterine cyst revealed fibromuscular tissue, lined by a single layer of serous type epithelium, consistent with a serous cystadenoma. There was no evidence of borderline changes or invasive neoplasia.

Conclusion

Our patient represents an incredibly rare case of uterine serous cystadenoma. It is difficult to ascertain how the cystadenoma has arisen. It may have arisen in a paraovarian cyst which become adherent to the uterus, or possibly via endosalpingosis. Although our case revealed a benign pathology, clinicians must be vigilant in the management of pelvic cysts in peri-menopausal women, to ensure rare pathology is not missed.



(OP07) Oncology and surgery

The role of HPV in the transformation of ovarian epithelial tumors

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Context

There is a lot of evidence of the link between human papillomavirus (HPV) infection and the development of cancer of the female genital organs. It is believed that the p16, E6, E7 oncoproteins, expressed by highly oncogenic HPV types 16 and 18, are specific markers of neoplastic processes in the tissues of the cervix. The role of human papillomavirus infection in the malignant transformation of ovarian epithelial tumors remains poorly understood.

Objective

The objective is the study of the expression levels of p16 INK4a, E6, E7 oncoproteins, vascular transforming growth factors VEGF, TGF- β 1, and tumor necrosis factor TNF- α in ovarian tissue in patients with HPV.

Methods and patients

170 samples of ovarian cysts tissue from women of 3 groups were examined: control group I - 50 samples from patients with negative HPV status, II - 70 with HPV positive, III - 50 with an indication of antiviral and immunomodulatory HPV therapy in history.

Interventions

Determined oncoproteins E6 and E7, p16INK4a, vascular endothelial growth factor (VEGF), transforming growth factor TGF- β , and tumor necrosis factor TNF- α , HPV status.

Main outcome measures

The content of expression factors in each group and the association with the development of malignant ovarian neoplasms were analyzed.

Results

Growth factors were found both in the main research group and in the control group. 24.0% of neoplasms of group I were positive for VEGF. In group II, a positive reaction of ovarian tumor structures with VEGF was determined in 2.9% of cases. Tumor necrosis factor TNF- α was found in 20.0% of the studied neoplasms of group III and in 21.4% - in patients of group II, with TGF- β 1 - 34.0%, which is 2 times more often than in group I. 6.0% of group I, 10.0% of group II, and 8.0% of group III observations turned out to be positive for E6 and E7 oncoproteins.

Conclusions

The presence of p16 INK4a oncoprotein in 65.7% of patients, with HPV-positive status, as well as the expression of growth factors VEGF (70.0%) and TGF- β 1 (64.3%) in conditions of a reduced level of TNF- α is a sign of an unfavorable clinical course of the diseases. HPV patients with borderline neoplasms with high p16INK4a, VEGF and TGF- β 1 values constitute a risk group for malignancy of cystadenomas and require dynamic observation.



(OP07) Oncology and surgery

HPV as a predictor of the development of neoplastic processes endometrium

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Context

The associations of endometrial hyperplasia and human papillomavirus (HPV) infection, underlying diseases, are the subject of close study.

Objective

Determination of the associative relationship of endometrial hyperplastic processes with the presence of various types of HPV viruses, the level of nonspecific factors of antiviral and antitumor protection.

Methods and patients

HPV-positive 30-49 y.o.women with (patients of the main group) and without (control group) hyperplastic processes of the endometrium, according to histological verification.

Interventions

The patients of the main and control groups were diagnosed with HPV types 6, 11, 16, 18, 26, 31, 33, 35, 39, 44, 45, 51, 52, 53, 56, 58, 59, 68, 69, 73, 82, viral load - the number of copies of the virus (Lg). All patients underwent determination of the level of interferon (IFN) in the blood serum, tumor necrosis factor (TNF- α).

Main outcome measures

HPV types 16, 18, 31, 33, 35, 56, 58, and 73 were found in all groups. Type 82 has been associated with complex atypical hyperplasia and atypical hyperplasia. Endometrial adenocarcinoma - with 6,16,18,31,33,35,51,56,58,73 types. A high viral load revealed - 3-5 copies, as well as associations with a decrease in the level of IFN, TNF- α .

Results

All patients with endometrial hyperplastic processes had a significant decrease in the level of serum IFN, TNF- α in comparison with the control group, as well as high titers of the HPV viral load. All hyperplastic processes of the endometrium were associated with the presence of various types of HPV, atypical forms of endometrial hyperplasia, endometrial adenocarcinoma - with a high viral load and low levels of IFN and TNF- α .

Conclusions

These morphological features of endometrial hyperplasia are associated with the presence of HPV infection and a decrease in immunological resistance. The question of the primacy of viral infection or a decrease in the immunological resistance of the organism in the development of hyperplastic processes can be controversial; however, the data obtained indicate the presence of this correspondence.



(OP07) Oncology and surgery

ERAS in gynecological surgery: a randomized trial

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Context

The enhanced recovery after surgery (ERAS) concept is based on a multimodal approach to improve the functional rehabilitation after surgery.

Objective

This study aimed to validate an ERAS protocol in gynecologic surgery and to measure the adherence to the protocol items

Methods

We conducted a prospective randomized trial enrolling consecutive patients from a single institution.

Patients

Affected by benign or malignant gynecological diseases (endometrial cancer and advanced ovarian cancer, excluding cervical cancer).

Interventions

We randomly assigned patients to undergo standard perioperative care or ERAS.

Main outcome measure(s)

The primary outcome is a shorter length of stay in favor of ERAS. Secondary outcomes include measurement of adherence to the protocol items: comparison of postoperative pain, vomiting, and nausea; anesthesiologic and surgical complications up to 30 days after surgery; rate of readmissions; the time to event in hours for bowel movements, flatus, drinking, hunger, eating, and walking; and the quality of recovery using a validated questionnaire (QoR-15). Finally, we explored the length of stay (LOS) in the prespecified subgroups at randomization, based on the type of surgical access and gynecologic disease.

Results

A total of 168 women were available for analysis: 85 women (50.6%) were assigned to the standard group, and 83 women (49.4%) were assigned to ERAS, and the groups were similar for baseline characteristics. Seventy-two patients (42.9%) underwent surgery for benign disease, 48 (28.6%) for endometrial cancer, and 48 (28.6%) for ovarian cancer. Women enrolled in ERAS had a shorter LOS (median: 2 [interquartile range, 2-3] vs 4 [interquartile range, 4-7] days; $P < .001$). A decreased rate of postoperative complications was noted for ERAS, as well as an earlier time to occur for all the events. Mean adherence to protocol items was 84.8% (95% confidence interval, 79.7-89.8), and we registered a better satisfaction in ERAS group. The shortening of the LOS was confirmed also in the prespecified subgroup analysis.

Conclusion

Application of ERAS in gynecologic surgery translated to a shorter LOS regardless of surgical access and type of gynecologic disease. Adherence to protocol items in the setting of a randomized trial was high.



(OP07) Oncology and surgery

Real-life efficacy of a multi-ingredient coriolus versicolor-based vaginal gel in high-risk HPV patients: the papilobs study final results

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Objectives

The objective was to evaluate the efficacy of Papilocare® -a multi-ingredient Coriolus versicolor-based vaginal gel- on repairing high-risk (HR) HPV-dependent low-grade cervical lesions and HR-HPV clearance in real-life practice.

Methods

Observational, multicenter, prospective, one-cohort study (PAPILOBS study ClinicalTrials.gov: NCT04199260). Vaccinated or not HPV-positive women aged > 25yo with Pap smear (Ps) of ASCUS or LSIL and concordant colposcopy were included during routine clinical visits in Spain. Patients were treated with Papilocare® 1 cannula/day for 21 days during first month + 1 cannula/alternate days for 5 months. After this 6-month period, patients with altered Ps and/or HPV persistency were treated for a 6-month extension treatment period with the same dosage. Analysis of HR-HPV patients with normal Ps and concordant colposcopy image (primary endpoint) and patients with HR-HPV cleared (totally or partially together with negative Ps and normal colposcopy) at 6/12 months is presented. The study was approved by an institutional review board and informed consent was signed by patients.

Results

At 6 months, data of 178 and 176 patients for Ps/colposcopy and HR-HPV presence, respectively, were available. 67% of patients (119/178) had negative Ps and concordant colposcopy. HR-HPV clearance was observed in 57.4% of patients (101/176). Data of 31 and 55 patients included in the 6-month extension treatment period for Ps/colposcopy and HR-HPV presence, respectively, were available. At 12 months, 54.8% (17/31) of patients had negative Ps and concordant colposcopy and HR-HPV clearance was observed in 60% (33/55). Considering all study period, 76% and 70.6% of patients repaired HR-HPV-dependent cervical lesions and cleared HR-HPV, respectively.

Conclusions

In this real-life study, repairing of HR-HPV-dependent low-grade cervical lesions and clearing HR-HPV were achieved after a 6-month treatment with Papilocare® (extending it up to 12 months if needed) in 3 out of 4 patients. These findings are consistent with the Paloma Trial's' ones (ClinicalTrials.gov NCT04002154) and other observational studies results.



(OP07) Oncology and surgery

Facts on uterine tissue morcellation, how to exclude a sarcoma?

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Objective

In female genital malignancy treatment laparoscopic procedures are valuable for early cervical cancers, endometrial cancer, early tubal and ovarian cancer and sarcomas. Minimal invasive procedures have also completely replaced explorative laparotomies. Can endometrial sarcoma be detected preoperatively?

Methods and patient(s)

Even with optimal preoperative imaging, unexpected uterine sarcoma can be detected in histopathology after uterine conventional and endoscopic fibroid surgery. In case of inadvertent morcellation of an unexpected uterine sarcoma the clinical outcomes, due to the rapid intraperitoneal dissemination of malignant tissue during the procedure can be negatively influenced. In a specific study we determined the prevalence of uterine sarcoma in women undergoing hysterectomy or myomectomy for benign uterine fibroids. We performed a retrospective study over 11 years. The total number of women operated for uterine fibroids was 2,297. Of this, 938 (42.5%) women had myomectomies and 1,269 (57.5%) women had hysterectomies. In myomectomies the most frequently used surgical method was laparoscopic myomectomy in 591 (63%) cases, followed by hysteroscopy myomectomy in 306 (32.62%) cases, and laparotomic myomectomy only in 41 (4.37%) cases. In hysterectomies, laparoscopic approaches significantly dominated in 1,163 (61.1%) cases, showing laparotomic approaches in 491 (25.82%) cases and vaginal approaches in 247 (12.99) cases.

Result(s)

Only one patient with endometrial stromal sarcoma (ESS) was not preoperatively diagnosed and treated as symptomatic uterine fibroid; this patient underwent laparoscopic supracervical hysterectomy. In the post-operative histopathological examination ESS was detected.

The patient was 49 years old and had shown normal LDH values and no suspicion in imaging techniques. Thus, our incidence of sarcomas among women who underwent benign uterine fibroid surgery is $\frac{1}{2,297}$ (0,043%).

Conclusions

Laparoscopic power morcellation should be performed only in cases with no suspicion of malignancy. Patients, who undergo laparoscopic surgery with power morcellation should be informed about the possible risks of morcellation in cases of rare not suspected malignant disease. Patients older than 45 years should not receive any tissue morcellation without an endobag. Principally power morcellation should only be allowed within an endobag. This is already a must for ovarian tissue, but for myomas will still seem to be reluctant, why?



(OP07) Oncology and surgery

Analyses of cervical adenocarcinoma (CAC) series: the relevance of mismatch repair proteins (MMR) status

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Context

The prevalence of cervical adenocarcinoma (CAC) has increased worldwide over the last past decades, exhibiting worse outcomes compared to squamous cell counterpart regardless of treatment. The prognostic and predictive relevance of several clinicopathological and molecular features, as mismatch repair proteins (MMR) status, is still under investigation.

Aim

Asses MMR status and estro-progestinic receptors (ER/PgR) expression in a mono-institutional series of CAC highlighting their correlations with tumoral clinico-pathological features.

Patients and methods

All CACs were retrospectively retrieved from the Division of Pathology of the University Hospital of Pisa (IT) from 2015 to 2021. Representative samples were selected, and histologic subtype, grade, and Silva pattern (according to WHO/IECC criteria) were annotated.

MMR status was immunohistochemically assessed with the four-antibody approach (MLH1, PMS2, MSH2, MSH6). Immunostainings were performed on ROCHE-Ventana Medical System.

Results

40 CACs have been collected. Patients' mean age was 48,15y (range: 32-76y). Most CACs were HPV-associated usual type (36/40) of which 24 were invasive and 12 in situ. Rare subtypes present were: minimal deviation (1/40), clear cell (2/40), and invasive stratified mucin-producing carcinoma (1/40).

All cases with lymphovascular invasion were G2 or G3; those with also perineural invasion were all G3 and Silva pattern C.

21 CACs were ER-positive, while 8 expressed both ER and PgR. No differential ER/PgR expression was observed with a dichotomic age stratification (55y). Interestingly, all G3 cases were PgR-negative and showed a lower ER expression. Similarly, Silva pattern C CACs were PgR-negative with absent/lower ER expression. Whereas all CACs with pattern A were both ER and PgR-positive. Only 7 CACs were MMR deficient (MMRd), and all were usual type (4 invasive and 3 in situ). The heterodimer MLH-1/PMS2 was the most frequently altered (6/7), only one case had just MSH6 loss.

Conclusion

Remarkably, even if MMRd is a rare event in CAC, both invasive and in situ usual type CACs can be involved, highlighting how this is an early event in tumorigenesis. Survival outcomes and treatment response in MMRd cervical cancer are still largely under-investigated; however, these patients could benefit from novel tailored therapeutic approaches. The association with Lynch and related syndromes justifies the screening for other associated malignancies and clinical genetic counseling.



(OP07) Oncology and surgery

Comparison of intravenous granisetron and ondansetron in preventing nausea and vomiting in epithelial ovarian cancer patients receiving paclitaxel-carboplatin chemotherapy using MASCC Antiemesis Tool (MAT) Assessment

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Context

Ovarian cancer is the second most common gynecological cancer in Indonesia. The combination of platinum (carboplatin) and a taxane (paclitaxel) is considered as the first line of chemotherapy for ovarian cancer. The side effects of these chemotherapeutic drugs are nausea and vomiting, which may affect patient's quality of life. Antiemetic medication options given to cancer patient are including granisetron and ondansetron. However, the effectivity of granisetron compared to ondansetron in preventing nausea and vomiting following chemotherapy is still controversial.

Objective

The aim of this study is to compare intravenous injection granisetron and ondansetron to prevent nausea and vomiting in epithelial ovarian cancer patient treated with carboplatin and paclitaxel, using The MASCC Antiemesis Tool (MAT).

Methods

A prospective, randomized, and double blind clinical study was performed with 60 epithelial ovarian cancer patients receiving carboplatin and paclitaxel in Dr. Sardjito Hospital. Patients were divided into two groups: the control group is patient who treated with 8 mg ondansetron injection, whereas the intervention group is patient who treated with 1 mg granisetron injection. The assessment of nausea and vomiting is performed using MAT score at 12, 24 and 48 hour following the administration of chemotherapeutic agents. Mann-Whitney test was used in this study to assess the MAT score differences between patient groups.

Results

Among 60 study participants, 32 patients (53.3%) were < 50 years old and 28 patients (46.7%) were > 50 years old, there was a statistically significant difference between age on the MAT score ($p=0.00$). The results of the MAT score at 12-hour were significantly lower from the 24 and 48-hour time points ($p=0.00$, $p=0.00$), but the 24-hour MAT score was not significantly different from the 48-hour MAT score ($p=0.211$). There were statistically significant lower MAT scores in granisetron group compared to ondansetron group at the 12, 24, and 48 hour time points ($p=0.00$, $p=0.00$, $p=0.00$, respectively).

Conclusion

Intravenous granisetron was more effective than intravenous ondansetron as an antiemetics, in epithelial ovarian cancer patients who received carboplatin-paclitaxel chemotherapy.



(OP07) Oncology and surgery

Real-life experience of the vaginal gel DeflaGyn® in Germany

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Context

DeflaGyn® is a vaginal gel that contains SiO₂, selenite, and citric acid. The medical device was marketed in 2020 in Germany. It promotes spontaneous remission and regression of unclear cervical smears, but was also shown to support the clearance of high-risk types of the human papillomavirus (hr-PV) and p16/Ki67.

Objective

To learn about the real-life experience of gynecologists who recommend the vaginal gel to their patients in case of abnormal cervical smear tests to support the watchful waiting period.

Methods

Twenty-two German gynecologists documented in case-report files their real-life experience in the treatment of patients with DeflaGyn® during the watchful waiting period after an unclear cervical smear test and/or positive for hr-HPV.

Patient(s): In total 40 women received DeflaGyn®. They were between 20 and 65 years old (mean age of 37.98 years) and had a mean BMI of 22.45 kg/m². 27.5% of women were smokers, three women received at least 1 dose of HPV vaccine and two women had concomitant infections.

Interventions(s)

Use of DeflaGyn® with a usual treatment period of 3x 28 days.

Results(s)

Before treatment with DeflaGyn® most women were diagnosed with Pap IIID1 (LSIL; n=22), Pap IIIp (ASC-H; n=6), or Pap IIID2 (HSIL; n=6), 77.5% of them (n=31) tested positive for hr-HPV. After treatment with DeflaGyn® 30 women were diagnosed with either Pap I or Pap IIa and the number of women tested positive for hr-HPV reduced to 13 (42.5%). In one case a woman was diagnosed with Pap II (NILM) while tested positive for HPV type 16. After treatment with DeflaGyn® she was tested negative for all hr-HPV analysed. Another case was a woman previously diagnosed with Pap IIID1 and CIN II and received laser therapy of the portio. Afterwards she was diagnosed with Pap I (NILM) combined with a recurrent positive test for hr-HPV she received DeflaGyn®. After the treatment with the vaginal gel, she was tested negative for hr-HPV. Most of the patients mentioned that the vaginal gel was well tolerated.

Conclusions

The real-life experience of DeflaGyn® upon German gynecologists shows that women within the age span of 20 to 65 use the vaginal gel during the watchful waiting phase. For both cervical smear tests and hr-HPV infections DeflaGyn® positive results have been documented while the patients' feedback was overall very positive.



(OP07) Oncology and surgery

Wound dehiscence in a post caesarean section oncologic female patient: a case report

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Context

Wound dehiscence is a risk factor that can occur following any surgical intervention. However there are certain cases where the risk factor of wound dehiscence occurring in a patient is greater than others.

Objective

Assess the risk factors of wound dehiscence in a maternal oncologic patient.

Patient

We received a referred patient with the diagnosis G3P1A1 GA 27 weeks 5 days, mother with cervical cancer stadium IIIB. Patient complained of spotting since 11 weeks pregnancy with a history of post coital bleeding and leukorrhea 5 months before pregnancy. Initially the planned management for the pregnancy was termination at 34 weeks through caesarean section followed by radiotherapy. However, at 33 weeks patient underwent and emergency caesarean section on indication of fetal compromised. Nine days later, the patient came in complaining of pain at the surgical site, delaying radiotherapy; 1 month after surgery occurred surgical site dehiscence. On physical examination, on the abdomen, there was pressure pain and dehiscence occurred at medial line of the scar from operative procedure measuring 5cm and it exerted a yellowish-brownish pus approximately 500cc. On bimanual examination, a mass of 5 cm size was found, brittle and easy to bleed, the right parametrium was normal, the left parametrium was fixated. Post caesarean section hemoglobin was 9.2 g/dl; hemoglobin further decreased to 7.7 g/dl when the patient returned 9 days later with the complaint of pain at the surgical site. Albumin was relatively low, from 1.92 g/dL post caesarean section to 1.95 g/dL at 9 days afterwards, respectively. Culture sampling of the pus, the bacteria was sensitive to tetracycline and ciprofloxacin and the patient was administered tetracycline and ciprofloxacin orally and 2 weeks later, closure of dehiscent wound was conducted.

Conclusion

Risk factors that influence surgical site complications are divided into major, moderate, minor and rare. In this case, the patient had a major pre-operative risk factor of having conducted emergency surgery, as well as 2 moderate patient-related risk factors, hypoalbuminemia and anemia. Incidence of surgical site infection is also higher in oncologic patients as well as oncologic patients has a weaker cellular and humoral immune system thus slowing the immune response, providing a higher risk of infection occurrence. Associated poor nutrition or intake from cancer patients could also be a factor in slowing down the healing process.



(OP07) Oncology and surgery

Transabdominal cerclage (TAC) for prevention of late abortion

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Objective

To assess the interest of TAC performed by laparoscopy in recurrent late pregnancy loss

Methods

We discussed indication of TAC after one or two pregnancy loss (between 18. and 25 amenorhea weeks) in patients well informed of the need of a cesarean section after TAC and wishing to decrease the risk of recurrence.

TAC was performed through laparoscopy in a simplified manner (i.e. without dissecting the space between uterine artery and isthmus) and using a mesh of with an anterior knot).

A systematic hysteroscopy was done when the cerclage was performed before pregnancy in order to detect chronic endometritis patients: 49 patients were enrolled in the study from 2012 to 2019. All patients were duly informed and signed a consent form prior to the intervention

Main outcome measures

Out of 49 patients, 23 have an history of one late abortion, 21 have had 2 late abortions and 5 an history of 3 abortions. 44 patients have had their cerclage prior to be pregnant and 5 before 12 weeks of pregnancy

47 patients were able to have a cesarean section after 36 weeks, 1 pregnant of twin underwent the operation at 10 weeks of pregnancy and had a failure at 25 weeks leading to the mesh removal after uncontrollable uterine contractions, she underwent 6 months after a new TAC and successfully deliver a singleton at 38 weeks.

Out of 44 patients having had cerclage prior to the pregnancy, 10 (22,7%) had an chronic endometritis with plasmocytes at the endometrial biopsy and were treated by antibiotics during one month.

No infection and no mesh rejection were observed in this serie.

Results

Laparoscopic cerclage was effective in 48 out of 49 patients (97%).

Conclusions

Laparoscopic cerclage seems to be a valid option to prevent late abortion, providing the patient well informed of the need to be delivered by cesarean section. Procedure may be performed before or during the first trimester. Usually TAC is proposed after at least 2 late abortion and a failure of conventionnal McDonald cerclage. We believe, due to the terrible burden of late abortion on patient, it is possible to propose TAC after only one or two abortions.



(OP08) Obstetrics 2

Experiences of healthcare professionals on pregnancy terminations due to fetal anomaly: a phenomenological study

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Context

Special health care needs of women and family who have a difficult process after pregnancy termination due to fetal anomaly should be handled by health professionals. However, healthcare professional who will provide care after perinatal loss may also be affected, and emotional impact may be reflected in health care.

Objective

It is aimed to determine the opinions and experiences of the healthcare professionals working in the field of women's health regarding pregnancy terminations due to fetal anomaly with this study.

Methods

This qualitative study is based on a phenomenological approach. The study was conducted in Antalya, Turkey between December 2018 and April 2019. The sample of the study consisted of 26 participants including nurses, midwives, specialists, and assistant doctors who have encountered pregnancy termination process due to fetal anomaly at least once. The study data were collected via an individual in-depth interview technique using a semi-structured survey form. Then, content analysis was made over the data transcribed.

Main outcome measures

The main outcome measures of the study are to reveal the perceptions and attitudes of health professionals about pregnancy terminations and to determine whether there is a difference in approach to pregnancy terminations among health professionals from different disciplines.

Results

After qualitative analysis, the study data were handled under two themes as "1-How are healthcare professionals affected during the termination process?" and "2-what do healthcare professionals do in the termination process?". Under these two themes, the difficulties and facilitating factors in the pregnancy termination process for health professionals were revealed; In addition, the approaches of health professionals to pregnancy terminations were determined. It has been concluded that doctors have a more mechanical approach to pregnancy terminations, while nurses and midwives have a more emotional and compassionate approach.

Conclusions

It was determined that healthcare professionals involved in the termination of pregnancy due to fetal anomaly were affected in different ways in the process and there were some variables that determine this effect. To facilitate the process, it can be suggested to strengthen health professionals by improving editable factors.



(OP08) Obstetrics 2

Did COVID-19 pandemic change the way of labour?

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Introduction

The COVID-19 pandemic was declared on March 11 2020, so several measures were then taken in our maternity to control the spread of the virus. These included: restriction of visits/company during delivery, appointments; COVID-19 tests to all women in labour; use of IPE by health professionals.

In Portugal, several maternities induced labour to all women at 39 weeks, for a better control of COVID-19. Our maternity did not.

Objectives

Comparison between characteristics of deliveries from March 11 to December 31 2019, and deliveries from March 11 to December 31, 2020.

Methods

Statistical analysis of the data basis of births in 2019 and 2020, comparing the same period from both years, between March 11 and December 31. Inclusion criteria was singleton pregnancies, cephalic presentation, and mothers with a negative covid test. In 2019, 825 women were included, and in 2020, there were 784, with a total of 1,609 women. The statistical analysis was through SPSS, Cramer's χ^2 and chi-square test.

Results

Between March 11 and December 31 2019, 825 women with a negative covid test delivered a single baby, in cephalic presentation. Of these, 6.2% were pre-term births. Regarding the type of birth, there were 52.6% eutocic births, 11.6% births with a suction cup, 3.4% births with forceps, and 32.4% births by c-section. Of the c-sections, 36% were elective, 55.9% urgent, and 8% emergent. 30.7% of all births were induced. There were 4 cases of newborns with an Apgar index <7 at 5 min, and 1 fetal death.

In the same period in 2020, 784 women with a negative covid test delivered a single baby, in cephalic presentation. 5.5% were preterm. There were 52.4% eutocic births, 12.5% births with a suction cup, 4.1% births with forceps, and 31% births by c-section. Of the c-sections, 41.2% were elective, 52.3% urgent, 6.6% emergent. 28.3% of all births were induced. No cases of newborns with an Apgar index <7 at 5 min, but there were 4 cases of fetal death.

Conclusions

Comparing the same period of time between 2019 and 2020, there were no statistical differences in the number, type of birth, or induced labour. There was a significant statistical difference (p value: 0,5) for cases with an Apgar index <7 at 5 min. In 2019 there was only one case of fetal death, while in 2020 there were 4 cases, which could be from the lack of availability of appointments, or fear to go to the hospital.



(OP08) Obstetrics 2

Allocation criteria for higher than low risk pregnancies

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Context

After midwife-led birth centers as well as home births had been included into Social Security Statute Book (§134a SGB V) and thus became covered by German Public Health Insurance contract negotiations on flat rate costs have followed.

Objective

The section on quality management concerning allocation criteria for out of hospital births needed an update now, as evidence based as possible.

Methods

12 catalogues from 11 countries, which do have documents for choice of birthplace, have been identified via literature studies, links to the homepage of the ministry in charge or direct correspondence.

Results

Obstetrics presents the same problems worldwide of how to cope with higher than low risks. The resulting overview table shows how very similar the solutions really are and thus helps to define how responsibility can be shared between midwives and obstetricians.

Conclusions

The specific regulations concerning quality management in the contract between self-employed midwives and the German Public Health Insurance have been updated on this basis. The overview table could also serve as an important contribution for international exchange, comparison of results and further development of obstetric care in the respective systems of Social Security.



(OP08) Obstetrics 2

Revisiting the importance of maternal age

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Context

The identification of high-risk pregnancies is a critical component of obstetric care. This assessment includes maternal age with maximum risk attributed to the extremes of the reproductive period, but ongoing changes potentially decreased the effect of age in late pregnancy. Medicine became more effective in the prevention, detection and management of conditions associated to unfavorable obstetric outcomes. Women worldwide have increasing resources and education. They have less children and invest more in each pregnancy. They are also more likely to have comorbidities at any age. Society has more pathways open to women and lifestyle choices became diverse increasing the gaps between the health status of women with the same age.

Objective

This study aims to explore the association between age and obstetric outcomes in late pregnancy previously to the COVID-19 pandemic.

Methods

Consult of the records of all deliveries after 24w gestation in Hospital do Espírito Santo de Évora (Portugal) in 2017 and 2018. Statistical analysis with SPSS.

Patients

2,222 women (2,262 births), with an average age of 31 years (min. 14; max. 47) (≤ 17 years: 30 patients; 18-29y: 800; 30-39y: 1,228; ≥ 40 y: 158). 51% were multiparous (≤ 17 years: 10%; 18-29y: 35.4%; 30-39y: 60.0%; ≥ 40 y: 71.5%).

Main outcome measures

maternal mortality, fetal mortality, Apgar Score, birth weight, weeks of gestation, singleton/twin delivery, type of delivery, urgency of cesarian section.

Results

With age there was an significant rise in:

- preterm births (≤ 17 years: 6.7%; 18-29y: 9.8%; 30-39y: 9.7%; ≥ 40 y: 16.5% - Cramer's V p 0,05)
- deliveries by cesarean section (≤ 17 years: 13.3%; 18-29y: 26.3%; 30-39y: 36.5%; ≥ 40 y: 49.4% - Cramer's V p 0.000)
- non-urgent cesarean sections (≤ 17 years: 25.0%; 18-29y: 36.2%; 30-39y: 54.1%; ≥ 40 y: 61.5% - Cramer's V p 0.000)

Although without significance, the incidence of twin deliveries increased with age, and there was a trend towards lower birth weights.

There were no differences in Apgar Score at the 5^o min, in fetal mortality (n=12) or in maternal mortality (n=0).

Conclusions

The data from our Center suggests that maternal age continues to be associated to obstetric outcomes in the third trimester. However, teen pregnancy didn't stand out as high-risk. That was true for pregnancies at 40 years of age or above, but a bigger propensity for medical intervention may explain some of the discrepancies that were found.



(OP08) Obstetrics 2

How to improve placental perfusion and umbilical artery vascular resistance in second trimester of singleton pregnancy?

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Objective

The aim of our study was to analyze the therapeutic effects of pravastatin /L-arginine therapy on improvement of placental perfusion and decrease of umbilical artery vascular resistance in singleton pregnancies with increased umbilical artery pulsatility index for gestational age.

Methods

In this study 12 pregnant patients, with isolated increased umbilical vascular resistance and normal uterine artery doppler findings, were included. Pravastatin 40 mg / L-arginine 1500 mg per day, was administered when umbilical artery pulsatility index was measured above limits for gestational age. Patients were scanned in 2-4 week interval to follow up changes in vascular resistance in umbilical artery.

Results

12 pregnant patients had singleton pregnancy. Median gestational age, when increased umbilical vascular resistance was detected and therapy introduced, was 23 weeks (18-30 weeks). Therapy was introduced when PI values in the umbilical artery were above normal limits for gestational age. Improvement of umbilical artery PI values was confirmed in 11 patients. Median period of improvement in umbilical circulation was 2 weeks. Fetal cerebral, aortal, renal circulation and uterine arteries vascular resistance remained normal throughout pregnancy. Median gestational age at delivery was 40 weeks. Median 1/5 min Agar score was 9/10. 11 neonates were born without signs of intrauterine asphyxia. Mean neonatal weight was 3331±389 g. In one patient, who had normal umbilical artery vascular resistance until 30th week, therapy was introduced after significant rise of umbilical artery PI to 1.5. Fetal condition was intensively monitored and umbilical artery PI values continued to rise until 35 weeks when AEDV occurred. Fetal cerebral circulation showed initial blood redistribution towards central nervous system. Pregnancy was carefully monitored and, when cardiotocographic monitoring indicated imminent asphyxia, cesarean section was performed at 35 weeks of pregnancy. Neonatal weight was 2400 g, Apgar score was 7/8. Histopathological examination of the placenta confirmed placental infarction.

Conclusion

In patients with isolated increased umbilical artery vascular resistance, increased placental perfusion and decreased vascular resistance in umbilical arteries was achieved after administration of Pravastatin 40 mg/L-arginine 1500 mg daily. Administration of this therapy reduced the incidence of premature delivery due to fetal asphyxia.



(OP08) Obstetrics 2

Tocilizumab and remdesivir as possible effective treatments In COVID-19 infection in pregnant women

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Context

Physiologic immune suppression and cardiopulmonar changes experienced by pregnant women confers additional risk for COVID-19 infection, morbidity and mortality. SARS-CoV-2 has rapidly spread globally making urgent need for therapeutic options. Remdesivir, the first drug licensed for COVID-19 treatment, is a nucleoside prodrug with activity against coronaviruses supposed to shorten the time of recovery in hospitalized patients requiring oxygen therapy. Pregnant women were excluded of clinical trials for justifiable reasons, therefore we have no strong evidence of efficacy in this population. Considering that ten percent of all pregnant women infected by COVID-19 will have severe symptoms, potential treatment options are more than necessary at this point of the pandemic. Tocilizumab is a recombinant and humanized IgG monoclonal antibody against IL-6 which does not appear to increase the risk of birth defects and has limited use to severe COVID-19.

Objective

To expose Tocilizumab and Remdesivir as possible effective drugs for treating moderate to severe COVID-19 cases in pregnant women. Methods – multiple electronic databases were searched for studies and case relates evaluating the safety and effects of Tocilizumab and/or Remdesivir in pregnant population.

Main outcome measure(s)

Predictions can be made based on Remdesivir chemistry and pharmacokinetics, as it is rapidly hydrolysed by intracellular esterases to a nucleoside monophosphate analogue requiring several steps of metabolism to generate the active intracellular nucleotide triphosphate analogue suggesting that it is unlikely to cross the placenta in important amounts.

Result(s)

All the articles searched reached consensus in determining that the main clinical outcome was recovery, both by using Tocilizumab and Remdesivir isolated. There was no adverse effects and recovery time was shortened.

Conclusions

Remdesivir has *in vivo* activity against Ebola virus and MERS-CoV, probably also has effect on SARS-CoV-2, it's also well tolerated by pregnant women, with no severe adverse affects. Despite the fact that it is still necessary further study and randomized controlled trial to strongly correlate remdesivir and tocilizumab to clinical improvemet, the accumulated data show promising results for these drugs as viable therapy.



(OP08) Obstetrics 2

Cervical insufficiency: late diagnosis and management. A case report

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Context

Cervical insufficiency is defined as the inability of the uterine cervix to retain a pregnancy in the second trimester due to dilation of the cervix without uterine contractions. Unfortunately, diagnosis is mostly based on a patient history of prior midtrimester loss, therefore when it occurs in the first pregnancy we are faced with an advanced condition that lacks solid protocols on what treatment to follow.

Objective

To show a successful treatment of a second trimester pregnancy with cervical insufficiency through the combined use of three types of treatment methods. Methods: the data was obtained through review of the patient's medical record.

Patient

KEL, 29 years, fifth pregnancy.

About the previous gestations:

- 1st: C-section at term due to breech fetal presentation
- 2nd: C-section at term due to maternal desire
- 3rd: miscarriage followed by curettage
- 4th: premature deliver at 22 weeks of pregnancy due to total cervical dilation followed by premature rupture of membranes. A C-section was performed due to cormic fetal presentation. Neonatal death after 5 days. A new pregnancy occurred after 40 days, despite regular use of condoms.

Interventions

During the current pregnancy, pre-natal exams were performed including cervical measurement and evaluation at 12 weeks, with normal results. Progesterone supplementation was initiated at the end of the first trimester. At 20 weeks and 6 days, during the morphological ultrasound, a transvaginal ultrasound was also performed in order to evaluate the cervix. It was found to have a funnel-shaped appearance and it measured 15 mm in length indicating cervical insufficiency. A day after the diagnosis, a McDonald cerclage was performed without any complications. Five days later a cervical pessary was inserted around the cervix. The patient presented excellent pregnancy evolution until 37 weeks, when the pessary and cerclage stiches were removed. Immediately after the removal the patient was 5 cm dilated and presented a thin cervix. A C-section was performed due to a recent hysterotomy.

Main outcome

A 6.6 pound healthy girl was born. The patient also underwent a tubal ligation in accordance with Brazilian law, which allows the procedure to be performed concomitant with delivery if after three or more C-sections.

Conclusion

When we face pregnancies on the verge of birth before viability, a treatment that includes the three interventions above mentioned can be effective.



(OP08) Obstetrics 2

Creating a new system about autonomic nervous system activity: FANTE

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Context

Fetal Autonomic Nervous sysTem Evaluation (FANTE) is a non-invasive tool able to evaluate the autonomic nervous system activity in fetus. Autonomic nervous system is a key-regulator of the fetal homeostasis during the prenatal and postnatal life and its modulation could be important to stimulate autonomous nervous system (ANS) maturation and development.

Objective

Primary endpoint was creating table and graphs containing several parameters of heart rate variability (Rrsd, RR interval standard deviation; power spectral density, PSD; Ptot), sympathetic (low frequencies, LFn) and parasympathetic activity (high frequencies, HFn), related to gestational age. Secondary endpoint was finding statistical differences in FANTE values between physiological pregnancies babies and pathological pregnancies' ones.

Method

All FANTE registrations were acquired using 12 derivations placed on the maternal abdomen. In every session, 10 min basal FANTE (bFANTE) were registered, avoiding external noises or other stimulations.

Population

171 women between the 24th and 38th week with a singleton pregnancy, physiological or pathological, were recruited in this study. 46 patients were recruited outside the hospital in our outpatient clinic, while 125 were recovered in our Obstetrics (Physiological and Patohlogical) Unit. A weekly FANTE registration was performed.

Results

RR mean increase regularly during period from 25 to 42 weeks with statistical relevance ($r=0.4026$, $p<0.0001$) as like as RMSSD ($r=0.3503$, $p<0.0001$) and SDNN; in fact this value increases regularly after 25 weeks ($r=0.3857$; $p<0.0001$). Both LF and HF increase during second and third trimester of pregnancy (LF: $r=0.3857$, $p<0,0001$; HF: $r=0.3332$, $p<0.0001$), while LF/HF ratio decrease without statistical relevance. However when we have considered only physiological pregnancies (N=94) excluding pathological ones (IUGR, SGA, pPROM, preeclampsia, intrauterine death), LF/HF ratio decreased statistically with gestational weeks ($r=-0.361$, $p=0.0004$).

Conclusion

FANTE could be developped and used to define ANS development and could give a relevant contrinution on early diagnosis about ANS disfunctions and to assess future risk on developping diseases in preterm babies. However there are several limitations which have to be solved in order to gain relevant results and further studies (based on bigger populations) need to be held in future.



(OP08) Obstetrics 2

Abdominal ectopic pregnancy - A clear diagnosis with a challenging management

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Ectopic pregnancies (EP) affect 1% to 2% of all pregnancies, most occurring in the fallopian tubes. Around 1% of EP are found at the abdominal cavity, with the fertilized ovum attached to reproductive organs, uterine serosa, omentum, bowel or mesentery.

A 34 years old woman presented to the ER on 15/03/2021 with abdominal pain and abnormal uterine bleeding.

The patient had history of HSIL (conization in 2020), never having had surgery or currently taking any medication.

G5P5 (5 eutocic deliveries) with amenorrhea of 4w and 6d.

The pregnancy test was positive.

Bimanual examination revealed a firm and closed cervix, right deviated uterus, severe pain in the left adnexal area, with a rubbery mass of 12/14 cm diameter and pain in the Douglas pouch.

The ultrasound (US) exhibited a deviated uterus, clear endometrial line, thicker at the fundus. In between the left adnexal area and the Douglas pouch a gestational sac was seen with a live fetus, CRL 53mm and BPD 24,7 mm, compatible with a 14w+1d pregnancy.

Admission was recommended for further evaluation and management, which was fiercely denied by the patient, even after a detailed explanation of the risks.

On 22/04/2021 the patient showed up at an obstetrics appointment, referring a “4 months old pregnancy” sic.

The physician performed a US that exhibited a fetus compatible with a 14w pregnancy, without heartbeats.

It was stressed it was a nonviable pregnancy that must be managed in the hospital. The patient remained determined against admission.

The following day the patient presented to the ER with abdominal pain, and after a thorough explanation of the risks she faced, the patient finally consented admission and surgery was performed the same day.

Firstly the medical team tried a laparoscopic approach, but considering the severe bleeding from the retrouterine mass, it was decided to convert to laparotomy.

The ectopic mass evidenced a large area of fibrin and extensive adhesions to the bowels. The gestational sac was artificially ruptured and a dead fetus was retrieved and sent to pathology. The placenta was noted to be attached to the posterior wall of the uterus/Douglas pouch.

Abdominal ectopic pregnancies present high morbidity and mortality, therefore their effective diagnosis and management are of utmost importance. Doctor/patient communication is often challenging, but its effectiveness is crucial for the successful management of a patient's disease.



(OP08) Obstetrics 2

Placental growth factor increases actin depolymerisation and cell stiffness in human endometrial stromal cells

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Objective

An adverse uterine micro-environment can trigger unfavourable events resulting in miscarriage or late pregnancy complications, such as pre-eclampsia. A successful pregnancy is dependent on well-timed modification of the bio-mechanical parameters in the endometrium including cell migration, cytoskeletal rearrangements, establishing cell polarity and matrix stiffness. Factors influencing endometrial actin dynamics remain poorly understood. Placental growth factor (PLGF) is abundant in the human endometrium and previous studies in cancer revealed a putative link between PLGF and cytoskeletal rearrangement. Therefore, the present study explored whether PLGF modifies actin cytoskeleton, shape and stiffness in benign human endometrial stromal cells (ESC).

Methods

The effect of PLGF (20ng/ml for 6 days) on cytoskeletal regulators Rac1 and PAK1 was studied using qRT-PCR and western blotting. Further, the impact of PLGF on globular to filamentous actin (G/F actin) ratio was measured using flow cytometry, immunofluorescence and western blot approaches. Finally, the cell stiffness (the elastic modulus), cell surface area and cell volume were investigated by atomic force microscopy (AFM), imaging and flow cytometry.

Results

As a result, PLGF increased Rac1 and PAK1 transcript and protein levels. PLGF decreased G/F ratio levels in ESCs pointing to actin depolymerization. Further, treatment with PLGF dramatically increased cell stiffness with minimal change observed in cell surface area and cell volume. The effect of PLGF on actin depolymerization was blocked by inhibition of Rac1 and PAK1.

Conclusion

In conclusion, PLGF leads to an increase of Rac1 and PAK1 activity with subsequent actin depolymerization and cell stiffening. Thus, endometrial PLGF influences cell dynamics by modulating G/F actin directly in ESCs. Aberrant PLGF signalling and perturbed cytoskeletal arrangement could be an important determining factor leading to pregnancy complications such as miscarriage or pre-eclampsia.



(OP08) Obstetrics 2

Pregnancy in woman with Fowler syndrome

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A favourable outcome of a 31-year-old pregnant woman with underlying Fowler's syndrome along with focal epilepsy, Hypothyroidism and Asthma. Fowler's syndrome is a cause of urinary retention in young women.

The abnormality lies in the failure of urethral sphincter to relax, hence the main concern is to ensure adequate bladder emptying. Our patient went through self-catheterisation and suprapubic catheters after which she had the Mitrofanoff procedure to help manage her symptoms.

Upon getting pregnant the main concern was recurrent urinary tract infections and pelvic pain requiring hospital admissions for parenteral antibiotics and analgesia. She underwent Induction of labour at 39 weeks and delivered a healthy infant. Post-natal recovery was complicated with worsening of seizures, was managed with support of neurology team input.



(OP08) Obstetrics 2

Temporal trend of near miss and its regional variations in Brazil from 2010 to 2018

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Cases of maternal near miss are those in which women survive severe maternal complications during pregnancy or the puerperium. This ecological study aimed to identify the temporal trend of near-miss cases in different regions of Brazil between 2010 and 2018, using data from the Hospital Information System (HIS) of the Unified Brazilian Health System (SUS).

Hospital admission records of women between 10 and 49 years old with diagnosis included in the ICD-10 and codes indicating near-miss events were selected. From 20,891,040 admission due to obstetric causes, 766,249 (3.66%) near-miss cases were identified, 31,475 women needed admission to the ICU and 1,259 died.

Cases were found to be more predominant in black women over 35 years old from the North and Northeast region. There was a trend of increase in near-miss rates of approximately 13.5% a year during the period of the study. The trend presented a different behavior depending on the level of development of the region studied. The main causes of near miss were preeclampsia (47%), hemorrhage (24%) and sepsis (18%).

The elucidation of the temporal trend of near miss can contribute to the institutionalization of public policies that aim to reduce the rates of maternal morbidity and mortality.



Poster Session





Adolescence

Lipschütz ulcer: a diagnosis to remember

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Context

In clinical practice genital ulcers are a frequent complaint, but the diagnosis is sometimes challenging. Lipschütz ulcerations usually appear in non-sexually active adolescents or young women who report a sudden onset of one or more painful and necrotic vulvar ulcerations. These ulcers may have a symmetrical “kissing lesions” pattern and sometimes are preceded by flu or mononucleosis-like symptoms. The true incidence and etiology of this condition remain unknown, however, the main hypothesis is that it represents a clinical manifestation of hypersensitivity reaction to a viral or bacterial infection.

Patients

We present two clinical cases of healthy and sexually inactive young girls.

Case 1

10-year-old girl admitted to the pediatric emergency room (PER) with vulvodynia, dysuria and vulvar lesions, preceded by fever and odynophagia for the past 3 days. Physical exam showed multiple necrotic ulcerations on the left labia minora covered by grey exudate and exuberant labial edema. Laboratory tests revealed mild leukocytosis with neutrophilia and increased C reactive protein, serological exams were negative for active infection by Cytomegalovirus, Herpes Simplex Virus, Epstein Barr Virus and Syphilis.

Case 2

9-year-old girl presented to the PER with acute vulvodynia and vulvar lesions, preceded by odynophagia and fever. On physical examination stood out: three pericentrimetric necrotic ulcerations with regular and well delimited margins, two of them on the inner surface of the labia majora of the vulva, “kissing lesions” with symmetrical appearance, and one on fourchette.

In both cases, the presumptive diagnostic of Lipschütz ulcer was made and the patients were treated with lidocaine for about 2 weeks, and clobetasol propionate in case 1. Complete resolution of the ulcers was achieved in less than 6 weeks.

Conclusion

Lipschütz ulcer is a clinical diagnosis and one of exclusion. The ulcerations tend to heal spontaneously in 3-6 weeks without sequelae and the treatment is primarily supportive. Despite being an apparent infrequent cause of genital ulcers, in order to offer the best treatment and avoid unnecessary distress, Lipschütz ulcer should not be forgotten and physicians should learn how to recognize this condition.



Abnormal Uterine Bleeding

Establishing a risk prediction model for abnormal uterine bleeding caused by primary endometrial disorders (AUB-E)

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Context

Due to the diagnosis of abnormal uterine bleeding caused by primary endometrial disorders (AUB-E) depending on exclusion, it is a lack of specific detection means, and etiology is not clear.

Objective

A case-control study was carried out to analyze the epidemiological characteristics between AUB-E and control groups, explore the risk factors, and establish a risk prediction model.

Methods

Data were collected by a self-designed health questionnaire. Next, PSM was used to match the controls as the condition of "Age" with a ratio of 1:2. After that, exploring the epidemiological distribution of the two groups was conducted. The Logistic regression model was established with significant variables and evaluated.

Patients

84 patients with AUB-E and 170 healthy controls were permanent residence in Zhejiang Province.

Intervention

Not applicable.

Main outcome measure

Combine with self-reported HMB and assessed by the Pictorial Blood Assessment Chart (PBAC) to diagnose AUB-E relied on the AUB diagnostic guidelines, both at home and abroad.

Result

The median age of all participants was 42 (35, 47) years and ranged from 22 to 51 years. The Logistic regression model was made with 7 variables with statistical significance, including education degree, occupation type, tea-drinking habit, sugar diet, history of diagnosis and curettage, history of fallopian tube operation, and BMI between AUB-E patients and controls. The Logistic regression analysis showed that educational level (x1) ($p = 0.003$), tea-drinking (x3) ($p = 0.018$) and BMI (x7) ($p = 0.011$) were significant for disease prediction. Lower education level (OR = 3.642; 95% CI: 1.550 - 8.555) and increasing BMI (OR = 1.119; 95% CI: 1.026 - 1.221) were risk factors for AUB-E, although tea-drinking habit (OR = 0.437, 95% CI 0.220 - 0.866) might be a protective factor. The sensitivity and specificity of the model were 41.0% and 91.9%, the positive predictive value and negative predictive value were 75.56% and 71.84%. The AUC was 0.740 ($p = 0.000$) with 95% CI 0.671-0.808.

Conclusions

Primary education and below and increasing BMI are risk factors for AUB-E, and tea-drinking is a protective factor.



ART

Prothrombotic biomarkers during controlled ovarian stimulation for assisted reproductive techniques

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Context

Controlled ovarian stimulation (COS) for assisted reproductive techniques (ART) is associated with a hypercoagulable state and an increased risk of venous thrombosis. The impact of the different ART protocols on coagulation biomarkers is unknown.

Objective

To assess the evolution of coagulation biomarkers throughout and after the ovarian stimulation comparing 3 different ART protocols.

Methods

Observational multicentre cohort study.

Patients

Infertile women undergoing COS for ART in 2017-2019 were included.

Interventions

None.

Main outcome measures

Our primary outcome was endogenous thrombin potential (ETP) assessed by calibrated automated thrombinography (using 5 pM of tissue factor). ETP was measured before stimulation (baseline), on the day of ovulation triggering (triggering) and seven days after triggering. Three protocols were prescribed according to the standards used and without hormonal pre-treatment: agonist protocol with hCG trigger (ag-hCG); antagonist protocol with hCG trigger (atg-hCG) or GnRH agonist trigger (atg-GnRH); evolution of ETP was estimated and compared among groups using mixed effects linear regression model.

Results

A total of 64 women, mean aged (SD) 37.8 (2.8), participated to the study: 24 received ag-hCG, 16 atg-hCG, and 24 atg-GnRH. The mean serum estradiol levels in atg-GnRH were statistically higher at triggering and lower 7days after. Overall, ETP evolution over time was statistically different between groups ($p=0.013$). If values were similar at baseline and increased at triggering in each group, the greatest difference occurred between triggering and 7days after triggering: while ETP continued to increase in ag-hCG (+110) and atg-hCG (+170), it remained stable in atg-GnRH (+0). The mean ETP in atg-GnRH were 1270 at baseline, 1490 at triggering and 1480 seven days after. In Ag-hCG and Atg-hCG, values were 1280, 1440, 1550, and 1260, 1430, 1600, respectively. Protein C and protein S levels were stable, while D-dimers, fibrinogen and factor VIII increased at triggering and 7days after in all groups

Conclusion

The hypercoagulable state was higher and persistent after stimulation in the ag-hCG and atg-hCG groups compared to the atg-GnRH group. Further studies are required to evaluate the differential effect of estradiol and multi-follicular ovulation on coagulation markers and the duration of the induced hypercoagulable state.



ART

Inequalities in Assisted Reproduction Technology (ART) utilization within countries of the G20

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Objectives

To assess whether there are inequalities in ART utilization across the G20 countries and, if so, are they correlated with national wealth measured by growth domestic product (GDP) per capita and affected by accessibility for ART treatment.

Design

Analysis of total ART cycles obtained from international and national registries for 2016 of the G20 countries, excluding the European Union. Growth domestic product (GDP) and population size for that year were retrieved from relevant World Bank data documents. ART utilization was calculated by dividing the total cycles by the country's women at reproduction age (15-49y) population, and described as cycles per million population (cpm). ART utilization was correlated to GDP and national pro-natalism policies affecting accessibility- mainly government funding and/or insurance reimbursement.

Results

The 19 countries of the G20 comprised of 4.49 Billion people (range 24M-1,374M) (61% of total world population in 2016). There was large variability in GDP and ART utilization across the 19 countries of the G20. The mean ART utilization was 4,065 cpm (range 143-17,156cpm) with a strong positive correlation to GDP ($r=0.54$; $p=0.015$). Higher utilization rate of ART was seen in the 12 countries that provide government funding and/or insurance coverage for IVF and ICSI compared to the seven countries with no such cover (5,714 vs 1,239 cpm; $p=0.008$) although there was no significant difference in the mean GDP between these two groups (\$36,329 vs \$23,603; $p=0.08$)

Conclusions

The strong correlation between national wealth measured by GDP per capita and ART utilization highlights the inequalities of ART provision even among the largest world economies. Higher-income countries have higher utilization rate of ART, while less wealthy countries cannot offer government reimbursement for this treatment and individuals cannot afford it. Only when most countries will implement policies that promote and enable publicly funded ART treatment will this utilization rate gap close, but this might be a very difficult and far-off target for many of the poorer economies regardless of their size.



Breast

Controlateral axillary node recurrence after initial breast cancer with sentinel lymph node negative

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Objective

Controlateral Axillary's Metastasis (CAM) may be present at the time of primary breast cancer diagnosis or following prior breast cancer treatment as a recurrence. Late CAM is a rare event after breast cancer with negative axillary's nodes. CAM is associated with an aggressive histopathological feature. We present a case report of a patient with CAM.

Methods

The patient was primarily treated with conservative surgery followed by chemotherapy and radiotherapy. The follow-up was performed with mammography, breast ultrasonography, CT scans, bone scintigraphy and also PET-CT.

Patient

The 47 years old patient was had a tumor in her right breast. The biopsy confirmed an invasive ductal carcinoma, 25 mm diameter, margins negative, Grade 3, Triple-Negative, and Sentinel lymph nodes negative. Chemotherapy with EC -Taxol was started after the surgery, followed by radiotherapy. Twelve months after the treatment, an axillary node in her left armpit (controlateral) was detected clinically and the core biopsy confirmed metastasis. On the contrary the imagery of the ipsilateral axilla was free of metastasis and neither metastasis were found. The node was removed and a second line chemotherapy was offered plus radiotherapy of the controlateral susclavicular area. Twenty-eight months later, the patient presented metastatic nodes in the mesothorax.

Intervention

Initially, we performed partial mastectomy on her right breast and followed by adjuvant treatments: Chemotherapy and Radiotherapy (RT). Subsequently, with second chemotherapy (Xeloda) plus RT. The recurrence in the thorax was managed with thoracotomy and excision of the pathological nodes.

Results

2 years after the second recurrence, the patient is without pathological findings, and regular follow-up is performed.

Conclusions

Therefore we report this case of controlateral node recurrence and later in the mediastinum without any metastasis in the ipsilateral axilla and other organs. This no classical pathway of recurrence shows that breast cancer could present very strange behavior when recurrence occurs.



Breast

Risk factors of synchronous breast and thyroid cancer: a controlled multicentric study

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Objective

To identify possible risk factors in synchronous or metachronous breast and thyroid cancers.

Methods

The data from four gynecological clinics: three in Greece (Athens, Alexandroupolis, Ioannina) and one in Germany were collected from June 2017 to June 2020. The statistical analysis was performed with version 20 of the SPSS statistical package. The Chi-square test was used and a p -value <0.005 was considered statistically significant. Patients: The patients were divided into two groups: the first group of 58 patients with breast cancer and a personal history of thyroid cancer. The second group (control group) included 50 patients with only breast cancer with the same characteristics: age, parity, type of pregnancy, treatment for sterility, polycystic ovaries, regularity of the menstrual cycle, breast density, BMI, family history of cancer, blood group, and histological results of breast cancer.

Results

The only factors related with the association of breast and thyroid cancer were: history of abortion and multiparity [more than one delivery ($p < 0.001$)]. An immunological disorder is probably related.

Conclusions

Among many risk factors, the patients of our study with higher number of pregnancies or abortions developed more frequently thyroid cancer plus breast cancer. These findings should be confirmed with larger series.



Contraception

Usability and efficacy of an atraumatic uterine cervical traction device during IUD placement: a pilot study

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ASPIVIX SA

Alignment of the uterine cervix with the vaginal canal is often required during insertion of an intrauterine contraceptive device (IUD). Currently, the available instruments are traumatic tenacula, which could cause pain and bleeding and therefore represent an obstacle for certain patients to pursue their medical follow-up. Aspivix™ is a new device, which enables atraumatic traction of the cervix while respecting its specific semi-circular anatomical shape through a system enabled by a vacuum chamber.

The pilot study is a single arm non-comparative study. This aim is to assess the usability, the safety and the efficacy of the device in a minimum of 10 women received IUD using this atraumatic device. We prospectively collected the device efficacy (ability to insert IUD with Aspivix™ device alone without recourse to conventional tenaculum), usability (number of placements attempts before traction can be applied, number of spontaneous releases), safety (adverse events, cervical bleeding and ecchymosis), patient-reported pain scores at specific time points during IUD insertion procedure and patient satisfaction.

13 participants were included. 11 participants had a successful IUD insertion, 7 with Aspivix™ device alone (54%) and 4 after switch to standard single tooth tenaculum. 2 out of 13 participants (15%) experienced IUD insertion failure irrespective of the device used – Aspivix and tenaculum - due to cervical stenosis. The usability of the device was satisfactory in 77%. In 9 out of 13 cases, the practitioner reported spontaneous releases of the device from the grasped tissue. No bleeding or only limited ecchymosis were caused by the Aspivix™ device. No adverse events were reported. Participants reported almost no pain while the Aspivix™ device was applied. The participants, who had the IUD insertion achieved with Aspivix device alone strongly agreed that they were overall satisfied with the procedure.

The Aspivix™ device can be used to hold and manipulate the cervix during IUD insertion with efficacy, safety, and usability. Characteristics of the device that are appreciated by the practitioners included the lack of pain, absence of trauma to the cervix, maneuverability, and ease of use. Its use requires a short learning curve to avoid releases. With the results of this pilot study, a comparative study with the standard single tooth tenaculum will be performed.



Contraception

Spontaneous anterior abdominal wall expulsion of female sterilisation filshie clips - a case report

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Introduction

Filshie clips ligation is a common procedure for female sterilisation. Rarely, Filshie clips may dislodge and migrate through tissue planes (0.6%).

Case

A 35-year-old Chinese lady presented to the Gynaecology clinic with a few-month history of a 6x5cm superficial, firm, tender, and mobile infra-umbilical lump with purulent discharge and surrounding erythema. She was afebrile and her inflammatory markers were not raised.

Obstetrical history included three lower segment caesarean sections via Pfannensteil incision, and Filshie clip postpartum sterilization three years ago. She denied other medical or surgical history.

Computerised tomography showed a 2.1cm hyperdense soft tissue in the infra-umbilical anterior abdominal wall containing two ligation clips.

She opted for conservative management with antibiotics. The clips were expelled spontaneously from the abdominal lump in succession over the next month— both were closed and complete.

Discussion

A literature review on tubal ligation complications revealed one other case report of delayed spontaneous anterior abdominal wall expulsion of Filshie clips. Filshie clips have also rarely been reported to migrate through tissue planes involving bladder, appendix, inguinal canal, vagina, urethra, and rectum. The pathophysiology is unclear. A chronic low-grade inflammatory process – rather than infective – was suggested, raising the possibility of an allergic reaction to titanium or silicone. Incorrect clip application must also be considered.

Conclusion

Spontaneous anterior abdominal wall expulsion of Filshie clips is a rare complication. When patients are counselled for tubal ligation, risks of clip migration and expulsion should be discussed. Sterilisation history should also be sought in females with abdominal pain.



Contraception

Metabolic effects of the 4 mg drospirenone-only pill compared to 75 µg desogestrel

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Context

Progestin-only pills (POP) have less impact on metabolic and haemostatic parameters than combined hormonal contraceptives (CHC). A novel POP containing 4 mg drospirenone (DRSP; 24/4 intake regimen) with a contraceptive efficacy comparable to CHC, a good cardiovascular safety profile and a highly acceptable bleeding profile has been marketed. Its influence on metabolic and haematological and haemostatic laboratory parameters compared to a POP with 75 µg desogestrel (DSG) is described here.

Objective

Assessing the impact of the new 4 mg DRSP POP on a variety of laboratory parameters including lipid-, carbohydrate-, haematological and bone metabolism parameters as well as coagulation factors compared to the 75 µg DSG POP.

Methods

Prospective, randomized, double-blind, double dummy, multicentric clinical phase 3 trial over 9 treatment cycles. 1,190 participants were randomized to use DRSP 4 mg (24/4) or DSG 75 µg (28 active tablets). Haematology and biochemistry laboratory parameters were assessed in all subjects. In a subset of 68 subjects haemostatic, carbohydrate metabolism and bone metabolism parameters were evaluated.

Patients

1,190 women at risk of pregnancy between 18-45 years.

Main outcome measures

Cholesterol (total, LDL, HDL), triglycerides, fasting glucose, serum insulin, C-peptide, Haematological (Haemoglobin, Red blood cell count, haematocrit) and haemostatic (coagulation factors VII, VIII, Protein C activity, ATIII activity, D-Dimer, APC resistance) parameters, bone metabolism markers (bone alkaline phosphatase, CTX).

Results

Cholesterol (total, LDL and HDL) and triglyceride levels decreased in both groups with a stronger reduction for triglyceride levels in the DRSP group (-0.111 mmol/L (DRSP) vs -0.226 mmol/L (DSG); $p = 0.0351$). No relevant changes were observed for albumin, bilirubin, TSH, insulin, plasma fasting glucose or bone remodelling markers. Differences in the changes of haematological parameters were observed (erythrocytes: mean (SD) changes (DRSP/DSG): -0.022 (0.2810) vs 0.046 (0.065); $p = 0.002$; haematocrit: +0.010 (0.0298)% vs. 0.015 (0.0303)%; $p = 0.043$), but not considered relevant. There was no sign for coagulation induction.

Conclusions

No relevant impact of DRSP 4 mg on metabolic, haematological or haemostatic parameters was observed, confirming the beneficial safety profile of the novel POP.



Contraception

Contraceptive choices of women before and after voluntary termination of pregnancy

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Context

Unplanned pregnancies are a worldwide public health issue. The World Health Organization (WHO) has estimated that 3 out of 10 of all pregnancies end in induced abortion and nearly 50% of all these abortions are unsafe. In Portugal, since 2007, Voluntary Termination of Pregnancy (VTP) can be done before 10 weeks of gestation for non-medical reasons.

A good family planning and the knowledge about contraceptives methods can prevent unplanned pregnancies and be lifesaving.

Objective

In this retrospective study, we aimed to investigate the contraceptive choices before and after VTP in a Portuguese Hospital from January 2010 until June 2021.

Methods

Data was collected from clinical files of women who made a VTP at our hospital, during the considered time period, and analyzed with SPSS.

Results

A total of 5,220 women were included in this study, with an average age of 28 years old (range. 13-48). Approximately 12% were ≤ 19 years-old. 83% of women were Portuguese. The majority of them were employed and 16% were students. Half of them were single and more than 50% studied at least until high school.

Before VTP, 35% of the women were not using any contraceptive method. Previous to the VTP, the most frequent method used was oral contraceptive (37%), followed by preservative (22%) and natural methods (5%). Long-acting reversible contraceptives (LARCs) were only the choice in less than 1% of the population.

When a contraceptive method was used before the VTP the main mentioned reason for failure was the incorrect use of the method, and this was more frequent with oral contraceptives. Approximately 20% mentioned method failure, although the use was correct, and 23% indicated not to know what happened.

After the VTP the preferred contraceptive method continues to be oral contraceptive, however LARCs became more popular, being chosen in approximately 46% of the cases.

Conclusion

Contraceptive choices of women tend to change to more effective methods after the counselling done during the VTP. Said that, we can conclude that easy access to information and contraceptive methods can be one of the tools to prevent unintended pregnancies and their complications.

Portuguese legislation benefits the universal access to family planning appointments and the availability of free contraceptive methods in the National Public Health System.



Contraception

Cardiovascular safety of the new progestin-only pill containing 4 mg drospirenone in a 24/4 regime

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Context

After approval by the FDA and several European authorities, the new progestin-only pill containing 4 mg drospirenone has been marketed on the US market in fall 2019 and in the first European countries in spring 2020. During the clinical development of the pill, the safety profile with a special focus on the cardiovascular risk profile has been evaluated extensively.

Objective

To develop a new contraceptive method with 4 mg non-micronized drospirenone that combines a high efficacy and a profile with low cardiovascular risk.

Methods

Three Phase III studies has been performed: 2 in Europe and 1 in the US. These studies investigated in over 25,000 cycles the efficacy of drospirenone 4 mg and its possible cardiovascular risk profile.

Patients

Women of child-bearing age (18 to 45 years) were recruited. About 41.9% and 16.6% of the patients displayed at least one risk factor for venous thromboembolism.

Main outcome measure

Incidence of venous or arterial thromboembolic events (VTE / ATE), hemostasiological data, blood pressure and ECG data was collected and analyzed.

Results

In all three studies, no single case of VTE was documented. Hemostasiological parameters remained unchanged. In patients with baseline values between 130 and 140 and/or 85 to 90 mm HG a small decrease in RR was observed., while no change was found in normotensive patients. There was no influence on ECG parameter.

Conclusion

The clinical trials document a very high cardiovascular safety profile. Hence, the new estrogen-free oral contraceptive with non-micronized drospirenone in a dose of 4 mg and 24/4 regime expands the options for contraception for women, even for women with cardiovascular risk factors.



Contraception

Satisfaction with LNG-IUS 12 in German women: Findings from the Kyleena® Satisfaction Study

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Context

Prior clinical trials have demonstrated that levonorgestrel-releasing intrauterine systems (LNG-IUSs) are associated with high satisfaction and continuation rates. Here we report the results from German participants in the Kyleena® Satisfaction Study (KYSS), which is the first to provide real-world data on satisfaction with LNG-IUS 12 (also known as Kyleena®).

Objective

To evaluate satisfaction with LNG-IUS 12 in routine clinical practice.

Methods

This prospective, observational, multicentre, single-arm cohort study was conducted in 8 countries, including Germany, from 2017 to 2018.

Patient(s)

Women who independently chose to use LNG-IUS 12 during routine counselling were subsequently recruited into the study.

Main outcome measure(s)

Overall satisfaction rate with Kyleena at 12 months (end of observation) or at premature discontinuation.

Result(s)

In the subset of German participants in KYSS, there were 506 successful LNG-IUS 12 placements, with insertion attempted in 508 women. Of these insertion attempts, 458 (90%) were rated 'easy' by the clinician and 416 (82%) women undergoing insertion rated the pain as 'none' or 'mild'.

The German study population had a mean age of 32.3±8.8 years, and 305 women (60%) were parous. Oral hormonal contraceptives (152 women, 30%), hormonal IUS (94, 19%) or barrier methods (90, 18%) were the most frequently reported methods of prior contraception. The most common motivations for choosing LNG-IUS 12 were the lack of need for a contraceptive routine (174, 34%), high contraceptive reliability (159, 31%) and low hormone dose (158, 31%).

Of the German participants with satisfaction data available, 388/443 (88%) were satisfied or very satisfied with LNG-IUS 12 at 12 months. Satisfaction rates were similar for parous (238/274, 87%) and nulliparous (150/169, 89%) women. The majority (299/406, 74%) were also satisfied with their menstrual bleeding profile at 12 months.

The 12-month continuation rate was 84% (427/508). The majority of discontinuations were due to loss to follow-up (43/508, 9%) or treatment-emergent adverse events (24/508, 5%).

Conclusions

The results from German participants in KYSS demonstrate high satisfaction rates regardless of parity and reflect the suitability of LNG-IUS 12 for a broad population, including nulliparous women.



Contraception

Current landscape of oral contraceptives from gynecologists in Germany

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Context

When prescribing oral contraceptives, gynecologists have the choice between different types of pills: combined as well as progestin-only pills, pills of different molecules and concentrations that translate into various non-contraceptive benefits. This spectrum of oral contraceptives allows the physician to consider the individual needs and health status of the patient.

Objective

The assessment aimed to understand the physicians' perception towards currently available contraceptives, to learn about their treatment choices as well as the factors affecting the treatment choices.

Methods

Eighty-four gynecologists in Germany participated at the computer-assisted web interview. Thirteen different patient profiles were introduced to the doctor. They were asked about their prescribing behaviour of oral contraceptives and the key factors that influence their prescribed product choice.

Results(s)

Young teenager with a normal BMI are considered at lowest risk for deep venous thrombosis (DVT). Gynecologists preferably prescribe combined pills with ethinylestradiol and levonorgestrel for this patient group. In case women smoke or are 40 years or older progestin-only pills become the first choice. A middle-aged woman that smoke 10-20 cigarettes per day is considered at highest risk for DVT. Smoking was the key driver to prescribe progestin-only contraceptives instead of combined pill with levonorgestrel followed by age and BMI. A good safety profile is the most important factor for physicians when prescribing oral contraceptives. Progestin-only pills were associated with the lowest risk for DVT. In line, combined pills with progestins of the 3rd and 4th generation that are associated with an increased risk for DVT are not considered in the daily practice except the combined pill with ethinylestradiol and dienogest to control acne.

Conclusions

The generated data shows that physicians are aware of the thrombotic risk of contraceptives, and it is most important for the doctor to prescribe oral contraceptives with a low risk profile for thrombotic disease. Smoking followed by age are the most important factors that are associated with an increased thrombotic risk leading to the prescription of progestin-only pills.



Endometriosis

Results of spontaneous pregnancy after surgical treatment of endometriosis by systematic peritonectomy of the posterior compartment of the pelvis, series of 91 cases

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Context

Pelvic peritonectomy for endometriosis has been associated with increased fertility rates.

Objective

To evaluate the results of spontaneous pregnancy in a series of 91 cases of women operated on for endometriosis by the same surgeon following the same standardized technique, based on complete peritonectomy of the posterior compartment of the pelvis.

Methods

Observational and descriptive study of a series of 91 patients with infertility due to endometriosis as the only probable cause, operated in the last 6 years by the same surgeon using the same systematized technique and followed up for a period of 18 months awaiting the outcome of spontaneous pregnancy.

Patients

We studied 91 patients with primary or secondary infertility, who had other causes of infertility (tubal, ovulatory and male factor) excluded, with a diagnosis of endometriosis, operated for endometriosis by the same surgeon over a 6-year period. Patients with probable causes of infertility other than endometriosis were excluded from the study. Patients with grades I, II, and III endometriosis (ASRM) were included. The patients studied were between 21 and 39 years old.

Interventions: All 91 patients underwent videolaparoscopy for endometriosis after investigation of the causes of infertility. The surgical procedure was performed using a technique for the most complete possible removal of previously diagnosed endometriotic lesions (physical examination, specialized ultrasound or magnetic resonance imaging). In all cases, complete removal of the entire diseased peritoneum from the posterior compartment of the pelvis was performed.

Main outcome measure(s)

All 91 patients were followed for a period of 18 months awaiting the outcome of spontaneous pregnancy or not. Of these patients, 63 (69.23%) had a positive result for spontaneous pregnancy in the follow-up period. Of these patients, 59 (64.83) of them managed to reach full term with live children, 4 (4.39%) had a miscarriage in the first trimester.

Results

The surgical technique proposed for endometriosis resection promoted spontaneous fertility in 69.23% of the cases studied.

Conclusion

The technique based on the systematic removal of endometriotic lesions by complete peritonectomy of the posterior compartment of the pelvis with rational use of energy, bipolar or ultrasonic, has been shown to be effective in increasing fertility outcomes in patients with endometriosis as the only cause of infertility.



Endoscopy

Contribution of hysteroscopy in recurrent pregnancy loss

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Introduction

Recurrent abortion (RA) is defined as three or more consecutive pregnancy losses at less than 24 weeks of gestation. Since that uterine anomalies (UA) are considered among one of the multiple recurrent pregnancy loss aetiologies, hysteroscopy has been suggested to be one of the routine investigative procedure for recurrent abortions.

Material and methods

Retrospective analysis of 52 cases of recurrent abortions investigated by hysteroscopy. All included women fit the definition of recurrent abortion presented above. In case of uterine anomalies, appropriate hysteroscopic treatment was performed.

Results

Hysteroscopic examination was considered Normal in 35 women (67.3%) and revealed Uterine Anomalies (UA) In the 17 remaining women (32.7%)

*Acquired Anomalies found in 12 women (23%):

- Intrauterine adhesions in 7 women (16.6%)
- submucous myomas in 3 women (7.1%)
- polyps in 2 women (4.8%)

*Congenital Anomalies found in 5 women (14.3%):

- 4 cases of septate uterus
- 1 case of bicornuate uterus

Conclusion

In 25 to 30% of women with recurrent spontaneous miscarriage, hysteroscopy will reveal congenital or acquired uterine anomalies. many of the anomalies detected are amenable to therapy and appropriate hysteroscopic treatment,when applicable, may improve ongoing pregnancy rate.



Endoscopy

Polypectomy for all?

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Context

Endometrial polyps (EP) are a common uterine pathology that affects most frequently post-menopausal women. Although generally considered a benign pathology, the literature mentions the possibility of malignant EP in 0 to 12.9% of all EP. Hysteroscopic polypectomy is the standard treatment for EP with increased dimensions (>2cm) or symptomatic EP. Major bleeding, uterine perforation, fluid overload, thermal injuries and infections are the most frequently mentioned complications of hysteroscopic polypectomy.

Objective

Determine how often complications occur during hysteroscopic polypectomy in the gynecology department in Hospital Espírito Santo Évora (HESE).

Methods

A retrospective study of all patients, from January 2008 to December 2019, that underwent hysteroscopic polypectomy at the gynecology department in Hospital Espírito Santo Évora (HESE), comprising a sample of 1676 women. Hysteroscopic polypectomy was performed with an Olympus® 5mm surgical hysteroscope and Versapoint® system with bipolar electrode (Springle and Twizle), with subsequent histological diagnosis.

Results

A total of 1676 hysteroscopic polypectomies were performed and the mean age of the patients was 60.2 years. Of these women, 40 (2.39%) had malignant EP. There were complications in 42 (2.5%) women, which included vagal reactions in 34 (2.03%) and uterine perforation in 8 (0.48).

Conclusions

In our study, complications during hysteroscopic polypectomy occurred in 2.5% of all of the procedures and the most common complication was vagal reaction. Even though the prevalence of malignant polyp was only 2.39%, we consider that since there is a low frequency of complications, hysteroscopic polypectomy is a valid treatment for all polyps.



Ethics

Workplace bullying among health care professionals

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Context

Conducted at Liaquat University of Medical and Health sciences, a teaching hospital Jamshoro, Sindh, Pakistan.

Target Audience

Post graduate trainees, house officers, medical officers.

Issue

Bullying of doctors is a very serious issue globally. The quality of care of patients is related directly with the performance of healthcare workers, which can diminish if we don't provide safe, healthy, friendly environment to our frontline workers.

Assessment of issue and analysis of its causes

Workplace harassment is a huge issue because of its antagonistic effect on the well-being of affected people. A cross-sectional study was conducted at LUMHS, Jamshoro from 1st January 2021 to 31st March 2021 and it comprised of 75 postgraduate residents, house officers and medical officers. After assuring them of confidentiality, their consent was taken. The doctors then were interviewed by a questionnaire asking them about incidents of bullying, aggression, violence and harassment during duty hours and its social and psychological effects. A MDT meeting was held between the administrative staff, doctors and nurses before starting the the data collection as well as after results, for feedback.

Interventions

Bullying amongst health care workers is a major issue. It has been related with undeniable degrees of occupation instigated pressure, tension, gloom, focus issues, uncertainty, absence of activity and lower levels of occupation fulfilment. Finding ways to stop it will not only improve the quality of life of the doctors but also cause improvement in health system. Strategy for improvement: Departmental policies have been made to tackle the issue. Designated officer has been assigned to look in the complaints. Flow chart of bullying behaviour have been made and posted in every room. The project was presented in the audit meeting and feedback was taken from the doctors, nurses, administrative officers. Dissemination of recommendations was done to the hospital staff via meetings and emails. We will implement the changes in one year time and re audit to evaluate the impact.

Measurement of improvement

The data was entered and analysed using SPSS 22. We concluded that: the main source of undermining or harassing was by administration 12%, Faculty 34%, senior colleagues 42.6%, Colleagues 16%, paramedics 15%, and patients attendants 13%. 26% complaint about the behaviour to higher authorities. The ways of discriminatory behaviours were mocking/scoffing & making hurtful comments in 42.66%, discouragement on work done in 45.6%, giving too much work in 22.6 percent, exclusion from practical workload /OT list in 18.66%. Effects noticed on personality/ behaviour were sadness in 41.33%, aggression 32%, changes in sleep pattern in 12%, headache/palpitations in 34.6%, loss of interest in activities 41.33%, poor performance at work 18.6%, lack of confidence 46.66%, fear to go to workplace 20% and avoiding the bully in 29.3%.

Impact

1. We simplify the pathways for the ways to address this issue. 2. We have highlighted and educated the importance of good workplace behaviour so it improves the quality of life of a doctor and indirectly the care of the patient. 3. It was difficult to extract the data, due to the reluctance of many doctors to participate in this study. Only after assuring them of anonymity and confidentiality, they agreed to participate in this study.

Lessons learnt

Workplace bullying is a problem worldwide and it creates havoc with the lives of the doctors. In order to have a better healthcare system, we need effective measures to tackle this issue and to protect our doctors from it. In future, I would like to question doctors from other departments to see its prevalence there.

Message for others

Serving in safe and healthy surroundings is the basic right of every healthcare worker in order to take healthy decisions and to give quality patient care so policymakers need to take preventive measures to protect healthcare workers from it. Involvement of stakeholders such as patience patients and carers and family members. Post graduate trainees, house officers, medical officers.



Infective Diseases

Epidemiological aspects of COVID-19 in pregnant women in the state of Amazonas, Brazil

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Pregnant women if infected with COVID-19 are vulnerable and considered as a risk group. The objective was to analyze the epidemiological aspects of COVID-19 cases in these women registered by the Brazilian Obstetric Observatory COVID-19 (OOBr COVID-19) and reported from 2020 to 2021 in the State of Amazonas, Brazil. The stratified variables were hospitalization, gestational age, age group, antiviral used in treatment, frequent symptoms, complications, ICU admission, type of ventilatory support and deaths.

A total of 565 diagnosed cases of SRAG by COVID-19 in the Amazon were confirmed, of these 546 (96.6%) of the women required hospitalization, 9 (1.6%) were not hospitalized and 10 (1.8%) did not report. The highest number of cases was recorded in the third trimester of pregnancy 291 (51.5%), followed by the second trimester 130 (23.0%), unreported gestational age 76 (13.5%) and by the first gestational trimester 68 (12.0%). The women affected were predominantly young adults, aged 20 to 34 years 363 (64.2%), followed by 35 years or older 108 (19.1%) and under 20 years 94 (16.6%).

Regarding the antiviral used in the treatment, 283 (50.1%) used Zanamivir and 137 (24.2%) used Oseltamivir, but 145 (25.7%) did not report the medication used. The most reported symptoms were cough 356 (63.0%), fever 335 (59.3%), dyspnea 301 (53.3%), respiratory distress 299 (52.9%), odynophagy 184 (32.6%), low saturation 143 (25.3%), fatigue 94 (16.6%), diarrhoea 68 (12%), vomiting 67 (11.9%), anosmia/hyposmia 56 (9.9%), ageusia 49 (8.7%) and abdominal pain 40 (7.1%).

The most frequently associated complications were asthma 19 (3.4%), diabetes 18 (3.2%), cardiovascular 17 (3.0%), obesity 9 (1.6%), hematological 4 (0.7%), neuropathies 3 (0.5%), immunodepression 2 (0.4%), liver 1 (0.2%), pneumopathies 1 (0.2%) and kidney disease 1 (0.2%). Seventy (12.4%) of the women required ICU, 364 (64.4%) did not need it and 131 (23.2%) did not report it. 108 (19.1%) required noninvasive ventilatory support (NIV), 50 (8.8%) required invasive ventilation (VI), 240 (42.5%) did not need ventilatory support and 167 (29.6%) did not report. Fortunately, 449 (79.5%) of the pregnant women with COVID-19 were cured and only 45 (8.0%) died, but there is no information on 71 (12.6%). Due to complications, and scarcity of information during pregnancy, systematized care and vaccination in this risk group is needed.



Infective Diseases

Assessment of the *in vitro* short time bactericidal activity of two local treatments against bacteria involved in aerobic vaginitis

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Context

Aerobic vaginitis is the name given in 2002 to a vaginal infectious entity which was not recognised as such before. It is one of the most prevalent cause of abnormal vaginal discharge in women after bacterial vaginosis. It is characterized by dysbiotic vaginal microflora containing aerobic, enteric bacteria, variable levels of vaginal inflammation and deficient epithelial maturation.

Objective

To compare the kinetics of bactericidal activity of two antibiotic treatments (combination versus standard) against five common aerobic microorganisms involved in aerobic vaginitis.

Methods

Products tested: Neomycin-Polymyxin B-Nystatin (NPN: marketed vaginal caps) and Clindamycin (standard treatment: initial concentration 20 mg/mL).

Dilutions: 1/2, 1/4, 1/8, 1/16, 1/32, 1/64 and 1/128 (V/V).

Strains: *Streptococcus agalactiae* (Gram +), *Escherichia coli* (Gram -), *Klebsiella pneumoniae* (Gram -), *Klebsiella aerogenes* (Gram -), *Pseudomonas aeruginosa* (Gram -).

The bactericidal activity of each product on the five strains was assessed by dilution-neutralization method according to product dilutions and to the contact time, i.e. 1h and 4h. Assays were performed with serum (10% Fetal Calf Serum) to explore potential interferences. The higher log reduction, the more efficient product/dilution tested.

Results

Gram +: Regarding *Streptococcus agalactiae*, NPN combination showed log reductions higher than 3 log after 1h of contact for dilutions 1/2 to 1/16. The increase in contact time from 1h to 4h, led to progressive reduction of inoculi reaching 4 to 5 log for all tested dilutions. On the contrary, the standard treatment Clindamycin demonstrated no effective bactericidal activity at all tested dilutions after 1h and 4h except a slight bactericidal activity after 4h contact at dilution 1/2.

Gram -: Regarding Gram negative bacteria, NPN presents a global high activity on all tested strains with log reductions higher than 3 log while Clindamycin showed only bactericidal activity after 4h contact at dilution 1/2 and otherwise no effective bactericidal activity at all other tested dilutions after 1h and 4h of contact.

Conclusion

This *in vitro* study, performed in conditions close to use (in the presence of serum, after dilutions and for short contact times), underlines the best bactericidal activity potential of the combination Neomycin-Polymyxin B-Nystatin on the main bacteria involved in aerobic vaginitis in comparison with the reference treatment, Clindamycin.



Fibroids

Cost-effectiveness of Relugolix combination therapy for the treatment of moderate to severe symptoms of uterine fibroids in pre-menopausal women in England

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Context

Uterine fibroids (UF) are common benign tumours that grow within the uterine wall and commonly result in heavy menstrual bleeding and painful periods, which negatively affect quality of life (QoL). Relugolix combination therapy (CT) is a novel long-term pharmacological option for treatment of UF. The efficacy and long-term safety of Relugolix CT have been proven in clinical trials and it has been shown that the use of Relugolix CT, without interruption, could have the potential to reduce or delay the need for invasive surgical options but its cost-effectiveness (CE) has not yet been assessed.

Objective

Estimate the CE of Relugolix CT compared to Best Supportive Care (BSC) in the treatment of moderate to severe symptoms of UF in England.

Methods

A decision analytic CE-model was developed to compare the Relugolix CT and BSC scenarios. BSC was comprised of non-steroidal anti-inflammatory drug (NSAID) and iron supplementation. Both treatment alternatives included withdrawal to surgery as needed and Relugolix CT patients could also withdraw to BSC. The model utilized the perspective of the National Health Service (NHS) in England and the treatment effect of Relugolix CT was derived from clinical trials data using an algorithm that linked reduction in menstrual blood loss (MBL) with improvement in EQ-5D. The robustness of the results was explored via deterministic and probabilistic sensitivity analyses (DSA, PSA).

Patients

Adult pre-menopausal women with moderate to severe symptoms related to UF.

Intervention

Relugolix CT: 40 mg relugolix, 1 mg estradiol (E2), and 0.5 mg norethisterone acetate (NETA) combined in one pill.

Main outcome measures

Lifetime costs and health outcomes, expressed as quality-adjusted life years (QALYs), discounted at 3.5% and combined into an incremental cost-effectiveness ratio (ICER).

Results

The base case comparing Relugolix CT versus BSC showed incremental costs and QALYs of £5,390 and 0.315, respectively, resulting in an ICER of £17,111 which is below the generally accepted CE-threshold in England. The sensitivity analyses showed the ICER was mostly sensitive to changes in the modelled QoL inputs, cost of Relugolix CT and patient monitoring but remained relatively stable and below £20,000.

Conclusions

Long term treatment of symptomatic UF with Relugolix CT instead of BSC is likely a cost-effective treatment strategy in England.



Fibroids

Umbilical parasitic fibroid: a late sequela of laparoscopic myomectomy

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Context

Parasitic fibroids are rare ectopic implantations of uterine fibroid outside of the uterus. It can be spontaneous or iatrogenic in origin. An iatrogenic cause is linked to an unintentional seeding of fibroid fragments during laparoscopic myomectomy or hysterectomy. Superficial implantations in accessory port sites have been described in several cases.

Objective

To our knowledge, this is the first case in English literature which reports a parasitic fibroid at the umbilicus port site, growing not only superficially but also extending intra-abdominally. In this case study, we want to bring across the important message of avoiding uncontained morcellation at all cost to minimize parasitic seeding.

Methods

Written informed consent was obtained from patient for this case study.

Patient

A 53-year-old lady was referred to our center for a growing umbilical mass. Her imaging workup revealed the mass likely to be a dumbbell shaped umbilical parasitic fibroid. This was likely due to a remnant growth from her previous laparoscopic myomectomy done 13 years ago. She underwent total abdominal hysterectomy, bilateral salphingo-oophrectomy and resection of rectus sheath fibroid, joint managed by Gynaecology and General Surgery team. Histology confirmed findings of benign fibroids.

Results

Although parasitic fibroids over port sites are mainly benign, they are a potential dire long-term complication of laparoscopic gynecological surgery. In most cases, patients will require surgical excision for symptomatic relief. To reduce the risk of port site implantation, care should be taken to ensure careful contained morcellation, extraction of specimen, inspection, irrigation and closure after laparoscopic myomectomy. Physicians should be well informed about this risk and provide adequate counselling preoperatively.

Conclusion

It is our responsibility to let patients know about the possibility of dissemination of fibroid fragments during laparoscopic surgery, perhaps requiring future repeat surgeries.



Fibroids

Implications of large fibroids in pregnancy: A multidisciplinary approach

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Context

Fibroids are the most common pelvic tumours in pregnancy, with a prevalence of 10.7% in the first trimester. Most fibroids do not affect pregnancy; however, some may adversely impact pregnancies.

Objective and methods

We report a case of a pregnant lady with large uterine fibroids, documenting her antenatal management, details of her delivery and postpartum interval myomectomy.

Patient

Our patient is a 28-year-old primiparous lady who was booked early with a private obstetrician. Her fetal anomaly scan showed a healthy fetus with no abnormalities. However, it detected large uterine fibroids. In view of the potential maternal and neonatal complications associated with large fibroids in pregnancy, the patient transferred to our hospital for subsidised care.

An MRI Pelvis done at 26+1 weeks showed multiple fibroids with evidence of degeneration. The largest anterior wall fibroid measured 15.3x20.2x23.1 cm. It is inferior to the gestational sac and displaces the fetus superiorly and to the left of the fibroid. This resulted in mass effect on adjacent bowel loops and compression to the right proximal ureter with upstream right hydronephrosis.

A high-risk consult meeting was conducted to discuss the timing of delivery and potential intraoperative complications. The patient was seen by our neonatal, interventional radiology and anaesthesia colleagues pre-operatively for assessment and counselling. She received corticosteroids for fetal lung maturation at 33 weeks gestation.

Intervention and main outcome

She underwent prophylactic internal iliac artery balloon placement and midline caesarean section at 34 weeks. A baby girl with birth weight of 2109 g was delivered. The remaining uterine repair was uneventful. She remained haemodynamically stable throughout surgery and intraoperative blood loss was 500 mls. She recovered well and was discharged on postoperative day 4.

A repeat pelvic scan done 10 weeks postpartum showed an enlarged uterus with fibroids which extended to her upper abdomen. The patient opted for surgery due to constant abdominal pressure from the large pelvic mass.

She underwent an open myomectomy. Intraoperatively, there was a 20 cm necrotic and degenerated looking posterior wall intramural fibroid and 2 anterior wall subserosal fibroids measuring 6 cm and 1 cm. The total intraoperative blood loss was 1200 mls. She was transfused with 3 pints of packed cells intraoperatively.

Result

She recovered well postoperatively, histopathology returned as benign leiomyomas and she remains asymptomatic with regular menstrual cycles. Her most recent pelvic scan done 18 months post myomectomy was normal, with no fibroids detected.

Conclusion

Our case demonstrates the importance of multidisciplinary care, adequate counselling and anticipation of potential intraoperative complications in the management of a patient with high-risk pregnancy.



Genetics & Genomics

Translocation (11;22) in couples with reproductive disorders

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Context

The most common recurrent constitutional translocation in humans is the t(11;22)(q23;q11), due to a highly specific Alu-mediated recombination. The clinical features of t(11;22) carriers are variable according to the translocation form (balanced or imbalanced). Balanced translocation carriers have often a normal phenotype whereas their offspring may have the derivative 22 and Emanuel syndrome.

Objective

Here, we determine the clinical features of this translocation among patients presenting in our genetic counselling for reproductive disorders between 2000 and 2010.

Methods and patients

We retrospectively investigated a 10-year interval of our experience of genetic counselling for reproductive disorders at the medical university of Sfax in Tunisia. We reviewed medical files and medical genetics counseling charts of t(11;22) carriers patients.

Results

Among 3000 consultations, only two familial t(11;22) were recorded in two Tunisian unrelated male patients. The first case was infertile (3 years of primary infertility) with severe oligozoospermia (4,8M SPZ/ml) and a personal history of three failed ART attempts. In his paternal family history, there were many cases of ocular malformations and mental retardation. The second was the father of a dysmorphic male having a severe mental retardation with autistic traits and behavioral troubles (particularly hyperphagia and difficult controlled food-seeking). Cytogenetic formula were respectively: 46,XY, t(11;22) (q24;q11) and 46,XY, t(11;22) (q23;q11). The malformed child of the second patient had an unbalanced form of the t(11;22) translocation. He carried the derivative der(11) chromosome and missed one of the two chromosomes 22: 45,XY,-22, der(11) t(11;22) (q23;q11).

Conclusion

This study showed the paternal origin of the t(11;22)(q23;q11), the variability of reproductive disorders in male carriers who may manifest infertility, recurrent pregnancy loss or the birth of unbalanced offspring and the occurrence of another form of 3:1 meiotic segregation with tertiary monosomy and a derivative 11 encompassing a part of chromosome 22. Live birth karyotype included a single chromosome 22 and was compatible with an unbalanced partial monosomy 22. We conclude that chromosome and molecular studies must be offered to t(11;22) families, in particular sperm and preimplantation genetic testing to provide couples with appropriate genetic counseling and the necessary information regarding their reproductive risk.



Genetics & Genomics

Caplin-10 gene involvement in risk occurred in polycystic ovary syndrome in Tunisian population

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Context

PCOS is a multifactorial disease influenced by both environmental and genetic factors. Given the relationship between PCOS and type 2 diabetes mellitus (T2DM) or impaired glucose tolerance, several T2DM candidate genes have shown significant evidence for a genetic contribution to PCOS pathogenesis including CAPN10. However, recent studies on the relationship between CAPN10 and PCOS remain highly controversial potentially owing to high variation of single nucleotide polymorphisms (SNPs) frequency in CAPN10 between ethnic populations.

Objective

The aim of the present study was to investigate the possible role of the CAPN10 gene polymorphisms UCSNP-43 (rs3792267), UCSNP-19 (rs3842570) and UCSNP-63 (rs5030952) in conferring susceptibility to PCOS in Tunisian women.

Methods - Patient(s)

The diagnosis of PCOS was based on the Rotterdam criteria. Clinical information was recorded for all participants. Endocrine (Follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone and progesterone) and metabolic (Glucose levels, insulin, serum lipids) parameters were determined by conventional methods. CAPN10 genotyping was carried-out by direct PCR and PCR-RFLP. Linkage disequilibrium pattern in the genomic region explored was determined by HAPLOVIEW4.2 while reconstruction of haplotypes was done using PHASE 2.1. ARLEQUIN 2.000 was used for phylogenetic distribution of haplotypes in the population and determination of population genetics parameters.

Main outcome measure(s)

Study subjects included 127 women with PCOS and 150 healthy women.

Result(s)

Six haplotypes were observed. We did not find relationship of individual SNP or of their combination as haplotypes with PCOS. However, one haplotype H4 (121) was specifically associated with the obese phenotype of PCOS ($P < 0.025$; OR = 1.72) and correlated with glucose levels ($P < 0.047$; 7.68 ± 0.29 vs. 7.03 ± 0.19). Moreover the pair of haplotypes 112/121 (H1/H4) was strongly associated with high blood-pressure in PCOS group ($P < 0.012$; OR = 14.4).

Conclusions

Our findings confirms that CAPN10 is implied in metabolic disturbances in PCOS and highlights the role of haplotypes as strong and efficient genetic markers. Although no SNP taken alone displays a reliable association with the susceptibility of PCOS, they yet may be associated with various phenotypes of the disease. Further analysis among large series of Mediterranean or African women should be conducted.



Genetics & Genomics

Turner syndrome genotype and phenotype correlation

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Turner syndrome (TS) is the most common sex chromosomal abnormality seen in females affects 25 to 50 / 100 000 live female births. It is characterized by the absence of all or part of a second sex chromosome which results in a variety of clinical features. Major clinical features of TS are short stature and primary amenorrhea. Different karyotype abnormalities may cause different phenotypic features.

In this study the main objective was to find out the correlation between the cytogenetic abnormalities and the phenotypic features in patients with Turner syndrome.

In our study we enrolled 130 patients, their age ranging was from 1 year to 55 years, The mean age at diagnosis 16 years. The most frequent reason for consultation is short stature in 50%, primary amenorrhea in 17% of cases, in 15% of cases suspicion of TS and 8% confirmed diagnosis of TS. The Fish study is practiced in 23% of karyotypes. The cytogenetic abnormalities were, 43% monosomy, 25% simple mosaic, 17% isoXq, 8% structural abnormalities, 3% triple X, 4% with Y chromosome. The low birth weight is found in 44% of cases. Neonatal lymphoedema is found in 32% of cases. Stature delay was severe in 56% of cases (-4 SD). For clinical dysmorphism we found 19.23% of severe phenotype, 28.46% of moderate phenotype, 31.53% of light phenotype and 20.76% absent. 100 patients reached the age of puberty during follow-up, a complete spontaneous puberty with menarche occurred in 19 patients (19%). Cardiac exploration by echocardiography and cardiac MRI returned pathologically for 46% of patients, there are five patients operated on for cardiac malformations. For the correlation study; There are positive and significant genotype phenotype correlations for neo-natal lymphoedema more found in the two groups: monosomy and iso Xq. For spontaneous growth and final height without GH treatment the shorter one for both monosomy and iso Xq groups. The most severe dysmorphic syndrome in the monosomy. Spontaneous puberty more common for mosaic at 41%. More pronounced ear deafness for the monosomy group, higher AMH levels for the mosaic group, and higher FSH level for the monosomy group.

The phenotype / genotype correlations are not significant for birth weight, age at diagnosis, BMI, final height with GH, cardiac and renal abnormalities, autoimmune disorders (hypothyroidism and celiac disease), hepatic and bone abnormalities.



Genito-urinary syndrome

Condition of the mucous membrane in postmenopausal women with cystocele III- IV stage POP-Q

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Context

Surgical treatment of postmenopausal women with stage III-IV genital prolapse (GP) presents significant difficulties due to the duration of the disease against the background of pronounced structural changes in the tissues of the urogenital tract. Objective. To study the effect of local forms of estriol, progesterone in combination with lactobacilli on the histological features of the vaginal mucosa in postmenopausal women with cystocele III-IV stage POP-Q.

Methods

All patients underwent clinical and laboratory examination: general and gynecological examination, morphological examination of biopsies of the mucous membrane of the anterior wall of the vagina. Patients. The study involved 70 women with GP III, IV stage POP-Q in combination with genitourinary menopausal syndrome. The patients were randomized, blindly, into two groups. Interventions. In the first (1) group, vaginal forms of estrogen, progesterone, and lactobacilli were used as preoperative preparation. In the second (2) group, preoperative preparation was not performed.

Results

It was revealed that the most characteristic changes in the vaginal mucosa in postmenopausal women with genital prolapse are focal dystrophy, moderate infiltration with mononuclear cells, as well as acanthosis and hyperkeratosis. A decrease in the intensity of the inflammatory process in the vaginal mucosa was found in the 1 group. Probably, this effect can be explained by the anti-inflammatory effect of progesterone and the ability of lactobacilli to form biofilms. A decrease in the severity of dystrophic processes in women of the 1 group was established. Obviously, this is due to the influence on the processes of proliferation and differentiation of cells of the vaginal epithelium under the influence of estriol and progesterone. High expression of ER-a in the basal, intermediate, and superficial layers of the vaginal epithelium in women of the 1 group was determined, while the expression of ER-b is less pronounced but exceeds the indicators of women in the 2 group.

Conclusion

The use of local therapy at the stage of preparation for surgical treatment with the use of vaginal forms of estrogen, progesterone and lactobacilli preparations can reduce the intensity of the inflammatory process in the vaginal mucosa, reduce dystrophic changes and their severity due to the complex effect on the processes of proliferation and differentiation of the vaginal epithelium and activate regeneration processes in tissues.



Gynecological endocrinology

Resistant ovary syndrome (Savage syndrome)

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Introduction

Patient with the resistant ovary syndrome are distinguished from those with premature ovarian failure by the presence of follicles in the ovary. Ovarian biopsy is done to test for primordial follicles in the ovaries. The resistant ovary syndrome is rare.

Case report

A 27-year-old null gravid woman presented with of secondary amenorrhea and infertility. Her menarche occurred at 16 years of age and was followed by fairly regular menstrual cycles of 30-35 days until the age of 21. When the cycle length changed to 40-60 days. At that time, her menses became more irregular, until they eventually ceased at 25 years of age. Routine laboratory tests showed serum FSH levels of 19-29 IU/mL (normal levels: 2-8 IU/MI) and LH levels of 16-30 IU/mL (normal levels: 2-15 IU/MI). The E2 level was less than 25 pg/ml. Serum levels of prolactin, androstenedione and DHEAS were normal. The inhibin level was 52 pg/mL (normal level \geq 45 pg/mL). Thyroid and adrenal hormone levels were normal, and no auto-antibodies against thyroid, adrenals or ovaries were detected. Karyotype was 46XX, laparoscopy was performed for ovarian biopsy.

The patient was then treated for hormone replacement with 2mg ethenylestradiol and 5 mg norgestrel per day administered sequentially for 3 months.

Discussion

Premature ovarian failure occurs in 1% of all women and in 0.1% of women younger than 30 years of age. This condition is characterized by secondary amenorrhea, infertility, hypoestrogenism, and elevated gonadotropin levels. Although premature ovarian failure is usually irreversible, some therapeutic approaches have resulted in successful folliculogenesis and ovulation in patients with a normal female karyotype.

Conclusion

The laparoscopy and ovarian biopsies are mandatory parts of the diagnostic procedures in younger women suffering from hypergonadotropic hypogonadism. We can speculate that improvements in *in-vitro* oocyt maturation techniques may offer hope for fertility in women with this syndrome.



Gynecological endocrinology

Puberty and fertility in girls with Turner syndrome study of 70 cases

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Background

Gonadal dysgenesis in Turner syndrome (TS) is the result of massive apoptosis of the oocytes during fetal life. Though the large majority of women with TS have dysgenetic gonads.

Objective

The aim of this study is to evaluate clinical and hormonal characteristics of puberty in young girls and adolescents with TS according to their age and to their karyotype.

Methods

This is a prospective study follows for 5 years a total of 70 girls with TS confirmed by karyotype. All the patients underwent routine clinical visits during which thorough clinical examinations including pubertal staging. Serum concentrations of FSH, LH, AMH and estradiol had previously been determined at standard clinical visits. Pelvic ultrasonography, and BMD were performed. Karyotypes Diagnosis of TS was confirmed by karyotyping using routine G-banding, including counting of at least 10 metaphases.

Results

The 70 patients were divided into four groups with a karyotype distribution of: 31% of the girls with monosomy, 40% with mosaicism, 17% with mosaicism and structural abnormalities and 12% with structural abnormalities alone. These patients were followed in our center between 2013 to 2018, with age range at diagnosis between 3 years to 18 years. mean age was 13 + 4 years. FSH level, pelvic ultrasonography, and BMD were performed. The average FSH of all patients was 55 + 44 ui/ml, according to the Karyotype the patients with mosaicism have the lowest rate (average FSH 36 ui/ml). There was no significant difference between other subgroup. 22% detectable AMH level, and an average AMH of 1.88 ng / ml (13.4 pmol / L). During follow-up, a complete spontaneous puberty with menarche occurred in 19 patients. 9 patients in mosaic group and 4 in monosomy. The average age at puberty induction was 17 + 2.66 years. The ovary/ovaries was/were described for all patients, being seen in 25/70 (35.7%). The BMD performed before and after puberty in 2/3 of the patients. The BMD was low in 75% of cases, and in 25% normal BMD which 50% of them were patients with mosaicism. For the correlation study; There are positive and significant genotype phenotype correlation higher AMH levels for the mosaic group, and higher FSH level for the monosomy group.

Conclusion

Our study demonstrates Although spontaneous puberty and menarche occur more frequently in non-45,X girls, the karyotype cannot be used to predict them. However, the chance of spontaneous menarche can be predicted based on gonadotropin values.



Gynecological endocrinology

Investigation of the receptor potential of the vaginal tract of women with androgen deficiency and female sexual dysfunction

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Context

The main complaint of women with androgen deficiency (AD) is a decrease in lubrication and female sexual dysfunction (FSD).

Objective

Study of vaginal epithelium receptors in women with androgen deficiency and reduced lubrication.

Methods

Immunohistochemical study of androgen receptor (AR) and estrogen receptor (ER) density in the distal parts of the vaginal tract of women of reproductive age 18-35 years. Used commercial immunohistochemical systems LSAB2 SystemHRP (Dako, USA). Statistical processing was performed using methods of variation and correlation statistics.

Patient(s)

We examined (n=16) patients with AD is a decrease in lubrication. 8 women of reproductive age 18-35 years with FSD and AD. The control group - 8 women of reproductive age without signs of FSD and AD.

Intervention(s)

Biopsy of the lower third of the vaginal mucosa using a dermopunch with a diameter of 3 mm.

Main outcome measure(s)

Immunoreactivity in the epithelium was 61.3% (55.7; 65.7), in the stroma 23.7% (14.3; 43.9), respectively (p <0.01). In the epithelial layer, the amount of ER was 73.8% (60.8; 87.2) against 52.1% (49.6; 54) in the stroma (p <0.05). The share of AR-positive cells in healthy women was insignificant and was 6.6% (3.6; 16.5), which is significantly lower compared to women with androgen deficiency 13.2% (7.2; 32.3) and others receptors.

Result(s)

The distribution of EP α reflects their participation in the regulation of the processes of proliferation and differentiation of the vaginal epithelium under the influence of E2. 8 women in the control group of the same age had a higher (2.3 times) density of EP α . EP β was detected in cells of the basal-parabasal layer, the intermediate layer and in isolated cases the surface layer of the vaginal epithelium. According to the results of immunohistochemical study of AR in the vagina, the proportion of AR-positive cells in healthy women was insignificant and amounted to 6.6% (3.6; 16.5), which is significantly lower compared to women with androgen deficiency 13.2%, 2; 32.3). Androgen deficiency and an increase in AR in the vaginal epithelium may cause a decrease in steroid-dependent lubrication.

Conclusions

2.3-fold increase in the density of stained EP α in women of the control group indicates the involvement of regulation of the processes of proliferation and differentiation of the vaginal epithelium.

The localization of androgen receptors (AR) in the basal layer indicates the safety of using local forms of androgens to overcome the reduction of lubrication.



Gynecological endocrinology

The effectiveness of therapy with myoinositol and D-chiro-inositol in a ratio of 5:1 in the treatment of clinical and biochemical hyperandrogenism, as well as improving the psychoemotional state of patients with polycystic ovary syndrome

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Context

Polycystic ovary syndrome (PCOS), which occurs in 5-15% of women of reproductive age, is manifested by anovulation and hyperandrogenism. Hirsutism and acne are the main clinical signs of hyperandrogenism. The combination of myoinositol (MI) with D-chiro-inositol (DHI) can normalize the hormonal profile of patients with PCOS and manifestations of androgen-dependent dermatopathy.

Objective

To evaluate the effectiveness of the combination of MI and DHI in a ratio of 5:1 in the treatment of acne and hirsutism and reducing the level of androgens in the serum blood. To analyze the level of anxiety and quality of life in patients with PCOS after 6 months of therapy.

Methods

An interventional single-center prospective study was conducted on the basis of the Department of Obstetrics and Gynecology No1 of the Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation from October 2020 to March 2021.

Patient(s)

The study included 47 patients with PCOS aged 26.5 ± 3.65 years with biochemical and clinical signs of hyperandrogenism.

Intervention(s)

The severity of hirsutism was assessed on the Ferriman-Gallway scale and acne according to the classification of G. Plewig, M. Kligman, in the study group of patients with PCOS. In all patients the following hormonal parameters were determined: luteinizing hormone (LH), follicle-stimulating hormone (FSH), anti-Muller hormone (AMH), dehydroepiandrosterone sulfate (DHEAS), total testosterone (total T), sex hormone binding globulin (SHBG), androstendione, free testosterone (free T) and free androgen index (ISA) were calculated. After receiving informed voluntary consent, patients with PCOS received an oral combination of 1000 mg MI and 200 mg DHI in a ratio of 5:1, 2 times a day after meals for 6 months. The hormonal profile of the patients was compared initially and after 6 months of therapy. Also the degree of anxiety on the Spielberg-Khanin scale, as well as the dermatological index of quality of life (DIQH) were determined initially and after 6 months of therapy.

Main outcome measure(s)

After 6 months of therapy of an oral combination of 1000 mg MI and 200 mg DHI in a ratio of 5:1, there was a decrease in the level of LH (8.1 ± 2.6 compared to 12.5 ± 4.5 IU/l, $p=0.001$), DHEAS (7.8 ± 1.2 compared to 8.4 ± 1.2 nmol/l, $p=0.013$), total T (1.7 ± 0.5 compared to 2.6 ± 0.6 nmol/l, $p=0.001$), free T (20.8 ± 5.7 compared to 34.2 ± 9.9 pmol/l, $p=0.001$), androstendione (11.6 ± 2.3 compared to 13.9 ± 2.5 nmol/l, $p=0.001$), ISA (2.8 ± 0.9 compared to 5.6 ± 2.1 , $p=0.001$).

Result(s)

Initially, acne was detected in all patients with PCOS: 21 (45%) had a mild degree, 18 (38%) had a moderate degree, and 8 (17%) had a severe degree, as well as hirsutism of varying severity. After 6 months of therapy, there were significant improvements in the treatment of acne. Total disappearance of acne was observed in 15 (32%), mild degree of acne was in 18 (38%), moderate degree of acne – in 12 (26%) and severe degree of acne – in 2 (4%). A decrease in the number of patients with severe and moderate hirsutism was by 7 and 9%, respectively. The score in points on the Ferriman—Gollway scale also decreased (8.7 ± 3.5 compared to 9.9 ± 4.2 points) ($p=0.056$). After 6 months of therapy the degree of anxiety significantly decreased, the number of patients with a slight effect of acne on the quality of life increased by 32%.

Conclusions

The results of the study showed that the combination of myo-inositol with D-chiro-inositol in the ratio of 5:1 can be considered as an effective treatment for correcting biochemical and clinical hyperandrogenemia in patients with polycystic ovary syndrome. There was an improvement in the psychoemotional state of the patients due to a decrease in anxiety and an improvement in the quality of life.



Gynecological oncology

Characterization of cognitive function in female classified as premenstrual syndrome by mood scores

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Accurate diagnosis of premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) is difficult because their symptoms range from physical to mental symptoms, and many adult women complain of such symptoms.

Objective

This study aimed to establish an objective method to identify PMS based on the female's mood and cognitive functions.

Methods

The subjects comprised 19 Japanese female aged 20–22 years, who were categorized by a gynecologist into three groups: PMDD (3 subjects), PMS (5 subjects), and non-PMS (11 subjects). During their follicular and luteal phases, the participants were subjected to perform the abridged Japanese version of the Profile of Mood States 2nd Edition (POMS) and the N-back task, which is a test of cognitive function. The oxyhemoglobin level around the frontal lobe was also measured during the N-back task by near-infrared spectroscopy.

Result

The subjects were clustered by Word method using their scores on the sub-items of POMS. In the follicular phase, two clusters were formed. Cluster 1 consisted of nine non-PMS female, who scored higher on items “Friendliness” and “Vigor-Activity”. All subjects in the PMS and PMDD groups were classified as Cluster 2. In the luteal phase, there were also two clusters: Clusters 1 and 2 comprised 12 and 7 subjects, respectively. Both clusters included subjects who were classified as PMDD, PMS, or non-PMS. We also calculated the integral value of oxyhemoglobin during the performance of the N-back task. The integral value represents the total amount of change in the oxyhemoglobin level and the level of brain activation. The integral values were significantly lower in Cluster 2 than in Cluster 1 ($p = 0.27$), and there was no difference in the luteal phase. The percentage of correct responses to the 2-back task was also significantly lower in Cluster 2 than in Cluster 1 ($p = 0.45$). These findings reveal that the female in cluster 2 had lower performance on cognitive task during the follicular phase.

Conclusions

The mood scores and the cognitive function during the follicular phase would be the parameters to identify PMDD/PMS from non-PMS.



Gynecological oncology

The trends of cervical cancer rates over two decades in Romania

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Context

Although cervical cancer mortality can be prevented through vaccination, screening, treatment of precancerous lesions, and widespread access to the diagnosis and treatment of invasive cancer, cervical cancer continues to be a global public health problem, with 56,987 new cases annually and 311,365 deaths per year; in 2018, low- and middle-income countries contributed with 52% and respectively 60% of these figures, due to the failure to implement prevention programs.

Methods

We analyzed the number of deaths and the mortality rates by cervical cancer, and also standardized rates using the direct method, over two decades.

Main outcomes

Romania, the eighth largest country and the sixth biggest population in Europe, has the highest proportion of rural population among European Union (EU) member countries. The epidemiological profile of cervical cancer is extremely unfavorable among women in Romania. In 2018, the vaccination rate for the 11-14 age group was below 10%, and the incidence of cervical cancer was 19.5 / 100,000 women, respectively 54% more compared to the European average. Cervical cancer screening is theoretically accessible to entire population, but participation rate remains particularly low (5% of the annual target for cervical cancer screening in 2018). In the period 2001-2016 there was a reduction of mortality by 58% in the EU and 56% in Romania, which, however, remains with the highest rate in Europe, 3.7 times higher than the European average. Of the 32,558 preventable deaths from cervical cancer registered in Romania between 2001-2019, 61% occurred in women under the age of 65, and 14% of them in young women under the age of 44. In the country, the rural population continues to be disadvantaged. Despite a greater reduction in rural mortality compared to urban mortality, the rural-urban mortality gap still accounts for 24% of the national rate in 2019.

Conclusions

Given that cervical cancer mortality rates are higher in Central Europe and East, the EU needs to step up the creation of accessible opportunities and changes related to cervical cancer screening, in order to reduce the mortality gap among EU Member States, and Romania needs to radically change the design of population screening.



Gynecological oncology

Primary solitary lymphoma of the uterine cervix: a case report

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Lymphoma is a common malignancy derived from cells of the immune system. Two anatomical groups are recognized. Nodal lymphomas affecting lymphatic nodes and tissues such as spleen or thymus and extranodal lymphomas affecting organs and tissues out of the lymphatic system, female reproductive organs included. Lymphoma of the uterine cervix is a sporadic disease, standing for a less than 1% of primary cervical tumors. It requires precise diagnostics and personalised therapy as no guidelines are available due to its rareness. Surgery, radiotherapy and chemotherapy are being used with almost similar results even when combined.

We present a case of solitary primary lymphoma of the uterine cervix in a 59-year-old woman presenting with postmenopausal vaginal bleeding. Gynecological examination revealed a bulky cervix and diagnosis of the diffuse large B-cell lymphoma was determined by biopsy. Subsequent extensive staging by MRI and PET-CT excluded additional lymphoma spread.

Chemotherapy and biological treatment were chosen as the therapy considering type of the lymphoma, its immunological profile and preference of the patient. After 8 cycles of the therapy no sign of metabolic activity in tumor was revealed by PET-CT imaging and patient was scheduled for a follow-up. She now remains in complete remission for 49 months.

We conclude that the presented case of primary uterine cervix lymphoma was managed successfully, although it needs to be emphasized that every such case is challenging due to often difficult diagnosis, lack of the evidence-based therapy guidelines and rareness of the uterine cervix lymphoma. More cases and widely shared experience will be needed to develop a reliable evidence-based treatment in future.



Gynecological oncology

Allopregnanolone modulate proliferation and migration in human breast cancer cells

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Context

Breast cancer is the most common malignancy in women. Currently, the endogenous progesterone (P4) role of breast cancer is uncertain. The understanding of its effects has been mostly related to the presence of its receptors but there is little evidence of the effect of its metabolites. Allopregnanolone (ALLO) is an active P4 metabolite and serum levels fluctuate similarly to P4 levels. We previously showed that ALLO regulates migration and myelination in Schwann cells through FAK and Src; and we obtained the first evidence that ALLO promotes proliferation, clonogenic capacity and migration in an epithelial human ovarian cancer cell line. Other authors related ALLO to tumoral progression in melanoma and glioblastoma. Nevertheless, its effects in breast cancer are unknown.

Objective

Evaluated the effects of ALLO on cell proliferation and cell migration in breast cancer cells in a two-dimensional (2D) culture, as well in 3D culture.

Methods

T47D and MDA-MB-231 human mammary cancer cells were used. Cells were treated with increasing concentrations of ALLO from 10^{-5} to 10^{-11} M. 2D cell proliferation was measured by MTT assay. 2D-cell migration was measured by a multi-well insert systems. T47D spheroids were performed on 96-well low attachment plate. 3D cell proliferation was measured by Feret diameter. Statistical differences between groups were analyzed using one-way ANOVA followed by Tukey's test.

Results

ALLO increases proliferation in a concentration-dependent manner on T47D (hormone-dependent) and MDA-MB-231 (triple-negative); with a maximum effective range of 10^{-6} - 10^{-5} M ($p < 0.001$ vs control). ALLO significantly increase MDA-MB-231 migration with a maximum effect of 10^{-9} M ($p < 0.001$ vs control). However, ALLO significantly reduced T47D migration (50% of reduction with ALLO 10^{-9} M; $p < 0.001$ vs control). On the other hand, on the 3D-culture T47D cells ALLO stimulates the growth of spheroids in a time and concentration-dependent manner; a maximum effect was observed at 96h with 10^{-7} M ($p < 0.01$ vs control).

Conclusion

ALLO stimulates MDA-MB-231 cell proliferation and migration, suggesting that ALLO may exert its action independent of classical hormonal receptors. ALLO significantly increased T47D cell proliferation on 2D and 3D cell model, but ALLO significantly reduced 2D cell migration. In short, it is difficult to draw an interpretation based on these results, but it may be compatible with the hypothesis that ALLO may be a regulator in tumor progression



Gynecological oncology

Fine-needle aspiration in the diagnosis and management of ovarian masses

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Context

Fine-needle aspiration (FNA) is a valuable tool in the diagnosis of ovarian malignancies to facilitate removal of ovarian masses.

Objective

The objective of this study was to examine the efficacy of FNA over a 10-year period at our institution.

Methods

A retrospective study of all FNA identified from a Pathology Department of a tertiary hospital between January 2011 and June 2021.

Intervention

The cytological findings and results were compared with the histological diagnosis. A retrospective chart review was conducted to retrieve data on clinical course and treatment.

Patients

This study identify 63 cases of ovarian masses sampled by fine-needle aspiration. The overall mean age of the patients was 56 years, whereas the mean age of patients with malignant lesions was 61 years.

Main outcome measure

The cytologic diagnostic was benign in 40 cases (65%) and malignant in 23 cases (35%). Two false negatives cases were noted; two metastatic adenocarcinomas. The falses negative specimens were sampling errors; no diagnostic tumor cells were present in the cyst aspirates. There were no false positive case.

Results

The overall sensibility and specificity of fine-needle aspiration was 92% and 100%, respectively. The positive and negative predictive values for the detection of malignancy were 100% and 95%, respectively. Size of tumor no has bearing of sensibility of FNA. The mean size of malignant tumors detected on the cytology was 10.5cm.

Of the 23 malignant lesions diagnosed on cytology, 13 were treated with primary surgery. Two patients were treated with neoadjuvant chemotherapy due to evidence of advanced stage disease followed by interval surgery. Six patients were treated with palliative care. There were no known complications resulting from the ovarian aspiration.

Conclusions

FNA of an ovarian mass is a minimally invasive procedure that can be considerate as a useful diagnostic modality in certain clinical situations, especially differentiating between benign and malignant lesions, for choosing an appropriate management course. In our study, it was high specific, with excellent positive and negative predictive value.



Gynecological surgery

Therapeutic approach to a very rare case of uterine anomaly of uterus communicans septum with cervix duplex without vaginal septum and Asherman syndrome

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Objective

To report a rare Müllerian anomaly case, discuss its accurate diagnostic ways and hysteroscopic treatment modality.

Method

33-year-old patient with a history of preterm birth, complaints of pain and miscarriage was evaluated both clinically and surgically. Bimanual vaginal and speculum examination showed two cervixes without vaginal septum.

Hysterosalpingography pointed a lower segment septum communicating between two cavities.

Interventions

Diagnostic Laparoscopy revealed the bulge of the uterine fundus so that anomalies associated with bicornuate uterus has excluded. Continuing the intervention, left cervix which was closer to the size and appearance of normal cervix, chosen for hysteroscopic entrance. The immature cervix had closed by an instrument during the session to prevent leakage of distension media. Hysteroscopy showed Uterus Bicervicalis and Subseptatus without vaginal septum. Widespread adhesions, thought to be due to previous curettage, were cleared. The septum resection, until uterine fundal myometrial tissue, were performed, then two open proximal ostium visualized.

Results

Müllerian anomalies are rare and there is no gold standard between their corrective approaches. In our case we did not choose to unify two cervixes, instead we preferred to enclose the smaller cervical os. This modality was assuring for cervical competence and an artificial protection from preterm delivery for future pregnancies. Later on her follow-up, she gave birth with cesarian section on 34th gestational week.

Conclusions

In cases with obstetric problems such as miscarriage and preterm birth, patients should be evaluated comprehensive with vaginal examination and imaging methods. Even after cesarian section, Müllerian anomalies should come to minds. Case-specific treatment should be applied.



Gynecological surgery

Comparison of the effect of Hyalobarier Gel vs 4DryField® PH on the formation of postoperative adhesions after myomectomy - an experimental study in ramli (rabbit)

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Purpose

To compare the effect of Hyalobarier Gel vs 4DryField® PH on the formation of postoperative adhesions after myomectomy in an experimental study in ramli (rabbit).

Methods

30 experimental animals were divided into three groups, A- control, group B- where preparation 4DryField® PH was used and group C - preparation Hyalobarier GEL. Subsequently, a simulation myoectomy was performed. According to the criteria, the antiadhesive effect after euthanasia was evaluated after 21 days.

Results

Statistical evaluation clearly showed a difference in antiadhesive effect in the scoring systems in groups B and C compared to control group A at a high level of significance.

Conclusions

We demonstrated a clearly statistically confirmed antiadhesive effect of Hyaobarrier Gel and 4DryField® PH on an experimental model of uretrus rabbit duplex. The effect of Hyalobarrier Gel is more significant in comparison of both preparations. Based on the results of the experiment, both preparations can be unambiguously recommended for routine practice.



Gynecological surgery

Assessment of women's reproductive health after urgent gynecological surgeries

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Context

Urgent surgical interventions, the frequency of which does not tend to decrease for a long time, can lead to further impairment of women's reproductive health.

Objective

Assessment of the frequency and severity of reproductive health disorders in women of reproductive age who have emergency gynecological surgery.

Material and methods

The state of reproductive health of 200 women aged 19 to 42 years was analyzed 1.5 - 2 years after emergency surgery. Laparoscopic access for "acute abdomen" was performed 121 (60.5%) surgery: for ovarian apoplexy (38; 31.4%), impaired tubal pregnancy (54; 44.6%) and complicated ovarian cysts (29; 24%). Open laparotomy was performed in 79 (39.5%) patients: in 25 (31.6%) due to ectopic pregnancy with massive intra-abdominal bleeding, in 22 (27.9%) - complicated ovarian cyst (torsion or rupture of the cyst capsule), in 16 (20.3%) - due to ovarian apoplexy, in 16 (20.3%) cases due to complicated tuboovarian tumor of inflammatory origin.

Results

The mean age of women was 28.9 ± 6.2 years. Before surgery, menstrual disorders: dysmenorrhea (7; 3.5%), opsomenorrhea (44; 22.0%), abnormal uterine bleeding (16; 8.0%) occurred in 67 (33.5%) patients, inflammatory diseases of the lower genital tract - in 52 (26.0%) women, inflammatory diseases of the pelvic organs - in 11 (5.5%) patients. Reproductive losses (spontaneous miscarriages up to 22 weeks of pregnancy) before surgery were observed in 29 (14.5%) women, 23 (11.5%) patients were examined and treated for infertility. It was noteworthy that after surgery, hormone therapy was prescribed only in 12 (12.6%) of the 95 cases where it was indicated; intraoperative prevention of malignant disease was performed in 17 (8.5%) cases, and postoperative courses of anti-malignant therapy were performed only in 5 (2.5%) cases. Analysis of the state of reproductive function after surgery showed an increase in the incidence of dysmenorrhea (29; 14.5%, $p < 0.05$), menstrual disorders (from 30.0% to 46.5%), infertility (from 11.5% to 22.5%, $p < 0.05$). Non-cyclic chronic pelvic pain developed in 52 (26.0%) patients in the absence of such before surgery.

Conclusions

The lack of pathogenetic justified intra- and postoperative measures after urgent surgical interventions leads to an increase in the frequency of reproductive dysfunction, which requires the development and improvement of differentiated rehabilitation therapy in accordance with the nosology that caused the urgent surgical intervention.



High risk pregnancy

Placental dysfunction and premature labor - issues of priority and interconnection

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Context

Spontaneous premature birth is one of the most important problems of modern obstetrics, as it causes a high level of perinatal and infant morbidity, disability and mortality. The strategy of perinatal risk involves identifying risk groups of pregnant women, in relation to which it is necessary to use predictive tactics, the development and implementation of which is currently a priority task.

Objective

Evaluation of the frequency and timing of the development of placental dysfunction, the course and outcome of pregnancy in women with a history of preterm birth.

Material and methods

A retrospective analysis of the medical records of 300 patients, whose previous pregnancy ended in premature birth, was carried out.

Results

The average age of the analyzed cohort was 29.3 ± 4.2 years. All patients had a history of preterm labor. The frequency of preterm birth in the analyzed cohort was 22.7%, while the population frequency in our region was 5.2%. The course of pregnancy in women with a history of preterm birth was associated with the threat of termination in the early (13.3%) and late (up to 21 + 6 weeks) (18.7%) gestational periods, polyhydramnios (11.3%), preeclampsia (22.0%), premature placental abruption (6.7%), antenatal fetal death (4.7%), premature rupture of the membranes (42.7%). Early formation of chronic placental dysfunction was noted in 81.3% of pregnant women in this cohort, which was manifested by a violation of hormonal homeostasis and utero-placental-fetal blood flow in the period of 30-34 weeks. The risk of very early preterm birth increases 1.4 times, early preterm birth - 1.6 times, which leads to an increase in perinatal morbidity and mortality. Among the disadvantages of managing this cohort of pregnant women, non-systemic examination and treatment at the stage of pregnancy planning, the lack of a differentiated approach to the management of pregnant women with the development of complications of gestation were noted.

Conclusions

A retrospective analysis of the course and outcome of pregnancy in women with a history of preterm birth substantiates the need to improve predictive perinatal and obstetric tactics and introduce these principles into real clinical practice.



High risk pregnancy

The association between the depressive tendencies of mothers with infants after the first month of life and their feelings toward their children

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Context

The incidence of postpartum depression is reportedly 10-15%, indicating a link between child abuse and the lack of social support during pregnancy. In Japan, uninterrupted health measures are provided to pregnant women and infants starting from pregnancy. However, there is inadequate uninterrupted support one month postpartum. Therefore, the relationship between the depressive tendencies of mothers with infants after the first month of life and their feelings toward the infant must be clarified, and uninterrupted postpartum support considered.

Objective

To determine the association between the depressive tendencies of mothers with infants after the first month of life and their feelings toward their children.

Methods

A survey was conducted on mothers with one-month- to one-year-old infants, enrolled in an online medical application, between October 2020 and March 2021. 90 mothers responded and were included in the analysis.

The Japanese version of the Mother-to-Infant Scale (MIBS-J) was used to evaluate the feelings toward the child; higher scores indicated more negative feelings. The Edinburgh Postnatal Depression Scale (EPDS) and Patient Health Questionnaire-2 (PHQ-2) were used to analyze the depressive tendencies. Respondents who scored at least nine points in the EPDS and one in the PHQ-2 were included in the depressive tendency group. To assess the association between depressive tendency and feelings toward the child according to the postpartum time, the respondents were divided into 2-4 (n=15), 5-8 (n=36), and 9-12 months (n=38) after childbirth. The Mann-Whitney U test was used to compare the MIBS-J scores regarding the presence of depressive tendencies based on EPDS and PHQ-2.

Result

In this study, the depressive tendency group comprised 34.1% (n=30) in the EPDS and 44.5% (n=40) in the PHQ-2, respectively. Significant differences were observed in EPDS ($p<0.01$), PHQ-2 ($p<0.01$), MIBS-J scores, as well as 5-8 months after childbirth (EPDS $p<0.01$ and PHQ-2 $p<0.01$). No significant differences were observed in 2-4 (EPDS $p=0.34$, PHQ-2 $p=0.52$) and 9-12 months (EPDS $p=0.08$, PHQ-2 $p=0.08$) postpartum.

Conclusion

Mothers may have depressive tendencies and have negative feelings towards their children even after just one month postpartum. As these negative feelings occur regardless of their depressive tendencies, they must be provided support, such as information on counselling institutions and social resources, to resolve childcare issues.



Infections and HPV

Real-life efficacy of a multi-ingredient *Coriolus Versicolor*-based vaginal gel in high-risk HPV+ women over 40 years old. Sub-analysis of an observational study

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Objectives

High-risk (HR) HPV clearance and resolution of HR HPV-dependent cervical lesions become difficult in peri and postmenopausal women. The objective of this observational study sub-analysis was to evaluate the effect of the Papilocare[®], a multi-ingredient *Coriolus versicolor*-based vaginal gel, on these endpoints in women over 40 years.

Methods

Observational, multicenter, prospective, one-cohort study (PAPILOBS study ClinicalTrials.gov: NCT04199260). Vaccinated or not HPV-positive women aged > 25yo with Pap smear (Ps) of ASCUS or LSIL and concordant colposcopy were included during routine clinical visits in Spain. Patients were treated with Papilocare[®] 1 cannula/day for 21 days during first month + 1 cannula/alternate days for 5 months. After this 6-month period, patients with altered Ps and/or HPV persistency were treated for a 6-month extension treatment period with the same dosage. Analysis of HR-HPV patients with normal Ps and concordant colposcopy image (primary endpoint) and patients with HR-HPV cleared (totally or partially together with negative Ps and normal colposcopy) at 6/12 months in the over 40 years subpopulation is presented. The study was approved by an institutional review board and informed consent was signed by patients.

Results

A total of 69 out of 179 evaluable HR-HPV patients were older than 40yo [mean(SD) age: 48.20(6.01)]. At 6 months, normal Ps and concordant colposcopy was observed in 73.5% (50/68) vs 64.5% (71/110) in younger than 40yo. HR-HPV clearance was observed in 59.7% (40/67) vs 56% (61/109) for older vs younger 40yo populations, respectively. Considering all study period (6 or 12 months), 81.2% (56/69) and 73.5% (50/68) of the older than 40yo patients repaired HR-HPV-dependent cervical lesions and cleared HR-HPV, respectively, in comparison to 72.7% (80/110) and 68.8% (75/109) observed in younger than 40yo. All comparisons were non-significant.

Conclusions

Papilocare[®] showed a clinically significant efficacy repairing HR-HPV low-degree cervical lesions and clearing HR-HPV in women over 40 years in a real-life study. These findings are consistent with the results observed in the Paloma trial (ClinicalTrials.gov NCT04002154).



Infertility

Comparison of ICSI results in a group of patients with and without oral L-carnitine, acetyl-L-carnitine and nutrients supplementation

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Introduction

Supplementation with various minerals, antioxidants and metabolic compounds has been shown to improve oocyte numbers and quality. A study on zinc supplementation showed that oocyte *in vitro* maturation improved preimplantation embryonic development in pigs (Yubyeol 2014). Systemic supplementation with vitamin C may also play a role in human fertilization (Wilson, 1973). The aim of our work was to evaluate the effect of the supplementation with metabolic compounds L-carnitine, acetyl-L-carnitine and specific nutrients on ICSI outcomes.

Material and methods

The study consisted of treating infertile woman with L-carnitine, acetyl-L-carnitine and nutrient during the two months preceding the ICSI cycle. The group of patients underwent hormonal treatment followed by follicular aspiration, intra-cytoplasmic spermatozoa injection and embryo transfer. For each couple, we calculated the rate of oocytes maturation, fertilization rate, cleavage rate, and top embryo rate and noted the presence or absence of pregnancy. 56 infertile women, who consulted at ART Reproductive Center; all women were the partners of men who had failed to conceive after 1 year of unprotected regular sexual activity. Inclusion criteria were as follows: nonsmokers, nonalcoholic women and not using any medication, women in good health by means of their medical histories and clinical examination.

Intervention

It was a prospective study on 56 infertile couples followed over a period of one year (February 2016- February 2017).

Results

The average age of the patients and the duration of infertility were respectively 35 ± 2.1 and 2.8 ± 1.3 years. The infertility origin was male in 70% and the type of infertility was primary in 84%. We obtained from the first cycle of ICSI (without carnitine) an average oocyte maturation rate of 69%, a fertilization rate of 55%, a segmentation rate of 58% and a good embryo rate of 40%.

Conclusion

In women under 35 years old and normal responder, significant improvements were noted in the number of mature oocytes, the type I embryos rate, the blastocyst rate and the type 1 blastocyst rate.



Infertility

Vitamin D concentration, anthropometric and hormonal changes in male patients with and without teratozoospermia

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Context

Teratozoospermia tends to be more common in male patients with obesity, age over 45 years, varicocele, and hormonal pathologies. Little is known about the vitamin D effect on sperm morphology.

Objective

The objective of this research is to determine vitamin D concentration in male patients with and without teratozoospermia and the association of its deficiency with different sperms variables.

Methods

The retrospective cross-sectional study was held by collecting the Infertility Treatment clinic's medical records of patients with and without teratozoospermia. Vitamin D concentration, anthropometric and hormonal changes were analyzed in 152 male patients. Vitamin D insufficiency was defined as 25(OH)D level in serum < 30ng/mL. For the statistical analyse Mann-Whitney U, Kolmogorov-Smirnov, and T-test were used.

Patients

The patients from 18 to 46 years with teratozoospermia (study group=76) and without teratozoospermia (control group=76) were included in the study.

Interventions

Interventions are not applicable.

Main outcome measures

Anthropometric data (age, height, weight, body mass index), hormonal data (thyroid stimulating hormone (TSH), testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH) were compared in the male with teratozoospermia and normal sperm. The level of vitamin D was detected in both groups and semen parameters (count in ejaculate, sperm pH, motility, concentration and morphology) in subgroups with D vitamin deficiency and normal levels were investigated.

Results

There was no statistical difference between the groups regarding age ($p=0.94$) and BMI ($p=0.09$). Vitamin D deficiency was statistically more often detected in patients with teratozoospermia comparing to controls (61.8% vs 38.2%, $p<0.001$). Among the patients with vitamin D deficiency defective sperm tails were confirmed statistically more often ($p<0.001$). There was no statistical difference between the subgroups in respect to FSH ($p=0.9$), LH ($p=0.49$), and TSH levels ($p=0.05$). Varicocele was diagnosed more often in patients with vitamin D deficiency (15.7% vs. 6.4%), approaching borderline statistical significance ($p=0.07$).

Conclusions

This study confirmed the important role of vitamin D on male fertility, particularly, its effect on sperm morphology. Adequate Vitamin D levels should be attained in cases of fertility treatment, especially in the regions where vitamin D deficiency is common.



Infertility

The prevalence of male infertility in correlation with oxidative stress (OS) – based on analysis of diagnostic data

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Context

OS is thought to be an important and probable cause of idiopathic male infertility. There is ample data in the literature on the correlation or causal relations between OS and male infertility.

Objectives

To determine the prevalence of male infertility correlation with oxidative stress based on diagnostic data analysis obtained sequentially in the Lithuania.

Study design

The study consisted of two stages. The first stage of the research included a retrospective study of male infertility using medical records of an infertility clinic. During the second stage of the research, according to the diagnostic Cleveland Clinic algorithm recommendations, a study was carried out to evaluate basic semen analysis and OS. Male infertility oxidation system (MiOXSYS) was used to detect OS.

Patient(s)

In the first part of the study, the retrospective studies were performed in “Infertility clinic” and were based on diagnostic data analysis from outpatient personal health records of 718 infertile couples who applied for infertility for the first time were analyzed. In the second part of the study, the basic semen analysis and “MiOXSYS” were performed on 49 male who applied for infertility for the first time per month.

Results

During the study, 718 couples approached the Infertility clinic, due to causes related to: factors causing male infertility – 234 cases (32.59%) as the leading cause of infertility in 138 cases (19.22%). Asthenozoospermia – 100 males (42.73%), oligozoospermia – 50 males (21.37%), oligoasthenozoospermia – 72 males (30.77%), azoospermia – 12 males (5.13%). Of the basic semen analysis and “MiOXSYS” were performed on 49 male who applied for infertility for the first time. Semen pathology was detected in 31 cases (63.27%), of which OS in 26 cases (87.1%). Normozoospermia was detected in 18 cases (36.73%), of which OS in 3 cases (16.67%).

Conclusion

The prevalence of causes of male infertility in our study is similar to the causes of male infertility provided by guidelines of the European Association of Urology (EAU). The initiated study showed the importance of the OS study, as a link with OS was found in 27 (87%) cases of pathological sperm and 3 (17%) cases of normozoospermia. The study requires continuity and a larger sample of subjects to obtain reliable data. Identifying the cause of changes in the semen opens opportunities for individualized, informed clinical management and treatment of infertility problem.



Labour and delivery

Decision to delivery interval for emergency caserean section

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Context

Conducted at: Altnagelvin hospital, main hospital for the North West of Northern Ireland. Target Audience: Obstetricians, Anaesthetists and Midwifery team.

Issue

It was observed that DDI in some cases was not up to the national standards and it could have been the reason for increase in NICU admissions.

The aim is to improve the quality of care provided to the women undergoing Emergency C- sections.

Assessment of issue and analysis of its causes

Risk management review of emergency sections reported through the Datix system identified the trend towards a prolonged DDI for emergency sections. We retrospectively reviewed the case notes of all emergency sections from July 2020 till February 2021. A MDT was held with midwives and labour ward consultants before starting the data collection as well as after results for feedback.

Interventions

On call registrar or labour ward co-ordinator should take the leadership role to ensure C- section is carried out within the time period. To introduce a structured proforma for documentation of timing of each step, from decision to transfer to theatre, to anaesthesia induction, to skin incision and delivery of the baby, so that it is easy to know where the delay occurs in C-sections.

Strategy for improvement

By introducing a formal drill for emergency C-sections in the home teaching program.

By putting up the posters in labour ward and theatre. By clearly defining the roles of each member of MDT to facilitate communication and effective management. By getting feedback from the staff at the end of the surgery as per WHO checklist and from patient during her stay in postnatal ward. The project was presented in the audit meeting and dissemination of the recommendations was done to the hospital staff via daily messages of the weekend emails. We will implement the changes in six months time and re-audit to evaluate the impact.

Measurement of improvement

Data was collected using Microsoft Excel sheets and analysis was done using Microsoft office. We concluded that: 1. Most delays occurred at the decision to transfer to theatre and anaesthesia induction. 2. Lack of leadership and communication during such C-Sections led to increased DDI.

Impact

We increased the awareness of correct categorisation of C-Sections which led to decrease in DDI in emergency C-Sections. All this led to better standard of obstetric care and improved fetomaternal outcome. Due to the pandemic in some sections it took increase time to wear PP kit. Absence of staff due to the pandemic and thus not complete awareness of the changes implemented amongst them.

Lessons learnt

Role of good leadership, effective communication and proper documentation leads to decrease DDI in emergency sections. I would like to see the psychological aspect also in women and their partners undergoing crash c-sections in future.

Message for others

Encourage good communication, team work, leadership and promote reflective practice for better learning and patient care. The changes led to improved care of labouring patients and promoted better team work and satisfaction. Involvement of stakeholders such as patient carers and family members. Anaesthetics, midwives, quality improvement team, labouring women.



Obstetrics

Post-caesarean section wound infection

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Surgical site infection (SSI) is one of the most common complications following caesarean section, and has an incidence of approximately 5%–10%. It places physical and emotional burdens on the mother herself and a significant financial burden on the health care system. With the global increase in caesarean section rate, the expectation is that the occurrence of SSI will increase in parallel, therefore its clinical significance.

Given its substantial implications, recognizing the consequences and developing strategies to diagnose, prevent, and treat SSI are essential for reducing post-caesarean complications.

Optimization of maternal comorbidities, increasing awareness, evidence-based surgical techniques and use of prophylactic negative pressure dressing in high BMI patients are some of the practices proven to be effective in reducing the incidence of SSI.

In this retrospective audit, we describe the risk factors for its occurrence, average increase in hospital stay, increased financial burden and summarize recent practices adopted to reduce SSI incidence. It is prudent that the surgical team who perform caesarean sections be familiar with these practices and make efforts to reduce SSI rates, to provide safe medical practice is high-quality and adequate costs.



Menopause

The Effects of 17 β -estradiol (E2)/micronized progesterone (P4) on vasomotor symptoms (VMS) and endometrial safety in postmenopausal women

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Context

Bijuva[®] (1 mg E2/100 mg P4, referred to hereafter as 1 mg/100 mg) taken once in the evening, is approved in the US, Canada and in several EU countries. In EU, the indication is treatment of estrogen deficiency symptoms in postmenopausal women with an intact uterus.

Objective

To evaluate the efficacy and safety of 1 mg/100 mg vs placebo in postmenopausal women with moderate-to-severe VMS.

Methods

REPLENISH was a randomized, double-blind, placebo-controlled study that evaluated oral 1 mg/100 mg capsules in postmenopausal women (age 40-65 years) with VMS. Women with ≥ 7 /day or ≥ 50 /week moderate-to-severe VMS comprised the primary efficacy population and were randomized to one of four active treatment doses of E2/P4 or placebo. Women who did not meet the efficacy VMS eligibility criteria were randomized to active E2/P4 doses only. Women who took ≥ 1 capsule were included in the safety population.

Co-primary efficacy endpoints were change from baseline in VMS frequency and severity at weeks 4 and 12 vs placebo.

Endometrial biopsies were performed and assessed by three pathologists. Bleeding profiles (based on daily bleeding/spotting diaries), including cumulative amenorrhea over thirteen 28 day cycles, were analyzed for the safety population.

Results

A statistically significant reduction in the frequency ($p < 0.05$) and severity ($p < 0.05$) of VMS was observed at week 3 and was maintained through week 12 for 1 mg/100 mg vs placebo. Percentage of responders at week 12, a secondary endpoint, were statistically significantly higher in the 1 mg/100 mg group vs placebo for $\geq 50\%$ reduction in VMS frequency (79% vs 58%, respectively; $p < 0.05$) and $\geq 75\%$ reduction in VMS frequency (68% vs 32%, respectively; $p < 0.05$).

Endometrial biopsies at 12 months showed no atypical cells. One case of simple endometrial hyperplasia without atypia was reported by one of three pathologists in the 1 mg/100 mg group.

During months 10 to 12, the amenorrhea rate with 1 mg/100 mg was 82.6% vs 94.6% with placebo. At Cycle 13, the amenorrhea rate was 90.2% with 1 mg/100 mg vs 97.8% with placebo. Discontinuations due to bleeding occurred in 1.4% of women with 1 mg/100 mg vs 0% placebo.

Conclusions

Bijuva[®] is a novel hormone therapy that improves moderate-to-severe VMS frequency and severity in postmenopausal women with an intact uterus and is associated with a high amenorrhea rate. Micronized progesterone, as a component of Bijuva[®], was associated with effective endometrial protection.



Menopause

Depressed symptoms and related factors in mid-aged women from Paraguay

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Objective

To determine the prevalence of depressive symptoms and related factors among mid-aged women.

Methods

This was a cross-sectional study in which 216 urban-living women from Asunción-Paraguay (aged 40–60 years) were surveyed with the 10-item Center for Epidemiological Studies Depression Scale (CESD-10) and a questionnaire containing personal and partner data.

Results

The median age of the sample was 48.7 ± 6.1 years, 48.1% were postmenopausal, 8.8% used hormone therapy, 39.4% psychotropic drugs, 43.5% had hypertension, 6.5% diabetes, 44.9% abdominal obesity, and 89.3% had a partner ($n=193$). Mean total CESD-10 score was 5.8 ± 5.6 and 25.5% of women had total scores 10 or more defined as depressed mood. Overall, 93.3% (180/193) of women having a partner were sexually active, with a median coital frequency of 8 times per month. Factors associated with higher CESD-10 total scores were: female age, educational level, marital partner status, menopausal status, psychotropic drugs, oral contraceptive use, sedentary lifestyle, partner age, coital frequency, erectile dysfunction and premature ejaculation.

Conclusion

As determined with the CESD-10 a quarter of this mid-aged urban female Paraguayan sample had depressed mood which was related to sexual, hormonal, partner issues, and other female aspects.



Menopause

A comparative study of efficacy of CO₂ laser treatment alone and in combination with platelet-rich plasma for vulvovaginal atrophy

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Study objective

Compare clinical efficacy of fractional CO₂ laser monotherapy and CO₂ laser combined with platelet-rich plasma (PRP) for vulvovaginal atrophy (VVA): treatment.

Design

A prospective cohort study.

Patients

The study included 48 women aged 49-60 years (median age 54.5) with symptoms of VVA: dryness, itching, burning, soreness, dyspareunia; the period of menopause (duration 2-5 years) without somatic pathology, without prior hormonal therapy, both local and systemic. The follow-up period was 12 months. The patients were randomized into two groups 1:1.

Interventions

Group 1 received CO₂ laser monotherapy (controls); Group 2 underwent CO₂ laser treatment combined with PRP. Each woman received three sessions of CO₂ laser at four-week intervals. Patients of Group 2 had 3 additional PRP treatments of the vulva and vagina 14 days after each CO₂ laser session.

Measurements and main results

The symptoms of VVA were assessed before the first session and 1, 3, 6, and 12 months after laser treatment. The findings were assessed using a questionnaire (Visual Analogue Scale), the Vaginal Health Index (VHI), including pH and assessment of vaginal cell maturation, the Vulval Health Index (VuHI), the Female Sexual Function Index (FSFI), the Quality of Life Inventory (QOLI), and the Satisfaction with Life Scale (SWLS).

Both groups showed reduction of VVA symptoms, improvement in vaginal elasticity, volume, moisture, and pH after the first session. After 3 sessions and within 12 months, the improvement was more pronounced and persistent in the combined treatment group.

The intensity of dyspareunia and vaginal dryness decreased from 9 (5-10) and 8 (0-10) at the baseline to 0 (0-6) and 0 (0-8) ($p < 0.001$). FSFI, QOLI, and SWLS scores increased from 10.4 (2-26.5) and 1 (0-8) at baseline to 27 (15.0-34.8) and 4 (2-8), respectively. The positive effect of combined treatment remained unchanged for 12 months in contrast to laser monotherapy.

Conclusion

The combined treatment with fractional CO₂ laser and PRP significantly increased its efficacy and helped achieve significantly better results in VVA treatment. PRP therapy combined with laser had a synergistic effect and contributed to a longer therapeutic effect. It is advisable to include this combination into VVA treatment algorithm and use it as an effective and safe method of treatment.



Obstetrics

Features of pregnancy and childbirth in women with myocarditis after COVID-19

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Context

Myocarditis in pregnant women is a risk factor for the development of complications of pregnancy and the condition of the intrauterine fetus. Point of interest is that the myocarditis in pregnant women, which developed after undergoing COVID-19. The aim of the study was to investigate the effect of covid-associated myocarditis on the pregnancy and childbirth.

Materials

We examined 25 pregnant women with myocarditis who were admitted for childbirth, who were divided into 2 groups: group 1 - 15 pregnant women with myocarditis who had undergone Covid during pregnancy and group 2 - 10 pregnant women with myocarditis who did not have Covid. The control group consisted of 12 healthy pregnant women. Anamnesis, data on the transferred covid infection, the severity of the disease were studied. PCR tests for covid-19 have been performed. Instrumental studies included ECG, echocardiography and ultrasound of the fetoplacental complex. There were no COVID-19 vaccinated among the surveyed pregnant women. Results. The age of the surveyed was averaged 28.3 ± 5.1 years. COVID-19 was transferred by pregnant women of group 1 in I-trimester - 11 women, in II-trimester - 4. Covid clinic was moderately severe - in 5 pregnant women, it was characterized by fever, cough. These pregnant women were admitted to a specialized hospital. In 10 women, the disease was mild, characterized by minor catarrhal symptoms, loss of smell and appetite, while the PCR test was positive. Myocarditis was first detected in group 1 at 32-35 weeks. The clinical picture of covid-associated myocarditis was characterized by complaints of severe weakness, rapid fatigue, palpitations, and shortness of breath during exercise. All pregnant women of group 1 had a negative PCR test upon admission to the hospital. In group 2 of pregnant women who did not suffer from covid, complaints of palpitations, shortness of breath during exertion, headaches, and swelling of the legs prevailed. Myocarditis was detected at 16-26 weeks of gestation, median 21.2 ± 4.8 weeks. Ultrasound of the fetoplacental complex in pregnant women of group 1 more often (53.3%) revealed signs of impaired uteroplacental-fetal blood flow of I-II degree compared with pregnant women in group 2 (40.0%). Labor was completed by surgically in 66.7% in group 1 and in 50% in group 2.

Conclusions

Covid-associated myocarditis develops in the third trimester of pregnancy is more severe and is the cause of operative labor.



Obstetrics

Analysis of carbohydrate and lipid metabolism in pregnant women with metabolic syndrome

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Context

The frequency of detection of obesity during pregnancy is 12.3–38%. Such patients are at 2–3 times higher risk of developing gestational diabetes mellitus (GDM), fetal macrosomia.

Purpose of the study

To analyze the state of carbohydrate and lipid metabolism in pregnant women with metabolic syndrome (MS).

Materials and research methods

Totally 88 pregnant women admitted to the perinatal center were examined. The main group included 48 pregnant women with MS. The comparison group included 25 pregnant women with gestational diabetes mellitus (GDM) with a body mass index (BMI) over 25 kg / m² before pregnancy. The control group included 15 healthy pregnant women. We studied the incidence of complications of pregnancy and childbirth, as well as parameters of carbohydrate and lipid metabolism.

Results and discussions

Pregnancy in women with metabolic syndrome was complicated by the development of a threatened miscarriage by 43.4%; mild preeclampsia - by 22%; severe preclampsia - by 15.8%; fetoplacental insufficiency - by 20.6%; cesarean section was performed in 45% cases compared to the pregnant control group. In the main group, GDM was detected in 70.4%; DM type 2 - in 29.6% of pregnant women. The highest HOMA-IR index was in women with insulin resistance, dyslipidemia and preeclampsia - 4.0, the lowest in women with preeclampsia and dyslipidemia - 2.6. The study of indicators of lipid metabolism revealed the presence of dyslipidemia in pregnant women with MS. In all investigated groups the lipid profile (low density lipoproteins (LDL) (146.91 ± 31.8 mg/dl) was 3 times ($p < 0.05$), triglycerides (201.25 ± 43.5 mg/dl) - 1.8 times, total cholesterol (243.56 ± 31.4 mg / dl) - 1.5 times higher than these indicators in pregnant women of the control group. The level of high density lipoproteins (HDL) was found within normal limits in all groups. The mean value of HDL of the main group was 81.19 ± 29.4 mg/dl, which 1.4 times higher than that of the control group.

Conclusions

In women with MS, pregnancy is more often complicated by miscarriage, preeclampsia, the development of GDM, fetal macrosomia and operative delivery, and is characterized by disorders of carbohydrate and lipid metabolism. This indicates the need for preparation for the planned pregnancy.



Obstetrics

Maternal abdominal and visceral fat tissue as predictors of GDM development

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Context

Gestational diabetes mellitus (GDM) is defined as glucose intolerance diagnosed in pregnancy; it is the most common metabolic complications of pregnancy, and it affects up to 15% of women, with great discrepancies among different studies. The increased prevalence of maternal obesity is a major factor in developing GDM.

A recent but reliable marker to quantify the amount of central fat is the ultrasound measurement of abdominal subcutaneous fat thickness (ASFT), which has been recently proposed in pregnancies, suggesting its possible role in predicting GDM and other metabolic alterations. Very little is known about the role of renal adipose tissue, as markers of maternal visceral fat (VAT).

Objective

To evaluate the effect of the sonographic measurement of maternal ASFT and VAT early in the first trimester of pregnancy as predictor GDM development.

Methods

Adipose subcutaneous and renal thickness was measured by transabdominal ultrasound in 454 consecutive pregnant women attending our antenatal clinics at 11-13 weeks' gestation. All women were followed longitudinally until birth. Data regarding fasting glycemia, pregestational weight, maternal weight gain, neonatal weight and neonatal centile were collected.

Intervention(s)

75g oral glucose challenge as diagnostic test for GDM, according to local guidelines.

Result(s)

395 women completed the study. 73 women (18.5% of the total) developed GDM.

As expected, women with higher pregestational BMI and higher fasting glycemia in the first trimester were at greater of GDM ($p < 0,001$). Interestingly, age and first trimester weight gain were not linked to GDM. In addition, both ASFT, measured in the lower and higher part of the abdomen, and VAT, evaluated as perirenal fat, were strong predictor in GDM development. However, when corrected for BMI, only ASFT remained statistically significant (lower abdomen $p < 0,001$, upper abdomen $p: 0,011$).

A ROC curve was performed to evaluate specificity and sensitivity of ASFT in the lower and upper abdomen. The sonographic measurement of ASFT in the lower and upper abdomen seemed to have a better specificity (62,75%) compared to BMI alone, but BMI demonstrated a greater sensitivity (79.45%).

Conclusions

ASFT, both in the lower and upper abdomen, seemed to have a crucial role in the development of GDM and the evaluation, in the first trimester of pregnancy, can be an early predictor of pregnancy-related metabolic complications.



Obstetrics

Placental Growth Factor (PlGF) impairs healthy endometrial angiogenesis by disrupting the NFAT5-SGK1 signaling axis

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Objective

Preeclampsia (PE) is a major obstetrical complication with life-threatening consequences for both mother and child. Poor trophoblast invasion through the endometrium into the spiral arteries is implicated in the pathogenesis of PE, although the mechanism of impaired vessel development in the endometrium remains poorly understood. Transcription factor Nuclear Factor of Activated T cells (NFAT5) is sensitive to hypertonic stress and regulates cellular homeostasis. NFAT5-regulated genes include serum and glucocorticoid inducible kinase 1 (SGK1), a key regulator of endometrial function. NFAT5 is reported to mediate pathological angiogenesis driven by placental growth factor (PlGF). In view of those observations, we hypothesized that PlGF may up-regulate the expression of NFAT5-SGK1 signaling axis in human endometrial stromal cells (ESCs) contributing to impaired blood vessel development.

Methods

ESCs were subjected to 20 ng/ml PlGF for 6 days or remained untreated. The effect of PlGF on NFAT5 transcriptional activation was studied using qRT-PCR, western blotting, ELISA, flow cytometry and immunofluorescence. Further, PlGF influence on NFAT5 downstream targets were inhibited using plasmids/inhibitors and quantified using western blotting. Cell proliferation and tube-forming ability were analysed using transwell and HUVEC tube formation assays. Lastly, endometrial NFAT5 gene expression in healthy pregnant and first trimester placentas of preeclamptic pre-symptomatic women (GDS3467) was examined using in silico analysis.

Results

Our results reveal that NFAT5 is activated by PlGF in ESCs. Enhanced NFAT5 levels leads to activation of downstream targets such as SGK1, HIF-1 α and VEGF-A. We also report, PlGF drives uterine angiogenesis by enhancing intercellular ROS production and by controlling inflammatory mediators via SGK1 signaling. Pivotaly, we show that deregulated levels of NFAT5 is associated with PE prior to onset of disease.

Conclusion

In conclusion, aberrant PlGF signaling stimulates the expression of NFAT5, SGK1, HIF-1 α and thus VEGF-A in ESCs. Accordingly, enhanced NFAT5-SGK1-VEGF-A levels increases angiogenesis and could thus contribute to the enhanced risk of pregnancy complications.



POI

Premature ovarian insufficiency - autoimmunological serum parameters and bone mass density

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Context

The prevalence of autoimmune disease in primary ovarian insufficiency (POI) remains unknown. It is still not clear whether women with POI should be screened for autoimmunity. A possible association of autoimmunity with decreased bone mass density in premature ovarian insufficiency patients has not been evaluated.

Objective

The objective was to focus on the incidence of elevated markers for autoimmunity, routinely evaluated in the patient population, as well as on dual-energy x-ray absorptiometry (DEXA) results and serum sex steroid levels to compare bone density (BMD) between POI women with and without suspected autoimmunity.

Methods

In this retrospective cohort study 75 chromosomally normal women who suffered from spontaneous POI and had been referred to the Clinical Division of Gynecologic Endocrinology and Reproductive Medicine from January 2015 to December 2019 were included.

Patients

After exclusion of one person with Turner syndrome, one woman with a fragile X repeat mutation, seven women using estrogen treatment and nine women with missing data, it resulted in a final patient population of 58 women with spontaneous POI.

Interventions

Patients had undergone complete evaluation of hormonal parameters, autoimmune screening and DEXA.

Main outcome measures

Main outcome parameters were the results of an autoimmune screening panel and of DEXA.

Results

Sixty percent of POI women showed abnormal DEXA results (minimal T-score < -1.0). The median age was 33 years. Any signs of autoimmunity were revealed in 21 women (36.2%). The most frequent abnormal results were increased thyroid peroxidase antibodies (24.1%) and thyroglobulin antibodies (20.7%). A longer duration of amenorrhea ($\beta = -0.015$; $p = 0.007$), any abnormality during autoimmune screening ($\beta = -0.940$; $p = 0.010$), and a lower body mass index ($\beta = -0.057$; $p = 0.036$) were associated with a lower minimal T-score.

Conclusions

In untreated women with POI a high prevalence of autoimmune alterations and diminished BMD could be found. Our data highlight the association between autoimmune abnormalities and decreased DEXA results.



Polycystic ovary

The prevalence and impact of polycystic ovary syndrome in recurrent miscarriage: a retrospective cohort study and meta-analysis

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Context

The use of different definitions and diagnostic approaches of polycystic ovary syndrome (PCOS) and recurrent miscarriage (RM) has led to a wide range of prevalence rates in the literature. Despite the persistent controversy about the factual prevalence of PCOS in RM, a vast number of studies have revealed evidence about their association with each other.

Objective

The goals of this study were to evaluate the prevalence of PCOS and polycystic ovarian morphology within the RM population, performing meta-analyses with the obtained data from this study, together with previous reports on this topic and evaluating reproductive outcome in women with RM and PCOS.

Methods

A retrospective cohort study with 452 women with RM and a meta-analysis were conducted. RM was defined as three or more consecutive miscarriages before the 20th gestation week with the same partner. PCOS was diagnosed according to the revised Rotterdam criteria. For the systematic literature review, we searched the Medline database to identify eligible studies and reviews on RM and PCOS and polycystic ovarian morphology.

Patients

All women with RM who underwent evaluation at the Department of Gynecology and Obstetrics of the Medical University of Vienna, Austria, from January 2003 to December 2018 were included.

Interventions

No intervention were used as this is a retrospective study.

Main outcome measures

The main outcome parameter was the prevalence of PCOS in RM patients.

Results

In the retrospective study, the prevalence of PCOS in RM was 9.5%. RM remained unexplained in 283 patients (62.6%). From all evaluated possible underlying causes for RM, only the presence of thrombophilic disorders was significantly associated with PCOS (PCOS: 20.9% versus no PCOS: 7.8%, $p = 0.010$). In the meta-analysis of three studies on PCOS in RM patients, an estimated pooled prevalence of 14.3% was found. In the retrospective data set, women in the PCOS group revealed significantly higher LH, testosterone, and AMH levels than age- and BMI-matched controls with unexplained RM ($p < 0.05$). Further miscarriages were significantly more frequent in PCOS women than in controls ($p = 0.031$).

Conclusions

The prevalence of PCOS seems slightly increased in women with RM. Women with PCOS suffering from RM showed a significantly higher risk for further miscarriage and decreased chances of having a life birth of about 18% which did not reach statistical significance. We assume that PCOS plays a moderate role in RM.



Prenatal diagnosis

Nursing care applied in accordance with humanistic nursing theory in pregnancy termination: a case report

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Context and objective

Pregnancy termination is the process of terminating the current pregnancy in some necessary situations such as fetal anomaly, regardless of the gestational week. Pregnancy termination process is generally performed by using drugs in accordance with international guidelines to ensure the expulsion of the fetus vaginally. In pregnancies older than the twentieth week, it may be necessary to perform a feticide (stopping the heart of the fetus) before the procedure. In this process, the woman goes through painful and uncomfortable processes while trying to cope with her loss. It is thought that this difficult process can be facilitated by nursing care for women. In this study, it was aimed to determine the nursing care needs of a woman who had pregnancy termination.

Methods

Nursing care was planned and applied by accompany and supporting a woman who had pregnancy termination due to fetal anomaly in Akdeniz University Hospital. In this process, observation findings and interviews with the woman were used while planning the care. Observation data together with the nursing diagnoses handled in the care process were reported as the results and conclusions of the study.

Main outcome measures

In the study, the care needs of a woman who had pregnancy termination due to fetal anomaly were determined based on her experiences in this process.

Findings

Ş.Ş. is 27 years old and in her 26 weeks and 3 days old pregnancy, “Cerebellar Vermian Hypoplasia” was detected in the fetus and she was hospitalized for termination. Feticide was made before the termination process. Mrs. Ş. stated that she felt like “educational material” during the procedure while giving feedback on the feticide procedure. For this reason, it has been determined that it is important to adopt a humanistic attitude in approaching individuals. It has been determined that the most prominent care needs during the termination process are related to the lack of information about the medical condition and treatment plan, fear, pain, nausea and the risk for complicated grieving.

Conclusions

A respectful and humanistic approach should be determined, adequate information should be given, and care should be planned to ensure physical-psychological well-being while giving health care to the woman whose pregnancy was terminated due to fetal anomaly.



Prenatal diagnosis

Ultrasound and Doppler findings following the SARS-CoV-2 infections during pregnancy

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Objective

The objective of this study was to investigate the possible effect of SARS-CoV-2 (SARS) infection on fetal growth and vascularisation using ultrasound and Doppler examination.

Methods

Pregnant women enrolled in this study attended the Rīga Maternity Hospital from May till July 2021 after confirmed SARS infection by RNA PCR. Ultrasound examination consisted of fetal anatomy, biometry, biophysical profile (BPP), and transvaginal cervical length (CL). Doppler examination included the interrogation of the umbilical artery (UA), middle cerebral artery (MCA), ductus venosus (DV), and uterine arteries (UtA). All biometry values and Doppler pulsatility indices (PI) were converted to z-scores, percentiles, and compared to controls without SARS infection history during pregnancy, matched by gestational age and parity.

Patients

The study and control group each included twenty-five participants with spontaneous onset of pregnancy. The gestational age of enrolled patients was in the range from 13+1 till 37+4 weeks. The exclusion criteria were gestational diabetes, hypertensive disorders, autoimmune diseases, multiple pregnancies, and smoking history.

Interventions

Interventions are not applicable.

Main outcome measures

The primary study outcome measurements were abdominal circumference (AC), estimated fetal weight (EFW), AFI, BPP, MCA PI, UA PI, UtA PI, DV PI, and CL. The secondary outcome was the evaluation of SARS symptoms.

Results

No fetuses with anatomical anomalies, abnormal Doppler and BPP evaluation were detected in both groups. There were no statistical difference in respect to AC ($p=0,54$), EFW ($p=0,82$), AFI ($p=0,59$), MCA PI ($p=0,88$), UA PI ($p=0,93$), UtA PI ($0,53$), DV PI ($p=0,65$), CL ($p=0,68$) measurements between the study group and controls.

The majority of patients encountered SARS infection during the second trimester (64%) and experienced mild symptoms (88%). The main symptoms were loss of smell and taste, subfebrile temperature, dry cough, headaches, and rhinitis. The average duration of illness was five days. Only 4% of patients required oxygen therapy and hospitalization.

Conclusions

There were no significant differences between women exposed to SARS infection during pregnancy and controls regarding ultrasound findings and Doppler values.

The more frequently observed symptoms of SARS infection in generally healthy pregnant women were mild.



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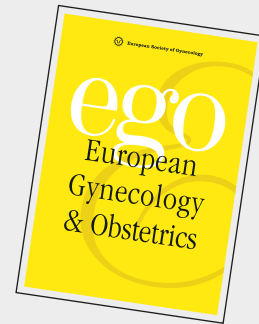
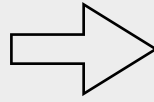
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