Palliative care in gynaecology

Jeannine Gambin [1], Maximilian Brincat [2]

[1] Department of palliative care and oncology, Mater Dei Hospital, Msida, Malta; [2] Department of Obstetrics & Gynaecology, Mater Dei Hospital,Msida, Malta

ABSTRACT

Despite advances in the management of gynaecological oncological diseases patients are still presenting at advanced or terminal stages of diseases. Up to 25% of women diagnosed with a gynaecological malignancy will die from recurrent disease. The art of palliative care is often lacking despite it offering so much relieve of suffering to those who have the disease and their loved ones. The World Health Organisation states that "palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and treatment of other problems, physical, psychosocial and spiritual". During this review we look through the most common challenges faced by patients with terminal gynaecological malignancies, and review how the optimal management of these complications improves the quality of care and therefore life of the patients.

KEYWORDS

Palliative care, pain, analgesia, bowel obstruction, ascites.

Introduction

Despite advances in the management of gynaecological oncological diseases, patients are still presenting at advanced or terminal stages of disease. Up to 25% of women diagnosed with a gynaecological malignancy will die from recurrent disease [1]. The art of palliative care is often lacking, even though it can offer considerable relief of suffering, both to those who have the disease and to their loved ones. We must also consider palliative care in chronic benign gynaecological conditions, such as chronic pelvic pain and lichen sclerosus. Since clarification of the aetiology and therefore a definitive cure may not be possible, such patients will benefit from proper long-term palliative care plans.

The World Health Organisation (WHO) states that "palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and treatment of other problems, physical, psychosocial and spiritual" [2]. The National Institute for Health and Care Excellence (NICE) describes palliative care as "the active holistic care of patients with advanced, progressive illness" [3]. Management of pain and other symptoms and provision of psychological, social, and spiritual support is paramount. A multidisciplinary approach is imperative to manage the multiple modalities that contribute to relieving symptoms. Palliative care is not solely for those who are terminally ill: it may be offered alongside curative care as well as end-of-life care [4].

Multiple randomised trials have shown that the addition of palliative care to usual oncological care either maintains or improves survival [5-10]. In the most well-known randomised trial of routine early integration of palliative care into cancer care, palliative care was associated with statistically significant improved survival [9]. Observation studies concluded that palliative care input led to significant improvements in patient care and symptom control [11-13].

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Contact

Maximilian Brincat; maxbrincat@gmail,com

Department of Obstetrics & Gynaecology, Mater Dei Hospital, Msida, Malta.

For the purpose of this paper, we shall be focusing primarily on palliative care in malignant gynaecological conditions, however similar complications may arise in benign conditions, which will share the same management.

Gynaecological malignancies

Ovarian cancer is the leading cause of death from gynaecological cancer in developed countries, with most patients presenting with advanced stage tumours, as defined by the spread of the disease outside the pelvis (International Federation of Obstetrics and Gynaecology (FIGO) stages III and IV). The estimated number of new ovarian cancer cases in Europe in 2012 was 65 538, with 42 704 deaths [14]. More than two thirds of patients are diagnosed at an advanced stage [14]. Although endometrial cancer has a better survival rate, it is the most common gynaecological cancer in developed countries. The number of newly diagnosed cases in Europe was nearly 100 000 in 2012, with an age-standardised incidence rate of 13.6 per 100 000. Most endometrial cancers are diagnosed early, however, five-year survival rates are much lower if there is regional spread or distant disease (68% and 17% respectively) [15]. Cervical cancer is the second most diagnosed gynaecological cancer, with more

than 58.000 new cases diagnosed and 24.000 patient deaths recorded in Europe every year [16]. Five-year relative survival in European women diagnosed with cervical cancer in 2000–2007 was 62%, ranging from 57% in Eastern Europe to 67% in Northern Europe [17]. The fourth most common gynaecological cancer is vulvar cancer, which has an annual incidence of 2.5–4.4 per 100 000 persons per year [18].

Palliative care issues in gynaecological malignancies

Common palliative care issues in gynaecology include communicating bad news, pain management, nausea and vomiting, gastrointestinal complications, recurrent ascites, tissue necrosis and fistulae.

Pain management

Pain is a very common complaint in patients with cancer, reported in 20% to 50% of patients with any type of cancer. About 80% of patients with advanced-stage cancer experience moderate to severe pain [19,20]. A review by the European Society of Medicine found that more than 40% of patients with advanced ovarian cancer and 70–75% of those with advanced cervical cancer experience pain that significantly impairs their quality of life [21].

A thorough assessment can aid in successful management of a patient's pain. It is important to carry out a holistic assessment which involves assessing the physical experience, psychological issues, the understanding and expectations of the patient and their family, their support network, and their current mental health. All these factors can affect how an individual experiences pain and how they will respond to treatments.

The WHO developed a pain management algorithm for cancer pain relief in the form of a three-step analgesic ladder [22]. It provides a framework for the pharmacological management of cancer pain starting with more simple analgesia such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) and stepping up to weaker opioids such as codeine followed by stronger opioids such as morphine. If a patient is in moderate or severe pain, it is important to consider starting a strong opiate straight away.

The opioid most commonly used is morphine. Newer opiates such as oxycodone are also becoming more popular and can be useful when patients cannot tolerate morphine. Patients can be started on a four-hourly dose, which can then be titrated up to a dose that alleviates pain without causing significant side effects. The total 24-hour dose is then converted into a 12-hourly sustained-release preparation, in conjunction with a breakthrough dose of one sixth to one tenth of the total 24-hour dose. The long-acting opioid dose can be adjusted every two to 4 days based on the prior days' need for breakthrough pain medication. An antiemetic should be prescribed regularly during the first week of treatment with the opioid, after which it can be switched to an as required medication. A regular laxative should also be prescribed.

If a patient cannot tolerate oral morphine due to severe vomiting or bowel disease that reduces absorption, then other routes may be used such as transdermal or subcutaneous. If a patient has renal impairment, alternative opiates such as alfentanil should be considered. Opioid intoxication can lead to respiratory failure, which can be identified by reduced respiratory drive, pinpoint pupils and unconsciousness. Death following opioid overdose may be prevented with early identification and the use of naloxone. Naloxone is an opiate antagonist that will completely reverse the effects of the opioid and it has virtually no side effect profile.

With advanced malignancies, cervical and endometrial in particular, patients can experience severe pelvic pain related to metastatic invasion into tissue and nerve endings throughout the pelvic floor. It can also be caused by bone metastases. In these cases, the pain is often refractory to simple and opiate analgesia. Neuropathic agents, such as pregabalin, amitriptyline and gabapentin, can be tried as adjuvants. Bisphosphonates, corticosteroids or NSAIDs can also be used for bone pain. These are not always successful, and it may be necessary to use other routes of analgesia delivery such as intrathecal or nerve blocks. The serious side effects of a sacral block need to be taken into consideration, such as loss of bladder and bowel control. Discussing all this with the patient is crucial as these side effects may be too significant for them to accept the procedure. An indwelling epidural is another option. Again, side effects need to be considered and discussed with the patient, such as lower limb weakness and urinary retention, however these usually resolve if the indwelling catheter is removed.

Radiotherapy can also be used to manage pain related to bone metastases, to reduce the symptoms of mass effect, and for localised metastasis. Studies have shown that up to 65% of patients will achieve significant pain relief both with a single dose (8 Gy), as well as with more standard dosing for targeted bone metastasis [23]. However, the time to optimal symptom control, even after short courses of radiotherapy, is usually measured in weeks to months after radiation treatments are delivered [23]. Therefore, when expected survival is short, palliative radiotherapy may have minimal, if any, clinical benefit for patients [23].

Nausea and vomiting

Nausea and vomiting affect 50–70% of patients with advanced cancer. Nausea can be caused by opiate medications, brain metastasis, gastrointestinal motility problems, ascites or biochemical alterations such as hypercalcaemia [24].

To manage nausea, patients should be started on a first line antiemetic medication, after which the possibility of adding additional agents for breakthrough nausea can be considered. The second agent should be of a different class to optimise nausea management and reduce the risk of side effects. If possible, therapy should be directed towards the most likely cause or causes, however this approach is limited, as most patients have multiple causes of nausea and vomiting.

Metoclopramide, a dopamine antagonist, may be effective in managing nausea related to opiates. As it acts as a prokinetic, it may also help with motility-associated nausea, which may be seen in non-obstructing carcinomatosis. However, if gastric stasis or obstruction is suspected, prokinetic agents should be avoided. Other agents such as cyclizine haloperidol and pro-

methazine also provide some patients with symptomatic relief, especially when the nausea is worse with movement. Haloperidol and promethazine can cause drowsiness which may limit their use in some patients.

Chemotherapy-related nausea is caused by stimulation of the serotonin-mediated chemoreceptor trigger zone, and it is best treated with serotonin antagonists such as ondansetron and granisetron. Radiation and corticosteroids, serving to lessen the mass effect at least temporarily, can help in the management of nausea related to localised brain metastases. Octreotide decreases peristalsis and gastrointestinal secretions. It can be used to try to control nausea and vomiting associated with intestinal obstruction or carcinomatosis ileus.

Non-pharmacological, environmental changes can also help to alleviate nausea. These include smaller, more frequent meals, ensuring a quiet and relaxing environment, hydration, and good oral hygiene. Although its value in the palliative care setting has not yet been fully explored, acupuncture has also shown some success, and might be considered as part of the treatment plan.

Bowel obstruction

Bowel obstruction is commonly seen in gynaecological malignancies, particularly ovarian cancer recurrence, and it is associated with a poor prognosis. Up to 50% of women with epithelial ovarian cancer have been reported to develop bowel obstruction during their illness [25]. The pathophysiology can include infiltration of the mesentery or bowel muscles and nerves by the tumour, inflammatory oedema, faecal impaction, and use of constipating drugs. Benign causes include adhesions, post-radiation bowel damage, inflammatory bowel disease, and hernia. Patients usually present with any of the following: nausea, vomiting, abdominal pain and distension, constipation, liquid stool.

A conservative approach is usually attempted first, and this usually involves intravenous fluids, fasting, insertion of a nasogastric tube, and medications for pain and nausea control. If bowel obstruction does not resolve within about 72 hours, other options are explored such as surgery. Surgery has a high risk of morbidity in these patients and can result in complications that may negatively impact their quality of life. Factors considered when deciding whether or not to opt for surgical management include the extent of the disease, the likelihood of the surgical resection being successful, the site of the obstruction, and the patient's life expectancy and comorbidities.

Other adjuvant agents that may be helpful, especially if surgery is not considered a beneficial option, include steroids and octreotide. Steroids are thought to decrease peri-tumoural oedema and can be given as a four- to five-day trial, and stopped if no benefit is obtained. The downside of steroid use is the risk of gastric ulceration, mood swings, hyperglycaemic episodes and infections [26].

Octreotide, a somatostatin analogue, is thought to reduce gastrointestinal secretions and motility. It has been evaluated in fifteen randomised controlled trials and observational reports for a total of 281 patients surveyed. It was found to have a therapeutic success rate of 60–90% [27]. Cost is a factor that prohibits its use. Hyoscine butylbromide is another alternative. It is an anti-muscarinic agent with antispasmodic and antisecretory properties. It cannot cross the blood-brain barrier and therefore has no drowsiness effects. It can be effective in reducing the unpleasant symptoms associated with intestinal colic when administered subcutaneously.

Recurrent ascites

Ascites is the excess accumulation of fluid in the peritoneal cavity. Ovarian cancer is the most common primary site of cancer that is associated with ascites [28]. It is a sign of advanced disease and has a poor prognosis, with only 11% of affected patients surviving longer than 6 months [28]. It can negatively affect quality of life and cause significant pain, nausea, vomiting, dyspnoea and increased dependency.

Diuretics are sometimes used in the management of malignant ascites. The efficacy of these agents is thought to decline with disease progression, and evidence for their use is weak. Side effects such as electrolyte disturbance and hypotension also limit their use. Cases of ascites due to hepatic metastases or portal hypertension, rather than ovarian malignancy, are more likely to respond to diuretics [29].

Paracentesis is a common intervention used to provide immediate short-term palliation of symptoms of malignant ascites. It can become more difficult to perform if the ascites becomes loculated due to disease or abdominal adhesions. It may also have a major impact on the patient's quality of life, as the procedure often requires a hospital stay and may have to be frequently repeated. To combat this issue, peritoneovenous shunts or catheter drainage can be considered.

Peritoneovenous shunting may be appropriate in patients with a longer life expectancy, although major risks, occurring in 6% of patients, include pulmonary oedema, pulmonary embolus and infection [30]. An alternative with less major risks is insertion of an indwelling intraperitoneal catheter. This involves tunnelling a catheter subcutaneously towards the peritoneal cavity. This solution can enhance patient autonomy and improve quality of life as these catheters are easy to self-drain and reduce the need for repeated hospital admissions for paracentesis. A review assessing the safety and efficacy of the use of indwelling intraperitoneal catheters for the management of refractory malignant ascites found it to be a safe and effective palliative strategy [31].

Anaemia and bleeding

Anaemia occurs in 68–77% of patients with advanced cancer. In gynaecological malignancies, particularly cervical and endometrial, it is usually due to vaginal bleeding [32].

Vaginal bleeding can range from spotting to heavy intractable bleeding necessitating acute admission and blood transfusion. Pharmacological agents that can be useful in these cases include antifibrinolytics such as tranexamic acid. For patients with endometrial carcinoma, progestogens such as medroxyprogesterone can be used. Vaginal packing in the acute situation for a patient with heavy bleeding is an effective temporary measure and can be improved by using dressings coated in vasoconstrictive/haemostatic agents.

Blood transfusion for patients with advanced disease is controversial: it is unclear what the benefit of blood transfusion

is in advanced cancer, who is most likely to respond, and also for how long. Studies have found that it can give temporary relief from symptoms such as fatigue and dyspnoea for up to two weeks [31].

When patients have a longer life expectancy, surgical measures such as uterine artery ligation or radiological arterial embolisation may be considered. Embolisation may be especially appropriate in selected cases of cervical cancer to control massive bleeding. Palliative pelvic radiotherapy has also been shown to be effective in controlling bleeding symptoms in some patients with locally advanced cervical cancer.

Fistulae

Fistulae and obstructions may occur as a result of primary tumour invasion, tumour recurrence or prior treatment (surgery or radiotherapy). Cervical carcinoma is the most common gynaecological malignancy resulting in fistula formation, with vesciovaginal fistulae occurring most frequently. These fistulae can cause constant leakage of urine or faeculent discharge, which can have a major impact on quality of life. It is important to ensure early involvement of colorectal surgeons in order to obtain optimal management and reduce morbidity.

Urological complications

Various cancers occurring within the abdomen, pelvis or retroperitoneum can cause infiltration of the bladder and ureter. This can result in hydronephrosis, and consequently a non-functional kidney. In gynaecological malignancies this complication is most often seen in cervical cancer. Hydronephrosis-related symptoms include pain, urinary tract infections, nausea and vomiting, renal failure and urinary tract bleeding [33].

Management usually involves relieving the obstruction, and patients can undergo stent placement or urinary diversion procedures such as a nephrostomy [33]. Hydronephrosis in cervical cancer patients is associated with notable morbidity. In a retrospective study by Rose *et al*., it was found that in patients with stage IIIB cervical cancer restricted to the pelvis, hydronephrosis at presentation is a significant prognostic factor associated with poor performance status and poorer survival [34]. These authors also found that relief of ureteral obstruction via stent or percutaneous nephrostomy is correlated with improved outcome.

Conclusions

Providing early and optimal palliative care plans has been shown to improve the quality of life of patients and their families facing the problems associated with life-threatening illness. This improvement is linked to the prevention and relief of suffering through early identification and treatment of other problems, physical, psychosocial and spiritual. The first steps to introducing care plans should involve all physicians. Working in a multidisciplinary manner ensures that patients promptly receive optimal and effective care.

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