Orphan symptoms in palliative care

Aoife Gleeson

Simon Noble

Abstract

Symptom management is the cornerstone of good palliative care. Symptoms of advanced disease, such as pain, nausea and dyspnoea, are readily assessed and frequently the focus of both consultations and research studies. However, there are many other prevalent symptoms that remain unaddressed in clinical practice if not highlighted by the patient or specifically sought by the healthcare professional. These symptoms may have a significant impact on remaining quality of life. This paper will focus on the assessment and management of some of these symptoms, including asthenia, constipation, dry mouth, pressure ulcers, hyperhidrosis, lymphoedema and pruritus.

Keywords asthenia; constipation; hyperhidrosis; lymphoedema; pruritis; wound care; xerostomia

What's new?

- There is limited evidence for use of exercise and psychological intervention in the treatment of asthenia
- There is currently insufficient evidence for the use of psychostimulants in managing asthenia in advanced cancer
- Further research is needed regarding interventions for managing lymphoedema

Asthenia

Asthenia is defined as lack or loss of strength or energy. It was traditionally used to define the subjective sensation of tiredness, while 'fatigue' was used to describe the symptom of tiredness after exertion. Both terms are increasingly used to describe the same constellation of debilitating problems: easy tiring and reduced capacity to maintain performance; generalized weakness (the anticipatory sensation of difficulty in initiating a certain activity); and mental fatigue (the presence of impaired mental concentration, loss of memory and emotional lability). Asthenia is the most common symptom experienced by advanced cancer patients, with a prevalence of 60–90% in various studies. It can be severely debilitating, affecting quality of life and daily activity.

Management

Asthenia is a challenging symptom to treat. Its pathophysiology is not fully understood and the research base for its management remains limited. Therefore, there is a lack of data supporting an established therapeutic strategy. Reversible causes of asthenia should be sought and treated, for example anaemia, infection, electrolyte abnormalities (hyponatraemia, hypokalaemia) and/or endocrine abnormalities (hypothyroidism, Addison's disease).

Non-pharmacological management of asthenia: there is some evidence of benefit from exercise, psychological interventions (patient education, cognitive behavioural therapy) and acupuncture.[1]

Pharmacological management: corticosteroids are frequently used to relieve symptoms of asthenia, but their effect usually lasts only 2–4 weeks and long-term use should be avoided because of serious long-term adverse effects. There is no consensus on the optimal type or dosage of corticosteroids, but most studies have used dosages equivalent to 40 mg/day of prednisolone. Megestrol and other progestogens have also been used, although without convincing evidence for their effectiveness.

Agents used in the management of cachexia such as thalidomide, omega-3 fatty acids, aspirin and other non-steroidal anti-inflammatory drugs may also have a beneficial effect on asthenia, but further studies are needed.

Psychostimulants such as methylphenidate and modafinil are increasingly used. However, there is insufficient evidence on the use of methylphenidate, and the role of modafinil in the management of asthenia in advanced cancer has yet to be established.[1,2]

Constipation

Constipation is a very common symptom in palliative care and can be associated with significant distress. The incidence of constipation in palliative care is estimated to be between 18% and 50%, but is higher (up to 87%) in opioid-induced constipation in patients receiving opioid treatment. Constipation can be associated with abdominal pain and distension, anorexia, nausea and vomiting, and may result in faecal impaction, intestinal obstruction, urinary retention or incontinence. Overflow diarrhoea resulting from constipation may wrongly be interpreted as overuse of laxatives by patients or healthcare professionals, leading to reduced compliance with laxatives and worsening of constipation.

Assessment primarily involves taking a history and performing a rectal examination. Plain abdominal radiography is sometimes useful in confirming the diagnosis (Figure 1).

General management

Reversible causes such as hypercalcaemia should be considered and corrected. Oral laxatives are generally used to treat

Aoife Gleeson *MD MSc MRCPI is Consultant in the Department of Palliative Medicine, Aneurin Bevan Health Board, Wales, UK. Areas of research interest are infection control in palliative care, sexuality in cancer and palliative care, and palliative care in non-malignant lung disease. Competing interests: none declared.*

Simon Noble *MBBS PGCE DipPalMed MD FRCP is Clinical Reader in Palliative Medicine at Cardiff University, Cardiff, Wales, UK. His clinical and research interest lies within supportive care of cancer patients, including the management of venous thromboembolism. Competing interests: none declared.*

Figure 1 Abdominal radiograph demonstrating faecal loading.

constipation, the choice of laxative being made on an individual basis.

Laxatives have historically been categorized under the four main headings: softeners, stimulants, bulking agents and osmotic agents. However, they can generally be considered in two groups: patients with hard stools will require a softening agent (e.g. docusate, lactulose, magnesium hydroxide with liquid paraffin), while those with infrequent soft bowel motions will need a stimulating agent (e.g. bisacodyl, dantron, senna). In practice and in keeping with recommendations from a pan-European working group on constipation management in palliative care, most patients require a combination of a softener and a stimulant laxative.[3]

Classification into oral and rectal laxatives is outlined in Table 1. Oral laxatives should be given regularly and the dose titrated according to effect. Dantron-based laxatives are relatively contraindicated in patients with urinary or faecal incontinence because of problems with skin irritation. Bulk-forming laxatives and attempts at increasing the fibre content of the diet are poorly tolerated in the palliative care setting. Prucalopride is a selective high-affinity serotonin ($5HT_4$) receptor agonist that has enterokinetic effects, enhancing gut motility; it is useful for women with chronic constipation when laxative therapy has failed.

Patients with advanced cancer sometimes require additional rectal measures such as suppositories and enemas. Patients with hard stools require a softening agent (e.g. glycerine suppositories, arachis oil enemas), whereas those with soft stools require a stimulating agent (e.g. bisacodyl suppositories, sodium citrate enema). It should be noted that arachis oil is contraindicated in patients with known nut allergies.

Management of opioid-induced constipation: for severe, resistant constipation, methylnaltrexone has been shown to work when other laxatives have failed. Methylnaltrexone is a peripherally acting opioid receptor antagonist. It is administered by subcutaneous injection and should be used with caution in patients with an increased risk of gastrointestinal perforation. It is also used in combination preparations with opioids to prevent the development of constipation.[4]

Hyperhidrosis

Hyperhidrosis is the secretion of an abnormally large quantity of sweat. Patients may experience generalized or localized sweating, which may occur throughout the day or predominantly at night. It is not always associated with pyrexia.

Causes of localized hyperhidrosis include spinal cord disease, cerebrovascular disease and peripheral neuropathy. Causes of generalized hyperhidrosis include endocrine disorders (e.g. acromegaly, hypoglycaemia, thyrotoxicosis, phaeochromocytoma, diabetes mellitus, diabetes insipidus, hypopituitarism), infection, hormone suppression treatments (e.g. tamoxifen, luteinizing hormone-releasing hormone analogues), neoplastic fever (e.g. Hodgkin's lymphoma, renal cell carcinoma, any solid tumour with liver metastases) and drugs including opioids, antidepressants (e.g. fluoxetine), aciclovir, naproxen and pentazocine.

Management

This includes treatment of reversible causes (e.g. infection, hypoglycaemia, thyrotoxicosis) and elimination of potential aggravating factors. Treatment of hyperhidrosis with pyrexia includes cooling measures (e.g. a fan), rehydration and antipyretics (aspirin, paracetamol, other non-steroidal anti-inflammatory drugs (NSAIDs)); corticosteroids may be effective in certain circumstances. In hyperhidrosis without pyrexia, treatment includes histamine receptor antagonists (e.g. cimetidine 400–800 mg twice daily), antimuscarinics (thought to act directly on the sweat glands rather than on the thermoregulation centre), NSAIDs (e.g. diclofenac 50 mg three times daily) and selective serotonin reuptake inhibitors (SSRIs; e.g. paroxetine, sertraline).[5]

Xerostomia

Xerostomia is the subjective sensation of a dry mouth. It is common in patients with advanced cancer and has been reported to occur in up to 77% of hospice in patients. It is a distressing symptom in up to 30% of patients dying from cancer.

It is usually associated with hyposalivation, although it can also result from a change in the composition of the saliva. Xerostomia in palliative care most commonly results as an adverse effect of prescribed medications (e.g. opioids, antimuscarinics, sedatives) and is also common in patients receiving radiotherapy for head and neck cancer.

Xerostomia may be associated with other symptoms including altered taste, difficulty swallowing and speaking, and pain or discomfort in the oral cavity. It may lead to dental caries, oral candidiasis (Figure 2) and other oral infections.

Management

This includes the treatment of reversible causes (e.g. medications). Symptomatic management relies on the use of saliva