



Palliating symptoms other than pain

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BACKGROUND

Symptoms other than pain are a heavy burden for patients with either malignant or progressive nonmalignant disease and significantly reduce quality of life.

OBJECTIVE

This article discusses the management of symptoms of malignant or progressive nonmalignant disease in the general practice setting.

DISCUSSION

The approach to management of the symptoms of malignant or progressive nonmalignant disease is the same, regardless of the diagnosis. Management includes evaluation, treatment – depending on the underlying pathological mechanism, explanation for both the patient and their family, and ongoing review of goals of care.

Symptoms other than pain are a heavy burden for patients with either malignant or progressive nonmalignant disease and significantly reduce quality of life. Although the symptoms of dyspnoea, nausea, constipation, fatigue, confusion, anxiety/depression, and itch are the most distressing for patients with cancer; they have also been identified as causing significant distress in patients with chronic lung, cardiac and renal conditions. The approach to management of these symptoms is the same, regardless of the diagnosis. Management includes evaluation, treatment – depending on the underlying pathological mechanism, explanation for both the patient and their family, and ongoing review of goals of care.

Management of common symptoms

Dyspnoea

Breathlessness is a complex physiological and psychological source of distress for 50–70% of palliative care patients.¹ Aetiology is often multifactorial, however it is important to identify the cause as this will influence the therapeutic intervention.

If oxygen and standard treatments including nonpharmacological measures (*Table 1*) are not adequately relieving the symptom, then opioids and benzodiazepines should be considered. Morphine mixture or low dose sustained release morphine has been demonstrated to provide relief of refractory dyspnoea with minimal side effects.² Morphine should be started at a low oral dose (2.5–5.0 mg every 4 hours) and titrated to an effective dose. Monitor the patient for constipation and treat with standard laxatives such as coloxyl and senna. Opioids should be used with care in the unstable patient with hypercapnia and acute exacerbation of disease. Hypercapnia is recognised by drowsiness, confusion, and a decrease in respiratory rate and depth.³ There is no convincing evidence that nebulised morphine offers any value compared to oral morphine.

Low dose lorazepam (0.25–0.5 mg sublingually) can be helpful for patients with anxiety associated with dyspnoea. Lorazepam is preferred due to its short duration of action. If a regular anxiolytic is required, then consider low dose diazepam or clonazepam, which are longer acting.

Nausea

Nausea and vomiting is a common and distressing symptom that occurs in a number of conditions. The choice of antiemetic requires an understanding of the aetiology and pathophysiology of that particular condition (*Table 2*).

In the palliative care setting, symptoms of nausea can be controlled for most patients using three antiemetics: metoclopramide, haloperidol or cyclizine.⁴ Antiemetics can be used in combination; use maximal doses of one drug before adding another antiemetic and don't combine drugs of the same class. For patients with significant distress, a subcutaneous infusion of metoclopramide with haloperidol via a Grasby pump can control the symptom quickly, allowing conversion to oral medication. Always remember general measures such as attention to odours, diet, presentation of food, and avoidance of situations to which the patient has become inappropriately conditioned.

Constipation

The approach to management of constipation would be the same as for any patient seen in the general practice setting. In palliative patients, aetiology is usually multifactorial and laxatives need to be used early, in sufficient doses and often in combination. A useful regimen is coloxyl and senna, two tablets twice per day, with the addition of either Movicol (up to 4–6 sachets per day) or lactulose (up to 20–30 mL twice per day) if required (*Table 3*).

Delirium

Delirium is a common symptom in geriatric and palliative patients, is underidentified in clinical practice, can be distressing for patients, and has a risk of complications. It is defined as a 'transient organic brain syndrome characterised by the acute onset of disordered attention and cognition, with disturbances of psychomotor behaviour and perception'.⁵

Aetiology is often multifactorial and investigations are usually required to identify reversible causes unless associated with the end stages of illness (*Table 4*).⁶ At a minimum, investigations include: pulse oximetry, basic blood screen, mid stream urine, and chest X-ray if relevant.

It is important to implement environmental and supportive measures. Review all medications and consider changing any opioid, especially if the onset of delirium is associated with a change of opioid dose or the patient's renal or liver function is compromised. Consider commencing a neuroleptic, especially if the patient is distressed or agitated. Low dose oral haloperidol (0.5–10.0 mg per day) is recommended as first line treatment; if side effects occur, consider olanzapine (4–10 mg per day) or risperidone (1.5–4.0 mg per day).⁷

Table 1. Management of dyspnoea in the palliative setting

- General reassurance and explanation
- Nonpharmacological: advice on posture, distraction and relaxation techniques, breathing exercises and flow of air across the face, physiotherapy, music therapy, occupational therapy and social work
- Standard treatment for existing conditions (eg. COPD, asthma, congestive cardiac failure [CCF]): maximise long acting bronchodilators, anticholinergics, steroids and antibiotics for COPD. Maximise diuretics, vasodilators, beta blockers, digoxin, ace inhibitors and aldosterone antagonists for CCF
- Treatment options for specific situations²³
 - pleural effusion: pleural aspiration + pleurodesis
 - pericardial effusion: aspiration
 - lymphangitis carcinomatosa: high dose dexamethasone
 - endobronchial disease: high dose dexamethasone, laser therapy, stenting, radiotherapy, chemotherapy
 - Hypoxia: oxygen
 - intermittent oxygen therapy for patients with intractable dyspnoea and chronic lung disease with significant hypoxaemia
- Morphine
- Benzodiazepines

Depression

Depression is underdiagnosed and undertreated in the terminally ill and can be difficult to diagnose as the symptoms of sleep and appetite disturbance, and lack of energy, are common in those with pain and end stage disease. Screening for depression is essential and treatment with antidepressants is recommended. Mirtazapine 30 mg per day is useful as the side effects of night time sedation and increase in appetite are beneficial in this patient population. If survival time is limited, there is some evidence that methylphenidate (5 mg twice per day) can be useful to improve symptoms.⁸

Pruritus

Pruritus is a rare symptom that may occur in end stage renal and liver failure or congestive cardiac failure (in addition to lymphoma and other cancers). It can be very distressing and difficult to treat. Pruritus has a complex physiology and there is limited understanding of the underlying mechanisms, however, there is evidence that histamine and serotonin receptors are mediators of itch. Management strategies include treatment of the underlying disease, topical treatments and oral medications (*Table 5*).⁹

Fatigue

Fatigue is a debilitating symptom that impacts on quality of life. It is a multifactorial, multidimensional problem

that is difficult to treat and requires a team approach to management. It is important to treat any reversible causes such as depression, anaemia or infection. Nonpharmacological measures shown to be of benefit include an exercise program, provision of information, and psychological interventions. Glucocorticoids or methylphenidate may be of value.¹⁰

Secretion management

Management of secretions can be difficult in the terminally ill patient, especially the patient with a progressive neurological disorder. Management includes: suction, postural drainage (not in terminal stage), saline nebulisers, mucolytics, and the use of anticholinergic medications

such as atropine eye drops, 1% 1–2 drops orally four times per day, hyoscine hydrobromide 0.4 mg three times per day subcutaneously or glycopyrrolate 0.2 mg 2–3 times per day subcutaneously (which is less sedating). In difficult cases, botulinum toxin injections of the salivary glands or low dose radiotherapy to the salivary glands may be considered.¹¹

Chronic conditions that benefit from a palliative approach

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is the single leading cause of death in Australia and the third largest contributor to the burden of disease in

Table 2. Common antiemetics used in the palliative setting

Antiemetic	Action	Indication	Dose
Butyrophenones			
Haloperidol	Dopamine antagonist, works at chemoreceptor trigger zone	Nausea due to drugs, metabolic disorders, sepsis, bowel obstruction	0.5–5.0 mg/day (oral/SC)
Prokinetic			
Metoclopramide	Prokinetic but also dopamine antagonist	Opioids, gastric irritation, gastric stasis, partial bowel obstruction, constipation	10–20 mg 4 hourly (oral)
Domperidone	Doesn't cross blood-brain barrier, not as effective prokinetic ⁴	Extrapyramidal side effects with metoclopramide	10–20 mg 4 hourly (oral/SC)
Antihistamine			
Cyclizine	Works at vomiting centre	Vestibular component, small bowel obstruction	50 mg twice per day (oral/SC, max 200 mg/day)
5HT₃ antagonists			
Ondansetron	Chemoreceptor trigger zone and the gut	Chemotherapy/radiotherapy	4–8 mg twice per day (oral/SC)
Tropisetron		Chemical, cerebral, abdominal causes when other antiemetics failed	1–2 mg/day (oral/SC)
Anticholinergic			
Hyoscine hydrobromide	Muscarinic antagonist works at vestibular system and vomiting centre	Motion sickness, small bowel obstruction	0.4 mg twice per day (SC)
Phenothiazine			
Levomopromazine	Multiple receptor antagonist	Other antiemetics have failed	6.25–25.0 mg/day (SC)
Other drugs			
Dexamethasone	Action uncertain	Raised intracranial pressure or in combination with other antiemetics	4–8 mg/day (oral/SC)
Octreotide	Reduces intestinal secretions	Bowel obstruction	200–500 µg/day (SC)
Benzodiazepines	GABA receptors	Anxiety	Lorazepam 0.5–1.0 mg/day (oral)

Australia.¹² A number of studies have demonstrated that patients with COPD at the end of life have physical and psychosocial needs at least as severe as patients with lung cancer. The common and most distressing symptoms include dyspnoea, fatigue, pain, insomnia, low mood and anxiety.^{13,14}

As well as symptom management, patients need support in daily activities, emotional support, social support and information.¹⁵

Motor neurone disease

Motor neurone disease and other progressive neurological diseases have a similar symptom profile to cancer patients (Table 6). There are particular issues in relation to swallowing, secretion management, nutrition, and respiratory complications that require input from a range of specialists including a neurologist, respiratory physician, dietician, speech pathologist and physiotherapist. Advance care planning should consider the preferred approach to nutritional and ventilatory support.¹⁶

Class IV heart failure

The symptoms of Class IV heart failure can be similar to those of end stage cancer – weakness, fatigue, shortness of breath, swelling of the abdomen and legs, nausea, constipation, depression, and poor quality of life.¹⁷ Patients may also develop symptoms secondary to uraemia such as nausea and itch. Management focuses on review of medications, optimisation of treatment for heart failure, and treatment of symptoms as they arise.¹⁸ The incidence of sudden death in this group of patients is up to 50%, which needs to be included in discussions about end of life care.¹⁶

Renal disease

Patients with end stage renal disease often have significant comorbid conditions including diabetes, heart failure and peripheral vascular disease that contribute to their symptom burden and poor quality of life. The most distressing symptoms in those ceasing dialysis are pain, fatigue, drowsiness, nausea, anxiety, and itch at similar rates to those with cancer.¹⁹ Advance care planning entails discussion of the complex issues around cessation of dialysis and addressing clinical, social and spiritual issues for the patient and their family.²⁰

Chronic liver disease

Chronic end stage liver disease has a terminal phase that is highly appropriate for palliative care. Common symptoms and signs of hepatic failure include liver capsule pain, ascites, jaundice, itch and electrolyte

Table 3. Laxatives for constipation²⁴

Mode of action		Oral agents	Suppository/enema
Predominant softening ↓ Predominant stimulant	Liquid paraffin	Paraffin	
	Bulk forming laxative	Fybogel	
	Surfactant	Coloxyl	Coloxyl
	Osmotic	Lactulose, Movicol	Glycerine/Microlax
	Saline	Epsom salts	Sodium phosphate
	Anthracenes	Sennakot	
	Polyphenolics	Bisacodyl	Bisacodyl

Table 4. Correctable causes of delirium⁶

- Increased intracranial pressure
 - tumour, trauma, hydrocephalus
- Hypoxaemia
- Metabolic disturbance (eg. hypoglycaemia, hyponatraemia, hypercalcaemia, hepatic or renal failure)
- Sepsis
- Drugs
 - multiple drug therapy (benzodiazepenes, opioids, anticholinergics, steroids, H2 blockers, central nervous system stimulants)
- Haematological conditions
 - severe anaemia, coagulopathy
- Depression
- Psychotic reaction to illness
- Alcohol or drug withdrawal

disturbances culminating in encephalopathy. One-third of deaths occur as a result of a significant gastrointestinal bleed, which can be extremely distressing to both the patient and their family. This needs to be discussed in depth with the family so that, if it should occur, they are better able to deal with the situation.²¹

Conclusion

In all these conditions, there is often a significant degree of psychosocial and spiritual distress due to the significant symptom burden, the prolonged illness and uncertain prognosis. Patients, and their families, have identified a need for advance care planning and discussion about wishes for end of life care to occur at an earlier stage.^{15,17,19,22}

A team approach to management is essential in order to provide holistic care which includes symptom management, advance care planning, support in daily activities, emotional support, social support and information for patients with both cancer and noncancer diagnosis in the palliative phase. The management team

Table 5. Treatment of systemic pruritus⁹

General measures	<ul style="list-style-type: none"> • Prevent boredom, anxiety, dry skin, heat • Treat skin infections • Discontinue drugs that cause pruritus • Eliminate common skin allergens (eg. perfume, soap) • Apply cold applications • Medicated baths
Topical treatments	<ul style="list-style-type: none"> • Lotions containing menthol, phenol and camphor • Tar compounds • Emollients • Topical anaesthetics • Capsaicin cream
Medications	<ul style="list-style-type: none"> • Antihistamine • Cholestyramine 4 g twice per day • Naltrexone 25–50 mg/day • Paroxetine 10–20 mg/day • Mirtazapine 15–30 mg/day • Ondansetron 4–8 mg twice per day • Doxepin 10–25 mg twice per day • Cimetidine 200 mg four times per day

Table 6. Symptoms of patients on admission to a hospice¹⁶

Symptom	Patient with motor neurone disease	Patient with cancer
Constipation	65%	48%
Pain	57%	69%
Cough	53%	47%
Insomnia	48%	29%
Breathlessness	47%	50%

will enlist a number of disciplines depending on each individual case, but might include allied health, pastoral care, specialist and generalist medical practitioners, community nursing, and specialist palliative care services for complex issues.

Summary of important points

- The approach to management of symptoms in palliative care is the same whether patients have a cancer or noncancer diagnosis – the focus is on control of symptoms and improvement of quality of life.
- Patients with progressive chronic conditions would like to have earlier discussion about end of life issues.
- Significant psychosocial support is required for patients and their families with chronic conditions due to the significant symptom load and uncertain prognosis.
- A team approach to care, often with the involvement of many disciplines and services, is essential.

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