CHAPTER 24
MEDICINES USED IN PALLIATIVE CARE

PALLIATIVE CARE

Palliative care is an approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness, regardless of whether or not they also receive life-prolonging treatment. It requires a multidisciplinary approach and aims to address physical, psychosocial, and spiritual problems.

Life threatening illnesses are where death is expected to be a direct consequence of the specified illness.
Analysis of available evidence suggested 11 common symptoms occurring in the advanced stages and end of life stages: anorexia, anxiety, constipation, delirium, depression, diarrhoea, dyspnoea, fatigue, nausea and vomiting, pain and respiratory tract secretions.
All symptoms should be managed by a multi-disciplinary team to ensure a holistic approach.

Note: Please be advised that the recommendations in this chapter are directed at treating common symptoms associated with end-of-life care (acute and sub-acute) - a component of palliative care. The approach to end-of-life care may differ from supportive palliative care. Refer to relevant sections for supportive palliative care, e.g. section 15.3.1: Depressive disorders.

Always refer to the latest National Guidelines on Palliative Care.

For management of pain in palliative care see chapter 26: Pain.

24.1 GASTROINTESTINAL CONDITIONS

24.1.1 ANOREXIA AND CACHEXIA

R63.0/R63.4/R64 + (Z51.1)

DESCRIPTION

Anorexia/cachexia syndrome is a complex metabolic process found in many end-stage illnesses. It is characterised by loss of appetite, weight loss and muscle wasting, and cannot be fully reversed by conventional nutritional support. It may impact significantly on the quality of life of patients, leading to increased anxiety and distress for both patients as well as family.

GENERAL MEASURES

Reduced food and fluid intake is expected at the end of life, and treatment of anorexia and weight loss may not be appropriate if these symptoms are not having a direct impact on quality of life. This should be explained to caregivers and family.

Management of anorexia and weight loss includes identification and, if appropriate, treatment of possible underlying cause(s). It may include the use of pharmacological and non-pharmacological treatment approaches.

Identify reversible problems that may contribute to or exacerbate anorexia/ cachexia including:

- Pain, nausea, heartburn, dyspnoea, gastritis, depression, constipation anxiety dysphagia, medication and fatigue
- Oral problems e.g. dry mouth, ulcers, candidiasis, etc.
- Odours e.g. fungating lesions, cooking smells, incontinence etc.
- Delayed gastric emptying due to local disease, autonomic neuropathy with early satiety and vomiting of undigested foods

If appropriate, moderate exercise must be encouraged, along with pacing of activities and good sleep hygiene.

Nutritional advice includes eating small amounts of enjoyable food frequently.

MEDICINE TREATMENT

If the anorexia and/ cachexia contributes significantly to decreased quality of life and the patient has a short life expectancy.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 0.5 mg/kg (e.g. 20–30 mg) daily.
  - The effect may be rapid but usually decreases after 3–4 weeks.
  - If there is no benefit after 1 week, stop the treatment.

LoE:III[i]

If symptoms of reflux or gastritis: see section 1.1.3: Gastro-oesophageal reflux disease.

If gastroparesis is present, see section 8.7.1 Diabetic neuropathies.

24.1.2 CONSTIPATION

K59.0 + (Z51.1)

DESCRIPTION

Constipation is the passage of small, hard faeces infrequently and with difficulty. Individuals vary in the weight they give to the different components of this definition when assessing their own constipation and may introduce other factors, such as pain and discomfort when defecating, flatulence, bloating or a sensation of incomplete evacuation. Constipation may also be secondary to other conditions e.g. dehydration, immobility poor diet, anorexia, tumour compressing bowel wall or hypercalcaemia.

GENERAL MEASURES

Ensure privacy and comfort to allow a patient to defecate normally.
Increase fluid intake within the patient's limits.
Encourage activity and increased mobility within the patient's limits.
Anticipate the constipating effects of pharmacological agents such as opioids, anticholinergic agents (e.g. tricyclic antidepressants), antacids, iron, 5HT3 antagonists and provide laxatives prophylactically.

MEDICINE TREATMENT

The combination of a softener and stimulant laxative is generally recommended, and the choice of laxatives should be made on an individual basis.

- Sennosides A and B, oral, 13.5 mg, 1 tablet at night.
  - In resistant cases increase to 2 tablets.

AND/OR *LoE:III[ii]*

Lactulose, oral, 15–30 mL 12–24 hourly. *LoE:III[iii]*

Severe constipation in patients who are unable to swallow:

- Bisacodyl, rectal, 10 mg suppository daily.

OR *LoE:III[iv]*

Glycerine (glycerol), rectal, 1.698 mL/2.4 g suppository when necessary. *LoE:III*

If these therapies are not effective, other options could be considered.

Note: Manual removal should only be undertaken if the patient has received adequate pain relief and sedation, if relevant.

REFERRAL/CONSULTATION

If bowel obstruction is suspected refer/consult for appropriate radiological investigations and, if appropriate, surgical interventions.

24.1.3 DIARRHOEA

A09.0/A09.9/K52.2/K52.9 + (Z51.5)

See Primary Health Care chapter: Medicines for palliative care: section 22.1.2: Diarrhoea.

24.1.4 NAUSEA AND VOMITING

R11 + (Z51.5)

GENERAL MEASURES

Treat the underlying cause and rehydrate the patient.
Reversible causes include medication, hypercalcemia, constipation, uraemia, gastritis, gastroenteritis, coughing and infections.
Manage odours e.g. cooking smells and fungating wounds.

MEDICINE TREATMENT

Treat the underlying cause.

- Metoclopramide, oral/IM/IV, 10 mg 8 hourly, 30 minutes before a meal.

<u>If metoclopramide is ineffective or contra-indicated (i.e. inoperable bowel obstruction):</u>

- Haloperidol, oral, 1.5–5 mg daily.

OR *LoE:III*[v]

Haloperidol, SC/IM/IV

- Initiate 0.5 mg 12 hourly.
- Titrate to a maximum dose of 5 mg 8 hourly. *LoE:III*[vi]

<u>Drug-induced parkinsonism:</u> *LoE:III*[vii]

ADD

- Anticholinergic agent, e.g.:
- Orphenadrine, oral, 50–150 mg daily according to individual response
  - Usual dose: 50 mg 8 hourly.
  - Maximum dose: 150 mg daily.
  - Use with caution in the elderly as it may cause confusion and urinary retention.

Note: Anticholinergic medicines (e.g. orphenadrine) should not be added prophylactically to antipsychotics to prevent extrapyramidal side effects.

<u>If haloperidol is ineffective/ inoperable bowel obstruction:</u>

- Promethazine, IM/IV, 12.5–25 mg, 4–6 hourly. *LoE:III*[viii]

Corticosteroids can decrease cerebral oedema: See section: 14.12.1 Brain oedema due to tumours and inflammation.

REFERRAL

Refer to the appropriate discipline if the underlying cause can be reversed e.g. bowel obstruction - refer to a surgeon.
Consult a palliative care trained doctor if the vomiting persists.

24.2 NEUROPSYCHIATRIC CONDITIONS

24.2.1 ANXIETY

F40.0-2/F40.8-9F41.3/ F41.8-9/F42.0-2/F42.8-9 + (Z51.1)

DESCRIPTION

Anxiety is defined as the apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension. Anxiety is characterised by excessive feelings of fear apprehension and worry. Anxiety may be associated with symptoms of depression, poor concentration, insomnia, irritability, panic attacks, sweating, tremor and nausea. It is a common symptom in Palliative Care and the complex multi-

causative nature of anxiety in patients with life threatening illnesses always require a multimodal approach.

GENERAL MEASURES

Address any contributing factors such as pain and dyspnoea. Consider other underlying conditions that may mimic anxiety e.g. electrolyte imbalance, hyperthyroidism, hypoxia, arrhythmias and many medicine side effects.
Assess for depression or any other previous psychiatric illness.
Include the caregivers
Ensure the patient and caregivers have received the desired amount of information around the nature of the disease, treatment, side-effects and outcomes.

MEDICINE TREATMENT

A multi-disciplinary team approach is recommended (including a spiritual carer).

Acute management of anxiety:

<u>For an acute episode or intense prolonged anxiety:</u>

- Benzodiazepine, e.g.:
- Diazepam, oral, 2.5–5 mg as a single dose.
  - Repeat if required up to 12 hourly. *LoE:III*[ix]
  - Duration of therapy: up to 2 weeks, taper off to zero within 6 weeks.
  - Avoid if liver function impaired.

OR *LoE:III*[x]

- Lorazepam, oral, 0.5–1 mg, immediately.
  - Repeat as necessary to control symptoms. *LoE:III*[xi]
  - Tablets may be crushed and administered sublingually. *LoE:III*[xii]

<u>Patient unable to take oral medication/ terminal sedation required:</u>
See section 24.5: Sedation in palliative care.

CAUTION

Benzodiazepines, especially diazepam IV, can cause respiratory depression.
Patients with liver dysfunction require lower doses.
Monitor patients closely. *LoE:III*[xiii]
In the short-term, benzodiazepines can aggravate delirium.

» In frail and elderly patients or where respiratory depression is a concern, reduce the dose by half. *LoE:III*[xiv]
» The safest route of administration is oral with the IV route having the highest risk of respiratory depression and arrest. Use the safest route wherever possible.
» Monitor vital signs closely during and after administration.

» Use haloperidol instead of benzodiazepines in patients with respiratory insufficiency.
» To avoid inappropriate repeat dosing allow at least 15–30 minutes for the medication to take effect. Repeated IM doses of benzodiazepines may result in toxicity owing to accumulation.

- SSRI e.g.:
- Citalopram, oral. *LoE:I*[xv]
  - Initiate at 10 mg daily for 2 weeks.
  - Then increase to 20 mg daily.

OR *LoE:I*[xvi]

Fluoxetine, oral.
- Initiate at 20 mg every alternate day for 2 weeks
- Increase to 20 mg daily after 2–4 weeks
- Delay dosage increase if increased agitation/panicked feelings occur.

LoE:III[xvii]

Note: Effect of SSRIs are only apparent after 2–3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

REFERRAL
Poor response to treatment.

24.2.2 DELIRIUM
F02.0-4/F02.8/F03/F05.0-1/F05.8-9 + (Z51.5)

DESCRIPTION
Delirium (confusion) is very common in the terminal stages of advanced disease and is associated with a short prognosis. When treatment of the underlying cause(s) of delirium is not possible or unsuccessful, pharmacological management is necessary. Causal treatment may not be indicated in patients with limited prognosis and pharmacological symptomatic therapy has to be initiated without delay.

GENERAL MEASURES
Assess for underlying causes e.g. infection or electrolyte imbalance.
Remove factors that can agitate the patient (e.g. full bladder, thirst, pain, constipation, medicines such as opioids, steroids, benzodiazepines, withdrawal of medicines, dehydration, liver or renal impairment and cerebral tumour).
Reduce polypharmacy.
Where appropriate, ensure adequate fluid and nutritional intake (not indicated in the pre-terminal stage).
Mobilise early when appropriate.
Monitor for sensory deficits and manage accordingly e.g. using hearing aids.

Keep the family involved and informed. Provide tools of care such as how to orientate and reassure the patient.

MEDICINE TREATMENT

- Haloperidol, oral/SC/IV, 0.5 mg 8 hourly.
  - Titrate dosage up as required and use the minimum dose that controls the symptoms.

LoE:III[xviii]

In the elderly or where there is no response or resistance to haloperidol:

ADD

- Lorazepam, oral, 0.5–1 mg 2–4 hourly as required.
  - Tablets may be crushed and administered sublingually.

LoE:III[xix]

OR *LoE:III*[xx]

Patients unable to swallow:

- Midazolam, SC/IV, 0.5–5 mg immediately.
  - Titrate up slowly.
  - Lower doses are indicated for patients with liver dysfunction.

LoE:III[xxi]

24.2.3 DEPRESSION

F32-3/F32.8-.9/F33.0-4/F33.8-9/F34.1 + (Z51.5)

DESCRIPTION

Depression is characterized by persistent feelings of extreme sadness and low mood associated with loss of interest in activities and inability to experience pleasure. There are often associated biological features of significant changes in appetite and weight, disturbed sleep, fatigue and poor concentration.

Diagnosis of major depression in a terminally ill patient often relies more on the psychological or cognitive symptoms (worthlessness, hopelessness, excessive guilt and suicidal ideation) than the physical/somatic signs (weight loss and sleep disturbance) described in depression in patients who are not terminally ill. The key indicators of depression in the terminally ill are persistent feelings of hopelessness and worthlessness and/or suicidal ideation.

Demoralisation is a phenomenon where hope and meaning is lost and where patients wish to hasten their death because they cannot foresee any future pleasure.

GENERAL MEASURES

Exclude physical reversible causes e.g. hypothyroidism, hyperthyroidism, or hypercalcaemia.

MEDICINE TREATMENT

- SSRI, e.g.:
- Citalopram, oral.
  - Initiate at 10 mg daily for 2 weeks.
  - Then increase to 20 mg daily.

OR *LoE:III*[xxii]

<u>If sedation is required:</u>

- Amitriptyline, oral, at bedtime.
  - Start with: 25 mg, increase by 25 mg/day at 3–4 day intervals.
  - Dose range: 75–150 mg daily.

Note: Effect of SSRIs are only apparent after 2-3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

24.2.4 FATIGUE

R53 + (Z51.5)

DESCRIPTION

Fatigue is defined as a subjective feeling of tiredness, weakness or lack of energy. The pathophysiology is not fully understood but will be multifactorial in most palliative care patients, including disease- and treatment-related causes. Fatigue may be severe, distressing and persistent, regardless of adequate amounts of sleep and rest.

GENERAL MEASURES

Treat underlying causes such as anaemia, depression, and infections.
Encourage aerobic exercises, where appropriate.
Ensure that the multidisciplinary team assists with activity pacing, assisted devices where indicated, and diet.

MEDICINE TREATMENT

Note: Because of limited evidence, consideration of steroids in palliative care should be restricted to use in the terminally ill with fatigue and a specific short-term treatment goal.
Fatigue can also protect patients at the end of life from physical and emotional distress.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral 0.5 mg/kg (e.g.:15–30 mg) daily, for 1 week.

LoE:III[xxiii]

24.3 PAIN

See chapter 26: Pain.

24.3.1 CHRONIC CANCER PAIN

See section 26.1.2: Analgesia for chronic cancer pain.

24.3.2 NEUROPATHIC PAIN

See section 26.1.4: Neuropathic pain.

24.4 RESPIRATORY CONDITIONS

24.4.1 DYSPNOEA

R06.0+ (Z51.5)

DESCRIPTION

Dyspnoea is the subjective unpleasant sensation of being unable to breathe adequately (breathlessness). Dyspnoea is a complex multidimensional symptom with physical, psychological, and emotional dimensions, especially anxiety. The intensity of dyspnoea is generally not related to the oxygen saturation.

Look for reversible causes, e.g. infection, pulmonary embolism, pleural effusion, bronchospasm and anxiety

The aim should always be to address the cause. However, in end stage disease symptomatic treatment is indicated.

GENERAL MEASURES

Ideally, include a physiotherapist and occupational therapist for pulmonary rehabilitation and to teach patients pursed lip breathing, pacing of activities, relaxation techniques, and positioning.

The use of a fan may reduce the sensation of dyspnoea.

Treat the underlying cause (e.g. antibiotics for underlying respiratory infection) wherever possible.

MEDICINE TREATMENT

- Morphine syrup, oral.
  - Starting dose: 2.5–5 mg, 4 hourly as required, titrating up slowly.

<u>Dyspnoea associated with hypoxaemia</u>

- Oxygen.

24.4.2 RESPIRATORY SECRETIONS

R06.0 + (Z51.5)

DESCRIPTION

Excessive respiratory tract secretions (also referred to as death rattle), is used to describe a rattling noise produced by accumulated secretions in the airway which oscillate in time with inspiration and expiration. Generally, respiratory secretions occur in patients who are extremely weak and close to death.

GENERAL MEASURES

Change position of the patient.
Explain to caregivers and relatives that the patient is not distressed by the secretion. Patients are not conscious that they are unable to clear secretions. Minimal oropharyngeal suctioning is required.

MEDICINE TREATMENT

- Hyoscine butylbromide, SC/IM, 20 mg.
  - Increase dose to effect to maximum of 120 mg.

LoE:III[xxiv]

24.5 SEDATION IN PALLIATIVE CARE

Y47.9 + (Z51.5)

Sedation in palliative care has unique objectives, and tolerance for some adverse effects may be greater than in other situations. There is also an emphasis on avoiding parenteral medication. Palliative sedation should be undertaken by clinicians experienced in the process and the advice of an expert should be sought where necessary. Sedation should only be started after discussion with, and with the consent of, the patient and/or family (when the patient is unable to consent).

The aim of sedation in palliative care is to ameliorate refractory suffering and not to hasten death.
Palliative care medication addresses symptoms such as pain, dyspnoea, nausea and depression. Managing many of these symptoms involves the use of medications which may have sedative properties. Palliative sedation involves the additional use of medication where sedation is the primary objective, and is appropriate only after standard care has proven unsuccessful.

GENERAL MEASURES

Pain must always be the first symptom to be excluded.
Always look for reversible causes of symptoms prior to prescribing sedation such as dehydration, hypoxia, concurrent synergistic sedative medicines, hypercalcaemia, renal failure, or infection.
Caution should be exercised and palliative care prescription examined for possible drug-drug interactions, prior to commencing sedation (or escalating doses of sedative medicines).
Dose escalation may be considered only if there is evidence of inadequate sedation.

MEDICINE TREATMENT

Dosing in frail, elderly patients should be titrated to effect.

- Lorazepam, oral, 0.5 mg 4 hourly.

- Tablets may be crushed and administered sublingually.

OR LoE:III[xxv]

Haloperidol, oral, 0.5 mg 4 hourly.

Patient unable to take oral medication or terminal sedation required:

- Midazolam, SC/IV:
  - Initial dose: 1–5 mg as needed
  - Titrate to effect.

LoE:III[xxvi]

24.6 END OF LIFE CARE

Z51.1

DESCRIPTION

Patients can be defined as being terminal when there is irreversible decline in functional status prior to death. It is essential during this time to ensure the ethical management of the dying phase and to minimise distress for the patient, family and fellow health care professionals by using a biopsychosocial and spiritual approach.

Signs of dying:

» The patient may gradually spend more time sleeping during the day and at times will be difficult to rouse.
» There may be decreased need for food and drink.
» The patient may become increasingly confused about time, place and identity of friends and family.
» Arms and legs may become cool to the touch and the undersides of the body may become darker in colour.
» Loss of control of bowel and bladder may occur.
» Urine output may decrease.
» Saliva and mucus may collect at the back of the throat as the swallowing and cough reflexes diminish. This sometimes causes a noise known as the “death rattle”.
» Vision and hearing may decrease.
» Breathing patterns may become irregular, with longer intervals between breaths.

GENERAL MEASURES

Communication is at the centre of care. The following aspects should be addressed:

» Honest, direct, compassionate and culturally sensitive information about the prognosis.
» Evaluation of the patient and family resources and needs, especially spiritual needs.
» Decision making on place of death as many patients want to go home.
» Education about patient care.

» Emergency contact details, especially if the patient wants to go home.
» Compassionate information about symptoms that might develop and how to manage them.
» Nutrition and hydration.

Discontinue all non-essential, futile procedures and medicines e.g. discontinue 4-hourly blood pressure measurements and vitamin tablets.
Ensure medicines are prescribed for symptom management and prescribe medicine when needed to pre-empt common symptoms during the terminal phase using the appropriate route of administration:
» Pain (see section above)
» Nausea and vomiting (see section above)
» Respiratory secretions (see section above)
» Agitation /restlessness/delirium (see section above)

Discuss feeding and hydration with the family. If the decision is to hydrate and/ feed, ensure gentle hydration and monitor oedema, especially in patients with hypoalbuminaemia. Hydration does not improve quality of life, survival, or symptom burden at the end of life, and should not be given as routine management. Rather offer sips of water if the patient is able to swallow.