Prescribing in Palliative Care

See also separate End of Life Care and Palliative Care articles.

Palliative care is defined as ‘the active total care of patients whose disease is not responsive to curative treatment’. It has traditionally been associated with the care of cancer patients but is also increasingly applied to the care of others with end-stage conditions such as motor neurone disease or heart failure (see also separate Palliative Care of Heart Failure article). Emphasis is placed on improving quality of life and relieving troubling symptoms rather than prolonging life. Good palliative prescribing is important but drugs are rarely the total answer; always consider the psychological, social and spiritual needs of the person. The use of non-drug measures is as important as medication in relieving suffering.

Wherever end of life care is undertaken, good communication and close multidisciplinary teamwork are essential. In primary care, the Gold Standards Framework has been shown to have considerable potential to improve end-of-life care. Its aims are to improve the quality of palliative care by focusing on the organisation of care of dying patients. Control of symptoms forms one of seven key tasks (the ‘7 Cs’) of the framework, the others being: communication, co-ordination, continuity, continued learning, carer support and care of the dying.

Where symptom control proves difficult, access to specialist palliative care expertise and advice is usually available through day or inpatient hospice care, Macmillan teams and hospital-based palliative care teams.

General principles

Try to follow a systematic approach to symptom control in palliative care:

- **Evaluation**: always try to diagnose the cause of symptoms (not necessarily the disease process - consider treatment side-effects, general debility and concurrent disorders) as the treatment's efficacy will depend on the underlying mechanism. For example, vomiting can be due to hypercalcaemia or raised intracranial pressure and require different treatments.
- **Explanation**: good explanation of the mechanism underlying the symptom and treatment options are crucial, as is involvement of the family, providing the patient agrees with this.
- **Individualised treatment**: the patient should determine treatment priorities. Set realistic goals of treatment together. Take precise drug histories - what is being taken currently, what has been tried before, problems with medication and concerns affecting concordance.
- **Supervision**: regular monitoring of symptom control is important in order to ensure that the treatment goals are being achieved and to avoid unacceptable side-effects.

Other important palliative care prescribing issues:

- **Prophylactic prescribing**: medication ‘by the clock’ for persistent symptoms.
- **Simple, acceptable treatment regimens**:
  - Aim to use the minimum possible number of drugs.
  - Consider size, shape and taste of medication.
  - Try to avoid inconvenient doses or dose intervals.
  - Consider the risk of adverse effects and drug interactions.

- **Written advice**: reinforce spoken instructions - a chart is usually helpful for the patient and family to work from, with timing, names of drugs and dose (as quantity of liquid, number of tablets, etc) and purpose outlined.
- **Continuity of care**: communication is essential between all prescribers (GP, out-of-hours service, palliative care specialists, nurse prescribers), nursing teams and pharmacists, so all are aware of changes and so that the patient and family are not confused by any alterations to medication made. Availability of equipment and drugs needs to be assured (particularly out-of-hours) and changes in prescriptions should be anticipated to avoid delays in obtaining vital medication.
- **Route of administration**:
  - Oral administration can be limited by severe nausea or vomiting, dysphagia, bowel obstruction, weakness or coma and so may not be an option for palliative care.
  - Rectal, transdermal and parenteral routes offer different options. Analgesia is available in suppository form (morphine, oxycodone) and transdermal preparations (fentanyl, buprenorphine) can also be useful, particularly in ambulatory patients where the oral route is difficult or where intractable constipation or other problems tolerating morphine develop.
  - Buccal or intranasal fentanyl may be useful for breakthrough pain (not uncontrolled background pain), as the fentanyl is swiftly absorbed, providing a more rapid onset of pain relief, compared with oral morphine.
- **Relative potencies**: care must be taken when switching between different opioids and different routes of administration. Patients who have already received weak oral opioids (eg, codeine, tramadol) should not be considered opioid-naïve when converting to stronger opioids, so require an adjusted starting dose.
- **Unlicensed use of drugs**: up to a quarter of palliative treatments involve the unlicensed use of drugs or by unlicensed routes.
Progressive disease: will alter how drugs are handled. In particular, worsening renal failure will lead to an accumulation of morphine-6-glucuronide (active metabolite of morphine). Signs of morphine toxicity may develop (increasing drowsiness, myoclonic jerks, delirium) and the morphine dose should be reduced down or the dose interval increased. Severe hepatic insufficiency will affect the metabolism of morphine and similarly may necessitate a dose reduction.[3]

Individual differences: some patients may require very high doses of morphine compared with others - this may reflect age (older patients tend to require less), use of adjuvant drugs and non-drug measures, pharmacokinetic differences (absorption, hepatic and renal function), pain tolerance threshold, previous use of strong opioids, duration of treatment and adequacy of management of other symptoms.[3]

Care of patients in the dying phase

Diagnosis of dying[7]
One of the biggest barriers to good care of the dying is healthcare professionals’ reluctance to diagnose dying. Recognising the key signs and symptoms is an important clinical skill. In cancer patients, death is usually preceded by a gradual deterioration in functional status:

- The patient becomes bed bound.
- The patient is semicomatose.
- The patient is able to manage sips of fluid only.
- The patient can no longer manage oral drugs.

The predictability of the dying phase is not as clear in some other chronic incurable diseases. Where a patient is recognised by their healthcare team to be in the dying phase (within days or hours of death), this can be communicated to the patient, if appropriate, and to the relatives. Appropriate care goals and prescribing can also be put into place to facilitate a ‘good death’.

Prescribing when providing end of life care[7]
Always consult local guidelines and protocols where available. See the British National Formulary for further information regarding drug doses and equivalent doses when converting from one drug to another.[8]

- Review current medication: stop medicines that are not providing symptom relief. Also, stop any inappropriate monitoring (such as blood tests and vital signs).
- Conversion to continuous subcutaneous infusion (CSCI): see also separate Syringe Drivers article. Essential drugs (eg, opioids, anxiolytics and antiemetics) should, in most instances, be converted to the subcutaneous (SC) route via a syringe driver. It is slightly more complicated where a patient has previously been using opioid transdermal patches (see below).

Use of SC diamorphine for pain control in dying patients:
- If already on oral morphine, divide the daily dose of morphine by three to provide the total 24-hour CSCI of diamorphine. For example, morphine sulfate (MST) 30 mg bd PO is equivalent to diamorphine 20 mg SC over 24 hours.
- If not already taking oral morphine, prescribe diamorphine 2.5-5 mg SC prn and, after 24 hours if three or more doses have been required, consider a continuous infusion via syringe driver.
- For breakthrough pain, intermittent prn SC injections of 1/6 of total 24-hour infusion dose should be given and the diamorphine dose increased by 30-50% when the syringe is renewed. This may not be indicated if the pain was due to a specific incident, rather than an increase in background pain.

- Other drugs that can be used in syringe drivers.[8]
  - Nausea and vomiting:
    - Haloperidol.
    - Levomepromazine.
    - Cyclizine (liable to precipitate if mixed with other drugs).
    - Metoclopramide.
    - Octreotide (requires consultant supervision).
  - Excessive respiratory secretions:
    - Hyoscine hydrobromide.
    - Glycopyrronium.
  - Bowel colic:
    - Hyoscine butylbromide (do not confuse with hyoscine hydrobromide).
  - Restlessness and confusion:
    - Haloperidol (little sedative effect).
    - Levomepromazine.
    - Midazolam (useful where a patient is restless or fitting).
Drug compatibility in syringe drivers - not all drugs can be mixed in a syringe driver. Those suitable to be mixed with diamorphine include:
- Cyclizine - may precipitate at higher concentrations (>10 mg/mL), with increasing concentrations of diamorphine or where a solution is older than 24 hours.
- Dexamethasone - care is needed with preparation to avoid precipitation
- Haloperidol - precipitation beyond 24 hours is likely where haloperidol concentration is greater than 2 mg/mL
- Hyoscine butylbromide.
- Hyoscine hydrobromide.
- Levomepromazine.
- Metoclopramide - discard if it becomes discoloured.
- Midazolam.

Patients using opioid transdermal patches - these can continue to be used into the last few days of life. However, titration is too slow to match any change in analgesic requirement at this time so, where there is increasing analgesic requirement, this should be given as diamorphine in addition to the patch: [6]
- Where pain is well controlled: continue the current patch regime, with diamorphine SC for breakthrough pain.
- Where pain is not well controlled:
  - Continue the current patch regime.
  - **In addition**, start diamorphine via a syringe driver with its dose based on the previous 24 hours’ breakthrough requirements.
  - For the new breakthrough dose, calculate the patch dose (diamorphine equivalent) and pump diamorphine delivery/24 hours and divide by 6.
  - Further increments in pump diamorphine doses should also be calculated based upon the patch dose, as well as pump diamorphine and breakthrough doses over 24 hours.

As required medication should be prescribed and available, including:
- Analgesics: eg, diamorphine/morphine (as-required dose will depend on regular dose).
- Antiemetics: eg, metoclopramide or levomepromazine.
- Sedative: eg, midazolam.
- Antisecretory drug: eg, hyoscine butylbromide.
- Delirium: haloperidol.

Anticipatory prescribing - should ensure that there is no delay in responding to a symptom likely to occur during the last days of life at home, such as pain, agitation, anxiety, breathlessness, nausea and vomiting and noisy respiratory secretions:
- Medicines should be prescribed so they are available in the home, with sufficient for use over a weekend (plus bank holidays). Do not omit water for injection.
- A ‘just in case’ box containing medications, syringes and needles, information leaflets, emergency contact details, etc is recommended.

Patient comfort: consider, for example, the need for mouth care and urinary catheterisation or pads where the patient is incontinent.

Monitoring: regular checks should be made to ensure good symptom control is maintained and to assess response to any changes in medication. Also important is regular monitoring of syringe drivers to check for precipitation and discoloration and to ensure the driver is running at the correct rate. If there is evidence of an injection site reaction, if the infusion is running too slowly or if there is pain or obvious inflammation, the injection site should be changed.

Common problems

Pain control
See separate Pain Control in Palliative Care article.

Nausea and vomiting
See separate Nausea and Vomiting in Palliative Care article.

- Nausea and vomiting are common in patients with advanced cancer but have many different causes - choice of antiemetic should be based on the cause wherever possible.
- In end of life care, broad-spectrum antiemetics that can be delivered via a syringe driver are chosen, most usually phenothiazines - haloperidol (effective for vomiting caused by morphine, hypercalcaemia and uraemia) and levomepromazine (broad-spectrum but sedating).
- Where bowel obstruction is the cause of the vomiting, cyclizine, hyoscine butylbromide and octreotide are suitable choices.

Restlessness
Consider:

- Pain/discomfort - the patient may not be able to communicate the source. Treat any reversible causes - eg, catheterisation for urinary retention, bowel care for constipation, hyoscine to dry up excess secretions in the throat.
- Opiate toxicity - the dose of morphine may need to be reduced as the patient’s renal function deteriorates.
- Biochemical abnormalities such as hypercalcaemia and uraemia may cause restlessness but, in the end of life phase, it is not usually appropriate to check for them. They may be associated with delirium.
- Psychological or spiritual distress.
Management options:

- Haloperidol - less sedating.
- Midazolam - sedating.
- Levomepromazine - highly sedating; use in place of haloperidol if the patient remains agitated despite haloperidol and midazolam.

**Dyspnoea**

See also separate Dyspnoea in Palliative Care article.

- Usually multifactorial, as it is almost always associated with anxiety.
- General measures - reassurance and explanation, upright positioning, good ventilation (fan, open window), chest physiotherapy and relaxation exercises.
- Drug measures - nebulised saline, oral or SC morphine (start with oral morphine or equivalent), benzodiazepines (eg, diazepam), oxygen (variable effect).

**Cough**[9]

- Consideration of whether a cough is dry or moist and the effectiveness of the cough will affect the choice of symptomatic treatment.
- Treat the underlying cause if appropriate and possible; consider co-existing disease.
- Cough can be very distressing and may worsen pain.
- Humidify the room and try simple linctus. If this is inadequate, use the appropriate strength of opioid (plus laxative) with regular or prn antiemetic for the first week if necessary.

**Excessive respiratory secretions ('death rattle')**

- This is particularly distressing for relatives.
- If present, this may be reduced by use of hyoscine hydrobromide or glycopyrrolate. Particular attention should be given to mouth care, as the treatment of secretions may cause an extremely dry mouth.

**Other common conditions**[8]

- Anorexia may be helped by prednisolone 15-30 mg daily or dexamethasone 2-4 mg daily.
- Capillary bleeding can be treated with tranexamic acid, which is usually stopped one week after the bleeding has stopped or is continued at a reduced dose. The use of gauze soaked in tranexamic acid 100 mg/mL or adrenaline (epinephrine) solution 1 mg/mL (1 in 1000) applied to the affected area is an alternative.
- Significant bleeding may be anticipated and if so the possibility is best discussed with the patient and family. Planning includes provision of dark sheets and towels. A rapidly acting benzodiazepine (eg, midazolam 10 mg IV or diazepam emulsion 10 mg IV) may be indicated.[10]

See separate Constipation in Adults, Dry Mouth (Xerostomia), Hiccups, Insomnia, Itching and Raised Intracranial Pressure articles.

**Palliative care emergencies**

Whilst anticipatory prescribing is vital, it is still appropriate that the doctor's bag should routinely contain injectable emergency medications to use in an unpredicted crisis.[11, 12] Good emergency symptom control may avert an unnecessary hospitalisation. Emergencies can include:[9]

- Severe haemorrhage.
- Choking - see separate Choking and Foreign Body Airway Obstruction (FBAO) article.
- Acute tracheal compression.
- Grand mal convulsions.
- Psychiatric emergencies (eg, panic, acute severe agitation, agitated delirium).
- Severe acute pain (eg, biliary or ureteric colic, intrahepatic bleed, bladder spasm, acute vertebral collapse, pathological fracture of a long bone).

**Ethical and legal aspects to end of life prescribing**

**Palliative sedation and the doctrine of double effect**[13]

Prescribing for patients at the end of life is often full of ethical anxiety for the prescriber, particularly in situations where a person at the end of life faces refractory symptoms. Palliative sedation is the poorly defined practice of continuous deep sedation used in patients at the end of life where normal medical treatment is failing to relieve severe symptoms of pain or agitation, and the ultimate option is to sedate beyond perception of these symptoms.

Doctors are duty-bound to relieve suffering but not to cause the patient's death. The use of medication to end someone's life constitutes euthanasia and is currently illegal in the UK. However, the doctrine of double effect is widely accepted and refers to the use of higher doses of opioids and sedatives to relieve end of life suffering without the intention of causing the patient's death, even though the risk of hastening death is foreseen. In reality, evidence suggests that palliative sedation in the last hours of life is not associated with shortened survival overall so that the doctrine of double effect need not routinely be invoked to excuse this aspect of end of life care.[14]
Disposal of medicines following death
See also separate Controlled Drugs article.

The Controlled Drugs (Supervision of Management and Use) Regulations 2006 came into force in England and Scotland in 2007 and were revised in 2013. Wales and Northern Ireland have equivalent legislation. Currently, all drugs once dispensed are the patient's property and pass to family on death. However, it is illegal to possess controlled drugs not prescribed for you. In the first instance, relatives should be encouraged to return unused medication to the community pharmacy or GP dispensing practice after their family member's death. Where this is not possible, good practice is for community nurses to destroy any unused controlled drugs, with another member of the team acting as witness, according to local standard operating procedures. Alternatively, unused controlled drugs can be returned by involved healthcare professionals to the community pharmacy for destruction. [15]

Further reading & references
- Treatment and care towards the end of life: good practice in decision making; General Medical Council (May 2010)
- General Palliative Care Guidelines for the Management of Pain at the End of Life in Adult Patients; Guidelines and Audit Implementation Network (February 2011)
- Raising awareness of dying, death and bereavement; Dying Matters
- National Council for Palliative Care (NCPC)

1. Gold Standards Framework
5. Control of pain in adults with cancer; Scottish Intercollegiate Guidelines Network - SIGN (November 2008)
6. Care of dying adults in the last days of life; NICE guidance (Dec 2015)
7. British National Formulary (BNF); NICE Evidence Services (UK access only)
8. Palliative care - cough; NICE CKS, July 2015 (UK access only)
9. Scottish Palliative Care Guidelines: Bleeding; Scottish Partnership for Palliative Care, NHS Scotland, June 2015
14. Controlled Drugs (Supervision of management and use) Regulations; Dept of Health, February 2013
15. The Controlled Drugs (Supervision of Management and Use) Regulations 2013

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