Symptom management in palliative care: optimizing drug treatment

This article provides an approach to symptom management and highlights how good prescribing is one of the essential skills required for the provision of optimal holistic palliative care.

In advanced progressive disease, although drug treatment is a major component of symptom management, reliance on drugs alone may well result in symptoms remaining unrelieved, and increased patient distress. This fundamental point is well illustrated by the case history shown in *Figure 1*. It reminds us that:

- Pains in patients with cancer may be cancer or non-cancer related
- Cancer patients often have multiple pains
- Muscular pains may be as severe or even more severe than cancer-related pain
- Some pains, however severe, do not benefit from the use of incremental doses of morphine
- Thorough clinical evaluation and explanation are vital initial steps
- Re-evaluation may lead to further changes in treatment in the light of initial results and/or undesirable drug effects.

To achieve the maximum possible success in symptom management it is necessary to adopt a systematic approach, such as is described below using the acronym *EEMMA*:

- *E*valuation
- *E*xplanation
- *M*anagement
- *M*onitoring
- *A*ttention to detail.

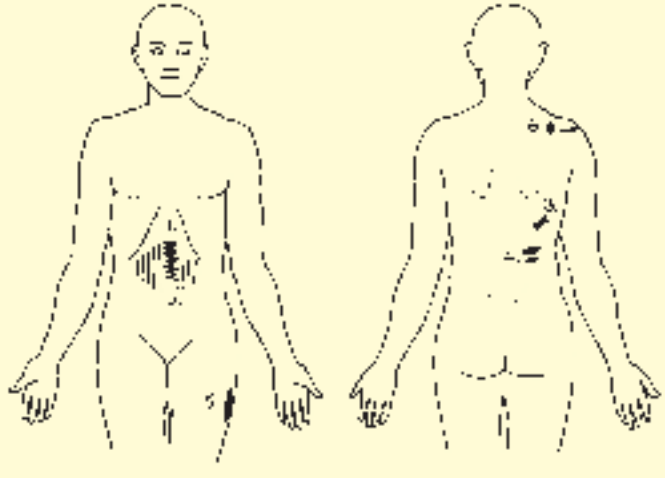
Dr Andrew Wilcock *is Macmillan Reader in Palliative Medicine and Medical Oncology, University of Nottingham, and Honorary Consultant, Hayward House, Nottingham University Hospitals NHS Trust, Nottingham NG5 1PB and* **Dr Robert Twycross** *is Emeritus Clinical Reader in Palliative Medicine, Oxford University, Oxford*

Correspondence to: Dr A Wilcock

Figure 1. Symptom management in practice.

A 63-year-old woman with a history of upper abdominal pain was found at laparotomy to have cancer of the pancreas with liver metastases. When seen 10 days postoperatively by a palliative care doctor she was receiving morphine 25 mg by mouth every 4 hours. This failed to provide adequate relief. She was drowsy, distressed and complained of insomnia. Clinical evaluation demonstrated the presence of six different pains:

1. Intermittent stabbing pain (postoperative wound pain)
2. Diffuse upper abdominal discomfort (probably constipation)
3. Rib pain (? Cracked)
4. Muscle spasm
5. Meralgia paraesthetica
6. Trigger point pain (supraspinatus)



It was explained to her that:

- Some of her pains were muscular
- The pain in her chest wall was probably caused by a rib fracture
- Her abdominal incision would probably continue to be uncomfortable on movement for several weeks, but would improve progressively
- Some of the abdominal pain was probably caused by constipation
- Some pains respond better to anti-inflammatory drugs and non-drug measures than to morphine.

The following measures were taken:

- The nurses were advised about the nature of the rib pain
- A non-steroidal anti-inflammatory drug was prescribed
- The dose of morphine was reduced to 15 mg every 4 hours in the daytime with 30 mg at bedtime
- A night sedative was prescribed
- A laxative was prescribed, and an enema planned for the following day.

The next day she had dramatically improved following a good night, and had minimal pain. The dose of morphine was reduced further and, after 3 days, she was taking only 5 mg every 4 hours with 15 mg at bedtime.

Evaluation

A wide range of symptoms may be experienced by patients with advanced cancer. Evaluation must always precede treatment, and is generally based on probability and pattern recognition. For example, hiccup in advanced cancer is often associated with gastric stasis or distension, and initial treatment planned accordingly.

What is the impact of the symptom on the patient's life?

The severity of a symptom is measured by determining the impact the symptom is having on a patient's life. Questions to ask include:

'How much does the pain [or other symptom] affect your life?'

'Do certain activities make it worse or make it better?'

'Is it worse at any particular time of the day or night?'

'Does it disturb your sleep?'

What is the cause of the symptom?

Causal factors include:

- The cancer itself
- Anticancer or other treatment
- Cancer-related debility
- A concurrent disorder.

Some symptoms are caused by several factors, and all symptoms are made worse by insomnia, exhaustion, anxiety and depression. Further, even when the cancer is responsible, a symptom may be caused by different mechanisms, e.g. vomiting could be caused by hypercalcaemia or by raised intracranial pressure.

What has been tried and failed?

This helps in planning the most appropriate management strategy by excluding certain treatment options, provided they were used optimally. If not, a further trial of therapy may be indicated.

Explanation

Treatment begins with an explanation by the doctor of the reason(s) for the symptom. This knowledge helps to reduce the negative psychological impact of the symptom on the sufferer. For example, 'The shortness of breath is caused partly by cancer itself and partly by the fluid at the base of the lung. In addition, you are anaemic.' If explanation is omitted, the patient may continue to think that his/her condition is shrouded in mystery. This is frightening because 'even the doctors don't know what's going on'.

Explanation may also be needed when using a drug beyond its licence (*Figure 2*). For example, although amitriptyline is widely used to treat neuropathic pain, the patient information leaflet lists only depression and enuresis in children as indications for its use. Without adequate explanation, patients have interpreted the use of amitriptyline to mean that the doctor thinks that they are just depressed and/or doesn't believe them about the pain, resulting in emotional distress and a lack of compliance with the treatment.

Management

Management falls into three categories:

- Correct the correctable
- Non-drug treatment
- Drug treatment.

Although the underlying disease cannot be cured, by adopting a multimodality approach it is often possible to obtain significant, sometimes complete, relief. Achievable goals should be set. For example, with inoperable chronic partial (sub-acute) intestinal obstruction, it is not always possible to relieve vomiting completely, and thus it is better to aim initially to reduce it to once or twice a day. It may also be necessary to compromise in order to reduce undesirable effects. For example, drug-induced dry mouth or visual disturbance may limit the dose escalation of an antimuscarinic drug, such as amitriptyline. Further, with some symptoms, such as anorexia, weakness and fatigue, helping the patient (and family) accept the irreversible physical limitations of end-stage disease is often the main thrust of management.

Figure 2. Using licensed drugs for unlicensed purposes.

In palliative care, up to a quarter of all prescriptions are for licensed drugs given for unlicensed indications and/or via an unlicensed route.

The licensing process for drugs regulates the activities of pharmaceutical companies and not a doctor's prescribing practice. The Medicines Act 1968 specifically safeguards a doctor's clinical freedom to legally use or advise a licensed medicine for indications or in doses or by routes of administration outside the licensed recommendations. Further, drugs prescribed outside the licence can be dispensed by pharmacists and administered by nurses or midwives.

The responsibility for the consequences of these actions lies with the doctor. Prescription of a drug (whether licensed use or route or not) requires a doctor, in the light of published evidence, to balance both the potential good and the potential harm which might ensue and to act with reasonable care and skill in a manner consistent with the practice of professional colleagues of similar standing. Thus the doctor must be fully informed about the actions and uses of the drug, and be assured of the quality of the particular product.

It has been recommended that when prescribing a drug outside its licence, a doctor should:

- Record in the patient's notes the reasons for the decision to prescribe outside the licensed indications
- Where possible explain the position to the patient (and family as appropriate) in sufficient detail to allow them to give informed consent; the patient information leaflet obviously does not contain information about unlicensed indications
- Inform other professionals, e.g. pharmacist, nurses, GP, involved in the care of the patient to avoid misunderstandings.

However, in palliative care, the use of drugs for unlicensed uses or routes is so widespread that such an approach is impractical. Few (<5%) palliative medicine consultants in the UK always obtain verbal or written consent, document in the notes or inform other professionals when using licensed drugs for unlicensed purposes or routes. Some half to two-thirds would sometimes obtain verbal consent (53%), document in the notes (41%) and inform other professionals (68%), when using treatments which are not widely used within the specialty, e.g. ketamine, octreotide, ketorolac. This is a grey area and each clinician must decide how explicit to be. Some institutions have policies in place and have produced information cards or leaflets for patients and caregivers.

Correct the correctable

Palliative care often includes disorder-specific treatment, but only when it is practical and not disproportionately burdensome. For example, patients with breathlessness and bronchospasm benefit from bronchodilator therapy. Likewise an emollient, such as aqueous cream applied topically, relieves pruritus associated with dry skin.

Non-drug treatment

For many symptoms, the concurrent use of non-drug measures is equally important, and sometimes more important. For example, palliative radiotherapy for metastatic bone pain, dietary modification in patients with taste changes, and advice about breathing technique and relaxation in patients with breathlessness.

Drug treatment

When treating a persistent symptom with a drug, it should be administered regularly on a prophylactic basis, and also 'as needed'. The latter alone is the cause of much unrelieved distress. It is important to keep the drug regimen as simple as possible. When an additional drug is considered, ask the following questions:

'What is the treatment goal?'
'How can it be monitored?'
'What is the risk of adverse or undesirable effects?'
'What is the risk of a drug interaction?'
'Is it possible to stop any of the current medications?'

Polypharmacy is common in palliative care. In one survey, patients received a median of seven drugs, four of which were either substrates, inhibitors or inducers of one of the five main cytochrome P450 isoforms. One in five patients were at risk of a clinically important or potentially clinically important drug–drug interaction.

Good prescribing extends to considering size, shape and taste of tablets and solutions, and avoiding doses which force patients to take more tablets than would be the case if doses were 'rounded up' to a more convenient tablet size. For example, it is better to prescribe modified release (m/r) morphine 60 mg (a single tablet) rather than 50 mg (three tablets: 30 mg + 10 mg + 10 mg).

Seek a colleague's advice in seemingly intractable situations

No one can be an expert in all aspects of patient care. For example, the management of an unusual genitourinary problem is likely to be enhanced by advice from a urologist or gynaecologist. Advice on prescribing in palliative care can be obtained from the Palliative Care Formulary (www.palliativedrugs.com), a hospital or hospice-based palliative care team, and/or pharmacists. Urgent referral to palliative care specialists should be made when pain and other distressing symptoms remain unrelieved or when complex psychosocial or spiritual issues remain unresolved. Sometimes transfer to a specialist palliative care unit is necessary.

Never say 'I have tried everything' or 'there's nothing more I can do'

Although it is sensible not to promise too much, it is important to assure the patient that you are going to stand by him/her and do all you can to help, for example 'No promises but we'll do our best'. However, instead of expecting immediate complete relief, be prepared to chip away at symptoms a bit at a time. When tackled in this way it is surprising how much can often be achieved with persistence.

Monitoring

It is not always possible to predict the optimum dose of opioids, laxatives, anti-emetics and psychotropic drugs. Undesirable effects put drug compliance in jeopardy. Adjustments will be necessary, particularly initially. This should be anticipated and arrangements made for ongoing supervision. Further, cancer is a progressive disease, and new symptoms occur; these need to be dealt with promptly.

Attention to detail

If a patient says, 'I take morphine every 4 hours', the doctor should ask, 'Tell me, when do you take your first dose?' 'And your second dose?' etc. When this is done, it often turns out that the patient is taking morphine q.d.s. (four times daily) rather than q4h (every 4 hours), and possibly p.r.n. (as required) rather than prophylactically. On one occasion, 'every 4 hours' meant 0800, 1200, 1600, 2000h. It was not surprising that this patient woke in excruciating pain at about 0300h – so much so that she dreaded going to bed at night.

Providing clear written instructions for drug regimens

Precise guidelines are necessary to achieve maximum patient cooperation. 'Take as much as you like, as often as you like' is a recipe for anxiety and poor symptom relief. The drug regimen should be written out for the patient and his/her family to work from. Times to be taken, name of drugs, reason for use (e.g. 'for pain', 'for bowels') and dose (x ml, y tablets) should all be stated (*Figure 3*). Patients should also be advised how to obtain further supplies, e.g. from their GP.

Rescue medication

Most patients need advice about what to do for episodic symptoms, particularly pain. Generally, it is good practice to err on the side of generosity in relation to the recommended frequency of p.r.n. medication, although how this is done varies according to the respective class of drug. Thus, for someone taking m/r morphine or metoclopramide, or an anxiolytic-sedative, indicate (in writing as well as verbally) that additional rescue doses of a normal-release preparation can be taken every 2 hours.

For inpatients, recommendations can generally be more generous because there are trained personnel to

monitor the effect of the additional medication, and to prevent serious toxicity. Thus, morphine can be prescribed q1h (every hour) p.r.n., with an increase in dose allowed if considered necessary.

Example
Patient taking m/r morphine 100 mg b.d.
Expected p.r.n. dose = 1/10–1/6 of total daily dose, i.e. 20–30 mg
Prescribe morphine tablets/suspension 20–30 mg q1h p.r.n.

This means that the nurses are less likely to be put in a position where they have to tell the patient, 'We're sorry, but you are not able to have any more morphine for another 40 minutes'. However, if two consecutive doses at the maximum frequency are insufficient, medical advice should be obtained.

Conclusions

It is the right of every patient to receive high quality palliative care, and it is the responsibility of all clinical teams to provide this for such patients under their care. Good prescribing is a skill, and makes the difference between poor and excellent symptom management. However, drugs must always be used within the context of a systematic approach to symptom management, which is encapsulated in the acronym EEMMA, a model which can be used in clinical and teaching practice. Generalists should make use of sources of advice on prescribing in palliative care and refer to palliative care specialists when pain and other distressing symptoms remain unrelieved or when complex psychosocial or spiritual issues remain unresolved. BJHM

Conflict of interest: AW and RT are directors of Palliativedrugs.com Ltd which promotes and disseminates information about the use of drugs in palliative care, through the website, CD-ROM and book versions of the Palliative Care Formulary. Profits from the company will be used to fund research and education initiatives in palliative care.

Further reading

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Name Sam Crowther Age 65 Date 5 May 2006

Tablets/medicines	*Breakfast*	*Midday meal*	*Evening meal*	*Bedtime*	Purpose
Morphine slow-release (MST) (100 mg tablet)		1		1	pain relief
Diclofenac slow-release (75 mg tablet)	1			1	pain relief
Co-danthramer strong (capsules)	2			2	for bowels
Metoclopramide (10 mg tablets)	1	1	1	1	for hiccups
Lansoprazole (15 mg oro-dispersible tablet)	1				for stomach
Diazepam (5 mg tablet)				1–2	for sleeping and relaxation

If troublesome pain: take morphine solution (2 mg in 1 ml) 15 ml, up to every 2 hours
If troublesome hiccup: take metoclopramide (10 mg) 1 tablet, up to every 2 hours
If bowels remain constipated: increase co-danthramer strong to 3 capsules twice a day

- Keep this chart with you so you can show your doctor or nurse this list of what you are taking
- Ask for a fresh supply of your medication 2–3 days before you need it
- Sometimes your medication may be supplied in different strengths or presentations. If you have any concerns about this, check with your pharmacist
- In an emergency, phone _____ and ask to speak to _____

Figure 3. Example of a patient's home medication chart (q.d.s. – four times daily); a modified version is necessary for patients on q4h (every 4 hours) medication.

KEY POINTS

Success in symptom management is more likely when doctors and other health professionals:

- Appreciate that pain and other symptoms are somato-psychic phenomena.
- Carefully evaluate the cause(s) of a symptom.
- Appropriately combine non-drug treatment with drug treatment.
- Use the right drugs in the right doses at the right time intervals.
- Are aware that the effective dose of a symptom control drug varies widely.
- Are aware that some pains respond poorly to opioid analgesics, and are familiar with the use of a range of adjuvant analgesics.
- Are similarly aware of the different classes of anti-emetics and laxatives, and are familiar with the underlying reasons for choice.
- Closely monitor patients and energetically treat undesirable drug effects, particularly constipation and nausea and vomiting in patients prescribed opioid analgesics.