PEER REVIEWED

Achieving pain control at the end of life

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Pain management at the end of life calls for the knowledge, skills and compassionate attitude of clinicians working within an interdisciplinary team created around the person who is dying. Many people express a preference to die at home, and in the vast majority of cases pain can be managed safely and effectively to facilitate this.

This article is dedicated to Mr BH and his family, who remind us that dying well at home is possible (see the first case study). Despite his youth, he approached death as he did life, without self-pity, keeping his eye on the ball being pitched and giving his all to his innings. – The authors

Death is inevitable, and clinician involvement in end of life care often occurs. It can be a challenging time for all. Pain is especially prevalent in the last week of life, and management in the terminally ill is often complex and confronting.[1,2] Despite the availability of resources and literature to support appropriate decision-making and the regularity with which medical practitioners are confronted with such situations, patients continue to suffer unnecessarily. This is largely due to clinician concern that opioids may hasten death, despite extensive evidence to the contrary.[3-6]

A clear preference exists in the wider community to die at home.[7,8] In the vast majority of cases, pain can be managed safely and effectively to facilitate this. However, this requires planning that recognises individuality and attends to details such as arranging adequate medication supplies and up-to-date contact details, organising the sharing of relevant information in a timely and accurate manner, and enabling patient and carer education to increase their confidence and capacity to manage pain.

Pain management is a core clinical skill that is often inadequately taught in medical training. Being able to competently relieve the pain of a dying patient is one of the most rewarding aspects of medical practice.

In this article, we review the prevalence of pain at the end of life (the last days to weeks of life), and the assessment and management of this pain, including intractable pain. The article focuses particularly on managing pain in the adult patient who is dying at home.

How common is pain at the end of life?

More people are living to older ages, and consequently have more chronic comorbidities.[9] Most deaths are now expected, and two-thirds occur between the ages of 75 and 95 years.[10] Sudden cardiac death is on the decline, and deaths relating to cancer are becoming more prevalent, with circulatory diseases and cancers each causing

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about 30% of deaths in Australia in 2012; about 9% of deaths in 2012 were due to respiratory causes.[11]

Pre-existing comorbidities in the elderly, such as arthritis and musculoskeletal disorders, may contribute further to pain experienced at the end of life.[2,12] Even before the dying process, over a quarter of elderly people experience clinically significant pain in the last two years of their lives. Some conditions are associated with a greater prevalence of pain; for example, 60% of patients with chronic obstructive airways disease report significant pain and 84% of patients with heart failure suffer severe pain towards the end of their lives.[13,14] For patients with cancer, a 2007 meta-analysis indicated that ongoing pain is experienced by 33% after curative treatment, 59% while on active treatment and 64% with advanced disease.[15]

Where people die in Australia

Most people in Australia express a preference to die at home, and yet most deaths occur in hospitals.[8,10] A recent online survey commissioned by Palliative Care Australia found that of the 1005 respondents, 56% had considered their preferred place of death and, of these, 74% expressed home as their preference.[7] These findings echo similar studies internationally.[16] Despite this, more than half of Australians die in hospital; in 2005, of the 131,595 recorded deaths in Australia, 54% died in hospital, 26% in aged care and only 20% at home.[17]

The importance of pain assessment

The key to successful pain management is always comprehensive initial assessment and ongoing evaluation.[18] Underpinning all elements is the therapeutic relationship within which this takes place. The physical aspects of pain are only one element to be addressed, alongside the psychological, social and spiritual dimensions that may be contributing to the pain experience and suffering. It is worth remembering that many patients with advanced malignancy have multiple pains, not all of which are directly due to cancer.[19]

Frequent review

The pain experience differs between individuals and may change over the dying period, and therefore the frequency at which assessment is required will vary. New back pain is of particular concern in patients with cancer, given the risk of spinal cord compromise from vertebral metastases and compression, and should always be carefully evaluated. Changes in pain due to disease progression or commencement of treatments that may reduce pain also require review and adjustment of analgesia.

The place of pain assessment tools at the end of life

Because pain management at the end of life is so individualised, the use of a pain diary is recommended to help patients and their carers understand, report and participate actively in pain management.[20] Delirium may be a frequent occurrence in elderly patients, and complicate pain assessment. There are numerous well-validated tools for evaluating pain, including the following:[21]

Key points

- **Good pain management at the end of life is based on comprehensive assessment (including psychosocial assessment) and diagnosis, careful titration of analgesics, attention to detail and frequent clinical review by the medical and nursing team.**
- **Opioids are the cornerstone of pain management at the end of life and, if used proportionate to pain, do not hasten dying. They are used in combination with other analgesics and titrated to efficacy and minimisation of adverse effects.**
- **With careful advanced planning, patients may die well at their home or residential aged care facility. This planning should involve GPs, community palliative care teams and the family, and be supported by hospital specialists as needed.**

- Initial Pain Assessment Tool – useful for documenting assessment findings[22]
- Abbey Pain Scale – a freely available tool that was developed to assess pain in patients with dementia, this may assist in assessing pain in patients with cognitive impairment of any cause.[23] It is based on observations of vocalisation, facial expression, body language, and behavioural, physiological and physical changes. In patients with cognitive impairment, the collateral history, sleeping pattern and presence of groaning and crying may suggest poor symptom control.

The Victorian Palliative Care Clinical Indicators for Pain help with auditing of the quality of pain management in palliative care patients, regardless of the setting of the care (Box 1).[24]

Approaches to managing pain

Case study 1 illustrates that with careful planning and good interdisciplinary co-ordination across the various care settings, patients can die well at home. Although cancer in the young is unusual, the management illustrated is applicable for all age groups.

Nonpharmacological measures

Pain management always requires attention to whole person care, and this is perhaps particularly important at the end of life, with the attendant grief of patient and carers alike. The importance of total pain care, incorporating physical, emotional, social and spiritual care, cannot be overemphasised. Physical strategies such as positioning of the patient, massage and distraction may be complemented by nonphysical dimensions of care including spiritual care, assisting with social and financial concerns and exploring the family needs. Life history review is one example of a creative validation of the dying person, and may be encouraged among the family and facilitated by volunteers or healthcare professionals.[25]

Establishing pain management goals, providing information and

1. Palliative care indicators for pain

The clinical indicators for pain listed below are recommended for implementation by the Victorian Department of Health (VDH) through the Palliative Care Clinical Network. Data specifications for each indicator are available in the VDH report *A Systematic Review for Palliative Care Clinical Indicators for Pain*.[24] Further information is available from the VDH's Palliative Care Program.

Pain assessment indicators

- Use of a validated pain scale
- Assessing pain for a new patient or new pain in a known patient
- Regular pain assessment

Analgesic prescribing indicators

- Prescribing for breakthrough pain
- Scheduled pain medication for severe pain
- Providing bowel regimen with opioids

Case study 1. An approach to dying well at home

Mr BH was a 23-year-old man with metastatic sarcoma. His illness spanned three years, beginning as he embarked on university studies. His pain was due to vertebral and other skeletal metastases. Additional symptoms were fatigue, insomnia and dyspnoea secondary to pulmonary metastases and pleural effusions. He expressed a deep desire to die at home, within his local community to which he was strongly connected. Despite his youth, he was accepting of his dying and received invaluable, unfailing support from his family, friends and local community.

Two months before Mr BH's death, a teleconference was held with cancer centre oncology and palliative care teams and his local general practitioner, community palliative care team and mother participating. This discussion provided the basis of his future care at home and allowed open discussion of possible terminal events and agreement on how they would be managed, with the focus on keeping him at home supported by local care providers.

Planning included:

- *establishing agreement that home death was possible*
- *choosing appropriate analgesics and routes of administration for maintenance and breakthrough pain management*
- *considering parenteral options for CSCI or ISCI administration in the terminal stage if he was unable to swallow*
- *agreeing that the family be taught to administer ISCI of opioids and antiemetics*
- *providing a supply of parenteral medication in the home*
- *discussing frequency of palliative care visits*
- *considering future potential clinical problems and their management, including discussion of terminal respiratory haemorrhage as a possible complication.*

Mr BH died at home surrounded by family. His cervical and shoulder pain increased in the last 48 hours, at which time the community team started a CSCI morphine 50 mg/24 hours with breakthrough subcutaneous morphine of 5 mg as required, replacing the 50 µg/hour fentanyl patch in accordance with dose equivalence of maintenance and breakthrough opioid needs. This provided more dose flexibility than the patch.

More than 80 friends and family members visited in that 48-hour period, with many stories and memories revisited. A few hours before his death, Mr BH told his mother, 'Mum, this is exactly how I wanted it to be. No hospitals and all my friends around me, thanks so much, this is perfect'.

Abbreviations: CSCI = continuous subcutaneous infusion; ISCI = intermittent subcutaneous injection.

educating carers are important elements of the management plan. In addition to analgesics, aetiology-modifying approaches should always be considered, such as judicious use of anticancer therapies (e.g. radiotherapy for localised cancer pain), tailored to the patient's prognosis and performance state.

Interventions are infrequently indicated at the end of life, with only celiac plexus block and intrathecal analgesia shown to have benefit over comprehensive medical management in specific situations.[26]

Pharmacological measures

In all but the most severe cases, adequate pain relief is achievable in the home environment within a reasonable margin of safety. The so-called analgesic ladder for treatment of cancer pain, shown in the Figure, guides the choice of analgesic according to the severity of pain and remains a widely accepted method for introducing analgesics for pain of any cause.[27] Drugs of use in the end of life setting are discussed below and listed in Box 2.

Many drugs are used off label in palliative care, utilising their actions beyond those for which they were licenced. This results in drugs used for different indications, by different routes and in different groups than specified in licensed use. Novel approaches are called for to overcome access barriers in the community.[28] Hospitals are often willing to supply such medications for patients on discharge for terminal care at home.

Nonopioids

Nonopioids such as paracetamol and NSAIDs are introduced as first-line analgesics for mild pain and may be continued when opioids are commenced, despite a lack of strong evidence for additive benefit.[27,29-31]

The well-recognised renal, gastrointestinal and cardiovascular toxicities of NSAIDs are of less relevance if the patient is in the last days or weeks of life and immediate pain relief is required.[32] However, there is limited availability of parenteral formulations of these agents.

When pain has a neuropathic component, tricyclic or newer antidepressants such as venlafaxine or duloxetine may be used.[31] Antiepileptic medications are perhaps the most useful agents in the treatment of neuropathic pain, particularly the newer agents gabapentin and pregabalin, albeit with the limitation of a lack of parenteral options.[31] On occasion, continuous subcutaneous infusion

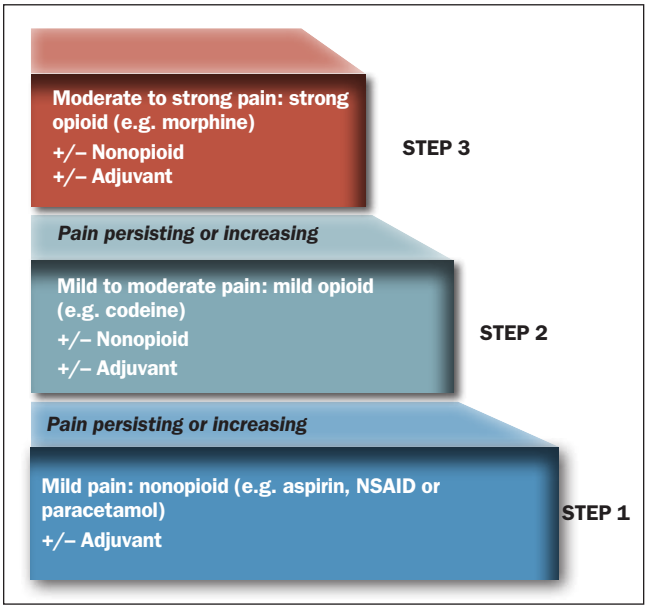

Figure. The WHO analgesic ladder.[26]

(CSCI) of lignocaine or ketamine may be trialled by specialist palliative care practitioners, although ketamine has not shown benefit in cancer pain when used with opioids and standard co-analgesics.[33]

Opioids

Where pain relief remains inadequate, a weak opioid such as tramadol (which combines mu-opioid agonism with serotonin and noradrenaline reuptake inhibition) may be added.[27,31] For more severe pain, more potent mu-opioid receptor agonists such as morphine are commenced.[27,31] In cases of severe pain at the end of life, early introduction of strong opioids is often indicated.[31]

Opioids are the cornerstone of good pain management at the end of life but are often underutilised, resulting in inadequate pain relief. This is largely due to clinician concern that opioids may hasten death, but there is no evidence that opioids hasten death when they are used proportionate to pain and titrated in accordance with readily available guidelines.[3-6,18,34] Also, patients often perceive opioids as a comfort measure for the dying rather than as a legitimate pain relief measure, a perception that needs to be countered as it leads to resistance to starting opioids and unnecessary untreated pain.[35]

Oral opioids are effective and are easier than injected opioids for patients to manage at home. Morphine remains the gold standard, with no evidence that newer, more expensive agents are more effective analgesics; alternative mu-opioid receptor agonists include oxycodone and hydromorphone.[31]

Although not recommended as first-line therapy, transdermal fentanyl or buprenorphine may be useful for patients with abnormal gastrointestinal function such as bowel obstruction or dysphagia.[31] Patients using transdermal preparations may be managed well by these means in the terminal phase, although if pain management becomes unstable more flexible preparations are preferable (see Case study 1).

2. Drugs of use in the end of life setting*†

Analgesics

Nonopioids

- Aspirin
- NSAIDs
- Paracetamol
- For treatment of neuropathic pain:
  - Tricyclic antidepressants – nortriptyline, amitriptyline
  - SNRIs – duloxetine and venlafaxine
  - Anticonvulsants – gabapentin and pregabalin
  - Continuous subcutaneous infusion of lignocaine or ketamine (specialist palliative care practitioners)

Opioids

- *Weak opioids*
  - Tramadol
- *Strong opioids*
  - Morphine (gold standard)
  - Hydromorphone
  - Oxycodone
  - Buprenorphine, transdermal (not first-line)
  - Fentanyl, transdermal (not first-line)

Antiemetics

- Haloperidol
- Metoclopramide
- Prochlorperazine

Laxatives

- Standard laxatives for opioid-induced constipation
- Methylnaltrexone

Anxiolytics/antipsychotics

- Clonazepam
- Haloperidol
- Olanzapine

Opioid antagonist

- Naloxone

Antisecretory agents

- Hyoscine hydrochloride
- Glycopyrrolate

* Not necessarily an all-inclusive list.

† Many of the uses of these drugs in the palliative care setting will be off-label.

Abbreviation: SNRI = serotonin and noradrenaline reuptake inhibitor.

Providing pain relief

Some useful online resources for GPs about the pain relief aspect of palliative care are listed in Box 3.

Analgesic doses

A key principle in the management of persistent pain at the end of life is to administer regular analgesia with provision for rescue doses

3. Pain relief in palliative care: useful resources

Cancer Pain Management in Adults
An evidence-based guideline providing brief, point-of-care recommendations for screening, assessment and management of cancer-related pain in adults is available on Cancer Council Australia's Cancer Guidelines Wiki at:
http://wiki.cancer.org.au/australia/Guidelines:Cancer_pain_management

Pharmaceutical benefits for palliative care
Information on preparations that may be prescribed for patients receiving palliative care is given at:
http://www.pbs.gov.au/browse/palliative-care
Provision is made for increased maximum quantities and up to three repeats on the initial authority prescription, providing up to four months' therapy in total

Syringe Driver Drug Compatibilities – Guide to Practice 2013
Detailed syringe driver drug compatibility information, provided by the Eastern Metropolitan Region Palliative Care Consortium (Victoria) Clinical Group, is available at:
http://www.centreforpallcare.org/assets/uploads/Syringe%20Driver%20Drug%20Compatibilities-%20Guide%20to%20Practice%202013(1).pdf

National Palliative Care Service Directory
A directory developed by Palliative Care Australia to assist the community and healthcare professionals access information about palliative care services, primary care services providing care at the end of life and a range of other services providing support to people with life-limiting illness is available at:
http://pallcare.gky.com.au/c/pc?a=apps&ap=bd

Palliativedrugs.com
An authoritative online resource for all palliative care prescribing. Online registration enables free access to most areas of the website. The *Palliative Care Formulary 5th edition* can be purchased in print or downloaded as a pdf from the website store.
http://www.palliativedrugs.com

for breakthrough pain. Breakthrough pain – pain that exceeds the usual background control – may be spontaneous (unexpected) or incident (expected or predictable; such as movement-related pain from spinal metastases).

Individuals vary widely in their requirements for analgesia. The Cancer Council Australia guidelines *Cancer Pain Management in Adults* recommends a starting dose of oral morphine in an opioid-naïve patient with normal renal and hepatic function is 20 to 30 mg per day in divided doses of long-acting or immediate-release formulations, with provision for additional doses of immediate-release opioid at the equivalent of one-sixth of the total 24-hour dose, administered one-hourly as necessary.[18] The patient should be advised to seek advice from healthcare professionals if three consecutive doses of rescue analgesia have not relieved pain.[18]

Clinicians should ensure that patients have access to opioids in the appropriate dose and format; some drugs will require PBS authority.[31]

Case study 2. The use of CSCI in the terminal phase of cancer

Mr MC, aged 68 years, had metastatic malignant melanoma, with bone, liver and peritoneal metastases. He had good pain control on slow-release hydromorphone 64 mg oral every 24 hours and up to two doses of 4 mg immediate-release hydromorphone each 24 hours for breakthrough pain. When he became semiconscious and unable to swallow he was commenced on the following CSCI delivered by syringe driver over 24 hours:

- *hydromorphone 16 mg*
- *midazolam 10 mg for anxiety*
- *haloperidol 2 mg for mild delirium.*

This was continued for two days until his death.

Clinical observations by Mr MC's family carers and community team, including noting his facial and verbal expressions, regular respiratory rate and relaxed posture, indicated his pain was well managed. He required occasional additional analgesia for breakthrough pain at position changes or when attending to his hygiene needs. His respiratory pattern changed to that of Cheyne-Stokes breathing 12 hours before death; this was explained to his carers. He was nursed on his left side, which was most comfortable for him, until his death, with his family maintaining a constant vigil.

Abbreviation: CSCI = continuous subcutaneous infusion.

Side effects of analgesics

Provision of analgesia for pain management at the end of life is often limited by side effects such as constipation, nausea, vomiting and sedation. Counselling patients and carers in advance about commonly occurring side effects is an essential part of management.

Medications to alleviate these side effects include regular prescription of standard laxatives for opioid-induced constipation.[31] In problematic cases, the peripherally acting mu-opioid receptor antagonist methylnaltrexone, administered parenterally, is effective in around half of patients.[31,36] Standard antiemetics, including metoclopramide (10 to 20 mg orally or by subcutaneous injection four times daily), haloperidol (0.5 to 1.5 mg orally or by subcutaneous injection twice daily) and prochlorperazine (5 to 10 mg orally three times daily), are frequently used in the treatment of opioid-related nausea and vomiting, although evidence for their efficacy in this role is limited.[31,37]

Delirium is common at the end of life and may be aggravated by opioids in the setting of renal impairment and dehydration. Anticholinergic load is high with many agents used in symptom control at the end of life, and contributes to delirium, particularly in the elderly.[38] Antipsychotic medication (e.g. haloperidol 0.5 to 2 mg by subcutaneous injection twice daily and 0.5 mg every two hours as needed to a maximum of 5 mg a day) may be necessary if the patient is at risk of self-harm and does not respond to reorientation and other nursing measures.

Respiratory depression due to opioid toxicity associated with

inability to rouse the patient may require naloxone in frequent small doses of 0.1 to 0.4 mg every two to three minutes by intravenous (if available) or subcutaneous injection until the patient's respiratory rate and level of consciousness is satisfactory.[39]

Antisecretory agents such as hyoscine hydrochloride and glycopyrrolate may be given subcutaneously to reduce terminal respiratory secretions, but may add to terminal delirium through their anticholinergic action.

Routes of administration

Several routes of administration are available for the different classes of analgesics used commonly in end of life care. When patients are unable to swallow, intermittent subcutaneous injection (ISCI) or CSCI are the most appropriate for the community setting.[31] In the hospital setting, these options are also highly effective and less burdensome to patients and their carers, with the CSCI route being unobtrusive and requiring minimal monitoring compared with intravenous administration. However, in the intensive care setting or occasional clinical situations such as the highly oedematous patient or the patient with a severe skin condition such as terminal cutaneous T cell lymphoma, the intravenous route may be necessary or more readily available.

CSCIs are administered with syringe drivers, which are able to co-administer multiple medications to provide relief for various symptoms.[40] When multiple agents are run simultaneously through a syringe driver, consideration should be given to drug compatibilities; in general, drugs with widely different pHs are less likely to be compatible (Box 3).[40,41] Several medications used in CSCIs in palliative care require specialist access but may be necessary for more complex symptom management. Caring for patients having drugs via CSCI at home is a partnership and must be closely co-ordinated to facilitate seamless care. Case study 2 is an example of a patient commencing a CSCI via a syringe driver in the terminal phase of cancer.

Refractory suffering at the end of life

In the vast majority of patients, pain can be well managed at the end of life by attending to whole person needs, physical, psychosocial and spiritual. However, in some patients distress may prove to be refractory, particularly when that distress arises from extreme existential suffering. In those situations, the use of sedation is an important and necessary therapeutic option. Careful guidelines have been developed to educate medical practitioners about sedation, in recognition of both the ethical complexities and the important benefits for some patients.[42,43]

Conclusion

Fear of dying is natural and widespread; many people associate cancer-related deaths in particular with intractable pain and suffering. The reality is far from this perception when attitude, skills and knowledge about pain management and palliative care are combined to care for a dying person. By reassuring patients of nonabandonment, commitment to providing every effort to assist with comfort care, respect for patient choices and openness to discussing all concerns raised, good pain management is possible at the end of life. **PMT**

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

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