

SYMPTOM CONTROL IN PALLIATIVE CARE

Dr Alethea Chung

INTRODUCTION

Palliative care is an approach that improves the quality of life of patients and their families facing life-threatening illness through the prevention and relief of suffering¹. One of the ways it achieves this is through the relief of distressing symptoms. The symptoms commonly experienced by cancer patients are pain, anorexia, weight loss, insomnia, dyspnoea, nausea and vomiting, constipation, fatigue, dysphagia and neuropsychiatric symptoms^{2,3}. But these are not dissimilar to those patients with end-stage renal, cardiac or liver diseases, or those with progressive neurological illness^{4,5}.

In fact, palliative care in non-cancer patients with life-limiting illnesses is expanding; contributing to 53.6% of hospice admissions in USA, while referrals of non-cancer patients to our local palliative care services have increased over the past few years^{6,7}.

The delivery of palliative care is no longer limited to the terminal phase of illness, but may start early in the disease trajectory, in conjunction with other life prolonging therapies. Good symptom control is essential during this stage to support patient through potentially toxic treatments, as it is when no further treatment is available.

For the purpose of this article, only management of pain, dyspnoea, nausea and vomiting, constipation and terminal delirium will be discussed.

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PRINCIPLES OF SYMPTOM CONTROL

These are:

1. Evaluate adequately to elicit cause(s) of symptom(s)
2. Correct underlying cause, whenever possible
3. Treat the symptom(s) that distresses the patient, not the doctor
4. Individualise treatment using appropriate therapies, and this may require a multimodality approach (e.g. using both drug and non-drug measures)
5. Agree on achievable realistic goals between doctor and patient (e.g. aiming for reduction of, rather than complete cessation of vomiting, in inoperable malignant intestinal obstruction)
6. Review the impact of treatment, and
7. Attend to the psychosocial and spiritual aspects of care.

ALETHEA CHUNG, Consultant, Palliative Medicine, National Cancer Center

I) Pain

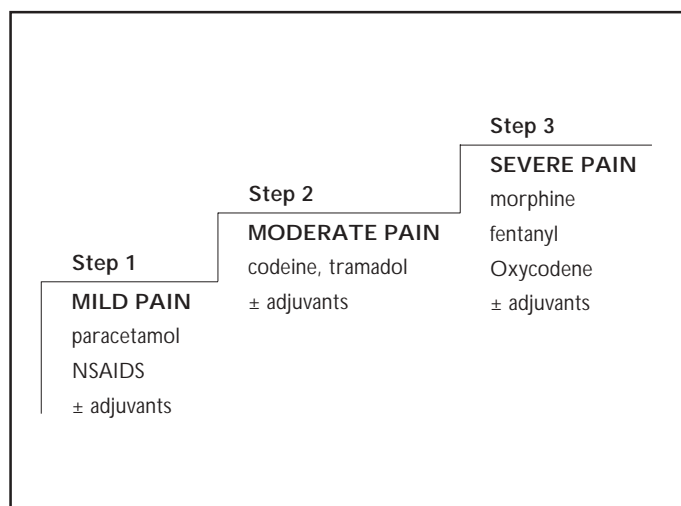
Pain is an unpleasant **sensory** and **emotional** experience associated with actual or potential tissue damage⁸. In other words pain is “what the patient says hurts”⁹. Hence, it is important to believe the patient, while appreciating that mood, morale and the meaning of pain to the patient, can modulate the experience. Pain can be both nociceptive and neuropathic. The former refers to pain resulting from chemical/physical stimulation of peripheral nerve endings with involvement of nociceptors, while the latter implies pain that arises from injury to the nervous system itself.

The principles of pain management are:

1. *Meticulous pain assessment:* This cannot be over-emphasised and includes detailed clinical history from patient to determine site(s), intensity, radiation, timing, duration, and quality of pain, and any aggravating/relieving factors, sensory disturbances, power loss, analgesic drug history, any associated anxiety/depression, and impact on daily life. It's not uncommon for patients with advanced illnesses to have multiple sites of pain, and detailed history of each pain is essential as each may have a different pathophysiology. Knowledge of dermatomes is also important for assessment of neuropathic pain. History taking should be followed by adequate physical examination and when appropriate, relevant investigations.
2. *Treatment of underlying cause if possible.* Examples are surgical fixation of pathological fractures, bowel clearance for constipation, surgery for malignant intestinal obstruction, or chemo/radiotherapy to shrink the tumour.
3. *WHO analgesic ladder.* This was developed by WHO in 1986 as part of global development of national cancer programs (see Figure 1). Since then, it has been widely used in management of pain. The key principles of the ladder are:
 - i) “by mouth” - oral route of administration for analgesics as far as possible
 - ii) “by the clock” - regular dosing
 - iii) “by the ladder” - to prescribe according to the ladder (see diagram). The steps illustrate the process of selecting a specific drug for a specific type of pain based on the intensity of the pain. E.g. someone with mild pain can be prescribed step 1 drugs as first-line, but someone with severe pain should be started on step 3 drugs instead.

- iv) “for the individual”- **The correct dose of opioid is the one that relieves pain without sedation.** There are no standard doses of opioids, i.e. no one-size-fits-all.
- v) Review, review, review! Regular monitoring is essential to ensure patient receives maximum benefit with minimum side effects.
- vi) Adjuvants may include tricyclic antidepressants, anticonvulsants, steroids, ketamine, lignocaine, and even interventional therapies, e.g. nerve blocks.
4. *Pain Scales.* These are useful tools for measuring pain intensity and for monitoring response to treatment. One useful scale to use in our local population is the numerical rating scale which requires the patient to rate verbally the pain on a score of 0 to 10, with 0 denoting no pain, and 10 the worst possible pain. Most patients are able to use this scale, even the elderly. For those who are unable, the categorical scale of none, mild, moderate and severe pain is an alternative.
5. *Non-pharmacologic measures.* These can often complement pharmacologic measures and should be considered when appropriate, e.g. physiotherapy, occupational therapy, massage, acupuncture and hydrotherapy.

Figure 1. WHO Analgesic Ladder



Do opioids hasten death?

There is a common perception among clinicians that opioids hasten death. This is probably true if opioids are given inappropriately and for the wrong reasons, e.g. large doses without previous titration, used for sedation instead of for pain or dyspnea. In fact, there are data to suggest that patients who received morphine during withdrawal of ventilatory support lived longer than those who did not receive morphine, suggesting that morphine may have a protective effect against the acute stress of critical illness¹⁰. In studies comparing those sedated for symptom control, with those who were not, there is no significant difference in survival or any correlation between opioid dose and time of death^{11,12}.

II) Dyspnoea

Dyspnoea is the sensation of shortness of breath (i.e. a symptom) and must not be confused with tachypnoea (a sign). The two may not always co-exist. It can be a very frightening experience for the patient. The interplay between dyspnoea and anxiety may be significant, so management of the latter is often necessary. Like pain, only the patient can tell us how bad it is; and it may be measured using similar scales to pain. The pathophysiology is complicated and not well understood. One possible mechanism is via stimulation of the mechanical receptors in the airways or chemoreceptors in the aortic, carotid bodies or brain stem. For causes of dyspnoea, please see Table 2.

Principles of management:

Correct underlying cause if possible

1. Morphine remains the mainstay of treatment, and principles of administering this is no different from pain, except that often low doses suffice and parenteral route may be preferable if the patient is very breathless. Morphine has been shown in randomised controlled studies to be effective for the alleviation of dyspnoea¹³.
2. Benzodiazepines have also been shown to be useful adjunct to morphine¹⁴.
3. Oxygen therapy is not useful unless there is hypoxaemia and it should be noted that a patient can be breathless without hypoxaemia.

Table 1. SUCCESSFUL USE OF MORPHINE

GUIDE TO SUCCESSFUL USE OF MORPHINE – for the doctor	GUIDE TO SUCCESSFUL USE OF MORPHINE – for the patient
Monitor patient at appropriate intervals	Educate patient on the use of morphine
Dose titrated to severity of pain	Warn about side effects
Understand addiction does NOT occur if used for pain	Empower patient to manage side effects
Understand respiratory depression does NOT occur with good dose titration	Address fears on morphine use
Learn to manage side-effects, e.g. nausea, somnolence, constipation	

Table 2. CAUSES OF DYSPNOEA

Cancer related		
1)	Intrathoracic – pleural effusion, pericardial effusion, lung primary or secondaries, lymphangitis carcinomatosa, mediastinal metastases.	
2)	Extrathoracic – ascites, hepatomegaly	
3)	Cachexia	
4)	Anaemia	
Treatment related		Non-cancer related
1)	Pneumonectomy	1) Pulmonary embolism
2)	Radiation	2) Pneumonia
3)	Chemotherapy	3) COPD/ CCF/ CRF

- Other modalities include steroids, bronchodilators (if evidence of bronchoconstriction) and diuretics (e.g. for lymphangitis carcinomatosa)
- Non pharmacological measures are equally important especially for anxiety alleviation. These include reassurance, gentle air flow (e.g. fan/ window), breathing exercises, and forms of relaxation therapy.

III) Constipation

Constipation is the decrease in the frequency of stools or difficulty in the passage of stools. The stools may be hard or soft. Causes include immobility, decreased food and water intake, general weakness, drugs (e.g. opioids, anticholinergics, iron, diuretics, 5HT₃ antagonists, etc), biochemical (e.g. hypocalcaemia, hypokalaemia), intestinal obstruction, pain on defecation (e.g. fissures), and social reasons (e.g. embarrassment with using commode or diapers). For assessment, thorough history of the patient's usual bowel habits, diet changes, medications, along with physical examination, including a rectal examination, are needed. It is important not to miss out on constipation from faecal impaction, which presents with spurious diarrhoea.

Table 3. LAXATIVES

Bulk forming agents		Osmotic laxatives	
Fybogel		Lactulose	
Fibrosine		Magnesium hydroxide/sulphate	
Methylcellulose		PEG	
Faecal Softeners		Stimulant Laxatives	
Liquid paraffin (Agarol)		Bisacodyl	
Docussate		Senna	

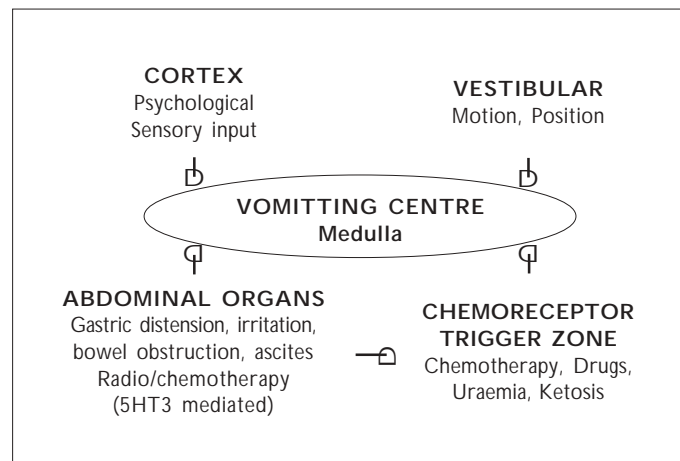
Principles of management:

- Treat underlying cause if possible
- Prevention is better than cure. Hence, patients starting on opioids should receive regular laxatives
- Laxatives are mainstay of treatment (see Table 3 for classification)

- Avoid bulk forming agents because it's likely to aggravate constipation if patient is unable to take sufficient amounts of fluid
- If impacted, rectal measures, e.g. enemas, suppository, manual evacuation, are needed alongside initiation of laxatives
- For paraplegic patients, it is important not to soften the stools too much, otherwise faecal leakage occurs. Besides regular stimulant laxatives, rectal measures (e.g. every 2 – 3 days) are often required.

IV) Nausea and Vomiting

Nausea is the unpleasant feeling of the need to vomit often, accompanied by autonomic symptoms. Vomiting is the forceful expulsion of gastric contents through the mouth⁹. Both can cause deep distress to the patient and carers. It's important to understand the pathophysiologic mechanisms involved to be able to initiate appropriate therapy. There are many neurotransmitter receptors responsible for conduction of neural impulses from various emetic stimuli to the vomiting centre in the medulla, which triggers the vomiting reflex. These include 5HT, histamine, acetylcholine and dopaminergic receptors. In particular, the chemoreceptor trigger zone is stimulated by metabolic derangements or drugs (especially opioids and chemotherapy agents). This then goes on to trigger the vomiting centre (refer to diagram below).

Figure 2. CAUSES OF VOMITTING

Principles of management:

- Identify underlying cause and treat if possible
- There may be more than one cause, and if so, combinations of anti-emetics may be needed
- Administer anti-emetics on a regular basis
- Use parenteral route of administration of anti-emetics (can be subcutaneous in home setting) if absorption is in doubt
- Titrate dosage according to response; give each drug an adequate trial of use at maximum dose before changing to another
- Combination of different anti-emetics may be needed if there are multiple causes

Table 4. DRUGS FOR VOMITTING

Cause of vomiting	Choice of drug
Drug/ toxin induced	haloperidol 1.5mg on/bd
Chemo/radiotherapy	ondansetron 4mg tds/granisetron 1mg bd ±dexamethasone 4-8mg od ±metoclopramide 10-20mg tds
Metabolic e.g. hypercalcemia	haloperidol 1.5mg on/bd
Raised intracranial pressure (e.g. brain metastases)	dexamethasone 4-8mg tds ±cyclizine 50mg tds/ haloperidol
Delayed gastric emptying (e.g. ascites, hepatomegaly, gastric outlet obstruction)	metoclopramide 10-20mg tds/qds or domperidone 10-20mg tds/qds
Bowel obstruction	sc haloperidol 1.5-3mg + buscopan 40-80mg infusion over 24h or sc ondansetron 8-24mg infusion/24h or sc granisetron 1-2mg od
Gastric irritation	stop irritant, e.g. NSAIDs or steroids H2 antagonists, e.g., omeprazole
Anxiety	benzodiazepines

- Treat constipation if present, as it can aggravate the situation
- Prokinetic drugs like metoclopramide, domperidone, should not be combined anticholinergics like buscopan and cyclizine which antagonises its action
- Prokinetic drugs should be used with care in intestinal obstruction as they may aggravate colic
- If the nausea/vomiting is opioid induced, consider switching to alternative opioids
- For malignant bowel obstruction, surgery bypass, if possible, is the best way to palliate symptoms; for those not amenable to surgery (e.g. multiple levels of obstruction or high operative risk), medical therapy (drugs+ NG/NJ tube) may be tried.

V) Delirium

This is an acute confusional state, associated with altered consciousness, disorientation, incoherent speech and poor concentration. It is not uncommon towards end of life. But it's important to exclude potentially reversible causes like sepsis, electrolyte disorders, hypoglycaemia, and drugs. Causes which are more difficult to treat are brain metastases, hypoxia, hepatic failure and psychological distress. It's also important to look out for urinary retention, faecal impaction and pain as possible aggravating factors if restlessness or agitation is present. Neuroleptics, e.g., haloperidol (5mg or more), olanzapine or risperidone may control agitated behaviour. Non-pharmacological measures include well lit room, and familiar face of close family member by bedside. Restraints are not advisable as they can aggravate confusion. If above measures fail and patient is in the terminal phase, sedation, e.g. with midazolam infusion, may be appropriate.

CONCLUSIONS

Good symptom control is essential part of palliative care, and the above discussion summarised management of some of the common symptoms experienced by patients with advanced illness, in particular, cancer patients. Psychological symptoms, e.g. depression, anxiety, etc, have not been discussed due to constraints of space, but identification and management of them is crucial if we are to improve the quality of life of our patients. To quote Dame Cecily Saunders, founder of the modern hospice movement, "Care of the dying... includes care of the family, the mind, the spirit as well as the body". How true indeed.

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RECOMMENDED READINGS

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