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 suffering. 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. But these are not dissimilar to those patients with end-stage renal, cardiac or liver diseases, or those with progressive neurological illness.

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.

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.

SFP2007; 33(3)Supplement: 57-60

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.

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I) Pain

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. In other words pain is “what the patient says hurts.” 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-fit-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.

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**Table 1. SUCCESSFUL USE OF MORPHINE**

<table>
<thead>
<tr>
<th>GUIDE TO SUCCESSFUL USE OF MORPHINE - for the doctor</th>
<th>GUIDE TO SUCCESSFUL USE OF MORPHINE - for the patient</th>
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<tbody>
<tr>
<td>Monitor patient at appropriate intervals</td>
<td>Educate patient on the use of morphine</td>
</tr>
<tr>
<td>Dose titrated to severity of pain</td>
<td>Warn about side effects</td>
</tr>
<tr>
<td>Understand addiction does NOT occur if used for pain</td>
<td>Empower patient to manage side effects</td>
</tr>
<tr>
<td>Understand respiratory depression does NOT occur with good dose titration</td>
<td>Address fears on morphine use</td>
</tr>
<tr>
<td>Learn to manage side-effects, e.g. nausea, somnolence, constipation</td>
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</table>
Other modalities include steroids, bronchodilators (if evidence of bronchoconstriction) and diuretics (e.g. for lymphangitis carcinomatosis).

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, hypokaelemia), 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 2. CAUSES OF DYSPNOEA

<table>
<thead>
<tr>
<th>Cancer related</th>
<th>Non-cancer related</th>
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<tbody>
<tr>
<td>1) Intrathoracic - pleural effusion, pericardial effusion, lung primary or secondaries, lymphangitis carcinomatosis, mediastinal metastases. 2) Extrathoracic - ascites, hepatomegaly 3) Cachexia 4) Anaemia</td>
<td>1) Pulmonary embolism 2) Pneumonia 3) COPD/CCF/CRF</td>
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4. Avoid bulk forming agents because it’s likely to aggravate constipation if patient is unable to take sufficient amounts of fluid
5. If impacted, rectal measures, e.g. enemas, suppository, manual evacuation, are needed alongside initiation of laxatives
6. 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 mouth. 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).

Table 3. LAXATIVES

<table>
<thead>
<tr>
<th>Bulk forming agents</th>
<th>Osmotic laxatives</th>
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<tbody>
<tr>
<td>Fybogel</td>
<td>Lactulose</td>
</tr>
<tr>
<td>Fibrosine</td>
<td>Magnesium hydroxide/sulphate</td>
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<tr>
<td>Methylcellulose</td>
<td>PEG</td>
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<table>
<thead>
<tr>
<th>Faecal Softeners</th>
<th>Stimulant Laxatives</th>
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<tbody>
<tr>
<td>Liquid paraffin (Agarol)</td>
<td>Bisacodyl</td>
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<tr>
<td>Docusate</td>
<td>Senna</td>
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Principles of management:
1. Identify underlying cause and treat if possible
2. There may be more than one cause, and if so, combinations of anti-emetics may be needed
3. Administer anti-emetics on a regular basis
4. Use parenteral route of administration of anti-emetics (can be subcutaneous in home setting) if absorption is in doubt
5. Titrate dosage according to response; give each drug an adequate trial of use at maximum dose before changing to another
6. Combination of different anti-emetics may be needed if there are multiple causes
**Table 4. DRUGS FOR VOMITTING**

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

7. Treat constipation if present, as it can aggravate the situation
8. Prokinetic drugs like metoclopramide, domperidone, should not be combined anticholinergics like buscopan and cyclizine which antagonises its action
9. Prokinetic drugs should be used with care in intestinal obstruction as they may aggravate colic
10. If the nausea/vomiting is opioid induced, consider switching to alternative opioids
11. 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.

**REFERENCES**

1. WHO definition of palliative care 2002.
7. Singapore Hospice Council Statistics FY05/06.

**RECOMMENDED READINGS**