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MANAGEMENT OF PAIN IN CANCER

-  While pain is a common symptom, occurring in up to 70% of patients with cancer, with a systematic approach up to 9 out of 10 patients will get satisfactory relief
-  The management of pain in cancer involves a thorough assessment and individualised treatment programme
-  The management plan should be reassessed regularly and adjusted as appropriate
-  The majority of cancer pain is and can be successfully managed in the community

INTRODUCTION

As discussed in the first bulletin on pain (NMIC Vol. 11 No. 5, 2005), pain is a subjective phenomenon¹. It is caused by stimulation of nerve endings or interference with nerve pathways, is perceived centrally, and is modified by physical, psychological, social and spiritual influences². Pain occurs in approximately one quarter of patients with newly diagnosed malignancies, one third of patients undergoing treatment, and three quarters of patients with advanced disease³⁻⁵. In addition, this is one of the symptoms patients fear most. Many cancer patients and their families believe that pain is inevitable or untreatable, or that addiction to opioids is likely when they are introduced in cancer pain management⁶. The perception of pain may be aggravated by anxiety or fear⁷ (of cancer spread, or possible impending death, or of ongoing suffering). Inadequately controlled cancer pain can have a profound effect on the patient and their carers. The core principles of pain management are a) a thorough assessment of the pain/pains to elucidate the potential cause, b) the development of a management plan using the WHO analgesic ladder, c) continued reassessment of the management plan and d) support of the patient and carers throughout the process.

ASSESSMENT OF CANCER PAIN

Given its frequency, all cancer patients should be asked at regular intervals whether they have any pain. If the patient has no pain, the continued absence of pain should be enquired about at every assessment. However, if pain is present, a comprehensive pain assessment is initiated. The standard means for determining how much pain a patient is experiencing relies on a patient's self-report. Severity should be quantified using a 0-10 numerical rating scale, a categorical scale, or the pictorial scale^{8,9}.

A comprehensive pain assessment involves a variety of components including a **history of the pain**; pain intensity; location; pathophysiology (somatic, visceral, or neuropathic); aetiology (direct effect of cancer or cancer treatment or non-malignant cause); response to current therapy; the patient's general medical condition; important psychosocial factors (i.e. associated anxiety or depression); and risk factors for under-treatment of the patient's cancer pain (i.e. past experience of unrelieved pain, patient's expectation that pain may be inevitable or poor history of pain).

The visual analogue scale (VAS) and numerical rating scale are two assessment tools for **pain severity**, which are quick to use and sensitive¹⁰. The VAS is a horizontal line 100mm long with the extremes being labelled from no pain to the worst imaginable. The patient marks a point on the line that they feel represents the severity of their pain. With the numerical scale, patients are asked to rate their pain from 0-10, with 0 representing no pain, and 10 the worst imaginable. Recording pain scores prior to and after intervention provides a relatively sensitive measure of efficacy.

To evaluate **pain intensity**, the patient should be asked how the pain interferes with their lifestyle (at rest, with movement, interference with activities). **Table 1** gives examples of questions to ask in relation to the pain⁶.

A **physical examination** and review of appropriate laboratory and imaging studies is necessary to complete a pain assessment. The goals and expectations of pain management should be discussed with the patient and his/her family, including level of comfort and function. A comprehensive history and physical examination establishes the cause of the pain in the majority of cases¹¹. Investigations may also be required to add further information¹¹ and to assist in formulating an effective management strategy.

Table 1: Useful questions to ask about the pain⁶

<p>“Tell me about the pain you have.”</p> <p>“What makes it better?”</p> <p>“What has / has not helped in the past?”</p>	<p>“Does the current medication relieve / reduce the pain?”</p> <p>“What problems/side-effects have you had with your pain medication to date?”</p>
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An accurate assessment should identify the cause, contributing factors, role of current or previous medications and the impact that each pain is having on the patient's quality of life¹⁰. There are different ways to categorise the types of pain that occur in patients with cancer. It can be defined on a temporal basis¹²: whether the pain is acute and/or chronic. Cancer pain can also be described in terms of the causes of the pain: due to the direct effect of the cancer, due to the effects of cancer therapy or due to a non-malignant cause. It can also be described in terms of the response of the patient's pain to standard management: be it simple or complex/difficult pain, which will be described in a subsequent section. The majority (up to 90%)⁷ of cancer pain occurs as a direct effect of the cancer, or as a result of its treatment, with 10% being unrelated to cancer. Some of the common causes of cancer pain are listed in **Table 2**. Patients rarely experience one single pain and reports indicate that up to 80% of patients can accurately describe two or more pains¹⁰. Each pain requires to be individually evaluated¹¹.

Table 2: Common causes of cancer pain^{7,12}

Direct effects of cancer	Effect of Cancer therapy	Non-malignant causes
Bone destruction Hepatomegaly Infiltration of pleura or peritoneum	Phantom limb pain (post-amputation) Post-mastectomy pain Post-radiation pain	Osteoporosis Osteoarthritis Diabetic neuropathy

In addition to pain, many cancer patients have a variety of **additional symptoms** including anorexia, cachexia, nausea, anxiety, depression, confusion and fatigue which may have an added impact on their pain¹³. Assessing the patient's and the carer's perception of the cancer pain is important¹⁰. Many patients and carers anticipate pain to be a feature of the illness as it progresses, and many have fears about medications that need to be explored to assist in the development of a management plan.

MANAGEMENT OF CANCER PAIN

The management of pain in a patient with cancer will be dealt with under the following headings: pharmacological management, non-pharmacological management, complex/difficult pain management and management of unrelieved pain. The key to successful management is to determine the underlying pain mechanism, and diagnose the pain syndrome prior to initiation of any therapy.

Pharmacological Management

Pharmacological therapy is the mainstay of cancer pain management¹. It requires an individualised approach through a process of continuous evaluation to achieve a favourable balance between pain relief and adverse effects with opioids, non-opioids and adjuvant analgesics¹⁴. The WHO analgesic ladder (see previous bulletins on pain - **Vol. 11 No. 5 & 6, 2005**)^{1,15} is an invaluable tool for guiding non-specialists in the logical use of analgesics for cancer pain and forms one part of the management plan. Using this treatment strategy up to 90% of patients obtain satisfactory relief from pain¹⁰.

Simple principles should be used when prescribing analgesics for cancer pain. Start at Step 1 of the WHO ladder and work up in a logical and clear fashion – inadequate pain control at one step requires a move to the next step rather than to an alternative drug of similar potency¹¹. Cancer pain requires regular analgesia¹¹. Breakthrough pain, which is characterised by a transient increase in pain between doses of an analgesic, should be treated with additional **short-acting medications**¹⁰. **Table 3** includes some of the basic principles for prescribing analgesics. The patient and their family should be advised of the likely side-effects of the analgesic therapy prescribed and their management¹⁰.

Table 3: Basic principles of prescribing analgesics in cancer

- Cancer pain requires continuous relief (“as required” use is inappropriate and ineffective in cancer pain management)¹⁰.
- Each patient's dosing regimen should be individually determined, and assessed on a daily basis, until the pain is controlled.
- Doctors should be familiar with the basic rules of the WHO analgesic ladder and only use those drugs, with which they are familiar^{2,16}.
- The oral route is always the preferred route¹⁷⁻¹⁹.
- When mild analgesics fail, change to a stronger analgesic (as per WHO analgesic ladder)
- Drug dependence is not a practical problem with cancer pain - while patients with cancer taking opioids do develop physical dependence (**and therefore opioids should NEVER be stopped abruptly**), they **RARELY** develop psychological dependence.²⁰

Opioids are the mainstay of drug therapy for cancer pain¹³. **Table 4** lists some of the principles for prescribing opioids. Opioid-naïve patients experiencing severe or increased pain should be commenced initially on regular short-acting opioids, laxatives, and adjuvant co-analgesics as indicated. **Psychosocial support** is needed to ensure that patients encountering common barriers to appropriate pain control (e.g. fear of addiction or side effects) or needing additional assistance (e.g. depression, rapidly declining functional status) receive appropriate care and attention.

Appropriate opioid selection may be difficult and depends on the patient's pain intensity and any current analgesic therapy. When starting opioids, an individual approach should be used to determine starting dose, frequency, and titration in order to achieve a balance between analgesia and side effects²¹.

After the initial treatment of acute pain, the patient should have a comprehensive reassessment. Once the patient has adequate pain control with the normal release preparation, consideration should be given to converting to the equivalent total daily dose of **sustained-release medication** (see previous bulletin **Vol. 11 No. 6, 2005**)¹⁵. This should be commenced at the time that the next normal release formulation was due. Patients with cancer pain should also have access to breakthrough analgesia, e.g. one-sixth of the total regular daily dose of the oral opioid in a normal release preparation^{10,14}. Patients with increasing levels of pain will require gradual escalation of the opioid dose until adequate analgesia or intolerable side-effects occur. In calculating this, the total daily opioid dose (regular and breakthrough analgesia) being used should be considered¹⁴.

Parenteral administration may be necessary when patients are unable to take oral medicines, for example, in the setting of nausea or vomiting, or when a patient is dying. Approximately 80% of patients with cancer will not be able to take oral opioids for some period before their death and parenteral methods of delivery can be used as an alternative. The relative potency of opioids is increased when they are given parenterally – the total oral daily dose of morphine should be halved to get the equianalgesic dose of subcutaneous morphine²² (e.g. a patient on a daily dose of MST 30mg BD should be transferred to 30mg subcutaneous morphine over 24 hours). **Specialist advice should be sought when changing a patient to this method of administration**^{7,10}.

In patients who are receiving high-dose or prolonged opioid administration it is important to observe for signs of opioid toxicity, particularly in the elderly and those patients with decreased renal function¹³. Signs include agitation, visual and auditory hallucinations, nightmares, vivid dreams, confusion and myoclonic jerks (see previous bulletin **Vol. 11 No. 6, 2005**)¹⁵. Management includes reducing the dose of opioid, ensuring adequate hydration, and treating the agitation with haloperidol²².

Table 4: Basic principles of opioid prescribing

- Before starting a patient on an opioid, explain to the patient and family the rationale for using the opioid, the expected result and the commonly experienced side-effects.
- The oral route is the route of choice.
- The patient should be prescribed regular analgesics – usually 4-6hrly if using short acting preparations or 12-24 hrly if using oral sustained release preparations (see Summary of Product Characteristics (SPC) for individual opioids).
- A short-acting analgesic for breakthrough pain should always be prescribed in addition to regular opioid – generally equivalent to one-sixth of the 24-hour baseline opioid dose ¹⁴.
- Co-prescribe laxatives, including a combination of a stimulant and a softening laxative.
- The patient and family should be advised that drowsiness may occur when opioids are introduced, but that it abates within 5-7 days. It is more frequently seen in the elderly and those with renal or hepatic impairment.
- There is no maximum dose ², although reassessment is required if rapid significant increases in opioids are required. Most patients require <200mg morphine a day ²².
- 30-60% of patients taking opioids for the first time will experience nausea and/or vomiting, however tolerance usually develops within 5-10 days. Treatment with an anti-emetic such as cyclizine may be required.

Morphine is the **most commonly used opioid** ²³ and is generally considered to be **the opioid of choice** for managing moderate and severe cancer pain ². The majority of patients tolerate morphine well, its use has been established in clinical practice in relation to safety and efficacy and there are a wide variety of formulations available, which allows flexibility in dosing intervals ¹⁰. When initiating morphine treatment, start with a normal release preparation at 5-10 mg every 4 hours. The starting dose of morphine however can vary between patients ⁷ and the optimal starting dose is determined by previous analgesic requirements ¹⁶. It may need to be reduced, particularly in those patients with renal impairment where accumulation of morphine metabolites can occur ¹⁰.

Oral morphine formulations: Normal release preparations have an onset of action after approximately 20 minutes and the peak drug level is reached after 60 minutes. They need to be given every four hours to maintain constant analgesic levels ¹⁰. These preparations are suitable for initiating therapy and also for treating breakthrough pain. Controlled release preparations have a slower onset (1-2 hours) and later peak effect (twice daily preparations 4 hours, and once daily 8.5 hours).

An increasing number of **alternative opioids** are available, including oxycodone, hydromorphone, fentanyl, buprenorphine and methadone. It is becoming increasingly common to switch to an alternative strong opioid ² in patients who are intolerant or unresponsive to morphine, which involves achieving a balance between analgesia and side effects ²¹. It is recommended that switching opioids should be carried out under the supervision of an experienced clinician/specialist, because the effect of switching opioids is variable and unpredictable ^{7,16}. See bulletin **Vol. 11 No. 5 & 6, 2005** for further information on individual opioids, including the side effects associated with the use of opioids ¹⁵.

Adjuvant therapy

Not all types of cancer pain are responsive to opioids and patients often require co-administration of other drugs and /or other intervention. Adjuvant or co-analgesic therapy may be required in those patients with bone pain, neuropathic pain or visceral pain, which may result in better pain control at lower doses of opioids. Subsequent treatment for each patient should be based on the patient's continued pain rating score.

The adjuvant analgesics most commonly used in the treatment of cancer pain include tricyclic antidepressants, anticonvulsants, corticosteroids and bisphosphonates.

Tricyclic antidepressants and anticonvulsants – Patients with difficult pain, such as neuropathic pain, should have a trial of a tricyclic antidepressant and /or an anticonvulsant. One drug should be introduced at a time, although they may occasionally be prescribed simultaneously ²². Please see previous bulletin (**Vol. 11 No. 5, 2005**) for further information on these medications ¹.

Corticosteroids can be helpful for those patients where the pain is caused or exacerbated by the mass effect of inflammatory oedema, such as pain due to acute nerve compression, visceral distension, increased intracranial pressure and soft tissue infiltration ²⁰. Short tapering courses of drugs given in initially high doses are advised.

Bisphosphonates have been used for the management of opioid-refractory bone pain. ¹

Non-Pharmacological Management

In the management of patients with cancer, consideration should also be given to non-pharmacological measures and input from a multidisciplinary team ⁶. The general practitioner (GP) and public health nurse (PHN) have a vital role to play in the non-pharmacological management by providing support to both the patient and family at this difficult and stressful time. A multidisciplinary team with good communication skills is very important for both the patient and the family, particularly around pain and analgesic issues ²⁴. In addition to the GP and PHN, the Home Care team are an invaluable resource in the non-pharmacological management of the patient and in particular for those patients who continue to experience pain.

A patient's perception of pain may be influenced by the patient's psychological health (anxiety, depression, insomnia) and spiritual concerns and, in addition, their family's experience of cancer – these factors need to be addressed.

Physical interventions with input from the Physiotherapist (thermal stimulation / ultrasound therapy / relaxation techniques / advice regarding exercise and proper positioning) and Occupational Therapist are included in the non-pharmacological aspect of management ¹⁷. Transcutaneous electrical nerve stimulation (TENS) is a way of controlling pain through the "gate" theory, where, it is believed, selective electrical stimulation of certain nerve fibres block signals causing pain impulses to the brain ²⁵. Its efficacy is unpredictable however and tends to decrease over time ⁶. Acupuncture has also been used – the response is similar to that seen with TENS ⁶. The use of complementary therapies – massage, aromatherapy, reflexology and meditation are increasing in popularity with patients and families, though the effectiveness of many of these has yet to be proven ⁶.

Complex / Difficult Pain Management

Some types of pain are complex, difficult to control and require a combination of pharmacological and non-pharmacological strategies¹³. This category of pain usually requires the skills of a specialist inter-professional team. Early referral to a specialist palliative care and / or anaesthetic pain service is obligatory. Examples of these pain types include neuropathic pain, visceral pain, bladder spasm, tenesmus (rectal spasm) and incident pain, which is episodically severe pain on a background of relatively well-controlled pain. **Table 5** provides the clinical features of different types of cancer pain.

Table 5: Clinical features and first-line management for different types of cancer pain

Sources of Pain	Clinical Features	Treatment Options
Bone	Worse on moving / weight bearing	NSAIDs Dexamethasone Opioids Radiotherapy
Obstruction of hollow organ	Colic type pain	Hyoscine butylbromide
Visceral involvement (Liver / Pancreas) Acute / Chronic	Constant severe pain radiating to the back or referred to the right shoulder May occur acutely with associated nausea	Opioids Dexamethasone Coeliac plexus nerve block
Neuropathic pain (nerve / CNS damage)	Severe / shooting / stabbing Radiating to dermatome	Adjuvant therapies Dexamethasone Opioids
Raised intracranial pressure	Headache – worse in the morning, lying or stooping Associated nausea	Dexamethasone Possible referral for radiotherapy

Unrelieved Pain

Failure to achieve pain control may occur for a variety of reasons, as listed in **Table 6** below. Inaccurate assessment of the pain, due to reasons relating to the patient or physician will lead to an inappropriate management plan and, ultimately, unrelieved pain. Frequent assessment of the patient with input from family members is helpful.

Table 6: Possible causes of unrelieved pain

Patient Reasons	Doctor Reasons
Reluctance to report pains ³	Inappropriate / inadequate prescribing ²⁴
Expectations that pain is inevitable ^{3,24}	Incomplete pain assessment ^{3,24}
Fears/anxiety about the meaning of pain ³	Misconceptions about opioids ^{3,24}
Fear of addiction to morphine ²⁶	Lack of communication with patient ²⁴
Aversion to side-effects ²⁶	Failure to use non-pharmacological measures where appropriate ²⁴
Lack of communication with doctor ²⁴	Failure to recognise the non-physical aspects of pain ²⁴
“Putting on a brave face”	Failure to identify a “difficult pain” ²⁴

ONGOING MANAGEMENT ISSUES

Pain relief is the goal and is achievable for the majority of patients with cancer pain. However as a patient’s cancer progresses, increases in previously controlled pain or the emergence of new pain commonly occurs. This aspect of cancer pain management requires ongoing expert input with frequent re-assessments of analgesic requirements and adjustment of the medications.

SUMMARY

Pain is one of the symptoms that patients with cancer fear most and is a common problem encountered in cancer. Pain can be due to the effects of cancer itself, to its treatment or be unrelated to the cancer. Many patients with cancer experience more than one pain and each requires assessment. With a standardised approach, using the WHO analgesic ladder, the majority of cancer pain can be managed.

Opioids are very effective in the pharmacological management of cancer pain, but only form a portion of the armamentarium. In addition non-pharmacological therapy has an important role in the management of cancer. It is important to identify those patients with unrelieved and difficult cancer pain. The majority of cancer pain can be managed in the community with a multi-disciplinary team, including support from the home care team and palliative specialists when required. The essential aspects of the management of the patient experiencing pain with cancer include a thorough assessment of the pain, development of a management plan and ongoing review of the patient.

References available on request. Date prepared: June 2006

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. Prescribers are recommended to refer to the drug data sheet or summary of product characteristics (SPC), also available on www.medicines.ie for specific information on drug use.

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