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Clinical experience

Pain control in palliative care settings

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Abstract

Background and Purpose: *The goal of palliative care is symptom control in patients with advanced disease and improvement of their quality of life.*

Materials and Methods: *Pain assessment can be done through numerous rating scales. It is important to quantify pain so that health care providers can provide the most sufficient pain therapy and determine the effectiveness of it.*

Results: *Morphine is the »gold standard« as pain medication in palliative care. Patients receiving palliative care often require frequent escalations in opioid dosage to attain good pain control. If the patient's pain cannot be controlled by using opioids co-adjuvant analgesics should be added.*

Conclusions: *In pain control therapy we should apply the cancer pain algorithm named »analgesic elevator« which is suggested by IASP.*

INTRODUCTION

Prevalence data indicates that there are currently about 18 million people living with cancer world-wide. At least 5,5 million have cancer pain. Prevalence of pain rates from 30 to 40 per cent in patients on active anticancer therapy and from 70 to 90 per cent in patients with advanced disease. *(1)* Pain impairs the patient's and caregiver's quality of life (QoL), worsens the prognosis and is still commonly under treated *(2)*.

The goals of palliative care are to control symptoms in patients with advanced disease and enhance their quality of life. No patient at the end of life should have unrelieved pain *(3)*. With the pharmacological approach, about 90–95% of patients get pain relief. Non-pharmacological approaches, neurosurgical or anaesthetic techniques may also relieve pain. This article addresses the pharmacological aspect of pain management.

Facts about pain

Many patients do not receive adequate control of their symptoms. Although education and training in the management of pain have increased for physicians and nurses, many patients do not receive adequate analgesia. More than 70% of cancer patients report pain *(4)* and more than 36% of patients with metastatic disease have pain severe enough to impair function *(5)*. The presence of pain usually implies a pathological process; in patients with cancer idiopathic or psychological pain is very rare *(6)*. Pain not only adversely affects the quality of life of patients, but also can be psychologically devastating because it can be a constant reminder of the incurable and progressive nature of the disease *(7)*.

Repeated comprehensive pain assessments are the cornerstone of adequate pain management. A complete history and a physical examination, with emphasis on the patient's symptoms are obtained, including information regarding the location, intensity, radiation, aggravating factors, timing, quality, and meaning of the pain. Medications and treatments are reviewed, and a psychosocial history is taken.

Pain assessment

The intensity or severity of the pain must first be quantified. Pain rating scales that have been used for more than a decade allow patients to quantify their pain so that health care providers can determine the effectiveness of the therapy. The most commonly used is the numeric rating scale. Pain is rated on a scale of 0–10, with 8–10 being severe pain, 4–7 moderate pain, and 1–3 mild pain *(8)* Other scales, including the visual analogue scale and the verbal rating scale, are available to quantify the patient's pain. Because most patients have variable tolerance to pain, patients should frequently be asked if the pain is interfering with their daily activities and some patients are unwilling to admit to having increased pain because this may be associated with progression of their underlying disease. This question often provides insight into the level of pain.

Pain assessment tools also give us various aspects of pain: location, quality, onset, duration etc. Precisely locating the discomfort can also help in determining the type and nature of the pain.

Pain management in the elderly is complicated by difficulties in pain assessment. Elderly patients may under report pain, and pain reports from cognitively impaired patients may be incomplete, but also valid.

All patients if possible should complete a standardised questionnaire or undergo a structured interview. The key to good pain management in patients with advanced disease is thorough and frequent assessment. The entire palliative care team can be useful in monitoring a patient's pain. *(9)* Patients are often unable to adequately rate their pain *(9)* and it may be necessary to monitor behaviour that could be indicative of pain in some patients *(10)* Behaviour such as mood swings, agitation, restlessness, and increased fatigue may all signify an increase in the patient's pain. But also patients can be sleepless, withdrawn, depressed or irritable when experiencing pain. Physicians and nurses have to be familiar with these manifestations and to recognise them as pain manifestation.

Actiology of pain

Pain may arise from different aetiology. It can be due to the direct effects of the cancer or caused by treatment of the disease. Surgery, radiation, and chemotherapy may all result in pain. The patient may also have chronic underlying disease that directly causes or contributes to pain. Visceral pain arises from direct stimulation of afferent nerves due to tumour infiltration of the soft tissue or viscera *(11)* This pain tends to be poorly localised and often ill defined. In cancer patients, visceral pain may be caused not only by direct tumour infiltration, but also by variable conditions such as constipation, radiation, or chemotherapy. Somatic pain in cancer patients is generally due to soft tissue inflammation or to metastatic disease of the bone *(12)*. Neuropathic pain is generally described as burning or electrical in nature. This type of pain is due to neuronal injury either by the effects of treatment or by tumour invasion. For example, cisplatin, vincristine, and procarbazine can be harmful to nerves. Neuropathic pain may not always be responsive to opioid therapy.

Pain management

Symptom control in the home setting may differ from that provided in a more traditional setting such as a hospital or nursing home. Pain management must be responsive to the patient's changing symptoms, and care must be taken to respect the family's wishes and limitations. Family members are often reluctant to give injections or administer medicines rectally. Breakthrough medications are often withheld for fear of getting their loved one »addicted« to opioids.

Treatment with analgesic drugs is the mainstay of cancer pain treatment *(13)*. WHO Expert Committee on Cancer Pain Relief and Active Supportive Care over two decades ago proposed a useful approach to drug selection for cancer pain which has become known as the WHO analgesic ladder (Figure 1).

WHO method for cancer pain relief when combined with appropriate dosing guidelines provides adequate relief to roughly 70-90 per cent of patients *(14)*.

Non-opioid drugs comprise paracetamol (acetaminophen), the non-steroidal anti-inflammatory drugs (NSAIDs) and nefopam. Non-opioids have a »ceiling« effect and therefore if a patient's pain is inadequately controlled and the maximum dose has been reached, then the drugs must be changed, supplemented with opioids, or an adjuvant drug added *(15)*.

Opioid use

Opioid receptors (mu, kappa, delta) are found in several areas of the brain, particularly in the periaqueductal grey matter and throughout the spinal cord. Based on their interactions with the various receptor subtypes, opioid compounds can be divided into agonist, agonist-antagonist and antagonist classes *(16)*. The agonist opioid drugs have no clinically relevant ceiling effect to analgesia, in contrast to both the partial agonists and agonist-antagonists drugs *(16)*. Jacox *et al. (17)* found that 75%–85% of patients received adequate pain control with oral, rectal, and transdermal drugs. Unfortunately, patients, their families, and some physicians may have unexpressed significant concerns and misconceptions about opioids. The physician must explain that patients with malignant tumours who take opioids do not become addicts, and »that we have lots of medications for the latter«.

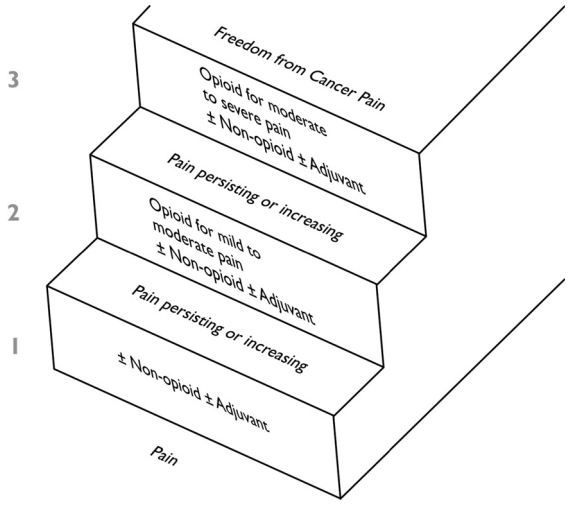

Figure 1. *The three step analgesic ladder.*

Morphine is often referred to as the »gold standard« in palliative care because it is effective, inexpensive, and easy to titrate, and it can administered using many routes including oral, rectal, parenteral, subcutaneous, and spinal. Morphine is a potent mu agonist drug that was first induced into clinical use 200 years ago. Today is the prototype opioid step III of the »analgesic ladder«. Morphine and morphine-like agonists (methadone, pethidine, hydromorphone, levorphanol, oxycodone, oxymorphone, fentanyl and phenazocine) are widely used to manage cancer pain while mixed agonist-antagonist analgesics (pentazocine, butorphanol and nalbuphine) play a very limited role in the management of chronic cancer pain *(18)*.

The goal of good pain management is to minimise both the patient's pain and the need for breakthrough medication. When comfortable on a given dosing regimen, the patient should be converted to a long-acting medication. All patients should have access to breakthrough medication since up to two thirds of patients with well-controlled chronic pain have transitory breakthrough pain *(19)*.

The most common side effects of opioids are sedation, constipation, emesis, confusion, hallucinations, urinary retention, dizziness and uncommon respiratory depression. Clinically important respiratory depression is a very rare effect in the cancer patient whose opioid dose has been titrated against pain. Close monitoring of the patient's symptoms through frequent reassessment dictates the need for titration of the opioid *(20)*.

Patients receiving palliative care often require frequent escalations in opioid dosage to attain good pain control. Foley *et al. (21)*. found that 20% of patients required three switches of their medication before finding an effective dose. Reassessment by the health care team is necessary after every medication change. Opioid use in older patients should be monitored closely. Older patients may require lower doses of opioids, and therefore these medications should be used cautiously in this patient population *(22)*. Opioids should never be discontinued abruptly in patients receiving chronic opioids as this may cause an acute withdrawal reaction.

Tolerance and Addiction

Tolerance is defined as the progressive decline of the potency of an opioid with continued use. Patients may also develop tolerance to the side effects of an opioid. Patients are often reluctant to increase the dose of their medication because they fear that the tolerance they have developed will lessen the effectiveness of the opioids at a later date. These patients should be assured that tolerance can develop as a normal result of opioid use and that a simple dose escalation is all that is usually required for additional pain control.

Fear of addiction (psychological dependence) is a major consideration limiting the use of opioids. The development of physical dependence and tolerance are distinct from the behavioural pattern seen in some individuals and described as »addiction« *(23)*.

Surveys of cancer patients and burn patients receiving chronic opioids during a long period, suggest that medical use of opioids rarely, if ever, leads to drug abuse or iatrogenic opioid addiction.

Infusion Therapy and Spinal Analgesia

If the patient's pain cannot be controlled by escalating doses of medication via the oral, rectal, or transdermal routes, more invasive therapy may be instituted. Opioids may be given via this route and may be titrated rapidly by patient-controlled analgesia. The subcutaneous route is limited due to variability in absorption of medications in each individual patient, depending on the amount of subcutaneous tissue. Venous access is a more effective method of delivering larger doses of opioids when rapid escalation is required. Medications are not limited by the concentration, and the variation in absorption is not a factor. However, not all patients have easily obtainable venous access, and central or peripherally inserted central venous catheter (PICC) line placement is often required. Spinal analgesia should be considered for patients with pain that is poorly responsive to conventional routes. This route should also be considered for patients with poorly controlled pain or for those who cannot tolerate the side effects of oral opioids.

Adjuvant analgesics (coanalgesics)

Adjuvant analgesics (coanalgesics) are administered with primary analgesics to enhance pain relief, treat pain that is refractory to the analgesics, or allow reduction of the analgesic dose for the purpose of limiting side effects *(24)*.

The adjuvant analgesics comprise an extraordinarily diverse group of drug classes (antidepressants, corticosteroids, anticonvulsants, local anaesthetics, neuroleptics etc.) and many of these drugs act like multipurpose analgetics. Focus on neuropathic pain as a target for

adjuvant analgesics in the palliative care setting derives from the relatively poor response of these pain syndromes to opioid drugs *(25)* and neuropathic pain is the usual indication for trial of a multipurpose adjuvant analgesic.

Cancer pain algorithm

Based on these data an alternative cancer pain algorithm known as »analgesic elevator« is suggested by IASP *(26)*. »Analgesic elevator« selects the strength of the opioid analgesic according to the current severity of pain:

1. For mild pain, non-opioid analgesic treatment should be initiated. If pain is not adequately controlled, then low doses of »strong« opioids should be added and titrated.

2. For moderate pain, low doses of »strong« opioids should be initiated and titrated, with or without non--opioids.

3. The treatment of severe pain obviously requires the immediate use of »strong« opioids, with or without non--opioids.

4. Invasive procedures should be considered as an alternative or adjunct to pharmacotherapy at any stage of disease with moderate or severe cancer pain.

5. Adjuvant drugs should be used for all stages when indicated.

6. »Weak« opioids should be dropped in the treatment of cancer, other than in countries where »strong« opioids are not readily available.

Although many studies support this suggested algorithm, further validation should be provided by prospective studies in broad populations of patients with cancer pain *(26)*.

CONCLUSIONS

Pharmacologic therapy is the mainstay of pain management in patients with advanced disease. The majority of patients can attain good pain control with the use of opioids and adjuvant medications. Simple means of administration such as oral, transdermal, or rectal can be used in managing the majority of pain syndromes. Principles of good pain management include a thorough initial assessment and frequent reassessment to monitor the efficacy of treatment and the onset of side effects. Opioids need to be titrated to attain good pain control. Many cancer patients have more than one pain syndrome, and multiple medications are often indicated. Frequent assessment, rapid intervention, and appropriate use of opioids and their adjuvants are requisites for adequate pain control and optimal quality of life.

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