Advances in pain control in palliative care

Pain in palliative care needs to be carefully assessed before treatment.

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The recent PainSA conference held in conjunction with the International Association of the study of Pain, Africa Association for the study of Pain, NeuroPsig and the London Pain Consortium, presented current physiological evidence of the importance of neuronal and synaptic activities involved in generating pain. The physiological evidence supports the inclusion of medication previously considered as co-analgesics or adjuvant analgesics as primary analgesics. This article looks at the assessment and management of pain in the palliative care setting and the current recommendations for the management of neuropathic pain.

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Pain in the palliative care setting can be caused by the illness itself, the treatment (radiotherapy, chemotherapy, antiretroviral treatment), concurrent disorders (tension headaches, urinary tract infection) or by general debility.[1] Thus a very careful assessment and a multimodal approach and understanding of pain are required.

Physiologically the different types of pain can be described as nociceptive (arthritis, cellulitis),[2] visceral (pancreatitis, peptic ulcers), neuropathic (herpes zoster, post-stroke pain) and mixed pain, a combination of the other types of pain found in certain disease states such as AIDS and cancer.

Many patients and health care professionals do not distinguish the pain experience from nociception, which describes the neural processes involved in the transduction of noxious stimuli.[3] Pain in the palliative care setting is not purely a nociceptive or physical experience but involves all aspects of human functioning: personality, affect, cognition, behaviour, and social relations.[4] Experimental evidence shows that acute persistent pain may promote biochemical and physiological changes in the peripheral and central nervous system, which may promote the continuation of pain.[5] Chronic pain (lasting longer than 3 months) has a negative impact on quality of life[6] and leads to anxiety, depression and sleep disorders. Because pain in palliative care is multidimensional, a multimodal approach is needed to address both the physical and the physiological factors (Fig. 1).

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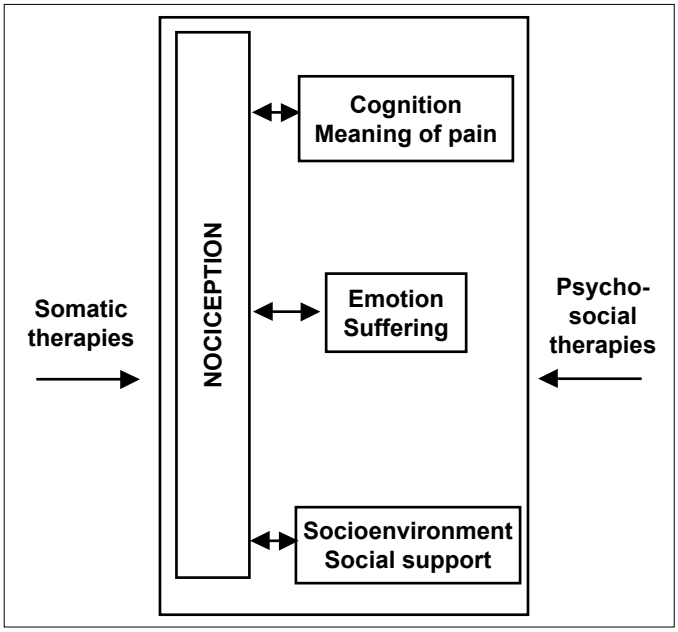

Fig. 1. The multidimensional nature of pain in terminal illness.

Pain assessment

The most important element of pain assessment in palliative care is to establish a good rapport with the patient and to show empathy and understanding of his/her pain and suffering. Encourage the patient to do most of the talking by asking open-ended questions (Tell me about your pain) and then zone in on more specific questions (Table I). Specific questions about the location, intensity, character and temporal profile of the pain, exacerbating factors and concomitant symptoms will help the clinician distinguish between the different types of pain.[7] Neuropathic pain is classically described as pricking, tingling, pins and needles, electric shocks or shooting, hot or burning, numbness, pain evoked by light touch or pain evoked by change in temperature. This type of pain is typically confined to a specific set of dermatomes. Nociceptive pain may be somatic or visceral pain. Somatic pain is typically well localised and is felt in the superficial cutaneous or deeper musculoskeletal system. Visceral pain is usually poorly localised, often described as deep squeezing and/or pressure and may be associated with nausea, vomiting and diaphoresis, especially when acute. Visceral pain can be referred to cutaneous sites away of the lesion (shoulder pain with diaphragmatic lesions).[8] The intensity of the pain can be measured by using visual analogue, drawings and verbal descriptors. A simple tool which is used in countries with varying degrees of literacy and numeracy is a closed fist for no pain and each digit indicating an increasing degree of pain up to five for the maximum. During the assessment the clinician must also determine how the pain affects the patient's mood, sleep pattern, physical activity and relationships. It is also important to find out what prior treatment has been used and its

Table I. Clinical assessment of pain[2]

- Believe the patient's complaint
- Take a careful history of the pain complaint to place it temporally in the progression of the patient's illness
- Assess the characteristics of each pain (site, referral pattern, aggravating and relieving factors and impact on daily living)
- Clarify the temporal aspects of the pain (acute, chronic, intermittent)
- List and prioritise each pain complaint
- Evaluate response to previous treatment
- Evaluate the psychological state of the patient and the effect of pain on it
- Perform a careful medical and neurological examination
- Order and review appropriate diagnostic test
- Individualise the treatment to the patient's circumstances and create realistic goals
- Provide continuity of care
- Empower patient and family caregiver to manage the pain, especially breakthrough pain
- Reassess the patient's pain response to treatment and compliance

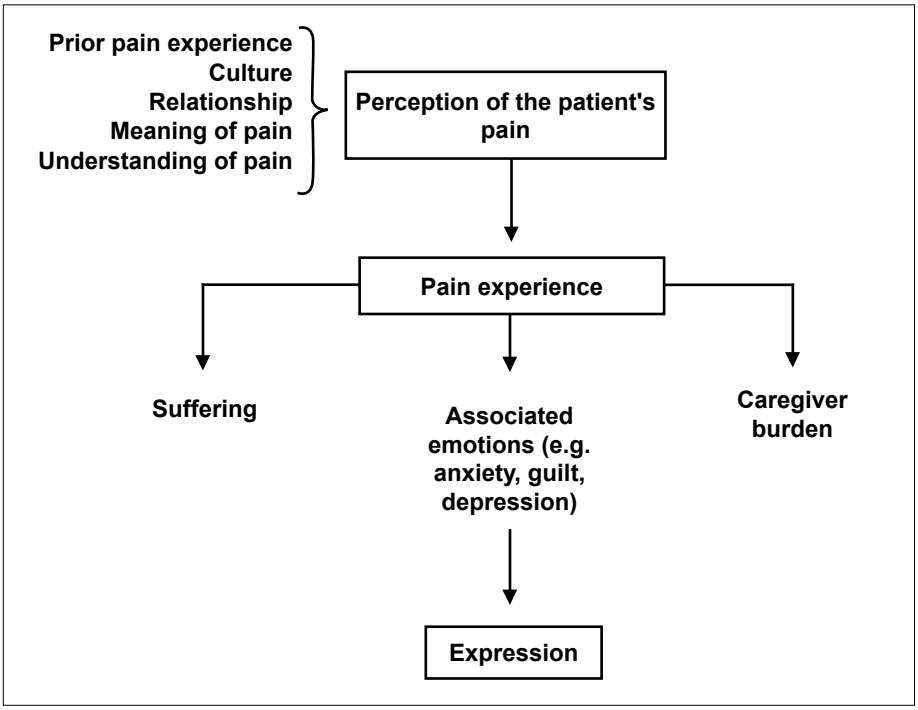

Fig. 2. Caregiver's experience of pain. (Adapted from Ferrell BR et al. Oncology Nursing Forum 1991;18:1315-1321.)

effect. If possible it is helpful to interview the family/carer, especially in the cognitively impaired patients, but not to rely only on proxy reports.

Somatic pain is typically well localised and is felt in the superficial cutaneous or deeper musculoskeletal system.

A family member in pain exercises a negative effect on the dynamics of a family. When patients are facing a life-threatening illness the meaning and understanding of pain and suffering must be explored with the family. Family caregivers' experiences with pain begin with their perception of the patient's suffering. This may vary dramatically and is influenced by many factors (Fig. 2) and may lead to long-term emotional distress in the caregiver.[9]

Examination

Examination of the patient should start when the patient walks into the clinician's office. Look for non-verbal signs, e.g. the patient who keeps his arm warm or pulls his shirt away from his body. The physical examination should be to the point and as non-invasive as possible. In neuropathic pain the clinician should try to localise the lesion by doing a systemic neurological examination. This should include a sensory examination to reveal somatosensory dysfunction, a motor assessment (muscle strength, tonus and fluidity of movement) and an examination of the tendon reflexes and cranial nerves. It is also important to assess the peripheral autonomic nervous system looking at temperature and colour of skin.

Management

Once the clinician has a clear understanding of the type of pain, its severity, possible cause and emotional component of the pain, pharmacological and non-pharmacological interventions can be implemented. Reversible factors should be addressed and a clear explanation of the cause of the pain given to both the patient and the caregiver. Treatment options must be discussed with both the patient and the caregiver so that they become active participants in the pain control. It is also important to establish realistic goals with the patient and to explain that individuals respond differently to medication and treatments.

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Respecting patient autonomy can be very difficult for clinicians when seeing their patients suffer pain. However, when patients are facing multiple losses, as most palliative care patients are, it is very important for the patient to maintain control of his/her pain management for as long as possible. Patients may be fearful of using morphine for reasons that need to be sensitively explored and explained so that patients can take full advantage of modern pain control methods without significant side-effects.

The World Health Organization has created a stepwise approach to the management of cancer pain known as the 'analgesic ladder' (Fig. 3).[10] This analgesic ladder approach is not an evidence-based guideline, but provides a systemic approach to the management of cancer pain,[11] especially in resource-limited areas.

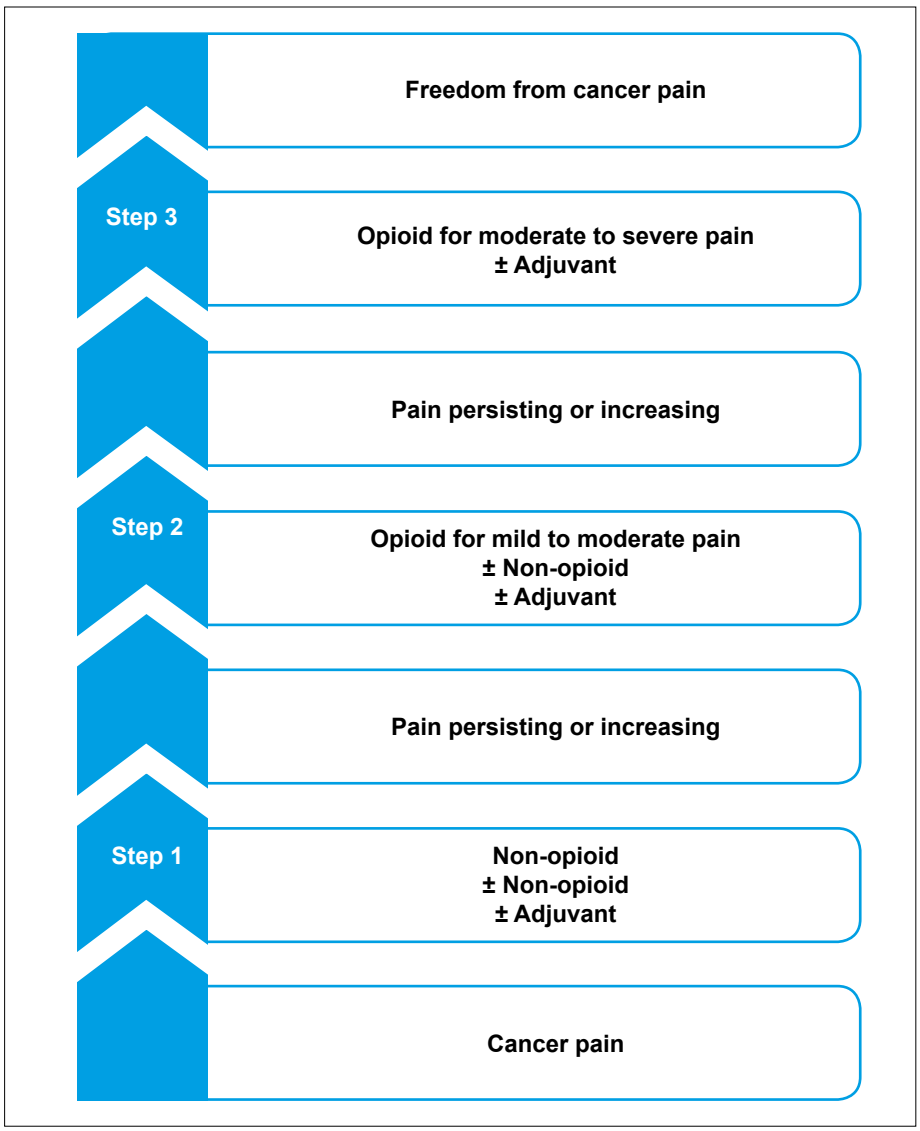

Fig. 3. WHO analgesic ladder.[10]

Table II. Common analgesics for cancer pain

Drugs	Indications
Non-steroidal anti-inflammatory drugs	Bone pain, soft-tissue infiltration, hepatomegaly
Corticosteroids	Raised intracranial pressure, nerve compression, soft-tissue infiltration, hepatomegaly
Bisphosphonates	Bone pain
Antidepressants, anticonvulsants	Neuropathic pain

Adjuvant drugs or 'co-analgesia' describe any drugs that have a primary indication other than pain, but are analgesic in some painful conditions (Table II).[13] The diversity and understanding of these drugs has developed over past decades and some of these drugs are now seen as first-line therapy for certain kinds of pain.

Advances in pain management

There is extensive literature regarding the physiology of the central and peripheral mechanisms of neuropathic pain and its management. The injury of a neuron produces change in the excitability in the injured neuron and neighbouring somatic neurons, causing ectopic action potential discharges. Three factors seem responsible: up-regulation of voltage gated sodium channels, down-regulation of potassium channels and possibly a reduction in the threshold of transient receptor potential (TRP) transducer heat-sensitive channels so that they can be activated at body temperature.[13] This ectopic activity may then directly initiate spontaneous sensation such as burning pain, paraesthesia and dysthethesia. N-methyl-D-aspartate (NMDA) receptors also play a major role in hyperalgesia and the enhancement of allodynia, a phenomenon termed central sensitisation.[14] Ketamine, a well-known NMDA receptor antagonist, has been used for many years in the treatment of neuropathic pain but causes significant central nervous system side-effects. A major way through which NMDA receptors work is through the influx of calcium channels and by decreasing transmitter release with calcium channel blockers (N type) and α2-δ binding drugs, pain reduction can be achieved.

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The International Association for the Study of Pain (IASP) has developed new treatment guidelines for the management of neuropathic pain[15] guided by improved understanding of the physiology of neuropathic pain and its management. It is especially in the treatment of neuropathic pain that new treatment recommendations have to be considered as first-line therapy. Factors to consider when choosing one neuropathic drug above another are: pain physiology; side-effects of the drugs; drug interactions; co-morbidities that can be alleviated by non-analgesic effect (e.g. depression, anxiety); cost and risk of abuse and over-dosage. In palliative care time becomes a very important factor and combination therapy may be needed for rapid onset of pain relief.

Recommended first-line treatment includes certain antidepressants (i.e. tricyclic antidepressants (TCA)), through their action as sodium channel blockers; dual reuptake inhibitors of serotonin and norepinephrine; calcium channel α2-δ ligands (i.e. gabapentin and pregabalin) and topical lidocaine. Traditionally the TCAs have been the most common drug used in the public sector in South Africa for treatment of neuropathic pain. They are inexpensive and placebo-controlled studies have provided support for the efficacy of TCAs in the treatment of neuropathic pain, especially in post-herpetic neuralgia and painful diabetic peripheral neuropathy.[16] TCA in randomised clinical trials have not differed significantly from placebo in the treatment of HIV neuropathy[17] and neuropathic cancer pain,[18] which are the two most common conditions treated in South African palliative care. TCAs are cardiotoxic and can cause sedation and have significant anticholinergic effects.[19] Regrettably there is not enough research conducted on the use of opioids in neuropathic pain despite WHO guidelines that suggest an analgesic drug in conjunction with an antidepressant or anticonvulsant for neuropathic pain in oncology patients.

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Duloxetine is a selective serotonin norepinephrine reuptake inhibitor SSNRI that has shown significantly greater pain relief in randomised clinical trials compared with placebo in patients with painful diabetic peripheral neuropathy.[20] Its main side-effects are nausea, sedation and dizziness.

Gabapentin and pregabalin are both calcium channel α2-δ ligands which decrease the release of glutamate, norepinephrine and substance P. Pregabalin and gabapentin have shown efficacy in a wide variety of neuropathic conditions and have no clinically important drug interactions, making them ideal drugs to use in the palliative care setting. Unfortunately, these drugs are difficult to obtain in the state sector and palliative care clinicians would like to see these drugs as part of the essential drug list (EDL). Gabapentin and pregabalin require dosage reduction in patients with renal impairment. It is also necessary to start at a lower dosage in the frail and elderly.

Studies have shown that lidocaine patch 5% improves pain in patients with post-herpetic neuralgia and allodynia,[20] but these patches are not available in South Africa. Lidocaine gel was shown to be effective in pain relief in patients with post-herpetic neuralgia and allodynia[22] but not in patients with HIV neuropathy.[23]

The main reason for not prescribing these drugs is still opiophobia among health professionals.

Opioid analgesics and tramadol are recommended as third-line treatment in the treatment of neuropathic pain in the general population. However, in neuropathic pain in cancer, acute neuropathic pain, episodes of exacerbation of pain and while titrating up medication these drugs are considered to be first-line medication. Opioid analgesics have demonstrated effectiveness in reduction of neuropathic pain.[24] Opioid analgesics are the mainstay for the treatment of moderate to severe pain in palliative care. When administered according to guidelines, opioids provide adequate pain relief for more than three quarters of patients with cancer pain.[25] The main reason for not prescribing these drugs is still opiophobia among health professionals.[26] Mist morphine (liquid morphine) is cost effective, and side-effects (constipation, nausea, vomiting and drowsiness) can easily be managed. Respiratory depression is rarely seen in the palliative care setting where morphine is introduced at low dose, administered orally and titrated slowly to achieve pain relief. Research has also demonstrated that the risk of addiction with the medical use of opioids is low.

Conclusion

It is always important to realise that any pain is not a homogenous entity and requires reassessment and adjustment of pain medication. The pain a patient has today might not be the pain he experiences tomorrow because of the physical and physiological changes patients in a palliative care setting face. Pain control is achievable in the African setting with good assessment, review and attention to detail.

Acknowledgement

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References available at www.cmej.org.za

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- Pain in the palliative care setting can be caused by the illness itself, the treatment (radiotherapy, chemotherapy, antiretroviral treatment), concurrent disorders (tension headaches, urinary tract infection) or by general debility.
- Physiologically the different types of pain can be described as nociceptive (arthritis, cellulitis), visceral (pancreatitis, peptic ulcers), neuropathic (herpes zoster, post-stroke pain) and mixed pain, a combination of the other types of pain found in certain disease states such as AIDS and cancer.
- Because pain in palliative care is multidimensional, a multimodal approach is needed to address both the physical and the physiological factors.
- The most important element of a pain assessment in palliative care is to establish a good rapport with the patient and to show empathy and understanding of his/her pain and suffering.
- Once the clinician has a clear understanding of the type of pain, its severity, possible cause and emotional component of the pain, pharmacological and non-pharmacological interventions can be implemented.
- The World Health Organization has created a stepwise approach to the management of cancer pain known as the 'analgesic ladder'.
- The International Association for the Study of Pain (IASP) has developed new treatment guidelines for the management of neuropathic pain guided by improved understanding of the physiology of neuropathic pain and its management.