UNIT NO. 6

PAIN MANAGEMENT IN PALLIATIVE CARE

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ABSTRACT

Good cancer pain management requires adequate pain assessment and monitoring, proficiency in prescribing opioid and non-opioid analgesics and adjuvant medications, and an understanding of the potential benefits and limitations of anti-neoplastic, anaesthetic, neurosurgical and behavioural modalities. A coordinated multidisciplinary approach is often needed. It is important for the family physician to recognize pains which are difficult to control using simple pharmacological means, so as to be able to refer appropriately and in a timely manner to a specialized team capable of dealing with complicated pain syndromes using a multimodal approach.

INTRODUCTION

The incidence of pain in patients with cancer increases with stage of disease. In patients with advanced cancer, 60 to 90% have pain. Up to 81% have pain at 2 or more sites, with one-third of patients reporting pain in 4 or more sites. Unrelieved pain decreases quality of life, interferes with function, appetite, sleep and social interactions, and may lead to depression and a wish to die. Pain is often considered an ominous symptom by cancer patients, though it may or may not signify recurrent or progressive disease. Effective treatment using relatively simple means is available, but often not achieved because of various patient, physician and systemic factors.

Evaluation of Cancer Pain

Good pain management starts with accurate assessment of the cause, type and pathophysiology of the pain. Health professionals should routinely ask about pain in cancer patients, and the patient's self-report should be the primary source of assessment. The intensity and temporal pattern of the pain should be documented using a validated pain scale, such as the 0 to 10 numeric scale, a four-point categoric scale or a non-verbal scale, such as the Wong-Baker faces. (Figure 1) Ongoing assessment is essential. This should be done at regular intervals, with each new report of pain, and at suitable intervals after each intervention, e.g., 15 to 30 minutes after parenteral therapy or one hour after oral therapy. In patients with more than one pain, each pain should be assessed and a likely cause assigned. Factors which may influence the response to analgesia, such as psychosocial factors and the meaning of the pain to the patient, should also be evaluated.

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Causes and Mechanisms of Cancer Pain

Pain in the patient with cancer may be related to the tumour itself or its treatment, or it may be unrelated to the cancer, e.g. due to osteoarthritis, peptic ulceration, or as a result of chronic debility, e.g., chronic constipation, deep venous thrombosis, decubitus ulcers.

Pain related to the cancer may be caused by direct tumour infiltration, bone metastases, obstruction of a hollow organ, such as bowel or bladder, distension of the capsule of a solid organ, e.g., liver, kidney, compression of nerves or spinal cord, and paraneoplastic pain syndromes, e.g., hypertrophic osteoarthropathy.

Cancer treatment may also give rise to pain, e.g., post-thoracotomy and post-mastectomy syndromes, fibrosis after head and neck irradiation, and mucositis or painful peripheral neuropathies after chemotherapy.

Defining the cause and pathophysiology of each pain forms the basis of rational therapy. Explanation to the patient of the cause and rationale of treatment is important to allay undue fears and ensure compliance with medications.

Identification of the possible pain mechanisms will guide the choice of treatment. Nociceptive pain is pain due to actual or potential tissue damage. It may be dealt with at the site of tissue damage with anti-inflammatory agents, such as the NSAIDs, by blocking transmission of the pain signal within peripheral nerves, e.g. with local anaesthetics, or alcohol or radiofrequency ablation, and/or by analgesics which modulate transmission of the pain signal at the spinal cord level or in the brain, e.g., with opioids. Pain due to colic may be treated with an antispasmodic, while pain due to muscle spasm may be treated with physical methods, with a muscle relaxant, or with trigger point injections.

Pain from tumour compression or infiltration of nerves is called neuropathic pain. It may be associated with sensory change, such as hypoaesthesia, paraesthesia (both of which may be described by the patient as numbness), or allodynia (pain caused by a non-painful stimulus). The quality of such pain is often different from nociceptive pain, and patients may describe it as a severe ache, or electric shock-like. The distribution of the pain along the course of a cutaneous nerve or within a

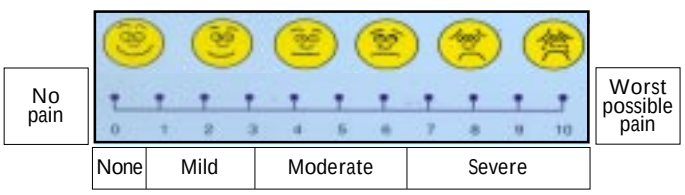

Figure 1: Pain Intensity Scales. Example of a Pain Ruler with Numeric Rating Scale and Verbal Rating Scale and the Wong-Baker faces for non-verbal adults and children.

dermatome is often helpful in diagnosis. Steroids may improve neuropathic pain caused by nerve compression. Antidepressants, e.g. amitriptyline, or anticonvulsants, e.g., carbamazepine, or sodium valproate, which modulate neurotransmitters within the central nervous system, have an increasing role in the management of neuropathic pain. Opioids are also useful, and may be used to control neuropathic pain as sole agents or in combination with adjuvant drugs.

Spinal cord compression may give rise to pain that has a neuropathic mechanism from epidural masses, but often, there may be associated bone pain from compression fracture of a vertebra, or facet joint instability.

Incident pain, such as that produced by coughing, movement or position, is particularly difficult to manage, as the level of analgesic needed may be greatly different at rest and during the incident. Some form of compromise, such as lifestyle adjustment, and acceptance that it may not be possible to abolish but merely reduce the pain during the incident, may be needed.

Cancer Pain Therapy

The principles of treatment outlined in the World Health Organisation (WHO) Cancer Pain Relief programme should be followed. Medications for persistent cancer-related pain should be administered on a round-the-clock basis with additional doses as needed. The simplest dosage schedules and least invasive modality should be used first. The preferred route of administration of analgesics is by mouth.

The choice of analgesic should start at the step of the WHO analgesic ladder appropriate for the severity of the pain. (Figure 2) If the pain persists or its severity increases, the next step of the analgesic ladder should be taken. Adjuvant medications, such non-steroidal anti-inflammatory drugs (NSAIDs) for nociceptive pain, or an antidepressant or anticonvulsant for neruopathic pain should be used with analgesics at any step of the ladder. Such adjuvants may have an opioid-sparing effect, with consequent reduction in side effects. The dose of analgesics should be titrated for each individual patient for optimal relief.

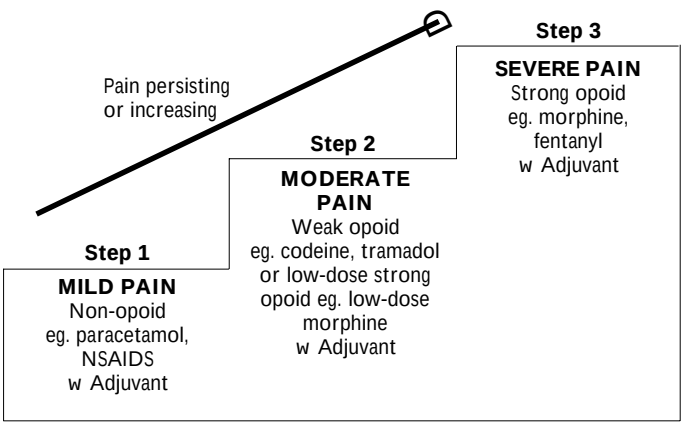

Figure 2: The World Health Organisation (WHO) Analgesic Ladder for Cancer Pain Management (modified).

It is important to be aware of the potential risks of analgesic and adjuvant drugs, e.g., the increased risk of gastrointestinal bleeding, renal impairment and heart failure with the use of NSAIDs. Common side effects of opioids, such as nausea on initiation of treatment, and constipation, should be treated expectantly and adequately.

Use of Opioids

The first step of the WHO Analgesic Ladder uses non-opioid drugs, such as paracetamol. The second step of the WHO Analgesic ladder recommends the use of weak opioids, such as codeine, dihydrocodeine and tramadol. If the WHO Ladder is followed and non-opioids at maximum doses do not control the pain, the starting dose of codeine may be 30mg 4 hourly, while the starting dose of tramadol may be 50mg three times daily. There is evidence that codeine exerts its analgesic effect through its conversion to small amounts of morphine. More recently, some groups have recommended the use of strong opioids in low dose for moderate pain, e.g. sustained-release morphine at 10mg at night or 12 hourly.

The strong opioids of choice for control of severe pain are morphine and fentanyl, and these are on the third step of the WHO Analgesic ladder.

If the second step of the WHO Ladder is followed and the pain is not controlled on maximal doses of codeine 60mg 4 hourly, or tramadol 100mg four times daily, these strong opioids may be started at a dose of morphine 10mg 4 hourly or fentanyl 25mcg per hour. However, if the second step of the WHO Ladder is not used, morphine-naïve patients should be given a much smaller dose, such as 2.5 to 5mg 4 hourly, depending on the severity of the pain, with a view to stepping up the dose within 24 hours. Because of the long wash-out period in case of overdosing, it is not recommended to start on the fentanyl patch in an opioid-naive patient if the dose of opioid needed is unknown.

Morphine is commonly available in Singapore in 3 forms: oral morphine mixture 1mg/1ml which works within 20 to 40 minutes, sustained-release morphine tablets, which achieves therapeutic blood levels at 4 hours and lasts for 12 hours, and injection morphine, which may be given through the subcutaneous, intramuscular, intravenous, epidural and intrathecal routes. Occasionally, morphine suppositories are available on special order from some pharmacies.

Oral morphine mixture is recommended to be prescribed 4 hourly for chronic pain because the higher dose needed to sustain blood levels on a 6 hourly regime may cause more side effects, such as somnolence. Sustained-release morphine tablets are prescribed 12 hourly, and occasionally 8 hourly when half tablets cannot be prescribed. Sustained-release morphine tablets are required to be swallowed whole and should not be cut or pounded. Pain breakthrough despite regular dosing should be treated by morphine mixture prescribed at the 4 hourly dose. These may be given up to one hour apart, which is the time needed to assess whether the breakthrough dose adequately controls the pain.

Fentanyl is available in injection form, but the formulation commonly used in cancer pain is transdermal, in the form of a patch. The 25mcg/hour fentanyl patch is approximately equinanalgesic to 10mg 4 hourly of oral morphine mixture. Dosing is proportional to the size of the patch in contact with the skin. To ensure correct dosing, the skin under the patch should not be broken or inflamed, and skin temperature should be normal. Because the transdermal system relies on the formation of a subcutaneous reservoir of the drug from which it diffuses into the subcutaneous capillaries, transdermal fentanyl takes about 12 hours to reach therapeutic levels. The patch is changed every 72 hours, but on removal, it takes about 12 hours for the subcutaneous reservoir to become depleted, so blood levels are maintained. It is therefore not safe to use the fentanyl patch for drug titration, nor for pain breakthrough. The fentanyl patch is useful for stable, chronic pain. Morphine mixture may be used for pain breakthrough in conjunction with the fentanyl patch, and also for initial dose titration.

Common side effects of opioids which the patient should be warned about includes nausea, which is transient on first starting a strong opioid. This wears off after a few days, and may be treated prophyllactically in the two-thirds of patients who will experience it. All opioids are constipating and this usually needs treatment with laxatives in adequate doses. Some patients experience somnolence or feel light-headed or giddy on first starting a strong opioid. Again, this wears off after a few days provided the dose is correctly titrated. Compliance is greatly improved if patients are warned about this. Less common side effects include dry mouth, skin itch (usually without a rash), and myoclonus at higher doses. If any of these become unacceptable, switch to another opioid may give good pain relief without the same side effects.

It is important to educate the patient and relatives that strong opioids like morphine do not cause addiction if used correctly for pain. Addiction, which is defined as psychological dependence leading to drug-seeking behaviour, almost never occurs. Physical withdrawal symptoms may sometimes occur if strong opioids are withdrawn too suddenly, and can be treated by bringing the dose up and decreasing at a slower rate.

It is not recommended to use pethidine in chronic pain because of accumulation of norpethidine, a metabolite that is a convulsant. Pentazocine is not recommended because it is a kappa opioid receptor agonist with unacceptable psychomimetic effects. The strong opioid buprenorphine has to be used with care because it has a ceiling effect, and is an antagonist of morphine at high doses if the two drugs are used together. Methadone has a place in cancer pain relief, but is difficult to titrate because of its long half-life of 15 to 60 hours on chronic use.

Uncontrolled Pain

Sudden severe pain in patients with cancer should be recognised as a medical emergency, and should be promptly assessed and treated. Causes include pathological fracture, rupture of an internal organ, subcapsular bleed or intraperitoneal. Spinal collapse with or without spinal cord compression may be a cause of pain exacerbation. The pain may be of a radicular nature, or there may be severe incident pain on movement or weight-bearing.

Sometimes, the patient may be in such severe distress as to make full assessment impossible until the pain level has been reduced. In this situation, the fastest and safest method of bringing the pain under control is with morphine by slow intravenous injection, titrating against the pain. The practitioner should sit at the bedside and give morphine intravenously 1mg at a time while talking to the patient and assessing the pain score. The intravenous bolus dose needed to bring the pain down to a score of 2 out of 10 would give an approximation of the 4 hourly dose needed for maintenance. Conversion of that dose to oral morphine using a 1 to 3 parenteral-to-oral morphine conversion would enable oral therapy to be instituted. Further investigations into the cause of the pain, e.g. by radiological imaging, and definitive treatment, such as fixation of fracture or surgery, can then be carried out.

Other modalities of treatment

Although analgesics are the mainstay of cancer pain management, a multimodal approach to treatment is often necessary. This includes treatment of the neoplastic process using radiotherapy, surgery, antineoplastic chemotherapy or hormonal agents. In certain pain syndromes where oral analgesic therapy gives suboptimal results, anaesthetic approaches using temporary or permanent nerve blocks, or intraspinal opioids with or without local anaesthetics via a tunnelled catheter or implanted port may be necessary. Physical approaches and neurostimulatory approaches, such as transcutaneous electrical nerve stimulation, may be helpful. Psychological approaches, e.g., using relaxation, or cognitive behavioural therapy, may also have a role in chronic pain management.

It is important for the non-pain specialist to refer promptly to a specialist pain management or palliative care team should the pain not respond to simple analgesic measures, so that other modalities of treatment can be instituted.

Beyond Pharmacotherapy

In the palliative care situation, severe distress may be expressed as pain by both the patient and the family. Less commonly, other physical symptoms, such as dyspnoea and vomiting, may mimic distress or suffering. This may be because the patient has no other way of expressing distress. Seeking medical attention for pain or physical symptoms is legitimate, while fear or anxiety seems less so. It is important for the medical practitioner to be aware of this, so that analgesics are not inappropriately exhibited. Sometimes, it may be impossible to diagnose emotional distress separate from an element of physical pain. Apart from a high index of suspicion, the test of titration with an intravenous dose

of morphine may be needed. If the patient falls asleep with only 1 or 2 mg of intravenous morphine despite expressing severe distress, this is an indication that physical pain is not the whole problem. There may be issues of anxiety over family, or finances, or existential distress, which need to be addressed. The physical pain has to be treated, and then other means to alleviate the source of distress, sometimes calling in the help of an interdisciplinary team, may be necessary.

FURTHER READING

MOH Clinical Practice Guidelines 5/2003 on Cancer Pain.

LEARNING POINTS

- Good cancer pain management begins with adequate pain assessment and monitoring.
- Proficiency in prescribing opioid and non-opioid analgesics and adjuvant medications is a must.
- An understanding of the potential benefits and limitations of anti-neoplastic, anaesthetic, neurosurgical and behavioural modalities is a must.
- It is important for the family physician to recognize pains which are difficult to control and refer patients to a palliative care team.
- Complicated pain syndromes require a specialized team and a multimodal approach.