

MAGNITUDE OF THE PROBLEM

In India, about 1 million new cancer patients are diagnosed every year. A statistical data suggest that approximately 60-80% patients, when they are diagnosed, are advanced cases & hence incurable. Often, their major symptom is moderate to severe pain. According to present estimates, about 56% cancer patients require relief of symptoms (palliative care) at any given time in India, however, only 28% are provided some sort of palliative care before they die. There is an immediate need to address this issue at all levels. Clinicians should reassure patients & their families that most pain can be relieved throughout the course of illness. Health professionals should encourage patients to be active participants in pain management. State regulatory bodies should not hamper the supply & collaborate with patients and their families taking the costs of the drugs & technologies into accounts in selecting pain management strategies.

PREVALENCE OF PAIN¹

A systematic review (2007) of 6000 patients including 54 studies during 1964-2005 found following prevalence of cancer pain. Despite clear world health organization guidelines (1986) pain still is a major problem.

- Pain after curative treatment, 33%
- Pain during active anticancer therapy 59%
- During advanced disease 64%
- At all disease stages 53%
- >33% patients grade their pain as moderate or severe

IMPORTANCE OF CONTROLLING CANCER PAIN

Pain control merits high priority for two reasons. First under-relieved pain causes unnecessary suffering. Because pain diminishes activity, appetite, and sleep, it can further weaken an already debilitated patient. The psychological effect of cancer pain can be devastating. Pain is defined as 'an unpleasant sensory & emotional experience associated with actual or potential tissue damage or described in terms of such damage. The perception of pain is modulated by the patient's mood, morale & the meaning of the pain for the patient. Pain in cancer may be caused by the cancer itself or by its treatment (radiation, chemotherapy & surgery) or its related debility or concurrent disorder.

CLASSIFICATION OF PAIN

Nociceptive

- Functional (physiological e.g. cramp, myofascial pain, colic)
- Organic (pathological e.g. trauma, cancer)
- Somatic pain arising from the covering of the body, i.e. skin, subcutaneous tissue
- Visceral pain arises from viscera.

Non-Nociceptive (Neuropathic)

- Nerve compression (e.g. sciatica)
- neural injury
- peripheral (e.g. post herpetic neuralgia)
- central sympathetically maintained pain

BONE METASTASES

Bone pain is the most common kind of pain caused by cancer. Upto 85% of patients dying from breast, prostate or lung cancer demonstrate bone involvement at autopsy. Bone pain affects 28% hospice in-patients, 34% in cancer pain clinic & 45% advanced patients at home. The gold standard treatment is radiotherapy.

Neuropathic Pain: Defined as pain arising due to lesion or disease in the somatosensory nervous system. It can be caused by cancer directly invading the nervous system or cancer treatment itself causing pain e.g chemotherapy induced peripheral neuropathy (CIPN), radiotherapy induced pain or pain caused by surgery i.e. phantom limb pain. Neuropathic cancer pain is caused by cancer directly while neuropathic pain in cancer is caused by treatment or due to co-morbid conditions e.g diabetic neuropathy, post herpetic neuralgia. Now treatment guidelines have been released by the International neuropathic pain group.²

PRINCIPLES OF PAIN MANAGEMENT

Relief of pain may be achieved by the following methods:

- Explanation
- Modification of pathological process
- Elevation of pain threshold
- Interruption of pain pathways
- Modification of lifestyles & immobilization

GOALS OF PAIN MANAGEMENT

- Relief at night

- Relief at rest during the day
- Relief on movement (this is not always completely possible)

PAIN ASSESSMENT

Assess relief in relation to each pain. Whether pain is somatic, visceral or neuropathic or mixed assess different components of each pain. If marked anxiety and/or depression, it may take 2-4 weeks to achieve optimum results. pain score should be assessed on 0-10 numerical rating scale (NRS), where 0 is "no pain" and 10 is "worst possible pain". Reassessment is a continuing necessity. Various QOL scales are available e.g. Mc Gill Pain questionnaire, Brief pain inventory (BPI).

PHARMACOTHERAPY OF PAIN: WHO LADDER APPROACH

Use of analgesics:

"By the mouth"-The oral route is the preferred route for analgesics, including morphine.

"By the clock"- Persistent pain relief requires preventive therapy. This means that analgesics should be given regularly & prophylactically. "As needed" medication is irrational & inhumane.

"By the ladder"-use a three-step WHO analgesic ladder:

Step 1: non narcotics (NSAIDS)

Step 2: mild opioids (Codeine, pentazocine)

Step 3: strong opioids (morphine)

If a drug falls to relieve, move up the ladder. Do not move laterally in the same efficacy group.

"For the individual"-The right dose of an analgesic is the dose that relieves the pain.

"Monitored treatment"-The response to treatment must be monitored to ensure that benefits of treatment are maximized & adverse effects minimized.

"Use adjuvant drugs"-A laxative is almost always necessary with an opioid: > 50% of patients need an anti-emetic.

ORAL ANALGESICS³

Oral analgesics are the mainstay of therapy for cancer pain. An estimated 70-90% of patients can be rendered relatively free of pain, when rational principles of pharmacological management are applied in a thorough & careful manner. The World Health Organization has adopted a 'ladder' approach to cancer pain management that relies exclusively on the administration of oral analgesia.⁴

I. Non-opioid (Non-narcotic) analgesics: These agents are effective when administered as the sole drug treatment for mild pain. They may be combined with opioids to treat moderate to severe pain.

Paracetamol is a safe step 1 WHO ladder analgesics. NSAID's have analgesic, anti-inflammatory & antipyretic activity. They can be given orally,

rectally, intramuscularly as well as by topical applications and are the first line agents for mild to moderate cancer pain. There is increasing evidence to suggest that these drugs may have unique role in management of certain kinds of pain from bone metastases. Side effects of NSAIDs should be carefully monitored. Cox-2 NSAIDs (e.g. Celecoxib, Etoricoxib) have been introduced in practice, which are considered relatively safe in terms of gastric mucosa and platelets.

II. Opioids: They are the mainstay treatment in moderate to severe cancer pain because of their effectiveness, ease of titration & favorable risk-to-benefit ratio. Opioids do not have a ceiling effect to their analgesic efficacy & will not reverse or antagonise the effects of other opioids within this class given simultaneously. Side effects include constipation, nausea, vomiting, itching, urinary retention, confusion, sedation & rarely respiratory depression if patient is not opioid naïve. Drug tolerance, physical dependence, addiction are no more big clinical issues.

Morphine is the most commonly used opioid for moderate to severe pain because of its availability in a wide variety of dosage and forms. It has well characterized pharmacokinetic & pharmacodynamic profile & relatively low cost. Recommended starting dose is usually 10 mg 4 hourly.

Guidelines for the use of opioids in the management of cancer pain

1. Start with a specific drug for a specific type of pain.
2. Know the pharmacology of the drug prescribed very well.
3. Adjust the route & dose of the drug as per patient's need & comfort.
4. Use drug combination for additive effects & reduce side effects.
5. Anticipate & treat the side effects aggressively.
6. Prevent acute withdrawal by slowly tapering doses.
7. Anticipate & manage complications like overdose, seizures & myoclonus etc.

III. Adjuvant Drugs:

Adjuvants play a major role for pains that are insensitive to opioids. They are also useful in counteracting the side effects of the pain medications like nausea, vomiting, itching, dyspepsia, constipation etc. The mainly used adjuvants are as follows:

1. Corticosteroids
2. Antidepressants (amitriptyline)
3. Anticonvulsants (gabapentin)

- 1060 4. Other drugs: Antacids, H₂ blockers, laxatives, stool softeners, antiemetics, antihistaminics & antipsychotic drugs etc. Radiopharmaceutical agents like bisphosphonates may be used in once a week infusion in bone metastasis with good relief. Inj calcitonin also has a role in pain relief due osteolytic lesions.

REFERENCES

1. van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, Schouten HC, van Kleef M, Patijn J. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Ann Oncol* 2007; 18:1437-49.
2. Nanna B Finnerup, Nadine Attal, Simon Haroutounian, Ewan McNicol, Ralf Baron et al Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurology* 2015; 143:162-173.
3. Bennett MI, Rayment C, Hjermstad M, Aass N, Caraceni A, Kaasa S. Prevalence and aetiology of neuropathic pain in cancer patients: a systematic review. *Pain* 2012; 153:359-65.
4. Zech DF, Grond S, Lynch J, Hertel D, Lehmann KA. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. *Pain* 1995; 63:65-76.