Pain Management in Cancer

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Citation

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Abstract

WHO estimates as many as 4 million people experience cancer pain on a daily basis. Pain is the most distressing symptom associated with cancer. However pain can be controlled easily in more than 80% of the patients to provide them with sufficient relief to function at a level they choose to and die relatively free of pain. Much of the pain management is not about what is new but about prescribing well what is already available. This article aims to improve the general practitioners confidence in prescribing in the palliative care setting and to encourage the timely and proper use of opioids.

CASE HISTORY

Mrs. XYZ is a 56 year old postmenopausal lady who underwent (Lt) side modified radical mastectomy for carcinoma breast. Histopathology showed a 6 x 4.5 x 4.5 cm infiltrating ductal carcinoma with 3/8 Lymph nodes positive for metastasis. Post operatively she received external radiation to the chest flap (35Gy/15F/3wks) and drainage area (40Gy/15F/3wks), systemic chemotherapy with FAC regimen x 6 cycles (5-FU:750mg/m^2, Adriamycin: 50mg/m^2, Cyclophosphamide: 750mg/m^2). On completion of treatment she was put on hormone therapy with Tab Tamoxifen 20 mg OD. One year after completion of her chemotherapy she complained of severe pain in the back for which she was put on diclofenac. Investigations revealed her to have multiple skeletal metastasis in the vertebrae, femur, scapula and mandible. Initial treatment was radiotherapy to the painful site at L4 vertebra with good results and when given an option Mrs. XYZ elected not to pursue second line chemotherapy or bisphosphonates. Hormone therapy was changed from Tab Tamoxifen to Tab. Letrozole 2.5mg OD. Two months later she presented with severe pain in the groin which radiated to her knees with a burning sensation precipitated even by light touch or cloth, pain score as assessed on the visual analogue scale was 8. She had difficulty in walking and was unable to sleep at night. She was shifted from NSAIDs to a combination of tramadol and paracetamol given 8hourly and tryptomer 50 mg HS was added. Her groin pain improved but the burning sensation persisted for which gabapentin 300mg BD was added. With the above treatment her pain was completely in control at rest and she had no trouble sleeping at night with a pain score of 1. Several weeks later Mrs XYZ presented with increasing dull ache in the right hypochondrium. Ultrasonography revealed metastatic lesions in the liver. She was finally shifted to morphine 20 mg 4 hourly and tryptomer and gabapentin continued. With the above treatment her symptoms were successfully managed and she is being regularly visited by the home care palliative team, who are glad to see a smile on her and her family's face as opposed to the distress with which she presented in the palliative clinic.

Palliative care is the active total care of patients whose disease is not responsive to curative treatment. It includes control of pain and other symptoms related to physical, psychological, social and spiritual problems. The goal of palliative care is to achieve the best possible quality of life for patients and their families[1]. Pain is a prevalent and feared symptom of cancer management and it is truly said: pain is a more terrible lord of mankind than even death itself. Good pain management is one of the central pillars of good palliative care[2].

Pain is what the patient says hurts and not what the physician or the family thinks. The patient Mrs. XYZ experienced bone pain with a component of neuropathic pain in the beginning and as the disease progressed she had developed an added component of visceral pain. The intensity of pain can be measured by many scales like the visual analogue scale, the numeric scale, the verbal descriptor scale, etc. Any one scale should be adopted and followed on each step for a particular patient to assess the response[3]. Drug therapy is the mainstay of treatment for

cancer pain while radiotherapy gives an additional advantage in specific situations.

Drug therapy for cancer pain consists of exploiting the WHO three step analgesic ladder for maximum pain control and minimal side effects. Step I includes the non opioids, chief among them being NSAIDS (ibuprofen, diclofenac, aspirin, naproxen) and paracetamol, prescribed for mild pain[1]. NSAIDS have analgesic, antipyretic, anti-inflammatory and antiplatelet actions. Clinically some patients respond better to one NSAID than to other. Treatment must hence be individualized. Gastrointestinal toxicity is the most common side effect which can be taken care of by prescribing simultaneous proton pump inhibitors. NSAIDS show a ceiling effect limiting their analgesia[4].

At the step II of the analgesic ladder are the weak opioids usually prescribed in combination with the non opioids for moderate pain[1]. Commonly available preparations are a combination of codein and paracetamol, tramadol and paracetamol. Tramadol is a centrally acting analgesic that acts as a weak stimulator of opioid receptors while inhibiting nor adrenaline and serotonin reuptake[5].

Strong opioids are the step III analgesics given with non opioids for patients with severe or rapidly escalating cancer pain[1]. Opioids do not have a ceiling effect. Well conducted clinical studies[6,7,8] have shown that potent opioids have no significant risk of addiction in those with cancer pain. Potent opioids include morphine, fentanyl, diamorphine, hydromorphine, buprenorphine and methadone. Various methods of drug delivery of opioids have been developed to maximize pharmacological effects and minimize side effects. Slow release non parenteral routes remain the preferred method of providing chronic opioid therapy. Morphine is considered to be the gold standard and is available as immediate release tablets, sustained release tablets, elixirs and injections. It is relatively inexpensive. The greatest long term adverse effect of opioids will be constipation. Stool softeners and laxatives should always be prescribed along with opioids. Other adverse effects include nausea and vomiting, however tolerance develops to these side effects which usually settle within a week. Uncommon side effects include sweating, urinary retention, anaphylaxsis and neurotoxicity[6].

GUIDELINES FOR PRESCRIBING MORPHINE

- Reassure the patient about the safety and efficacy of opioids.
- If the patient was previously receiving the equivalent of codein 180 mg/ day or more begin with 10 mg q4hrly.
- For opioid naïve patients start with 5 mg q4hrly immediate release tablets.
- Review daily during the titration phase.
- If the pain is not adequately controlled, increase each dose by 25-50%. Two third of the patients will never need more than 30mg q4hrly (SR 100mg 12 hrly)
- With immediate release tablets a double dose at bed time enables a patient to go through the night without waking in pain.
- Always prescribe a laxative and anti emetic along side.
- Morphine should be given along with a non opioid.
- For breakthrough pain, patients can be given 1/6 of the total daily opioid requirement.
- When dosing is stable with good pain control shift from immediate release to slow release preparations.
- If swallowing is difficult or vomiting persists morphine can be given per rectally by suppository (same dose as PO)

MYTHS

- Morphine does not cause clinically important respiratory depression in patients with cancer pain because pain acts as a physiological antagonist to the central depressant effects of morphine.
- Psychological dependence (addiction) does not occur if morphine is used correctly.
- Tolerance to morphine is not a practical problem.
- Physical dependence does not prevent a reduction in the dose of morphine if the patient's pain ameliorates.

BOTTOMLINE: Morphine and other strong opioids exist to be given not merely to be with held.

ADDICTION: Living your life for drugs

MEDICATION: Using drugs to live your life.

Transdermal Fentanyl is an alternative strong opioid, useful for patients with poor compliance with oral medication. Patches are available in strength of 25, 50, 75 and 100 mcg/hr for 3 days. Patch is usually applied on the upper arm or trunk. Steady state plasma concentrations are achieved only after 36-48 hrs, hence patients should use rescue doses liberally during the first 3 days. After the first 48hrs, if the patient continues to need two or more rescue doses of morphine, the patch strength should be increased by 25mcg/hr. Patches need to be changed after 72 hrs. Fentanyl causes less nausea and vomiting and is less constipating than morphine. However it is more expensive and the equvianalgesic doses are higher[9].

Radiation can be very useful in patients with bony metastasis. External radiation is used to treat patients with localized bony metastasis while intravenous radionuclides are used for patients with diffuse bony lesions. Strontium 89 and samarium 153 are FDA approved isotopes for use in bone metastases. However because of their restricted availability and limited indications, they are infrequently used[10]. External radiation in the doses of 8Gy/SF, 20Gy/5F, 30 Gy/10F are more commonly used. Pain relief rate is seen in 70-80% patients, and lasts for a median duration of 3 months. Pain relief starts 24-48hrs onwards. However patients frequently need retreatment for new lesions and recurring symptoms[11].

Bisphoshonates also have some analgesic effect but the main indication is to prevent skeletal morbidity with reduction of fractures. Patients with multifocal metastatic bone disease that is refractory to routine treatments may benefit. Analgesia, if it occurs usually appears within days but may accrue for many weeks with repeated infusions. Bisphosphonates analgesic effect appears to be dose dependent[12].

The WHO analgesic ladder brings relief in 80-90% of patients with cancer pain due to bone metastasis and visceral metastasis however neuropathic pain is usually less opioid sensitive and requires adjuvant drugs and co-analgesics. Neuropathic pain arises because of compression/ injury to peripheral or central nervous system. It is a severe burning kind of pain with a feel of tingling, pins and needles pricking, electric shock and may be precipitated by light touch or cloth itself. Management of neuropathic pain requires adjuvant drugs/ co analgesics like steroids, antidepressants and anticonvulsants[13].

The adjuvant/ co analgesic drugs should also be used in a scientific and graded manner similar to the WHO ladder. To begin with corticosteroids should be added for patients with symptoms suggestive of neuropathic pain or patients not responding well to opioids. Dexona is most commonly used at a loading dose of 16mg followed by once daily dose of 4-8mg . The safety of using the steroids on long term basis is however questionable. Drugs to be added or substituted when the nerve compression progresses to nerve injury are tricyclic antidepressants used alone or in combination with anticonvulsants. The most commonly used antidepressant is amitriptyline (25-75mg) which also takes care of concurrent depression. Among the anticonvulsants sodium valproate (200-1000mg), carbamazepine (200-1200mg/ day) and gabapentin (100-600mg tds) are commonly used. For patients not relieved by the above co-analgesics, oral anaesthetic agents like ketamine (25mg OD) and mexelitine can be tried[14].

Visceral pain example due to liver metastasis in our patient Mrs XYZ arises due to stimulation of nociceptors from infiltration, compression or stretching of thoracic, abdominal or pelvic viscera. Pain usually responds to increased doses of opioids. Steroids may reduce the peri-tumoral oedema in an encapsulated organ and further ease the visceral pain[15].

There may be some patients with intractable pain, toxicities of noninvasive analgesic therapy or poor compliance to treatment for whom certain surgical procedures can be used. Surgical techniques include anesthetic approaches (peripheral nerve blocks, autonomic nerve blocks) and neurosurgical approaches which includes neuroablative procedures (for nerve root, spinal cord, brain stem, thalamus, cortex, pituitary) or neurostimulatory procedures (for peripheral nerves, spinal cord and thalamus). However it is useful for well defined localized pain and requires good expertise[16].

Figure 1

Figure 1

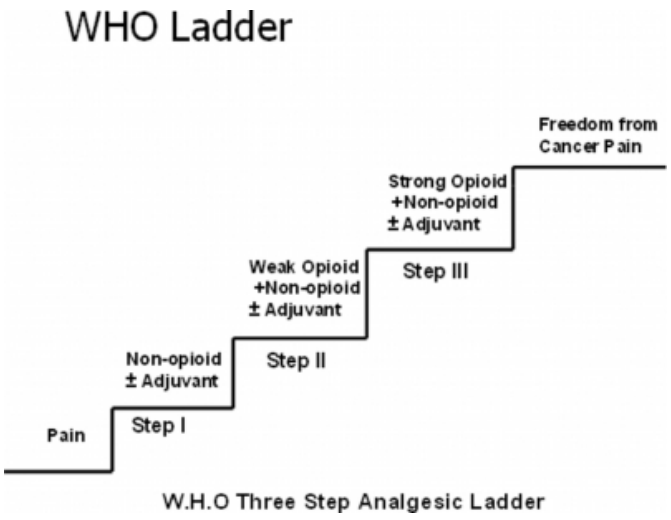
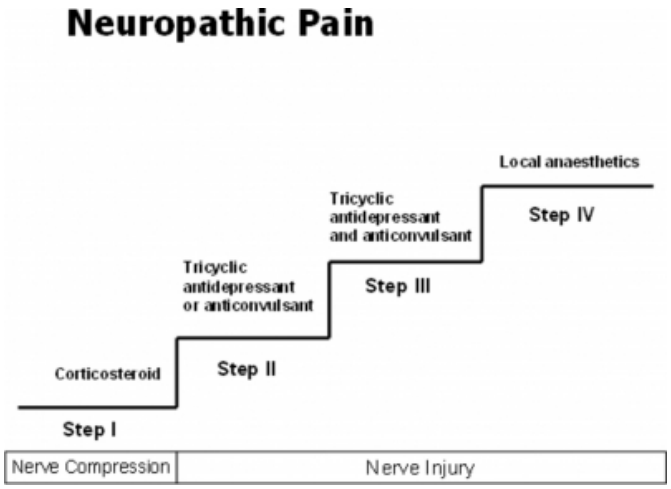


Figure 2

Figure 2



CONCLUSION

WHO estimates as many as 4 million people experience cancer pain on a daily basis. Yet not much has been said and done for them. Whatever funds are allocated for cancer patients are usually diverted for procurement of more machines and newer gazettes and latest technology. But what we must remember is that the goal of an oncologist and a physician in general is to cure sometimes, to relieve often and to comfort always.

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