International Journal of Pharmaceutical Research and Development (IJPRD)
Platform for Pharmaceutical Researches & Ideas
www.ijprd.com

CONTROL OF PAIN IN CANCER PATIENTS-RECENT TRENDS: A REVIEW

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ABSTRACT

Pain is perhaps best defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". Accurate assessment and diagnosis of the type of pain, its severity, and its effect on the person are necessary to plan appropriate interventions or treatments, and are an integral part of overall clinical assessment.

The severity of pain determines the strength of analgesic required and the type and cause of the pain will influence the choice of adjuvant analgesic. Paracetamol, aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), opioids for moderate pain, and opioids for severe pain form the basis of the WHO three-step ladder. Treatment should be adjusted from one step to the next according to increasing or decreasing pain severity, history of analgesic response, and side effect profile.

Paracetamol, aspirin, NSAIDs, opioids for moderate pain, and opioids for severe pain form the basis of the WHO three-step ladder. Treatment should be adjusted from one step to the next according to increasing or decreasing pain severity, history of analgesic response, and side effect profile. Radiotherapy is usually considered the most effective oncological treatment modality in relieving pain. It is especially effective in relieving pain due to bone metastases and when used for this indication produces few side effects.

KEYWORDS : *Method of pain assessment, the "WHO" analgesic ladder, chemotherapy, radiotherapy, adjuvant analgesics.*

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INTRODUCTION

Definitions of pain

Pain has been defined in many ways:

Pain is perhaps best defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". [1]

"Pain is a category of complex experiences,

not a single sensation produced by a single stimulus". [2]

Pain is a subjective phenomenon. It is a sensation in part of the body, always unpleasant, and also has an emotional component.

Pain due to tumors

There are many ways that tumors can cause pain in the human body.

(i) The pain is created directly by tumors, such as when a tumor stretches or distrasts normal tissues.

(ii) The pain is caused indirectly by reaction to tumor made chemicals, blockage of ducts from internal organs, bleeding into the tissues, collapse of bones, etc.

(iii) The treatment used to fight the cancer can also lead to pain problem.

ASSESSMENT OF PAIN IN PATIENTS WITH CANCER:

Effective control of pain in patients with cancer requires an accurate assessment. [3] Accurate assessment and diagnosis of the type of pain, its severity, and its effect on the person are necessary to plan appropriate interventions or treatments, and are an integral part of overall clinical assessment. The aetiology of the pain should also be considered: 5-10% of patients with malignant disease report pain due to conditions other than the cancer. [4]

Aspects of pain assessment

Pain is more than a physical phenomenon. [5] Despite this, the psychological, social and spiritual aspects of pain are not always considered. Comprehensive assessment of pain requires consideration of the following domains:

1. **Physical aspects / manifestations of pain**
2. **Functional aspect**
   - Interference with activities of daily living.
3. **Psychosocial aspects** [3, 6]

Aspects that lower pain tolerance	Aspects that raise pain tolerance
• Discomfort • Insomnia • Fatigue • Anxiety • Fear • Anger • Boredom • Sadness • Depression • Introversion • Social abandonment • Mental isolation	• Relief of symptoms • Sleep • Rest/or paradoxically physiotherapy • Relaxation therapy • Explanation/support • Understanding/empathy • Diversional activity • Companionship/listening • Elevation of mood • Understanding of the meaning and significance of the pain

- Level of anxiety, mood, cultural influences, fears, effects on inter-personal relationships, factors affecting pain thresholds (see Table 1).

Table 1: Factors affecting pain tolerance (adapted from Twycross and Lack) [7]

4. Spiritual aspects

Spirituality relates to ideas of meaning of purpose and of the continuity of life. It does not always include a religious component.[8, 9] Meaningful spiritual assessments come from understanding that there can be no one clear definition of 'spiritual needs'. It requires a 'person centred approach', focused on the individual. Spiritual pain is a result of the experience of illness which may threaten an individual with, spiritual disintegration, isolation and loss of meaning. [10]

Method of pain assessment

Diagnosis of the cause of pain and the functional and psychosocial impact [11] is achieved by full assessment (history, physical examination, investigations, standardized assessment tools.

Tool	Description / Setting
Memorial Pain Assessment Card	A simple, rapidly completed questionnaire which measures intensity, relief of pain, and psychological distress. Developed for use in hospitals.
Wisconsin Brief Pain Inventory	Widely used across cultures to assess pain. Measures intensity and relief of pain, psychological distress, and functional impairment. A valid and reliably tested tool used in research studies. A shorterned version has been used in research and in the hospice setting.
McGill Pain Questionnaire	One of the first pain assessment tools, which revolutionised assessment. The full chart is very detailed and time consuming to complete, but a shortened version is available. Used in research.
McGill Home Recording Chart	Developed for use at home
Simpler measures of pain intensity:	
Numerical Rating Scale (NRS)	The patient rates pain on a scale from 0 to 10
Visual Analogue Score (VAS)	The patient indicates intensity of pain on a 10 cm line marked from "no pain" at one end to "severe pain" at the other end
Likkert or Verbal Rating Scale (VRS)	The patient rates the pain verbally, e.g. "none", "mild", "moderate" or "severe".
Western General Hospital, Edinburgh Observation Chart	Under development in hospital setting

Table 2: Pain assessment tools and their applications

Time of assessment

In most cases the General Practicenor (GP) is the first point of contact when patients present with symptoms suggestive of malignancy. The timing of reassessment will depend on individual circumstances. If pain is difficult to control then asking the patient at home to assess regularly the severity of their own pain four times a day using a simple method will be beneficial. Sudden severe pain in patients with cancer should be recognised by all health professionals as a medical emergency and patients should be seen and assessed without delay.

Barriers to pain assessment

For pain to be accurately assessed and thereby appropriately managed, health professionals must be aware of the barriers to and the complexities of pain assessment. These include: The multidimensional, subjective nature of pain

- Lack of clearly defined language of pain
- Anxiety or depression
- Poor communication between patient and health care professional:
- under-reporting by patient
- under-assessing by health professionals/careers
- language/ethnicity
- impaired hearing
- reduced cognitive ability
- reduced level of consciousness
- incorrect attitude and knowledge deficit in health professionals regarding adequate pain control.

All health care professionals involved in cancer care should be educated and trained in assessing pain as well as in the principles of its control.

USE OF THE "WHO" ANALGESIC LADDER:

The severity of pain determines the strength of analgesic required and the type and cause of the pain will influence the choice of adjuvant analgesic (any drug that has a primary indication other than for pain management, but is analgesic in some painful conditions). Type, cause and severity can only be determined from a

thorough patient assessment. Effective use of the WHO ladder therefore depends on accurate regular pain assessment.

Paracetamol, aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), opioids for moderate pain, and opioids for severe pain form the basis of the WHO three-step ladder. Treatment should be adjusted from one step to the next according to increasing or decreasing pain severity, history of analgesic response, and side effect profile.

All patients with moderate to severe cancer pain should have a trial of opioid analgesia. Chronic pain in patients with cancer is usually continuous and where this is so, therapeutic plasma levels of analgesics must be maintained. This can only be achieved when the drug is given regularly at correct intervals according to the pharmacokinetic and pharmacodynamic profile of the drug. The cause and type of pain indicates which adjuvant analgesic should be used. [13, 14]

Choice of analgesic for cancer pain

Step 1: Mild pain

Drug option:

- Paracetamol
- Aspirin
- Non-steroidal anti-inflammatory drugs (NSAID's).

In multiple dose studies there is no comparative evidence for the superiority of paracetamol, aspirin or NSAIDs. In single dose studies of postoperative pain, NSAIDs are more effective than paracetamol, although paracetamol is also effective. The choice of non-opioid must depend on the individual risk/benefit balance for each patient. The side effect profile of each option is quite different. [15]

Paracetamol has minimal toxicity at recommended doses but at higher doses can cause fatal hepatotoxicity and renal damage. **Aspirin** may be difficult to tolerate at analgesic doses due the wide range of side effects. **NSAIDs** have a significant incidence of serious and potentially fatal problems. However those with existing renal disease cardiac failure, hepatic impairment and the elderly appear to be at higher risk of renal damage. Vigilance is required to detect if patients are

developing either of these problems. NSAIDs frequently cause fluid retention and may cause a rise in blood pressure, which may be detrimental in some groups of patients. [16]

Lower doses of misoprostol (200 µg twice or three times a day) significantly reduce the incidence of NSAIDs-induced damage whilst having a lower incidence of side effects compared with 200 µg four times a day.[17] Omeprazole is also effective at a dose of 20 mg daily in reducing the risk of gastric and duodenal erosions. No trials published to date have compared misoprostol to omeprazole for prevention of NSAID induced gastrointestinal (GI) damage. A dose of 20 mg omeprazole daily was as effective as 40 mg daily. [18]

The recent introduction of NSAIDs that selectively inhibit the isoenzyme cycloxygenase-2 (COX-2) may offer a reduced risk of gastrointestinal damage. Whilst there is clear evidence that the more selective COX-2 inhibitors such as rofecoxib do produce fewer serious GI adverse reactions in average risk patients in short term studies, there is little published data on whether this benefit extends to high risk groups or in chronic use. [19]

Step 2: Mild to moderate pain

Drug option:

- Codeine
- Dihydrocodeine
- Dextropropoxyphene
- Step 1 non-opioids.

In single dose studies of mild to moderate postoperative pain NSAIDs are more effective at treating pain than opioids alone or in combination with paracetamol or aspirin. Paracetamol in combination with an opioid for mild to moderate pain is effective and appears to be marginally more effective than paracetamol alone. [15] While the efficacy achieved by single doses of oral opioids such as codeine is poor, multiple doses may perform better. There is logic in adding an opioid to paracetamol (e.g. cocodamol forte, coproxamol) or a NSAID or in adding an opioid to paracetamol plus a NSAID. This may reduce the dose of opioid required. At therapeutic doses its analgesic effect is

similar to that of an opioid for mild to moderate pain in combination with a non-opioid.

Codeine demonstrates a dose response curve to pain relief. There is evidence that combinations of codeine 60 mg and paracetamol 600-1000 mg are more effective than paracetamol alone at doses of 500-1500 mg. No evidence was found in clinical trials or meta-analysis to support the superiority of cocodamol 8/500 over paracetamol alone. Many compound preparations containing codeine and dihydrocodeine have apparent sub-therapeutic doses (less than 30 mg) of these opioids and therefore are not recommended for the management of chronic pain in patients with cancer. [20]

Step 3: Moderate to severe pain

Drug options:

- First line - morphine, diamorphine **+** step 1 non-opioids
- Alternative - fentanyl, hydromorphone, methadone, oxycodone, phenazocine, + step 1 non-opioids.

The opioid of choice for oral use is morphine. The majority of patients tolerate oral morphine well and, due to the likelihood that patients will require to use medication chronically, the oral route is preferable to parenteral or rectal administration. Pain response is variable, but with dose titration a suitable level of analgesia can usually be achieved. The efficacy and safety of morphine is well established in clinical practice and the wide variety of morphine formulations available in the United Kingdom allows flexibility in dosing intervals. There is less long term safety data on alternative opioids. [13, 14]

Step 4: Acute or chronic pain

When acute or chronic pain occurs, urgent analgesia may be required, remembering that the normal breakthrough dose of analgesia for the individual is likely to be inadequate. In the acute pain situation retitration of opioid analgesia is usually necessary. This is achieved by substituting a normal release opioid for any slow release preparation. If nausea and vomiting accompanies the acute pain use the parenteral route.

Use of opioids in treatment of moderate to severe cancer pain

Opioids should be used for control of pain in patients with cancer as indicated in the WHO analgesic ladder. This section considers dosage, formulations, side effects, and methods of administration of opioids.

1) Opioid dose

The opioid dose required to control an individual's pain will depend on many factors and is not related to any one parameter. Patients require a wide range of opioid doses. For these reasons, it is necessary to titrate the dose of opioid against each patient's pain. Opioid side effects can be predicted and failure to minimise side effects, particularly sedation, will limit titration and therefore the level of analgesia which can be achieved. [21]

2) Oral morphine formulations

The time to onset of effect of the different morphine formulations varies, as does the time to peak drug levels. [15]

- **Normal release preparations**

Normal release morphine preparations have an onset of action of about 20 minutes and reach peak drug levels on average at 60 minutes. The rapid onset of analgesia makes these preparations more suitable for use in initiating therapy for severe pain and for treating breakthrough pain. When given every four hours these preparations will reach a steady plasma concentration and hence full effect within 12-15 hours. [22]

- **Controlled release preparations**

Controlled release morphine preparations have a slower onset and later peak effect. Many of the twice daily preparations have an onset of action of 1-2 hours and reach peak drug levels at four hours. The once daily preparations have a slower onset and reach peak drug levels at 8.5 hours. Controlled release preparations generally do not allow rapid titration for patients in severe pain, due to slow onset and the long dosing intervals.

3) Initiating and Titrating Oral Morphine

Pain severity, age, and previous use of opioids for moderate pain will be considered when

choosing the initial dose of opioid for moderate to severe pain. Extra care should be taken in patients with renal impairment. The active metabolites of morphine are cleared through the renal system. Therefore in patients with renal impairment, morphine metabolites may accumulate and lead to toxicity. In patients with renal dysfunction, smaller doses of morphine and longer dosing intervals are required. It is good clinical practice to avoid controlled release morphine preparations in patients with renal dysfunction.

4) Predictable side effects of morphine and other strong opioid analgesics

Opioids have predictable side effects. If these are not prevented or minimised, titration of analgesics will be limited. Sedation is the common limiting side effect to opioid analgesia and can cause a 'pseudo'-pharmacological ceiling dose. There may be some differences in side effect profiles between different opioids. Following are:

- Constipation
- Nausea and vomiting
- Sedation
- Dry mouth
- Less common side effects of opioids

5) Opioid toxicity.

Opioid toxicity can present as subtle agitation, seeing shadows at the periphery of the visual field, vivid dreams, nightmares, visual and auditory hallucinations, confusion and myoclonic jerks. The sedated patient may then become dehydrated with resultant renal impairment. For opioids with significant active metabolites which are excreted via the kidney, metabolites will accumulate and may cause further toxicity in patients with renal impairment. The presence of opioid toxicity is an indication that the opioid dose is too high for the patient at this particular time, and it may warn of developing renal dysfunction. [23]

6) Pharmacological tolerance

Clinically relevant pharmacological tolerance to opioid analgesia does not occur in chronic cancer pain management. Increases in analgesia usually coincide with disease progression.

7) Physical and psychological dependence

Psychological dependence on opioids (addiction) generally does not occur in cancer patients experiencing pain. Physical dependence on chronically administered opioids may occur in cancer pain patients. Sudden discontinuation of opioid therapy may lead to a physical withdrawal syndrome, which can be treated by administering a small dose of the opioid in question. However, abrupt discontinuation of opioids does not always produce this syndrome. [25]

- **Opioids and drug abusers**

Some drug abusers will develop malignancies. The prescription of analgesia in such cases nearly always results in anxiety and tension on all sides. Inadequate prescription of opioids in such cases will result in drug-seeking behaviour for pain relief, commonly referred to as pseudo addiction. If the pain is opioid responsive, prescription of opioid should lead to improved function and less pseudoaddiction.

8) Parenteral administration

When patients with moderate to severe pain are unable to take opioids by mouth, delivery by subcutaneous continuous infusion is effective. In addition the subcutaneous route can be used for prolonged periods of time. Indications for using the parenteral route are inability to swallow nausea and/or vomiting, gastrointestinal obstruction and any pathology limiting gastrointestinal absorption. In situations where pain control has been stable, fentanyl may be administered transdermally. Uncontrolled pain is not an indication for using the parenteral route if further titration by the oral route is possible. If a breakthrough injection is needed, the subcutaneous route is less painful than the intramuscular route. Patients requiring parenteral opioids should receive the appropriate dose of diamorphine via the subcutaneous route.

9) Alternative opioids suitable for the treatment of moderate to severe chronic pain

Changing opioids is rarely a solution to poorly controlled pain except where high doses are necessary and the first opioid is causing unacceptable side effects. The rationale for the use of these opioids is that for an individual patient

these drugs may have a better therapeutic index than morphine.

The alternative opioids for moderate to severe pain in patients with cancer have all been shown to be effective analgesics. However there is no evidence at present of any superior clinical analgesic effect for these agents over morphine. These alternative opioids can be tried in patients with opioid sensitive pain who are unable to tolerate morphine side effects. [27]

- Transdermal Fentanyl
- Hydromorphone
- Methadone and phenazocine
- Oxycodone

10) Management of postoperative pain in patients already on opioids

The team looking after the patient postoperatively must be aware whether the patient was taking opioids preoperatively. Patients taking opioids preoperatively need a larger than normal dose of opioids postoperatively. Patients are commonly given the standard postoperative analgesia and suffer pain as a result. If possible a pain specialist should be consulted. A patient-controlled analgesia (PCA) system should be used, set with a larger background and bolus dose than usual based upon the preoperative opioid dosage and a short lockout time. The use of NSAIDs in conjunction with opioids should be considered, as long as there are no contraindications.

ADJUVANT ANALGESICS

These drugs are used in combination with opioids and may result in synergistic effects producing better pain relief at lower dose of opioids; hence the patient may experience fewer opioid side effects.

1) Tricyclic antidepressants and anticonvulsants

Tricyclic antidepressants are effective in relieving neuropathic pain. Despite the possible differences in underlying pain causation, different tricyclic antidepressants are similarly effective in the different pain syndromes. There are no significant differences in efficacy between the different tricyclic antidepressants. [15]

The anticonvulsants carbamazepine, phenytoin, sodium valproate, clonazepam, and gabapentinare effective in treating neuropathic pain of non-malignant aetiology. Benefit was independent of pain characteristics. Gabapentin is licensed for the treatment of neuropathic pain and recent RCTs have demonstrated its efficacy. [28]

In clinical practice, tricyclic antidepressants appear better tolerated than anticonvulsants. The choice of antidepressant should be based on relative contraindications, possible drug interactions and risk of side effects for each patient. Tricyclics and anticonvulsants may be prescribed simultaneously. It is good clinical practice to introduce only one drug at a time.

2) Steroids

There is some evidence for the use of steroids as analgesics in patients with cancer pain. Clinical experience shows steroids to be useful adjuvant analgesics for raised intracranial pressure, severe bone pain, nerve infiltration or compression, pressure due to soft tissue swelling or infiltration, spinal cord compression and hepatic capsular pain. High dose dexamethasone up to 16 mg/24 hours may be required. The dose and duration depends on the clinical response to treatment. The last dose should be given at 6 pm as insomnia may be a problem if given later. [29]

3) Mexiletine

Mexilitene does appear to be effective in reducing pain associated with nerve damage but it carries a high risk of serious side effects. Mexiletine should not be used routinely as an adjuvant analgesic.

4) Ketamine

Ketamine has been used as an anaesthetic for 40 years. However at sub-anaesthetic doses it acts as an analgesic. This effect is chiefly mediated by blocking the N-methyl-d-aspartate (NMDA) receptors in the dorsal horn. The NMDA receptor is thought to be activated in clinical states where allodynia, hyperalgesia and hyperpathia are present. [30]

The use of ketamine as an analgesic is increasing in pain clinics and specialist palliative care units. It is generally administered

intravenously or subcutaneously. Ketamine may be indicated in neuropathic pain states, ischaemic pain, in acute inflammatory disorders and phantom limb pain. If successful ketamine will restore the patient's morphine sensitivity and opioid toxicity may occur.

Ketamine may cause transient hypertension and so caution is required if there is a history of hypertension, cardiac failure or cerebrovascular accident. Hallucinations, dysphoria and vivid dreams may occur when using ketamine.

SYSTEMIC ANTI-CANCER THERAPY

Response to systemic therapy used for pain control is likely to be delayed. Patients should also receive appropriate analgesics according to the principles outlined in section 4.

1) Chemotherapy

Palliative chemotherapy has been documented as being effective in the management of patients with pain from metastatic disease. Selection of appropriate chemotherapy should be made by an oncologist and its effect reviewed regularly by an oncologist. Where it is being used primarily for pain relief it is generally less appropriate than radiotherapy or endocrine therapy. The reasons are:

- Chemotherapy may already have been used earlier in the course of the disease.
- The response rates to chemotherapy for the common cancers with metastatic or locally advanced disease are relatively poor.
- Patients will have poorer performance status and as a consequence drug toxicity may be enhanced.

Chemotherapy for as following:

- **Breast cancer**

Patients presenting with locally advanced or inflammatory breast cancer or patients with metastatic disease may experience pain. In patients with symptoms mainly from widespread bone metastases and a reasonable performance status chemotherapy may achieve excellent palliation this area is discussed in the SIGN/SCTN guideline on breast cancer. Patients with locally advanced or inflammatory breast cancer should be treated with

systemic treatment as part of multimodality therapy. [31]

- **Lung cancer**

Chemotherapy can be effective and provide palliation for symptomatic extensive disease from small cell lung cancer (SCLC) causing pain, including cerebral metastases. This area is covered in the SIGN/SCTN guideline on lung cancer.

2) Endocrine therapy

Endocrine treatment is used frequently in two tumour sites: breast and prostate cancer. Endocrine therapy has the advantage of being much less toxic than chemotherapy but the response rates for palliation in breast cancer are usually lower and time to response is slower. This is due to patients having had previous treatment or who have endocrine non-responsive disease. This relatively poor and slow response rate may be unacceptable when the aim is palliation of pain.

- **Breast cancer**

Tamoxifen is recognised as first line endocrine therapy for breast cancer (see the SIGN/SCTN guideline on breast cancer). Most patients already will have received this treatment. The new aromatase inhibitors (e.g. anastrozole, letrozole) are replacing standard second line therapy (after tamoxifen), due to longer duration of response, survival advantages and less side effects. In patients with metastatic breast cancer who have progressive disease despite prior tamoxifen, the use of specific aromatase inhibitors such as anastrazole and letrazole should be considered. [32]

- **Prostate cancer**

Hormonal therapy is recommended for newly diagnosed patients with metastatic prostatic cancer. Medical castration using luteinising hormone-releasing hormone (LHRH) analogues is gradually replacing surgical castration because of patient preference and improved quality of life.

Many studies have examined maximum androgen blockade. A meta-analysis of this using nonsteroidal antiandrogens with LHRH or orchidectomy has produced inconsistent results when the end point has been survival benefit. Similarly, when the steroid anti-androgen

cyproterone acetate was combined with LHRH analogue, there was no advantage in terms of time to progression compared with monotherapy although side effects caused by LHRH analogue treatment alone were reduced. Maximum androgen blockade should be considered for management of patients with prostate cancer with worsening bone pain or progression on current single agent endocrine therapy. [33]

RADIOTHERAPY

Radiotherapy is usually considered the most effective oncological treatment modality in relieving pain. It is especially effective in relieving pain due to bone metastases and when used for this indication produces few side effects. A systematic review of the literature examined the evidence for using radiotherapy for painful bone metastases from all cancer sites and reported the difficulty in performing clinical trials in this patient group.[124] Guidelines for the management of metastatic bone disease in breast cancer have been published.

1) Bone metastases

A systematic review of the use of radiotherapy for bone pain showed complete pain relief at one month in 27% of patients, and at least 50% relief in an additional 42% of patients at any time in the duration of the trials included. Another systematic review on this subject highlighted difficulties in conducting these studies due to different treatments administered, variable fields and wide variation in performance status of patients. Radiotherapy using simple techniques and short fractionation should be employed. For wider fields, increased fractionation should be employed with anti-emetics. Radiotherapy should be considered for painful bone metastases. [34]

2) Prostate cancer

For prostate cancer, radioactive strontium is effective for pain control and may protect against the development of further painful bone metastases. However, strontium may take up to twelve weeks to give symptomatic relief. Therefore local radiotherapy should be considered for the main site of pain at the same time as administration of strontium. Hemi-body irradiation can also reduce the number of sites of bone pain. Radioactive strontium should be considered for the management of pain due to widespread bone metastases from prostatic carcinoma. [33]

3) Other sites

- **Brain metastases**

High dose steroids and radiotherapy should be considered for headache due to cerebral metastases.

- **Spinal cord compression**

This condition may be associated with pain and is considered an oncological emergency. The majority of patients who develop spinal cord compression suffer radicular pain for several weeks prior to overt expression of this condition. Depending on clinical factors, the patient should be treated with high dose steroids, analgesics, surgery, radiotherapy or a combination of modalities. Spinal cord compression requires urgent investigation and intervention. Urgent treatment should be given for all patients with spinal cord compression.

- **Pancoast tumour**

Management of patients with pancoast tumours is discussed in the SIGN/SCTN lung cancer guideline. [35]

CONCLUSION:

The pain is the major problem in the Cancer and there is many types of pain are associated in Cancer which should be assessed and treated by using various type of drugs for removing pain and make less troublesome to the Cancer patient.

The pain which are normal and easy to assessed and treat are treated by suing following categories of drugs.

- Non steroidal anti inflammatory drugs
  - Paracetamol, Aspirin,
  - Newer NSAID's which selectively inhibit the iso enzyme cycloxygenase-2 (cox-2) are used. Eq. Rofecoxib.
- Opioid Analgesics
  - Morphine, Diamerphine

- Fentanyl, Hydromorphone, Methodone, Oxycodone, Phenazocine.

- Adjuvent analgesics – These are used in combination of opioids due to synergistic effect for better pain relief
  - Tricyclic antidepressants
  - Anticonvulsants – Carbamasipine, Phenytoin, Sodium valproate, Clonazepam, Gabapentin.
- Steroids
  - Dexamethasone
- Mexiletine – Effective in reducing pain associated with nerve damage
- Ketamine – Used in neuropathic pain relief
- Systemic Anticancer Therapy
  - Chemotherapy, used to releave the pain from metastatic disease.
- Radiotherapy: Releaving pain due to bone metastates, Brain metastates, Prostate Cancer, etc.

The pain which is severe, not easy to treat and the further research is going on progress for employment of new drugs for such pain.

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