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Pain Management

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Abstract
Pain is a major health care problem. Pain is regarded as a symptom of underlying condition. Good pain management involves assessing the pain, followed by control of pain through pharmacological management and resolving underlying cause. Neuropathic pain is intractable pain caused by damage to nervous system. Peripheral neuropathy affects most people with Diabetes. HIV associated sensory peripheralneuropathy is the most prevalent neurological complication associated with HIV. According to Canadian guidelines Tri Cyclic Anti-depressants and Anticonvulsants are used as first line therapy for treating neuropathic pain. Cancer pain remains a clinical problem worldwide. Cancer therapy causes pain in patients receiving chemotherapy. Opioids remain the most effective pharmaceuticals in treatment of cancer pain. The goal of pain therapy for patients receiving chemotherapy is to provide them sufficient relief to tolerate the diagnostic and therapeutic approaches required to treat their Cancer.

Introduction

Pain is an unpleasant, sensory and emotional experience associated with actual or potential tissue damage[1]. It is an individual experience influenced by the patient perception, history and expression of pain. ex: ability to cope, mental wellbeing, previous experience of pain, communication skills, family or cultural background[2]. Pain is regarded as a symptom of an underlying condition. An immediate firing occurs in a reflexive action when a stimulus induces a reaction from pain receptors. Stimulus for temperature and touch have significantly lower firing than that of pain receptors and nociceptors. Pain receptors react due to stimuli such as cuts, scrapes, heat, chemical substances causing tissue damage and lack of blood circulation in specific area. The production of prostaglandins begin causing an irritation and signalling the body of an unpleasant feeling.

Types of pain[3]

There are several ways to categorise pain

1. Based on mechanism (Nociceptive & Neuropathic pain)
2. Based on duration (Acute & Chronic pain)
3. Based on etiology (Malignant or Non malignant pain)

4. Based on anatomical location (head, back or neck pain)

Receptors involved in pain

Pain receptors (nociceptors)

Types of pain receptors

Free nerve endings which are morphologically similar but functionally specific. They are classified according to their sensitivity into:

1.Polymodal pain receptors: These respond to combination of mechanical, thermal and chemical noxious stimuli.

2.Mechanical pain receptors: These respond to mechanical forces such as cutting, crushing, pricking or even firm pressure on tissues.

3.Thermal pain receptors: These respond to excessive changes in temperature above 45^0C and below 10^0C.

4.Chemical pain receptors: These respond to noxious chemical stimuli.

Distribution of pain receptors: Pain receptors are found in most tissues of body but varies in their density. They are abundant and widely spread in the skin and some internal tissues such as periosteum of the bone, arterial walls, joint surfaces, and tentorium in the cranial cavity, skeletal muscle, Parietal layer of serous membranes. Many of the deep tissues and viscera are poorly supplied with pain receptors. So, for pain to occur, painful stimulus must be intense and widespread. The deep and visceral pain are poorly localised. On the other hand, brain itself, and also the parenchymal tissues of the liver, kidney and lungs have no pain receptors. They are called "pain insensitive structures".

I Acute Pain

Acute pain is sudden in onset and is caused by something specific. It is sharp and gripping. It doesn't last longer than six months[2].Causes of acute pain include: Surgery, Trauma, dental work, burns, cuts, labour and child birth.

Principles of managing acute pain:

The primary aim of acute pain management is to provide treatment that reduces pain with minimal adverse effects. Secondary aim is preventing progression to chronic pain[2]. Patient should have a realistic expectation of what their pain management strategy will achieve– only analgesic regimen cannot remove all the experiences of pain. The effectiveness of an analgesic regimen can be attributed to not only pharmacological effects of medicine but also awareness that pain is being treated. Patients can be reassured that their pain is expected to improve with time and their requirements for medicines will decrease. Anxiety, depression, stress, insomnia, and catastrophising increase the likelihood that acute pain will become chronic, particularly post-surgery, patients who display any of these features will require additional reassurance that their pain is being managed and is expected to resolve. Regular assessment of pain improves management and outcomes. Patients prescribed with analgesics for acute pain should be followed up regularly to ensure that their pain is resolving and their medicine requirements are diminishing. Pain that is unable to be managed or that increases in intensity warrants consideration of other causes. ex: surgical complication, infection or alternative diagnosis ex-neuropathic pain.

Pharmacological treatment

A pharmacological treatment regimen for acute pain is based on WHO analgesic ladder.

The WHO analgesic ladder is widely accepted for management of nociceptive pain[4]. In patients with acute pain the ladder is generally used in reverse. Ex: In severe acute pain begin with Morphine at step-3, then as the pain resolves, reduce to Codeine at step-2 and continue with Paracetamol at step-1 until pain is negligible.

Figure 1 – WHO analgesic ladder for medicines[2].

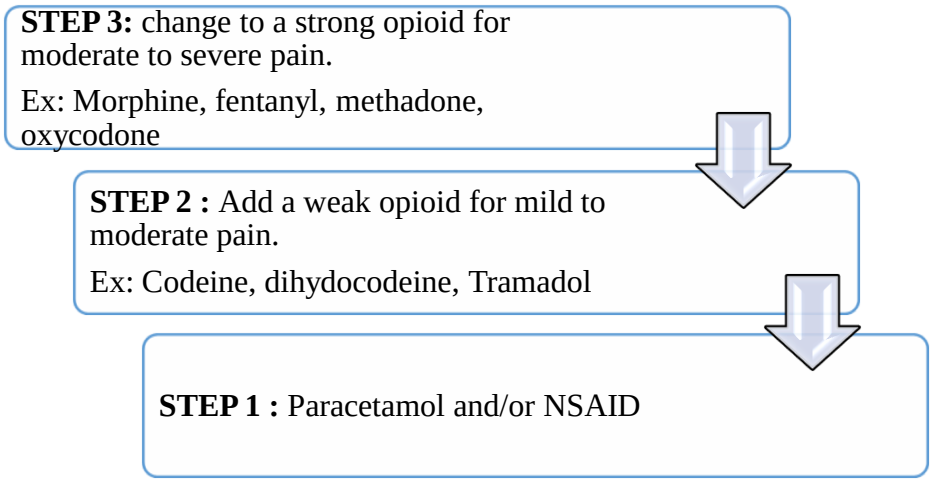

Table 1 Pharmacological treatment for Acute pain[5]

Sno	Drug	Dose	ROA	Frequency
I	Acetaminophen	325 – 650 mg or 1000 mg	PO PO	q 4 – 6 hours TID / QID
II	Aspirin	325 – 650 mg or 1000 mg	PO PO	q 4 – 6 hours q 6 hours
III	NON-SELECTIVE NSAIDS			
1	Ibuprofen	200 – 400 mg	PO	q 4 – 6 hours
IV	CYCLOOXYGENASE-2 SELECTIVE NSAIDS			
1	Celecoxib	100 – 200 mg	PO	BID
V	OPIOID COMBINATIONS			
1	Hydrocodone / Acetaminophen	2.5 – 10 mg / 325 – 625 mg	PO	q 4 – 6 hours
VI	OPIOIDS			
1	Morphine	10 – 30 mg	PO	q 3 – 4 hours
VII	DUAL-ACTION OPIOIDS			
1	Tapentadol	50 – 100 mg	PO	q 4 – 6 hours

II Chronic Pain

Chronic pain is defined as persistent pain, either continuous or recurrent, that affects patient's well-being, level of function, and quality of life[6]. Chronic pain is a pain that lasts longer than six weeks or more. This type of pain continue even after the injury or illness that caused it has healed or gone away. Pain signals remain active in the nervous system for weeks, months or years. Some people suffer chronic pain even when there is no past injury or apparent body damage. Chronic pain is linked to conditions including Headache, Arthritis, Nerve pain, Back pain, Fibromyalgia.

People who have chronic pain have physical affects that are stressful on the body. These include tense muscles, limited ability to move around, lack of energy and appetite changes.

Emotional affects of chronic pain include Depression, Anxiety, Anger, Fear of reinjury. Such fear might limit a person's ability to return to their regular work or leisure activities.

Types of chronic pain[6]

The ICSI work group divided chronic pain as 4 types Neuropathic, Muscle, Inflammatory and Mechanical pain.

Table 2 Pharmacological Treatment for Chronic Pain[7]

Sno	Drug	Dose	ROA	Regimen
I	NON-STEROIDAL ANTI-INFLAMMATORY DRUGS			
1	Ibuprofen	400 mg	PO	q 4 – 6 hrs
2	Diclofenac sodium	50 mg [EC] 100 mg [ER]	PO	BID/TID OD
3	Aceclofenac	100 mg	PO	BID
II	ANTI-DEPRESSANTS			
1	Amitriptyline	25 – 100 mg	PO	qhs
2	Doxepin	150 – 300 mg	PO	qhs
3	Imipramine	0.2 - 3 mg/kg	PO	qhs
III	ANTICONVULSANTS			
1	Gabapentin	300-1200 mg	PO	TID
2	Pregabalin	50 – 100 mg	PO	TID
3	Valproic acid	250 – 500 mg	PO	BID
IV	MUSCLE RELAXANTS			
1	Baclofen	20 – 80 mg	PO	TID/QID
2	Cyclobenzaprine	5 – 10 mg	PO	TID x 3 weeks
3	Metaxalone	800 mg	PO	TID/QID
V	OPIOIDS			
1	Codeine	15 – 60 mg	PO	q 4 – 6 hrs
2	Fentanyl	50 – 100mcg	IV/IM	x 1Inj
3	Hydrocodone	20 mg	PO	OD
4	Methadone	2.5mg	PO/SC/ IM/IV	q 8 – 12 hrs
5	Morphine	10 – 30 mg 2.5 – 10 mg 10 – 20 mg	PO SC/IM/IV Rectal	q 3 – 4 hrs q 2 – 6 hrs q 4hrs
6	Oxycodone	10 mg	PO	q 12 hrs
VI	TOPICAL NSAIDS			
1	Capsaicin	8 %		
2	Lidocaine	5 %		

III Neuropathic Pain

The International Association for Study of Pain, classified pain as Nociceptive pain & Neuropathic pain[8].Neuropathic pain, is defined as pain arising as a direct consequence of a lesion or disease affecting the somatosensory system[9]. Neuropathic pain may be classified as either peripheral or central in origin. Examples for Neuropathic Pain include

1. Diabetic peripheral neuropathy (DPN)
2. Post-herpetic neuralgia (PHN)
3. Antineoplastic therapy
4. HIV-induced sensory neuropathy
5. Tumour infiltration neuropathy
6. Phantom limb pain
7. Postmastectomy pain
8. Complex regional pain syndromes (reflex sympathetic dystrophy)and
9. Trigeminal neuralgia.

Deafferentation syndromes resulting in neuropathic pain include

1. Multiple sclerosis (MS)
2. Spinal cord injury (SCI)[9]
3. Central poststroke Pain and
4. Parkinson disease

Nociceptive Pain and Neuropathic Pain(NP) utilizes same nervous system pathways for transmission but significant physiologic differences exist in mechanism through which body processes and resolves these painful stimuli[10]. Nociceptive pain results from an obvious cause i.e, trauma, cancer metastasis, arthritis and is easy to identify. Neuropathic pain occurs in absence of identifiable cause.

The morbidity rate of neuropathic pain is estimated to be approximately 1%- 7% in developed countries, and several million people in Japan suffer from Neuropathic Pain[11]. NP results

from various aetiologies and can be categorised into either peripheral or central NP syndromes. Central NP is the result of a central lesion or disease such as stroke, multiple sclerosis or spinal cord injury, whereas peripheral NP occurs from dysfunction or damage to peripheral nerves[11]. A quarter of people with diabetes and 35% of people with HIV have neuropathic pain.8% of the general population in the UK experience pain of neuropathic origin[12]. In France, 7% of the general population are affected by NP[13]. A study in Canada reported that 17.9% of the general population reported chronic pain with neuropathic symptoms[14]; however, a recent Canadian study has reported lower percentages[14,15]. A study in the USA revealed that the prevalence rates for NP are determined by either clinical examination (9.8 %) or self-reporting (12.4%). It is difficult to obtain a true estimate, due to epidemiological studies using different methods of assessment and different definitions of NP[16]. A recent systematic review of epidemiological NP studies across the world by van Hecke *et al*., suggests that the prevalence likely lies between 6.9% and 10% in the general population[15].

Table 3 Estimated prevalence of neuropathic pain in United States[17]

Condition	Number per 100,000 Population
Diabetic Peripheral Neuropathy	600
Post-Herpetic Neuralgia	500
Cancer associated	200
Spinal cord injury	120
Causalgia and reflex sympathetic dystrophy	100
Multiple sclerosis	50
Phantom Pain	50
Post stroke	30
HIV associated	15
Trigeminal Neuralgia	15
Low back pain associated	2,100

Symptoms

Peripheral NP is the result of injury to nerve fibres due to various aetiologies including toxic, traumatic, ischaemic, metabolic, infectious or compressive damage. Positive symptoms are typically altered or painful sensations such as tingling, prickling, or pain described as shooting, stabbing, burning, or having an electric shock sensation[18]. Negative symptoms are described as diminished sensations due to loss of sensory function. Other symptoms include

Allodynia- Pain due to nonnoxious stimuli (clothing, light touch) when applied to the affected area. May be mechanical (eg, caused by light pressure), dynamic (caused by nonpainful movement of a stimulus), or thermal (caused by nonpainful warm, or cool stimulus)

Anaesthesia-Loss of normal sensation to the affected region

Dysesthesia- Spontaneous or evoked unpleasant abnormal sensations

Hyperalgesia- Exaggerated response to a mildly noxious stimulus applied to the affected region

Hyperpathia- Delayed and explosive response to a noxious stimulus applied to the affected region.

Hypoesthesia- Reduction of normal sensation to the affected region.

Paraesthesia- Nonpainful spontaneous abnormal sensations.

Phantom Pain- Pain from a specific site that no longer exists (eg, amputated limb) or where there is no current injury.

Referred Pain-Occurs in a region remote from the source[19].

Underlying Conditions

Neuropathic Pain has multiple aetiologies. Common underlying conditions that are associated with Neuropathic Pain include diabetic Peripheral

Neuropathy, HIV-associated Neuropathy[20], Chemotherapy-Induced Peripheral Neuropathy (CIPN), Post-Herpetic Neuralgia (PHN) and Trigeminal Neuralgia[18]. Although the aetiologies may vary, the signs and symptoms of Neuropathic pain can be similar[16].

Diabetic Peripheral Neuropathy

It is a condition that affects many patients with diabetes. The distal symmetrical polyneuropathy (DSPN) is the commonest clinical form of diabetic neuropathy, affecting more than 90% of the patients.

Generally, DSPN affects the toes and distal foot, but slowly progresses proximally to involve the feet and legs in a stocking distribution. It is also characterized by a progressive loss of nerve fibres affecting both the autonomic and somatic divisions, thereby diabetic retinopathy and nephropathy can occur[21]. Foot ulceration and painful neuropathy are the main clinical consequences of DSPN, linked with higher morbidity and mortality[22].

Diabetic Neuropathic Pain (DNP) is characterized by tingling, burning, sharp, shooting, and lancinating or even as electric shock sensations[21,23]. It is usually considered moderate to severe and often worse at night, causing sleep disturbances. The pain can be constant and accompanied of cutaneous allodynia, affecting the quality of life of patients, & impacts the ability to perform daily activities and has a negative influence on mood. The pain may also be a reason of withdrawal of recreational and social activities and may be associated with depression[21,24,25]. Several risk factors associated with DNP include worsening glucose tolerance, older age, longer diabetes duration, drinking alcohol and cigarette smoking[25]. Neuropathic Pain is thought to be the result of oxidative and inflammatory stress caused by metabolic dysfunction, which ultimately damages the nerve cells. Currently, only three agents are approved in the United States for the treatment of DNP: duloxetine, a selective serotonin and norepinephrine reuptake inhibitor (SSNRI), pregabalin, an anticonvulsant, and the dual-effect drug tapentadol, an opioid receptor agonist and norepinephrine reuptake inhibitor[26].

HIV associated Sensory Peripheral Neuropathy HIV-SN

It is the most prevalent neurological complication associated with HIV. This presents as a distal polyneuropathy in a symmetrical pattern that occurs in patients with both treated and untreated HIV infections. HIV-SN can be the result of injury to the nerve by the HIV virus or by medication-induced mitochondrial dysfunction of the nerve cells[27]. Risk factors of HIV-SN include exposure to neurotoxic antiretroviral drugs, increasing age, malnutrition, ethnicity, increasing height, certain genetic factors and comorbid conditions such as diabetes[28].Symptoms include bilateral tingling, numbness, or neuropathic pain starting in toes and spreading proximally; the pain frequently is described as burning or aching and is worse on the soles[29]. Patients frequently have impaired sensation and vibratory sense without pain. First line treatment includes amitriptyline or nortriptyline, pregabalin or gabapentin, duloxetine or venlafaxine. Second line therapy is tramadol or tramadol + paracetamol. Third line therapy is morphine or fentanyl, lamotrigine or topical capsaicin[30].

Chemotherapy induced Peripheral Neuralgia

It is the most common neurological complication associated with cancer treatment. Chemotherapy-induced peripheral neuropathy (CIPN) is a common dose dependent adverse effect of many anticancer drugs, such as platinum analogues, antitubulins (eg, taxanes and vinca alkaloids), bortezomib, and thalidomide[31]. It can present as sensory symptoms in the hands and/or feet, typically in a "stocking-glove" pattern; pain, numbness, or tingling, or motor symptoms, manifested as weakness, cranial nerve deficits, or autonomic neuropathy[32]. In many cases, CIPN improves once the therapy is discontinued; however, with Cisplatin and Oxaliplatin, it continues even after the drugs have been

discontinued[33]. Exact mechanism of CIPN is still unknown. The hypothesized mechanisms of taxane-induced neuropathy include the disruption of the axonal microtubule structure and a deficit in axonal energy supply from the toxic effect of chemotherapy on mitochondria in primary afferent neurons[32,34]. CIPN due to vinca alkaloid therapy is thought to be due to alterations in the neuronal cytoskeleton that cause axonal degeneration[34]. P latinum agents are thought to cause CIPN by exerting damage in the dorsal root ganglion through mitochondrial dysfunction and neuronal apoptosis, either by DNA crosslinking or oxidative stress[32]. First line therapy is amitriptyline or nortriptyline, pregabalin or gabapentin, duloxetine, venlafaxine or carbamazepine. Second line therapy is tramadol, strong opioids and/or topical lidocaine. Third line therapy includes SSRIs like paroxetine and citalopram, bupropiom, lamotrigine, topiramate, memantine and/or topical capsaicin[30].

Post-Herpetic Neuralgia

Post-Herpetic Neuralgia (PHN) is a chronic neuropathic pain condition that persists 3 months or more following an outbreak of shingles. Shingles, also known as acute herpes zoster, is associated with the reactivation of the dormant varicella zoster virus in an individual who has experienced chicken pox. PHN is associated with persistent and often refractory Neuropathic pain. Patients experiences multiple types of pain including a constant deep, aching, or burning pain; a paroxysmal, lancinating pain; hyperalgesia (painful stimuli are more painful than expected); and allodynia (pain associated with typically non-painful stimuli).The virus can affect the nerves through sensitisation (hyperexcitability) and deafferentation (sensory nerve death or damage)[27]. Pain is typically distributed unilaterally along spinal dermatomes or the ophthalmic branch of the trigeminal nerve[35]. The annual incidence rate per 10,000 population for post-herpetic neuralgia was 3.4 in the UK[36]. First line therapy for treatment of Post Herpetic Neuralgia is amitriptyline or Nortriptyline, pregabalin, gabapentin, topical lidocaine. Second line agents include morphine or fentanyl or topical capsaicin. Third line therapy includes baclofen or tramadol[30].

Trigeminal neuralgia

It is a most frequent cranial neuralgia. Patients with trigeminal neuralgia experience facial pain limited to areas associated with one or more branches of the trigeminal nerve[37]. Symptoms are the result of compression of nerve by vasculature or tumours. This type of pain is also caused by demyelination in patients with multiple sclerosis. Pain attacks begin suddenly and lasts for several seconds to a couple of minutes. The pain is usually unilateral in nature and is described as sharp, shooting, shock-like, burning and excruciating. These attacks are usually accompanied by involuntary spasms or contractions of the facial muscles. Trigeminal neuralgia is usually triggered by non-painful physical stimulation of a specific area that is located close to the pain[35]. The First line treatment is Carbamazepine or oxcarbamazepine. second line therapy is Lamotrigine or baclofen. Third line therapy includes gabapentin, pregabalin, amitriptyline, duloxetine, venlafaxine[36].

Treatment of Neuropathic pain

Table 4 Treatment for Neuropathic pain according to Japan Society of Pain Clinicians[38]

Sno	Drug	Dose	ROA	Regimen
I	CALCIUM CHANNEL α2-DELTA LIGANDS			
1	Pregabalin Diabetic neuropathy Postherpetic neuralgia Neuropathic pain	50mg 75 mg/ 50 mg 75mg	PO PO PO	TID BID/TID BID
2	Gabapentin postherpetic neuralgia	300 mg 300 mg 300 mg	PO PO PO	OD on Day 1 BD on Day 2 TID on Day 3

II	ANTI-DEPRESSANTS TCA			
1	Amitriptyline	75 mg	PO	QHS
2	Nortriptyline	25 mg	PO	TID/QID
3	Desipramine	100 – 200 mg	PO	OD
III	ANTI-DEPRESSANTS SNRI			
1	Duloxetine	20 mg	PO	BID
2	Venlafaxine	37.5 mg/25 mg	PO	BID/TID
IV	TOPICAL/LOCAL TREATMENT			
1	Lidocaine	5%		
2	Capsaicin	8%		
3	Botulinum toxin type A			
V	OPIOIDS			
1	Tramadol	50 – 100 mg	PO	QID
2	Tapentadol	50/75/100 mg	PO	QID

Table 5 Considerations of drugs by therapeutic lines for neuropathic pain[30]

Sno	Drug	Dose	Duration
First line drugs			
I	Tri-Cyclic Antidepressants		
1	Nortriptyline	25 – 150 mg/day	6 – 8 weeks
2	Amitriptyline	25 – 150 mg/day	6 – 8 weeks
3	Imipramine	25 – 150 mg/day	6 – 8 weeks
II	Serotonin and Norepinephrine Reuptake Inhibitors		
1	Duloxetine	30 – 120 mg/day	4 weeks
2	Venlafaxine	37.5 – 225 mg/day	4 – 6 weeks
III	Anticonvulsants		
1	Gabapentin	100 – 3600 mg/day	3 – 8 weeks
2	Pregabalin	150 – 600 mg/day	4 weeks
3	Carbamazepine	100 – 1200 mg/day	4 weeks
IV	Topical agents		
1	Lidocaine	3 plasters/day	3 weeks
Second line drugs			
I	Opioids		
1	Fentanyl	25 – 100 mcg/h	4 weeks
2	Morphine	15 – 200 mg/day	4 – 6 weeks
3	Tramadol	50 – 400 mg/day	4 weeks
Third line drugs			
I	Other anticonvulsants		
1	Lamotrigine	25 – 400 mg/day	4 – 6 weeks
2	Oxcarbazepine	300 – 1800 mg/day	4 weeks
II	Other antidepressants		
1	Citalopram	10 – 40 mg/day	4 weeks
2	Paroxetine	10 – 40 mg/day	4 weeks
3	Bupropion	100 – 400 mg/day	3 weeks
III	NMDA receptor antagonists		
1	Memantine	10 – 20 mg/day	4 – 6 weeks
IV	Topical agents		
1	Capsaicine	0.025 %	4 – 6 weeks
V	$GABA_B$ receptor agonists		
1	Baclofen	40 – 80 mg/day	4 weeks

IV Cancer Pain

Cancer causes pain as it invades bone, compresses nerves, produces obstructive symptoms in the pulmonary, gastrointestinal, and genitourinary systems, and distends involved visceral organs[39]. Cancer pain is one of the most feared entities in cancer and about 75% of patients required treatment for severe pain[40]. Data from WHO suggests that oral morphine alone can take care of 85% of patients. Pain has high prevalence in specific cancer types such as pancreatic (44%) and head and neck cancer (40%)[41]. Studies based on international surveys and WHO suggest that moderate to severe pain is experienced by 1/3rdof cancer patients who receive active therapy and 60-90% of patients with advanced disease. Bone pain is most common type. Cancer therapy causes pain

in 15% to 25% of patients receiving chemotherapy, surgery or radiation therapy.

The character of cancer pain is not fixed, it is recurring and often with complex multiple etiologies. 90% of pain contributes to tumour and its evaluation while rest is attributed to other pain generators. Out of these 90%, 70% is due to tumour invasion or compressing soft tissue bone or neural structures while 20% of pain is due to procedures related to therapeutics and evaluation.

Treatment of Cancer pain[42]

Figure 2: Treatment for cancer based on WHO Cancer pain ladder

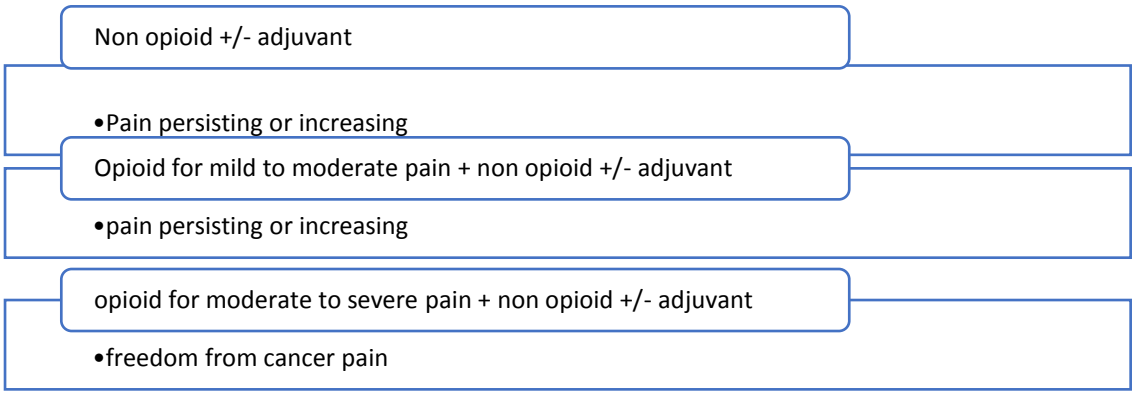

Table 6 Treatment for Cancer pain based on WHO[42]

Sno	Drug	Dose	ROA	Regimen
I	NON-OPIOID ANALGESICS FOR MILD PAIN			
1	Acetaminophen	500 – 1000 mg	PO	q 6 hours
2	Acetylsalicylic acid	325 - 625 mg	PO	q 4 hours
3	Ibuprofen	200 – 800 mg	PO	q 6 hours
4	Ketoprofen	25 – 75 mg	PO	q 6 – 8 hours
5	Diclofenac	25 – 100 mg	PO	50mg QID 100 mg BID
6	Mefenamic acid	250 – 500 mg	PO	QID
7	Celecoxib	200 – 400 mg	PO	OD/BID
8	Ketorolac	15 – 30 mg	IV/PO	q 6 hours
9	Naproxen	500 mg then 250 mg	PO	q 4 hours
II	OPIOIDS FOR MILD TO MODERATE PAIN			
1	Dihydrocodeine	60 – 120 mg	PO	BID
2	Codeine	30 – 60 mg	PO/IV/SC	q 4 – 6 hours
3	Tramadol	25 – 50 mg	PO/IV/SC	q 6 hours
4	Tapentadol	50 – 100 mg	PO	q 4 – 6 hours
5	Hydrocodone	10 – 20 mg	PO	OD
III	OPIOIDS FOR MODERAT TO SEVERE PAIN			
1	Morphine sulphate	10 – 30 mg 2.5 – 10 mg 10 – 20 mg	PO SC/IV/IM rectal	q 3 – 4 hours q 2 – 6 hours q 4 hours
2	Oxycodone	5 – 15 mg	PO	q 4 – 6 hours
3	Hydromorphone	2 – 4 mg 1 – 2 mg	PO IM/SC	q 4 – 6 hours q 2 – 3 hours
4	Fentanyl transdermal	12mcg/h	TTS	
5	Buprenorphine	Day 1: 8 mg Day 2: 16 mg Maintenance: 4 – 24 mg	Sublingual	OD
6	Buprenorphine	0.3 – 0.6 mg	IV/IM	q 6 – 8 hours
7	Buprenorphine transdermal	5 – 20 mcg/h	TTS	7 days
8	Methadone	2.5 mg	PO/SC/ IM/IV	q 8 – 12 hours
9	Nicomorphine	5 mg	PO/IV	
10	Oxymorphone	5 – 10 mg 0.5 mg	POIV/SC	q 12 hours x 3 – 7 days
11	Fentanyl	50 – 100 mcg	IV/SC	q 1 – 2 hours

Patient counselling plays an important role in the management of pain.

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