Acute Pain management in Onco Surgical Patient: Overview

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Pain is a complex multifactorial phenomenon which has a biological basis, huge psychological component, and a great social impact (Biopsychosocial model of pain) [1]. Broadly speaking pain can be classified into three broad categories—acute pain, that is the pain immediately following an operation or injury so it has an identifiable temporal and causal relationship to injury or disease, cancer pain which happens due to metastasis, invasion of tissues or inflammation from cancer and the third type of pain is chronic non-malignant pain like headache, backache, fibromyalgia or neuropathic pain. Chronic pain usually starts after tissue healing often without any specific identifiable cause in most cases persists beyond 3 months of the initial injury. Many scholars present a view that is acute and chronic pain may represent a continuum rather than distinct entities. In this chapter, we will limit ourselves to the definition of pain, the pathophysiology of acute postoperative pain, the assessment of the patients in pain, management of the postoperative patients and some challenges you will face in the ward. The aim of this chapter is not to impede the freedom of the clinician but to provide him with guidance to form a robust, evidence-based and acceptable working protocol. It will help the clinical staff to manage patient more proficiently and establish standardized care which can be audited against a standard to improvise and compare the outcome.

10.1 Introduction

International Association of the Study of Pain (IASP) [2] defines pain as 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage'. The old view was pain is beneficial as it warns us about the problem but contrary to the old view, it has been demonstrated that pain is not equal to damage. Pain is a stressor and it threatens homeostasis with a neurohumoral adaptive response which harms the patient. It is now established that the contribution of psychological factors in acute pain is as important as chronic pain [3]. So our aim should be to reduce preoperative anxiety, anxiety or depression by proper counselling and reduce the stress response to improve outcome.

The table below summarizes some of the salient systemic effects of acute pain, for example, following a laparotomy.

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Cardiovascular	Stress leads to increase in sympathomimetic amines like adrenaline and nor adrenaline causing an increase in heart rate, cardiac contractility, systemic vascular resistance and blood pressure. This leads to increase stress on the heart as it has to work more with less diastolic time for perfusion of cardiac muscles. This produces the oxygen supply-demand mismatch of the cardiac tissues causing myocardial ischaemia.
Respiratory	During operation, there is positive pressure ventilation of the lungs contrary to the normal negative pressure aspiration of air and oxygen. This disturbs the alveoli function leading to accumulation of protein-rich exudates in the dependent portions of lungs which are ideal for bacterial growth. So it is mandatory to have deep breathing exercises in the postoperative period to mobilize this fluid and prevent chest infection.
Renal	The effect of the activation of the renin–angiotensin system leads to sodium and water retention by active transport in the distal tubules. This leads to poor urine output and extracellular accumulation of water and tissue oedema. In compromised patients with low GFR (<50 mL/min/1.73 m^2) this can lead to postoperative acute renal failure.
Pancreas	Inhibition of insulin release and increase in glucagon leads to poor glucose homeostasis. Neoglucogenesis by the liver is also promoted by cortisol leading to further catabolism and increase in blood sugar levels.
Haemopoietic	General anaesthesia predisposes to Virchow's triad of venous stasis, abnormal coagulation and intimal damage; Immobility due to pain increases the chance of DVT and PE with fatal consequences [4].
Psychology and cognitive effects	Anxiety and pain are positively correlated [5]. The stressor effects of unrelieved pain have the potential to increase anxiety levels and interfere with activities of daily living, such as diet, exercise, work or leisure activities and to interrupt normal sleep patterns causing varying degrees of insomnia. Pain also results in a distressing cognitive impairment, such as disorientation, mental confusion and a reduced ability to concentrate [6].
Gastrointestinal	The override of the sympathetic system leads to a decrease in gut motility—paralytic ileus—postoperative nausea and vomiting. The GI mediated release of serotonin and its effect on the chemoreceptor trigger zone are also responsible for nausea and vomiting.
Immune system	Increased catabolism with negative nitrogen balance leading to dysfunction of T and B lymphocytes that increases the susceptibility to infection and poor wound healing. There is also the release of Interleukin-1 which stimulates the release of sympathetic mediators.

10.2 Pathophysiology of Acute Postoperative Pain

It is important to understand the basics of the pain pathway and know some of the neurotransmitters to understand the rationale behind the use of pain medications. The pain pathway has four important components: transduction, transmission, perception and modulation.

When pain is inflicted by a surgical incision at the tissue there is a degradation of cells with a release of chemicals [7] like histamine, prostaglandins, H+ ions, cytokines (IL1, TNF), chemokines (e.g. CCL3) and neuropeptides (substance

P) which stimulates the free nerve endings or nociceptors. Activation of the nociceptors leads to the development of action potential at nerve endings in a process called transduction (conversion of chemical to electrical energy). The pain impulse in the form of the action potential is now carried to the brain in a process called transmission. The impulse is carried by medium diameter, relatively fast, lightly myelinated A-delta and thin, slow conducting, unmyelinated C nerve fibres (both are first-order neurons) to a specific area of the grey matter of the spinal cord called substantia gelatinosa (Lamina II & III). (The grey matter in the spinal cord is divided into layers I to X known as Rexed laminas—see Fig. 10.1.)

The first-order neurons end at the lamina II and III and the second-order neurone starts. Most of the second-order neurone crosses over at this level to the opposite side and ascends as lateral spinothalamic tract (Lateral Pathway). Some second-order neurones do not cross, they ascend in the same side as fasciculus gracilis and cuneatus to the nucleuses of midbrain. These fibres (Medial Pathway) are important for fear, aversion and psychopathic components of pain perception and suffering.

Most fibres end in thalamus from where the third-order neurons arise. The third-order neurons go from the thalamus to various places of the brain including the sensory area of the brain so we can perceive (feel) the pain. Third-order neurons from thalamus also go to the areas like periaqueductal gray and locus coeruleus from where descending inhibitory tract begins and goes to the dorsal horn of the spinal cord. This completes the feedback loop of the pain. Some nerve fibres from the spinal cord and also from thalamus go to other areas of the brain like the medulla, brainstem, hypothalamus and amygdala (spinoreticular, spinomesencephalic, spinoparabrachial tracts). These are important to integrate the pain sensation with other responses like arousal, autonomic and emotional responses which leads to the expression of pain sensation and contribute to the suffering of pain.

A few words about the importance of dorsal horn is mandatory at this point.

The dorsal horn is the major site where modulation of pain signals happens.

- There is a complex interplay of the peripheral nervous system (the receptors and nerves) and central nervous system (brain and spinal cord).
- There are a huge number of excitatory neurotransmitters like glutamate, aspartate, calcitonin gene-related peptide which propagate

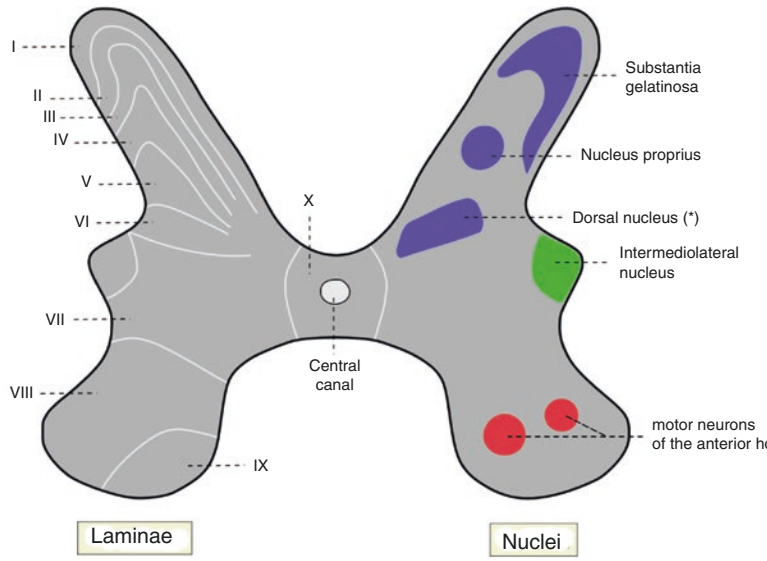


Fig. 10.1 https://en.wikipedia.org/wiki/Rexed_laminae

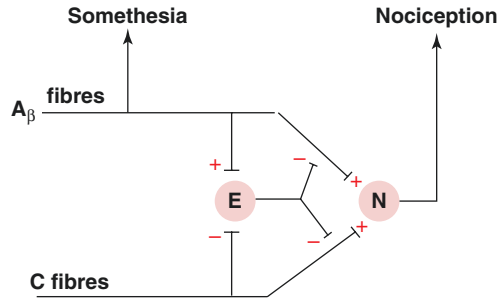


Fig. 10.2 Gate Control Theory of Pain: https://www.anaesthesiauk.com/article.aspx?articleid=100119. *E* Encephalinergic Interneuron

the pain signal and a host of inhibitory neurotransmitter like GABA and glycine which inhibit the pain propagation.

- On this dorsal horn the descending inhibitory fibres from periaqueductal gray and locus coeruleus terminates try to stop the pain (Inhibitory pathway).
- The dorsal horn is also influenced by non-nociceptive peripheral inputs by moderately myelinated, fast A Beta fibre which carries touch sensation. They can occupy the receptors and prevent excitatory neurotransmitters to activate it or can stimulate inhibitory interneurons and block the transmission of pain. This is the basis of the Gate Control Theory of Pain [8].
- The other inhibitory influences at this level are by higher-order brain function (e.g. distraction, cognitive input). These inhibitory mechanisms are activated by the brain to modulate the controlling responses to reduce the excitatory activity of C fibres.
- Thus, analgesia may be achieved by either enhancing inhibition (e.g. opioids, clonidine, antidepressants) or by reducing excitatory transmission (e.g. local anaesthetics, ketamine) (http://fpm.anzca.edu.au/documents/apmse4_2015_final) (Fig. 10.2).

Perception of pain is a complex phenomenon which involved recognizing of the intensity, quality and influence from medial pathway, defining and responding to pain. This brings us to the concept of global pain which is the resultant pain of all the conflicting influences in the spinal cord.

The concept is depicted as follows:

$$\text{Global Pain} = \underset{(\text{Lateral Pathway})}{\text{Pain intensity}} + \underset{(\text{Medial Pathway})}{\text{Pain suffering}} - \underset{(\text{Inhibitory Pathway})}{\text{Pain Suppression}}$$

It is a result of neural activity and is where pain becomes a conscious experience. Perception takes place predominantly in the cortex, but the limbic system and reticular systems are also involved. This becomes more important as the pain becomes chronic. The complex interaction between the various excitatory and inhibitory inputs alters the pain perception in a process called Modulation. A schematic diagram of the various projections is given in Figs. 10.3 and 10.4. Apart from modulation, pain is also influenced by culture, previous pain experience, belief, mood and ability to cope. The individual variation to pain makes it a dynamic experience and pins the importance that there cannot be a fixed plan to manage all patients. The same procedure in the same cohort of patients will elicit a different response. So, the treatment should be individualized and tailored to the requirement of the patient.

This brings us to the next section a careful assessment of the pain.

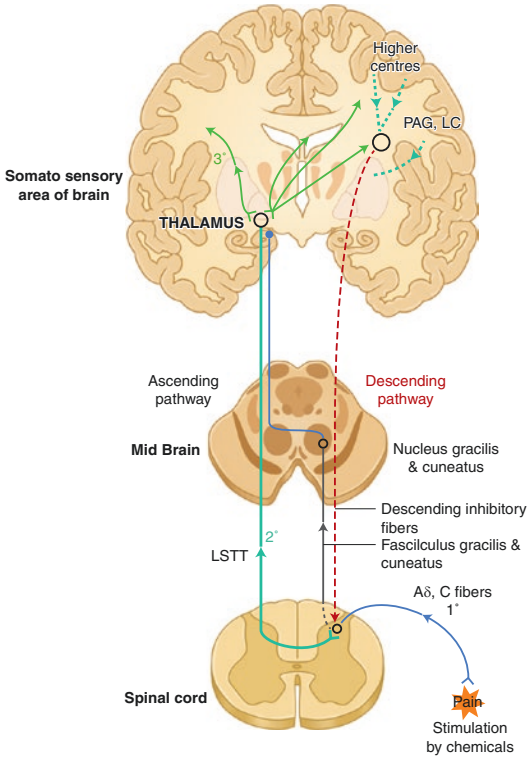


Fig. 10.3 The Afferent and Efferent Pain Pathways

10.3 Assessment and Documentation of Pain

Pain is a subjective phenomenon. So, it is reported by the patient and the assessment aims to find out the severity and quality of pain experienced by patients. When we assess the intensity of the pain we try to assess the Global pain.

Various scales have been used to assess pain but the main criteria to select one which is familiar to all staff, reliable, reproducible and easy to use in the postoperative period. I am going to explain here is an 11 point 0–10 Numeric Pain Rating Scale which is most commonly used in

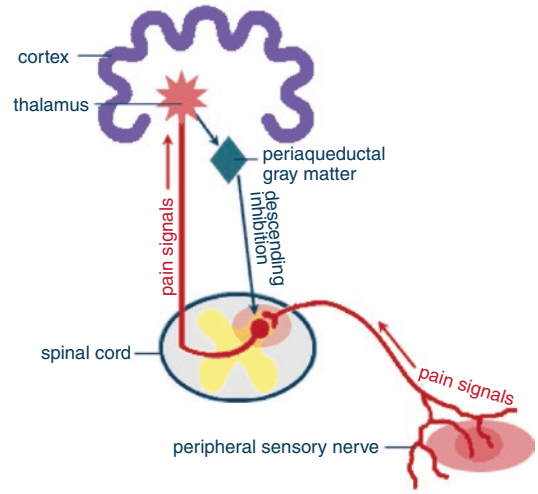
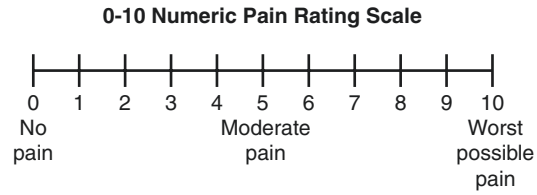
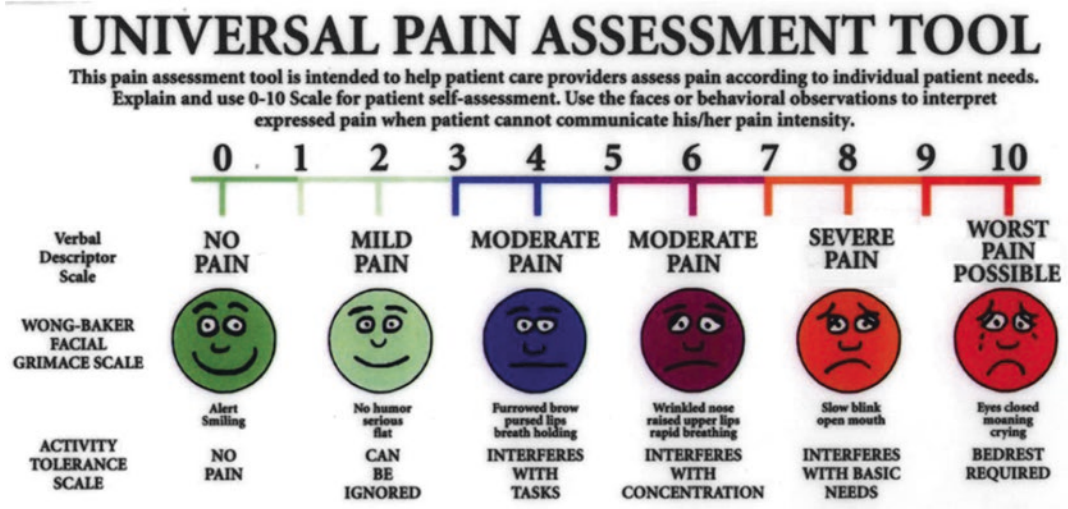


Fig. 10.4 A simple Diagram of the main pain Pathways. https://brainchemist.wordpress.com/2010/11/28/pain-sites-of-origin-pathways-and-neurotransmitters/

our unit. It is a 10 cm line with 0 to 10 written on it. 0 implies there is no pain at all, while a score of 10 means the maximum pain imaginable by the patient. The clinician aims to reduce the pain by 50% or keep it below a score of 3. A simple 4 point scale where no pain (= 0), mild pain (= 1 to 3), moderate pain (= 4 to 6) and severe (= 7 to 10) can also be used in patients who cannot comprehend it intellectually.



For children under 5 years, Wong–Baker FACES Pain Rating Scale is used. Recently a universal pain assessment tool is introduced which incorporates both the aspects.



For postoperative patients, it is important to assess the dynamic pain as well. It is important to use additional medications to manage pain during deep breathing, early mobilization or during procedures like dressing changes.

Along with routine vital signs and pain scores, we need to assess the side effects of medications. It is important to ask patients specific questions to find out whether they are suffering from nausea or itching and/or excessively sedated. The PONV risk score and the outline of management are given below [10, 11].

Risk factors for postoperative nausea and vomiting (PONV).

Patient Factors	Surgical Factors	Anaesthetic Factors
• Female. • History of motion sickness. • History of PONV.	• Gynaecological. • Abdominal. • Ear. • Testicular. • Laparoscopic .	• Inhalational anaesthesia. • Postoperative pain. • History of PONV. • Large doses of opioids.

There are several scales to assess the severity of nausea or sedation, one such is given below: Ask the patient to find out whether he is feeling

- No Nausea = 0.
- Nausea = 1.
- Vomiting = 2.

10.3.1 Management of Nausea and Vomiting

- Exclude hypoxia, hypovolaemia, hypotension, a full stomach.
- Ensure adequate analgesia.
- During the operation:
  - ensure that there are no contraindications to using either dexamethasone 2.5–4 mg iv and/or stemetil (prochlorperazine) 12.5 mg. IM or slow IV.
  - ensure that all suitable patients are prescribed Ondansetron PRN.
- If regular stemetil is ineffective or maximum dose is reached, add ondansetron 4-8 mg IV 8 hourly.
- Regular antiemetics may need to be given for a few days. Tolerance to nausea and vomiting caused by opioid drugs develops after 5–7 days.
- Regularly review the requirement for antiemetic therapy.

Sedation score is important as a trend towards increasing sedation may alert us to the adverse effects of opioids before respiratory depression becomes a problem. Sedation score like Pasero Opioid-induced Sedation Scale (POSS) can be used. But any standardized score which is acceptable and reproducible can be used. A simpler score is given below:

Sedation is scored as follows:

- 0 = None (alert)
- S = Sleeping normally.
- 1 = Mild (occasionally drowsy but easy to rouse)
- 2 = Moderate (frequently drowsy but easy to rouse)
- 3 = Severe (somnolent, difficult to rouse).

When the patient received a central neuraxial block it is mandatory to document the sensory and motor levels of the block. The sensory dermatomal level is often ascertained by use of ice cube in a plastic sheet or gloves. (Finding the cold response but not making the patient wet.)

Motor Block Score is assessed by the following score:

- 0 = No motor block. Free movement of legs and feet
- 1 = Unable to bend at the hip, able to bend knee, free movement of feet
- 2 = Unable to bend the knee, free movement of feet
- 3 = Unable to move legs or feet.

10.4 Review of Drugs

We will quickly review the common pain medications before we come up with management strategies. There are only 4 classes of analgesics: Paracetamol, Nonsteroidal Anti-inflammatory Drugs (NSAIDs), Opioid Medications and Anti neuropathic medications.

Paracetamol:

- Paracetamol, a centrally acting drug though the exact mechanism is not clear. It has a very good safety profile and should always be used regularly as it reduces the need for opioid and other analgesics [14].
- The maximum dose in a healthy adult weighing more than 50 kgs is 4 grams a day in divided doses. Doses should be reduced in low body weight and decompensated liver failure.
- Paracetamol can be given PO/PR/IV.
- It is difficult to estimate for how long paracetamol should be continued regularly following surgery as it depends on many variable factors including the patient's response to surgery. Consider converting from regular to 'as required' administration about 1–2 weeks after moderate surgery.

10.4.1 NSAIDs

In our unit, we extensively use NSAIDs in addition to regular paracetamol as baseline analgesia where not contraindicated. It is a very good analgesic used for short duration of action like 5–7 days. NSAIDs work by inhibition of prostaglandin synthesis at the periphery and can be broadly classified as non-selective cyclooxygenase inhibitor or relative selective cyclooxygenases type 2 inhibitors like parecoxib (iv formulation) or Celecoxib/meloxicam (oral formulation). The other group selective cyclooxygenase inhibitor like rofecoxib is withdrawn from the market due to adverse cardiovascular side effect.

Oral ibuprofen should be used where possible as it has the lowest gastrointestinal risk and relatively low cardiovascular side effects. If oral fluids are not tolerated, rectal or intravenous diclofenac may be used for short periods like 3 to 5 days. For all patients, the duration of NSAID use should be regularly reviewed as the GI risk increases significantly after 7–10 days. There are many contraindications to their use:

1. Renal dysfunction: NSAIDs may cause a deterioration in renal function and should be avoided in the presence of renal impairment (GFR < 75 mL/min/1.73 m^2).
2. Hypovolaemia and dehydration: NSAIDs should be prescribed with caution in hypovolaemic and dehydrated patients as they cause a reduction in renal blood flow and may precipitate acute renal failure.
3. Unstable asthma or asthmatic patients are known to be worsened by NSAIDs (about 10% of all asthmatic).
4. GI Risk: NSAIDs should be avoided in patients with active peptic ulceration. Gastric protective therapy (e.g., omeprazole 40 mg od) is advisable in patients at high risk of peptic ulceration and/or gastrointestinal bleeding. The r*ecognized additive GI risk factors are*:

(a) History of gastric or duodenal ulceration or gastrointestinal bleeding. (b) 65 yrs. of age (risk is highest above 75 yrs. but increases above 65 yrs). (c) Comorbidities like cardiovascular disease, renal or hepatic impairment, or diabetes. (d) Patients taking concurrent medication likely to cause GI irritation, e.g. corticosteroids, anticoagulants.
5. Coagulopathy.
6. Old age.
7. Allergy to NSAIDs.
8. Established cardiovascular disease: diclofenac 150 mg/day appears to be associated with a similar excess risk of thrombotic events (stroke and myocardial infarction) as coxibs, whereas low dose ibuprofen (<1200 mg/day) and naproxen 1000 mg/day appear to be associated with a lower risk.
9. Drug Interaction is very frequent with NSAIDs. Caution should always be exercised in patients taking drugs that interact, e.g. Lithium, methotrexate and warfarin.

OPIOID ANALGESICS (e.g.: Morphine, Fentanyl, Tramadol, Tapentadol, Buprenorphine).

These drugs are still the mainstay of acute pain relief and morphine is the opioid of choice as it is cheap, effective and side effects are easily recognizable and treatable. All opioids work by attaching to specific opioid receptors traditionally classified as mu, kappa and delta receptors.

Morphine can be given by many routes and is equally effective whatever the route, provided adequate doses are used. If the patient is nil by mouth, morphine may be given by either IM/SC injection or by IV-PCA (intravenous patient-controlled analgesia). If IV access is unavailable yet PCA remains the most appropriate method, subcutaneous PCA is equally effective [15]. When the patient is tolerating oral fluids the prescription may be changed to the oral route. A rule of thumb is 1 mg of IV morphine = 5 mg of IM/SC =10 mg of PO morphine. The figure below adapted from British National Formulary explains it well [16].

The major side effects associated with opioid use are:

1. Respiratory depression: usually of gradual onset and apparent as increasing sedation followed by a fall in respiratory rate.
2. Nausea and vomiting: should be treated without reservation.
3. Urinary retention: may necessitate bladder catheterization.
4. Constipation: may warrant regular prescription of a stimulant laxative, e.g. senna given at night.
5. Pruritus is rare but troublesome. Consider antihistamines and SC/IM naloxone 200cmg single dose. If severe with morphine convert to fentanyl IV (or patch) or buprenorphine patch. While using a patch either fentanyl or buprenorphine there should be an overlap period of 6 to 12 h, as they do not work instantly.
6. Long-term opioids (more than 3 weeks) are associated with other side effects like tolerance, dependence, addiction, suppression of immunity, suppression of pituitary adrenal axis, repeated falls and opioid induced hyperalgesia—phenomenon where increasing opioids increases the pain. So many countries have made it mandatory to reduce the use of opioids to a maximum limit for chronic patients. It is unlikely to happen in patients post operatively but many patients continue with the prescription if not discontinued at an appropriate time (https://fpm.ac.uk/opioids-aware).

All opioids should be prescribed with caution with a clear plan to deescalate and in reduced doses in presence to certain comorbidities [17].

1. Renal dysfunction.
2. Hepatic dysfunction.
3. Altered level of consciousness, e.g. Neurosurgery with a chance of raised intracranial pressure.
4. Respiratory dysfunction, e.g. chronic bronchitis leads to CO2 retention.
5. Obesity.
6. Sleep apnoea syndromes.
7. Elderly.
8. With a past history of addiction.

Oral opioids are the ‘step-down’ analgesia of choice following discontinuation of parenteral opioids. Sustained release oral morphine or codeine or tramadol can be prescribed as regular analgesics backed up by short-acting agents for

breakthrough pain depending on the intensity of pain and experience of the unit. The patients should be individualized and treated. Addition to opioids following postoperative short-term use (days to weeks) is not a concern. Problems of long-term use require sustained exposure and involve personal and social circumstances.

Tramadol is not a typical opioid. Apart from being a mu receptor agonist, it prevents the norepinephrine and serotonin uptake in the descending inhibitory fibres potentiating its effect [18]. It is used for moderate to severe pain, but not as effective in severe pain as other strong opioids. Side effects are similar to morphine except it is associated with less respiratory depression, less constipation and less addiction potential. Hallucinations and confusion are more common with its use and mostly happens with the first few doses. Concurrent use of antipsychotic and antidepressant medications especially those which prevent the reuptake of serotonin (e.g. SSRI) can cause serotonin accumulation and serotonergic syndrome in vulnerable patients.

Tapentadol is a new class of drug introduced in 2009. It can be given both orally and parenterally works via two mechanisms of action—mu-opioid receptor agonism and norepinephrine reuptake inhibition. The immediate-release formulation is approved in the US and European Union for moderate to severe pain, but it is currently unavailable in India [19]. The sustained release version which is available in India can be used in selected cases as a background analgesic where morphine is not tolerated. It has significantly less side effect profile in terms of nausea, vomiting, constipation and respiratory depression compared with stronger opioids [20–22].

Transdermal Fentanyl patches are used in some centres for the management of acute pain. It is not recommended as it is costly, not a superior method to others available, has a long latency period and cannot be titrated. It has no license to be used in acute pain.

Converting between transdermal fentanyl and fentanyl by other routes, or between transdermal fentanyl and other opioids is complex and will need expert input.

- A '25 microgram/hr' patch is approximately equivalent to 90–135 mg morphine orally in 24 h.
- If fentanyl patches are being used preoperatively, it may be appropriate to continue them perioperatively and use additional opioids (morphine, fentanyl) as required.
- The patches should be changed every 3 days.

For similar reasons, transdermal buprenorphine patches are also not recommended. But in chronic pain management, it is one of the opioids of choice being a partial agonist of mu receptors and good safety profile in the elderly population [23].

Pethidine has a short duration of action so it has a disadvantage in continuing pain. Repeated doses of pethidine increase the risk of neurological toxicity caused by the pethidine metabolite norpethidine. The use of pethidine is, therefore, not recommended.

Equivalent doses of opioid analgesics.

Drug Name	Dosage	Morphine Equivalent in 24 h
Codeine	60 mg	6 mg
Tramadol	100 mg	10 mg
Fentanyl patch	12mcg/hr	45 mg
	25mcg/hr	90 mg
	50mcg/hr	180 mg
	75mcg/hr	270 mg
Buprenorphine patch	5mcg/hr	12 mg
	10mcg/hr	24 mg
	20mcg/hr	48 mg

10.5 Local Anaesthetics

Local anaesthetics are drugs that cause a reversible loss of nerve transmission by blocking Na + channels. Local anaesthetics are formulated as hydrochloride salt so that they are water-soluble. It is used as a part of nerve blocks (e.g. Femoral nerve block), regional block (e.g. transversus abdominis plane block) or central neuraxial blocks (e.g. epidural blocks). Local Anaesthetics without preservatives and additives (apart from glucose at 80 mg/ml used in 'heavy' bupivacaine) are suitable for subarachnoid administration, as the preservatives carry the risk of producing arachnoiditis.

The commonly used local anaesthetic drugs are Lidocaine, bupivacaine, levobupivacaine and ropivacaine. The potency of the local anaesthetic is

mostly dependent on lipid solubility, but also vasodilator properties and tissue distribution of the drug. Local anaesthetics duration of action is dependent on their affinity and extent of protein binding. The drugs like prilocaine with less protein binding have a short duration of action, and, conversely, drugs like bupivacaine with more extensive protein binding have a longer duration of action.

The intrinsic vasodilator property of individual local anaesthetics influences potency and duration of action. At low concentration there is vasodilatation and the gradient is as follows: pril ocaine>lidocaine>bupivacaine>ropivacaine: and vasoconstriction at higher concentrations. Cocaineis the only local anaesthetics (rarely used now as local anaesthetics) is a vasoconstrictor. However, the total dose and concentration of administered local anaesthetic will also have a significant effect on a given clinical situation.

Local anaesthetics are generally ineffective when used to anaesthetize infected tissue due to the acidic pH of the surrounding tissues. The acidic environment polarize drug and changes it into ionic form so reducing the unionized fraction of drug available to diffuse into and block the nerve. There may also be increased local vascularity, which increases the removal of drug from the site. Intraoperative wound infiltration or regional nerve blocks or local anaesthetic infusions are preferred whenever possible to reduce the use of systemic analgesics.

Local anaesthetics have potential side effects when the recommended dose is exceeded. The management of local anaesthetic toxicity is described in the epidural section of the chapter.

10.6 Antineuropathics

These medications are also known as co-analgesics [5] and can be prescribed for nerve-related (neuropathic) pain or as a component of the multimodal approach of analgesia to reduce opioid consumption. The three types of medications most commonly prescribed for nerve pain include:

- Antidepressants or tricyclic antidepressants (TCA's), such as Amitriptyline and Nortriptyline. The newer selective serotonin reuptake inhibitors (SSRI) antidepressant medications are not considered as effective for this condition as tricyclic antidepressants. These work by preventing active reuptake of serotonin or nor adrenaline in the descending inhibitory fibres. The usual side effects are drowsiness, increase in intraocular pressure, arrhythmias, dryness of mouth and constipation.
- Anticonvulsants (also called neuroleptic medications) such as gabapentin and pregabalin. Pregabalin, a newly developed gabapentinoid is used in the perioperative period to manage pain due to its rapid onset of action, but we have to be careful about its addiction potential drowsiness which can impair recovery and recent studies suggest they are not useful in acute pain. The gabapentinoids are calcium channel blockers.
- The other group of antineuropathics which can be helpful in acute pain includes medications like ketamine, an intravenous anaesthetic and NMDA receptor agonist in low dose (0.25 mg/kg), or Clonidine, an alpha2 receptor agonist which also works on the spinal pathway or a 50% mixture of nitrous oxide and oxygen called entonox which stimulates NMDA receptors and higher centres in brain to produce analgesia.
- The list of antineuropathics can be extensive like carbamazepine, valproate, capsaicin bit these are rarely used in acute pain setting.
- So, we find we can influence the various channels which are expressed on the nerve fibres—sodium channel by local anaesthetics, calcium channels by gabapentinoids, or enhance effect by preventing active reuptake like amitriptyline.

10.7 Management of Acute Pain

The management of pain is multimodal and multidisciplinary. The most commonly prescribed medications are a combination of round the clock baseline medication and a medication to manage breakthrough pain. The breakthrough pain can be incidental like movement, or end of dose failure like just before the next dose.

Some concepts:

1. WHO Pain Ladder.

In 1986 the World Health Organization (WHO) presented the analgesic ladder as a framework that physicians could use when developing treatment plans for cancer pain. This therapeutic guideline paved the way for considerable improvements in the management of cancer pain [24, 25]. The WHO pain ladder has been modified and adapted in various forms even in the management of acute pain. Though the WHO recommendations are not evidence-based it has stood the test of time and most widely used pain tool. An outline for the use of systemic analgesics is given below:

Initial Analgesia is the responsibility of the anaesthetist. It is difficult to give an outline of what should be the ideal prescription but it depends on the patient, surgery, circumstances and familiarity of the unit.

(a) Minor Surgery:—Regular Paracetamol (PO/PR/IV) +/− Regular Ibuprofen PO for a short period like 3 to 7 days (or diclofenac PR/IV) +/− As Required Codeine/Tramadol up to 4 times a day.
(b) Intermediate Surgery:—Regular Paracetamol (PO/PR/IV) +/− Regular Ibuprofen PO for a short period like 3 to 7 days (or diclofenac PR/IV) +/− As Required Morphine (IM/PO) or Morphine IV-PCA.
(c) Major Surgery: —Regular Paracetamol (PO/PR/IV) +/− Regular Ibuprofen PO for a short period like 3 to 7 days (or diclofenac PR/IV) +/− As Required Morphine (IM/PO) or Morphine IV-PCA or Epidural or Paravertebral Infusions.

2. Step-down Analgesia.

After commencing the patients on initial analgesic, as they improve the analgesia should be optimized so the patients can be discharged home with a contingency plan. Step-down analgesia involves converting from the parenteral routes (IV, IM, SC, epidural) to the enteral routes (PO, PR). The norm is to start on regular oral paracetamol and NSAIDs (if not contraindicated) as soon the patient starts oral fluid. If the patient is on patient-controlled analgesia, oral opioids can be started when the daily consumption of morphine is less than 40 mg/day, keeping a close eye on the patient regarding his function, mobility, nausea, vomiting, drowsiness and gut mobility. Stepping down from epidural analgesia can take more time and patience. While PCAs are withdrawn in most cases by third postoperative day, (when the daily morphine requirement is less than 40 mg in 24 h) the epidural often runs till day five. The first step after starting the oral medication is to stop the epidural infusion temporarily for two to 4 hours and assess the patient in terms of pain and movement. A rough guideline can be as follows:

If oral intake of fluid has commenced and basic analgesics started, then assess the patient:

- If pain score = mild: use oral codeine 30 mg 4–6 hourly or Oral Tramadol 50 mg 6 hourly if the patient can tolerate, PRN.
- If pain score = moderate: use regular oral codeine 30 mg 4–6 hourly or Oral Tramadol 50 mg 6 hourly if the patient can tolerate and oral morphine 10–20 mg 2 hourly PRN for breakthrough pain.
- If pain score = severe: use regular oral sustained release morphine 30 mg 12 hourly or Oral Tramadol up to 100 mg 6 hourly if the patient can tolerate and oral morphine10–20 mg 2 hourly PRN for breakthrough pain.

3. Central Neuraxial Blocks like: spinal, epidural and paravertebral.

Neuraxial anaesthesia is the term for central blocks involving the spinal, epidural and caudal spaces [26]. It is a popular method of providing postoperative analgesia. It is safe, effective and frequently used technique especially in conjunction with enhanced recovery. Usually, a low concentration mixture of bupivacaine (0.1%) and fentanyl 2mcg/ml may be infused into the epidural space through an indwelling catheter. This provides excellent pain relief by interfering with the flow of 'pain signals' along nerves entering the spinal cord.

Plain bupivacaine may be infused into the paravertebral space through a paravertebral catheter (paravertebral analgesia) or through a catheter sited adjacent to a peripheral nerve to provide peripheral neural analgesia. The absence of opioid in this solution allows for additional systemic opioids to be used if required. The general term used for these techniques is 'loco-regional analgesia'.

10.7.1 Managing a Loco-regional Analgesia Patient in the Ward

- The anaesthetist is responsible for establishing the analgesic technique and also giving clear instruction about how to run the loco-regional anaesthesia. (Epidural, Paravertebral or Peripheral nerve block).
- Proper informed consent should be obtained from the patient before any loco-regional.
- The Patient must have an IV cannula in situ.
- In some hospitals for paravertebral and peripheral neural infusion bupivacaine, 0.125% is used from locked prefilled bags or syringes via infusion pumps.
- If a prefilled bag is used lines must be changed every 72 hours by the Acute Pain Team or by senior nursing staff. For epidural infusions, it can be used for up to 5 days when a 0.22-micron in-line filter is used.
- The rate of the infusions varies widely and normally ranges from 3 to 10 ml/hr. Boluses are only given if approved by senior registrars or consultant. Following a bolus patient should be observed for the effects and vitals should be monitored.
- Careful labelling of the epidural/paravertebral catheter and infusion line is essential. This is to distinguish them from intravenous lines and minimize the risk of inadvertent wrong route administration. In the UK only yellow dedicated lines with special adaptors can be used for loco-regional infusions. These must be specifically labelled as 'epidural' or 'paravertebral' or relevant to the peripheral nerve infusion, e.g. 'femoral nerve infusion'.

Documentation should involve: the timing of the procedure, any immediate complications while placing the catheter, along with the vitals, pain score, sedation score, nausea score, motor score and level of sensory analgesia. These should be recorded hourly for the first 24 hours after starting the infusion. Thereafter they should be recorded 4 hourly, or more often if either pain is poorly controlled or complications arise. While removing an epidural catheter, it is mandatory to document [27, 28])

1. The date and time of removal.
2. Condition of the catheter tip.
3. Bleeding, fluid drainage or Haematoma of the catheter site.
4. Patient tolerance.
5. Any complications and interventions.

If an epidural catheter remains in place the front of the drug chart must state 'epidural catheter in place' or have an epidural line sticker on it to alert staff to its presence. This is to minimize the risk of starting someone on oral anticoagulants before the catheter has been removed.

Managing the complications: The combination of low dose opioid and low dose local anaesthetic is given by the epidural route is safe and can provide excellent pain relief specifically targeted at the site of pain. In some patients with extensive incisions or operated on 2 different sites, for e.g., after oesophagectomy with an upper midline incision and neck incision an epidural infusion with local anaesthetic alone can be used for the upper midline incision along with a PCA morphine to manage the pain from the neck wound.

Nursing staff caring for patients with epidural/paravertebral infusions must be aware of the side effects of these procedures and their management:

1. Hypotension: Defined as systolic blood pressure is below 100 mm Hg in a normotensive adult. The blood pressure is a guide only; all patients should be assessed in terms of their preop blood pressure, current fluid status and end-organ perfusions like time and place orientation, urine output, capillary refill, etc. Management of the condition should always follow the 'SHIT' approach as outlined earlier. Also, it is prudent to use a vasoconstrictor like phenylephrine (50 to 100 mcg bolus) or ephedrine 3 to 6 mg.
2. Excessive sedation: defined as a sedation score of 2 or 3 may require intervention with naloxone apart from standard management. Naloxone (a mu receptor antagonist) is available as 1 ml ampoule containing 400 mcg to be diluted with 3 ml of sodium chloride 0.9%, making a total volume of 4 ml so each ml contains 100 mcg of naloxone. 1 ml of the above solution is given slowly through IV and repeated every 1 min until the sedation score

is 0 or 1 titrating the effect. Two important points must be stressed here. Using naloxone is an emergency and should not be delayed for authorization and the other point is naloxone is relatively short-acting. So there is a chance that the patient can be sedated after a while and should be observed closely.

3. Respiratory depression: defined as a respiratory rate of fewer than 8 breaths per minute. The management basics are again Airway, Breathing, Circulation and Naloxone administration if required.
4. Urinary retention: defined as the urinary volume of more than 500 ml with no urge to pass urine [29]. It may require a bladder catheterization. An additional dose of antibiotic covering Gram-negative organism should be used before catheterization if not contraindicated.
5. Itching: Epidural opioids may cause itching of sufficient intensity to be distressing. This is more likely to occur when the higher concentration of fentanyl is used and reversed by naloxone 25 mcg given SC or IM. If itching continues to be a problem, the epidural fentanyl/bupivacaine mixture may be changed to plain bupivacaine. In some cases, chlorpheniramine maleate or oral cetirizine can be given [30, 31].
6. Motor Block: defined a score of 2 or 3 in the absence of a recent epidural top-up with a local anaesthetic. It should be investigated as a matter of urgency. A detailed clinical examination is mandatory including signs of cauda equina syndrome. Epidural haematoma should be excluded and an urgent MRI is warranted. Early detection of epidural haematoma, within 6 h of onset, needs to be treated with emergency decompression surgery and is limb saving procedure.
7. Local anaesthetic toxicity: occurs if the epidural catheter is misplaced in an epidural vein resulting in accidental intravenous injection, or if the maximum safe dose of local anaesthetic is exceeded. Symptoms may occur sometime after the initial injection and include:
   - Tingling around the mouth—one of the earliest symptom.
   - Numb tongue.
   - Dizziness.
   - Light-headedness.
   - Twitching.
   - In severe toxicity, there will be a sudden loss of consciousness with or without tonic-clonic convulsions.
   - Cardiovascular collapse: sinus bradycardia, conduction blocks, asystole and ventricular tachyarrhythmias may occur.

It is a life-threatening emergency where we follow the mnemonic 'SHIT'

- S = Stop injection of local anaesthetic.
- H = Call for HELP.
- I = Intervene:

1. Maintain a clear AIRWAY.
2. initiate mouth-to-mouth, mouth-to-mask or bag and mask ventilation with 100% oxygen. Intubate if necessary.
3. Initiate CPR if necessary, following the current guidelines.
4. Control seizures: give a benzodiazepine or thiopental in small incremental doses.
5. Manage arrhythmias following the guidelines, recognizing that they may be very refractory to treatment and prolonged resuscitation may be necessary;

Consider treatment with lipid emulsion: Intralipid 20%0.1.5 ml/kg over 1 minute. Repeat the bolus dose twice at 5 min intervals if an adequate circulation has not been established.

- Continue CPR.
- Start an intravenous infusion of Intralipid 20% at 0.25 ml/kg/min.
- After another 5 min, increase the rate to 0.5 ml/kg/min if an adequate circulation has not been restored.
- Consider the use of the cardiopulmonary bypass.

T = Trace and Track to find out why the incident happened and formulate guidelines to avoid it.

10.7.2 Removal of Epidural Catheters

Most patients after major laparotomy or limb surgery receive anticoagulant to prevent venous thromboembolism right from day 0 or day 1 of surgery. The timing removal of the epidural catheter is important so the chance of occurrence of spinal haematoma is rare. Each patient should be individualized and the optimum timing is ascertained. If in doubt, discuss with an anaesthetic consultant and a consultant haematologist. In difficult cases like patients with suspected pulmonary embolism or acute coronary syndrome, further tests like platelet function assay and thromboelastography may be indicated [32, 33].

Timing of epidural catheter insertion/removal, or insertion of spinal needle, in patients given anti-thrombotic therapy

	Time to insertion of epidural catheter or spinal block	Timing of epidural catheter removal	Time to re-administering anticoagulant
Explanation: / Drug:	*Minimum* time required after last dose of anti-thrombotic therapy	*Minimum* time required after last dose of anti-thrombotic therapy	*Minimum* time required post insertion/removal before next dose of anti-thrombotic therapy
Unfractionated Heparin *Prophylaxis*	8-12 hours	8-12 hours	2 hours (delay by 24hours post insertion if traumatic insertion)
Unfractionated Heparin infusion *Treatment*	4 hours	4 hours	2 hours (delay by 24hours post insertion if traumatic insertion)
LMWH *Prophylaxis* (enoxaparin, tinzaparin or dalteparin)	12 hours	12 hours	2 hours (delay by 24hours post insertion if traumatic insertion)
LMWH *Treatment* (enoxaparin, tinzaparin or dalteparin)	24 hours	24 hours	2 hours (delay by 24hours post insertion if traumatic insertion)
Warfarin	INR<1.5	INR <1.5. Also, hold dosing for duration of epidural infusion and until 2 hours after catheter removed	Hold dosing for duration of epidural infusion and until 2 hours after catheter removed
Fondaparinux (Arixtra)	Not recommended. Use alternative anti-thrombotic agent. Discuss with Haematology		
Lepirudin infusion *Treatment*	4 hours, unless renal impairment then discuss with Haematology	4 hours, unless renal impairment then discuss with Haematology	2 hours (delay by 24hours post insertion if traumatic insertion)
Dabigatran (Pradaxa)	Contraindicated. Use alternative anti-thrombotic agent.	Contraindicated. Use alternative anti-thrombotic agent.	2 hours (delay by 24hours post insertion if traumatic insertion)
Rivaroxaban (Xarelto)	6 hours (though first dose usually post-op anyway)	18 hours	6 hours
Aspirin/NSAID Where no other anti-thrombotic agents used	No increased risk	No increased risk	2 hours (delay by 24hours post insertion if traumatic insertion)
In combination with other anti-thrombotic therapy (LMWH, clopidogrel etc)	Ideally omit for 5-7 days. As minimum, ensure LMWH timing is correct to minimise additional risk	Ideally do not restart until epidural catheter removed. As minimum, ensure LMWH timing is correct to minimise additional risk	Ideally do not restart until epidural catheter removed. If antiplatelet therapy critical, wait 2 hours after insertion (delay by 24hours post insertion if traumatic insertion)
Clopidogrel (Plavix)	7 days	7 days	Hold dosing for duration of epidural infusion and until 2 hours after catheter removed
Ticlopidine	14 days	14 days	Hold dosing for duration of epidural infusion and until 2 hours after catheter removed

4. Patient-Controlled Analgesia (PCA).

PCA is an effective and well-established method of managing postoperative pain. An IV-PCA puts the patient in charge of his/her pain control. Every time the patient presses the button a predefined small dose of opioid is injected in the bloodstream and keeps the patient pain free. The machine has also inbuilt mechanism to prevent the overdose. The advantages are:

- Gives the patient autonomy over their pain control.
- Minimizes delays in analgesia administration.
- Reduces nursing time involved in analgesia administration.
- Minimizes the side effects of the opioid.
- Improves staff and patient satisfaction.
- Minimizes the chance of overdose.

PCA consists of a syringe pump containing the desired opioid solution which is designed to deliver on-demand a pre-set amount of opioid (Bolus Dose) reliably and accurately. It is attached to the patient by a giving set with a non-return valve. The pump is activated by the patient pressing the attached dedicated handset. Each successful activation is indicated by a sound and a glowing light (depends on the make and model of the pump). The patient is told to press the handset when he/she experiences pain but the pump is activated only after a certain time set by the physician called Lock Out Time. The reasons for it are two-fold: firstly it allows time for the injected opioid to work, and secondly, it prevents the patient from inadvertently administering an overdose. The unsuccessful attempts are recorded as well as the effective boluses. This gives the clinician an indication of how well the pain is controlled and whether to increase the bolus dose. The pump has a battery facility to maintain drug administration if the pump has to be disconnected from a mains power.

There are provisions in some pump to give a background infusion or set in a 4 hourly limit for the opioid. Though age is not a contraindication to using an IV-PCA pump management of pain using PCA can be very challenging in patients with physical or mental disability. Patients need to be able to understand how to use IV-PCA effectively. The anaesthetist should explain to the patient before surgery how IV-PCA is used and is reinforced by the ward staff.

All IV-PCA pumps must be attached to the patient using a dedicated IV line or, if not possible, via a line incorporating a non-return valve. PCA can also be used via an s/c cannula if IV access is difficult [27]. The standard solution used is morphine 1 mg/ml. in a 50 ml syringe. A standard setup is 1 mg bolus dose delivered over 1 min with a lockout time of 5mins. Besides, a 40 mg 4 hourly maximum dose is incorporated in the setup.

In cases where morphine is not tolerated (for example allergic reaction) or unsuitable (for example in renal failure patients) fentanyl in a solution of 10 micrograms/ml may be used): fentanyl 500 micrograms made up to a volume of 50 ml with sodium chloride 0.9%. NSAIDs and/or paracetamol is given concurrently to decrease opioid requirements and provide good background analgesia.

10.8 Planning a Strategy for Pain Relief

The aim is to individualize patients and develop rational means to optimize drug therapy based on the patient's genotype to ensure maximum efficacy with minimum side effects. But due to limited information in this field and great inter-individual variability and magnitude of factors influencing pain perception and modulation it is not possible in the present day. The choice of analgesic depends on the patient, the type of surgery, the experience of the anaesthetist and also the infrastructure of the unit. The ability to procure opioids and other control drugs, training and expertise of the staff, the equipment and back up personnel available all are important factors.

The management starts in the preoperative period. It is important to identify the high-risk group of patients with preoperative pain, psychological vulnerability (catastrophizing), anxiety or having a history of drug misuse or on worker compensation. These patients should be preoper-

atively counselled by the anaesthetist and a detailed plan of postoperative care should be made keeping in mind the patient's wishes and requirements. The plan must be documented and made available on the day of surgery.

Patients for operations with a high incidence of nerve damage (e.g. thoracotomy) or with persistent pain or have a fast track recovery protocol should have a preoperative plan of putting a regional or neuraxial block. Proper explanation of these procedures with the risks involved must be informed at this stage. Preoperative pregabalin should be reserved for these patients [34].

Intraoperative pain management of the patient is a part of the balanced anaesthetic. Special care should be given to surgeries lasting more than 1 h [35], involving multiple dermatomes, young adults, intraoperative radiation or chemotherapy (HIPEC) or the high-risk patient group.

All plans should have a regular set of medications and an as required backup section. The regular medications must include paracetamol, NSAIDs where applicable and a sustained release opioid or epidural or PCA. The backup sections should include a quick and short-acting opioid or non-opioid which suits the patient's situation the most. The backup section will also contain an emetic and naloxone to prevent complications.

The concept of pre-emptive analgesia is now replaced by preventive analgesia which involves multiple interventions. Multiple agents have been tried to establish preventive analgesia including opioids, ketamine, dexmedetomidine, local anaesthetics and others. Epidural analgesia started before surgery has shown to have favourable outcomes in may trials [36] and probably the technique of choice in certain operations.

10.9 Some Special Problems

10.9.1 Analgesia Following Amputation

Patients with ischemic lower limbs often suffer severe, intractable and opioid insensitive pain and should be identified preoperatively.

1. The first method of choice:

   Where the placement of an epidural catheter is possible:
   - Insert an epidural catheter in the anaesthetic room preoperatively.
   - Provide *intraoperative* epidural anaesthesia using bupivacaine or levobupivacaine.
   - Maintain postoperative analgesia with an infusion of 'standard' epidural solution (bupivacaine 0.1% with fentanyl 2 micrograms/ml) for 3 days.
   - If the patient has pain preoperatively which is poorly controlled with opioids, the epidural catheter can be sited earlier, usually 1–2 days before surgery.
   - Epidural analgesia offers many advantages for these patients and should be considered for humanitarian reasons and to assist postoperative rehabilitation.
   - It is well established that epidural does not prevent or reduce stump pain or phantom limb pain[37].
2. Second method of choice.

   Where the perioperative placement of an epidural catheter is not possible:
   - Provide *intraoperative* analgesia with a peripheral nerve block (sciatic or posterior tibial) with bupivacaine or levobupivacaine [38, 39].
   - Maintain postoperative analgesia with a continuous peripheral nerve block for 3 days, using an infusion of bupivacaine 0.125%.
   - If a *continuous* peripheral nerve block is not possible postoperatively, an IV-PCA should be prescribed for postoperative analgesia. If the patient is not suitable for IV-PCA, sufficient alternative analgesia must be prescribed.
3. Third method of choice.
   - If neither an epidural nor continuous peripheral nerve block is possible, a spinal (subarachnoid) block may be used (unless contraindicated).
   - An IV-PCA should be prescribed for postoperative analgesia. If the patient is not

suitable for IV-PCA, sufficient alternative analgesia must be prescribed.
- For all cases prescribe:
- Paracetamol 1 g QDS and NSAIDs, if not contraindicated, should be prescribed as regular medications.
- Patient should also be prescribed a regular antineuropathic medication.

The treating team should have a low threshold to involve psychologist and physiotherapist early in the care pathway.

10.9.2 Analgesia for a Patient Dependent on a High Dose of Opioid

These are the patients who are on a prescribed dose of opioids. These opioid users are suffering from cancer pain, chronic non-cancer pain or patients on opioid rehabilitation or maintenance program.

The problems with these patients are [40]:

1. They are tolerant to opioids.
2. Often they under treat themselves in fear of becoming an addict.
3. They have physical dependence so will develop withdrawal symptoms when the dose is reduced or missed.
4. Some of them can exhibit drug-seeking behaviour.

The goal of managing these patients is to provide the baseline opioid requirement (even by converting to equivalent dose if not taking orally) to prevent withdrawal and treat the acute pain with short-acting opioids and adjuvants like NSAIDs and nerve blocks.

10.9.3 Analgesia for a Patient with Opioid Addiction

Before we understand the principles of managing these patients we must be familiar with certain terms:

Tolerance: Tolerance is the decreased sensitivity of patients to opioids following prolonged use. This results in less effect from the same dose and there is a need for progressively larger doses to achieve the same effect.

Physical Dependence: Physical dependence is the physiological adaptation to a drug characterized by the emergence of a 'withdrawal' syndrome if either the drug is stopped abruptly, the dose is reduced or the drug is antagonized. Physical dependence should be presumed to have occurred if repeated doses of opioids are given for 10–14 days or more.

Psychological Dependence: Psychological addiction is a pattern of substance use characterized by

- Compulsive use of a substance to experience its psychological effects or to avoid the effects of its absence (withdrawal).
- Aberrant substance-taking behaviours.
- Continued use of opioids despite the risk of physical, psychological or social harm to the user [41].

Managing these patients is often challenging requiring the need for deep involvement of carers/family and psychologists.

Problems with these patients:

1. An unknown quantity of the drug.
2. Often there is a mixture of different drugs.
3. Other factors like peer and family pressure, personality disorders, genetic predisposition, mental, physical and socio-economic context should be addressed.
4. Long-term opioid users tend to report higher pain scores, making pain scores less useful in assessing opioid requirements in these patients. High pain scores alone should not invariably prompt an increase in opioid dosage. An objective assessment of function should help to assess analgesic requirements, e.g. ability to cough, ability to ambulate.
5. Inadequate analgesia is more likely to cause anxiety, repeated demands for analgesia and reinstatement of drug-seeking behaviours.
6. Prevention of withdrawal symptoms.

10.9.4 Principles of Managing Addicted Patients in Acute Pain Include

- To provide pain relief by identifying the cause of the acute pain and treat with simple analgesics and local nerve blocks wherever possible [40].
- As far as possible, try to establish a patient's current baseline opioids requirement.
- Avoid buprenorphine, benzodiazepines and methadone for acute pain.
- To prevent and/or manage drug withdrawal syndrome to enable acute treatment.
- Start on antineuropathics like Pregabalin before the operation and continue throughout including the postoperative period up to 7 days and up to 14 days in some units.
- Use PCA Morphine is strongly recommended for most of the major procedures. In some patients, opioid-sparing agents like ketamine (1 mg/ml) can be added to the PCA solution.
- Early referral to involve specialist teams, e.g. community drug and alcohol service, psychiatric services are strongly recommended.

10.9.5 Analgesia for An Elderly Patient

Elderly people represent the fastest-growing segment of our society and undergo surgery more frequently than other age groups. Management of postoperative pain in older patients may be complicated by some factors, including a higher risk of age- and disease-related changes in physiology and disease–drug and drug–drug interactions. Physiological changes related to ageing need to be carefully considered because ageing is individualized and progressive. Assessment of pain management needs to include chronological age, biological age, about renal, liver and cardiac functions, and the individual profile of pathology and prescribed medications. Also, ways in which pain should be assessed, particularly in patients with cognitive impairment, must be considered. NRS is the most commonly used pain scales for the elderly. In older patients with mild to moderate cognitive impairment, the VRS is a better tool. For severe cognitively impaired patients, behavioural scales validated in the postoperative context, such as Doloplus-2 or Algoplus, are appropriate [42–44]. Pain treatment in the elderly is based on the principle 'start low and go slow'. Evaluation of treatment efficacy and incidence and severity of adverse events should be monitored closely.

10.9.6 Management of Patients with Acute Neuropathic Pain

Neuropathic pain is defined as 'Pain initiated or caused by a primary lesion or dysfunction in the nervous system' [2]. Management of acute neuropathic pain can be very challenging. It is an acute sharp pain that does not respond to most standard pain killers. In some operations the chance of nerve damage is high and antineuropathics should be started in the preoperative period. Examples of such operations and diseases are given below:

1. Postoperatively.
   - Post-thoracotomy.
   - Post-mastectomy.
   - Post-amputation.
2. Associated with cancer.
   - Pancreatic cancer.
   - Apical lung tumour pressing on brachial plexus.
   - Pelvic nodes pressing on sacral roots.
   - Spinal bony metastases.
3. Post-trauma.
   - Spinal cord injury.
   - Post-amputation.
   - Third-degree burns.
   - Brachial plexus avulsion.
   - Sacral root injury secondary to a fractured pelvis.
   - Major crush injuries of upper & lower limbs.
4. Medical conditions.
   - Viral infections, e.g. acute herpes zoster/postherpetic neuralgia/HIV-AIDS.
   - Trigeminal neuralgia.
   - Diabetic neuropathy.

- Alcoholic neuropathy.
- Demyelinating diseases, e.g. multiple sclerosis.

It is important to identify acute neuropathic pain early as early intensive treatment can prevent disability and improve prognosis. The salient features to be identified during careful history taking and clinical examination and sometimes investigations. The salient features of the neuropathic pain are:

- History of injury or disease-causing possible damage to peripheral nerves or spinal cord.
- Clinical evidence of damage to peripheral nerves or spinal cord: sensory loss, muscle weakness, bowel or bladder sphincter disturbance and reflex abnormalities.
- Clinical evidence of increased sympathetic activity: alterations in skin colour, temperature and texture, sweating, and nail and hair growth.
- Delayed onset of pain after an injury.
- Pain in the area of sensory loss.
- The character of pain: burning, shooting, stabbing, 'electric shocks'.
- Pain responding poorly to opioids.
- Spontaneous or paradoxical pains.
- Pain elicited to stimuli not normally painful (allodynia).
- Exaggerated pain to painful stimuli (hyperalgesia).
- Unpleasant abnormal sensations with areas of hypoesthesia where the pain is the most.

Treatment should start as soon as acute neuropathic pain is suspected. It often takes 2–3 weeks before a noticeable difference in pain score is achieved. The other problem is most of the antineuropathic drugs have multiple side effects. There is no particular drug of choice but any of the antineuropathic trials can be started if it is not contraindicated. Amitriptyline can be a first choice as the NNT (numbers needed to treat = number of patients needed to be prescribed so that one patient has a 50% reduction of pain) is around 2.3. Recently the perioperative use of pregabalin is advocated by many authors to decrease the postoperative opioid consumption and reduce the incidence of long-term neuropathic pain [34].

10.9.7 Analgesia for Patients with Renal Impairments

Renal impairments are common, especially in the elderly population. Patients with renal impairment and acute pain problems pose a clinical challenge and should be referred to the Acute pain team. Some of the drugs like NSAIDs cannot be used in chronic kidney diseases (unless they are dependent on dialysis) and the chances for opioid accumulation with subsequent respiratory depression are paramount. The protein binding of the opioids and other drugs also change in renal failure making the patient more prone for side effects.

In general, the following principles apply as a guide:

- Use non-opioid analgesics like local infiltration and paracetamol whereever possible to minimize opioid requirements.
- Start with small doses of short-acting opioids, e.g. fentanyl or alfentanil instead of morphine in these patients. Morphine is metabolized to morphine 6-glucuronide which is more potent than morphine and its accumulation in renal failure can lead to drowsiness and respiratory depression. It is often wise to confirm appropriate dosing intervals with a clinical pharmacist, particularly if renal replacement therapies are employed.
- Use as a required dosage with close monitoring in preference to regular dosing as this allows for varying effects in response to the accumulation.
- Regular dosing with longer dosing intervals (e.g. 8 hourly instead of 4 hourly) may be feasible for some patients, alongside regular sedation scoring.

As mentioned earlier it is wise to avoid opioids with active metabolites (e.g. morphine)

which has predominant renal excretion. These include morphine, diamorphine and codeine derivatives which produce toxic metabolites which accumulate in renal failure. Buprenorphine is metabolized in the liver to norbuprenorphine and buprenorphine-3-glucuronide. The parent drug is excreted unchanged via the biliary system but the metabolites are excreted by the kidneys. Although the metabolites have little analgesic action in humans, they do accumulate in renal failure and there is no robust study to recommend or reject its use [45]. In most cases buprenorphine transdermal patch up to 10 mcg/hr. is often used in these patients for chronic pain. Tramadol is successfully used in many units with increased dosing interval to 8 to 12 h. Tramadol is metabolized in the liver to one active metabolite, O-desmethyl-tramadol and 90% of the parent drug and its metabolites are excreted by the kidneys. Immediate-release tramadol would be our first choice analgesic for patients with renal failure with mild to moderate pain or as step-down analgesia.

Tapentadol is a new class of drug which has been successfully used in patients with renal failure when eGFR is more than 25 ml/min/1.73 m2. It is also recommended to be used for moderate to severe pain [46]. But most studies used the immediate-release version of tapentadol which is not available in India [47]. Using a sustained release drug in renal failure is not a good choice. More studies are required to establish the use of the drug in renal failure patients.

It has been suggested alfentanil for severe pain in renal failure [48]. Alfentanil is metabolized in the liver to non-toxic metabolites which are excreted. Only 1% of the parent drug is excreted unchanged by the kidneys. However, short bolus with titration is the safest approach. Infusion of alfentanil can increase context-sensitive half-life and accumulation. It is also not widely available in India so in Indian scenario probably fentanyl in short boluses of 10mcg iv or 25mcg subcutaneously is the only readily available drug.

10.10 Delivery of Care

Acute pain management requires a team approach involving the patient, a multidisciplinary team (consisting of pain physicians, pain nurses, junior doctors, physiotherapist, psychologist and occupational therapist) and family/careers. All these elements make up The Acute Pain Service (APS). Postoperative acute pain management starts in the preoperative period with patient preparation and managing patient expectations. It is important to stress the postoperative management during the preoperative visit. The goal of preoperative preparation is to:

1. Ascertain patient's expectation and understanding.
2. Provide patients with relevant information—an information leaflet is a good way to communicate as the patient can go back and read and refresh himself.
3. Discuss possible options with patients.
4. Identify problem patients like opioid-dependent patients.

The preoperative consultation helps the patient to make an informed choice about pain management and improve their cooperation.

The first line of the service is the recovery and the ward nurses who receive the patients from the theatre, assess their pain and provide analgesia. The job of the recovery staff can be summarized as follows:

1. Provide information and reassurance to the patient.
2. Ensure the regional block is working well.
3. All the types of equipment like PCA and Epidural infusion pumps are correctly prescribed and running. Prescriptions can be standardized across a hospital to reduce confusion among the ward staff. They can be preprinted in the sticky labels for reducing drug prescribing errors.

Types of a sticky label (covering the first-line analgesia):

- For morphine intramuscular or subcutaneous (IM/SC) prescription.
- For morphine intravenous patient-controlled analgesia (IV-PCA).
- For fentanyl intravenous patient-controlled analgesia (IV-PCA).
- For epidural analgesia: for continuous infusion bupivacaine 0.1% + fentanyl 2 microgram/ml for bolus doses ('top-ups') bupivacaine 0.1% + fentanyl 2 microgram/ml.
- For morphine IV bolus administration in critical care areas only.
- For fentanyl IV bolus administration in critical care areas only.
- For antiemetics like ondansetron.
- For Naloxone for overdose.

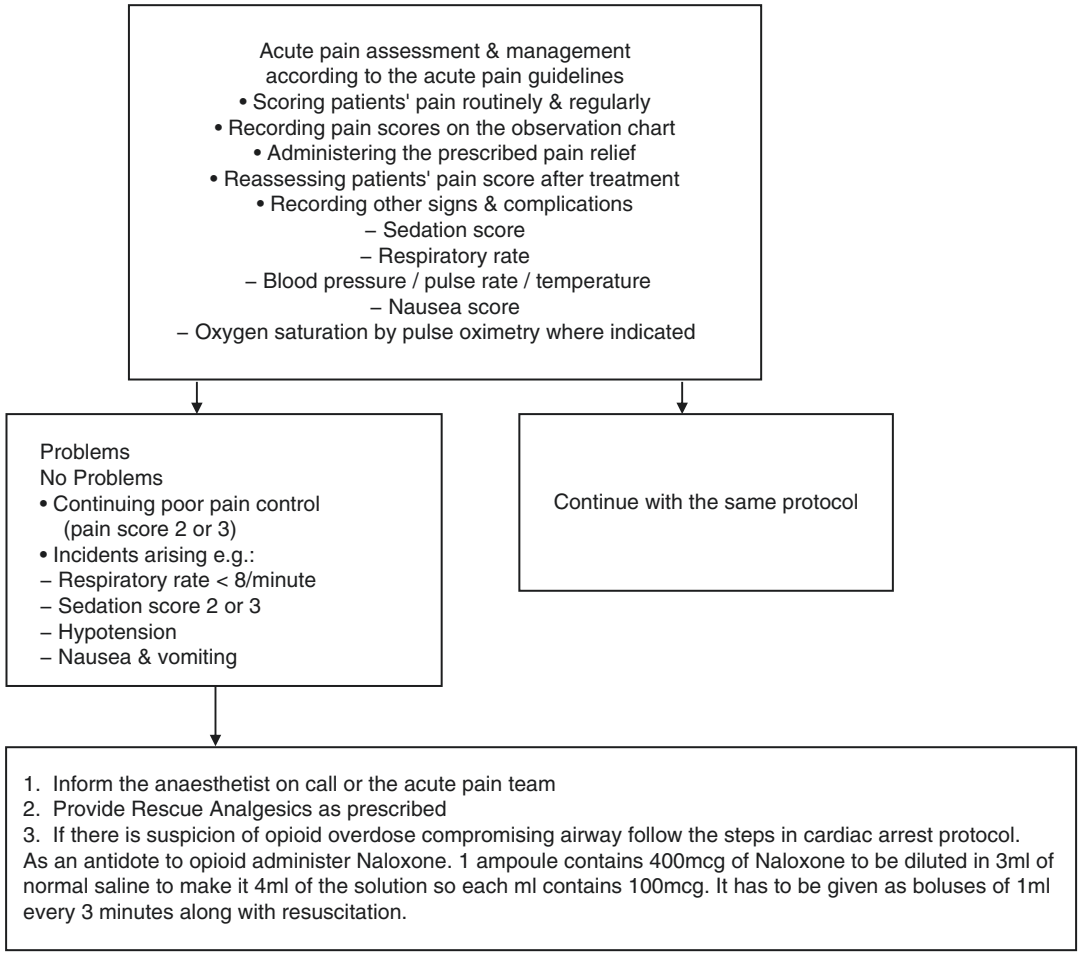
4. Liaise with the medical staff, pain team and the anaesthetist to identify and manage difficult patient.
5. Administer iv pain killers under supervision according to protocol. A commonly used protocol is to give iv morphine 1 mg every 5 minutes to a maximum of 10 mg.
6. Re-measure and record patients' pain score, sedation score, respiratory rate and nausea score along with other vital signs following specific pain relief interventions on the appropriate observation chart.
7. Ensure that no patient is discharged from the recovery ward until the following criteria are met:
   - Pain score of 1 or less at rest and 2 or less on movement (in a 4 point scale).
   - Nausea is controlled.
   - Appropriate analgesia and antiemetics are prescribed.

The second line forms the ward resident doctors who will manage most cases and identify potential difficult cases. The medical resident is the key person in delivering care. His job involves:

1. Manage and coordinate the day to day operations.
2. Be available to reassure the patient and boost the clinical staff.
3. Manage any critical incidents like drug overdose or hypotension following epidural boluses proficiently.
4. Prescribe rescue medications as appropriate for the patient.
5. Liaise with the anaesthetist or Acute pain team to manage difficult patients.
6. Maintain clinical records activity.

The acute pain team and the anaesthetic service form the third line careers who give their input in specialized situations only. The acute pain team will review all of the following patients:

- All patients with epidural infusions. This will enable the team to monitor adverse effects and change drug infusions as required.
- Patients with patient-controlled analgesia.
- Patients with pre-existing and complex pain.
- Patients on long-term opioid therapy.
- All patients awaiting limb amputation.
- Patients with renal or liver impairment.
- Patients undergoing surgery who are under the care of the haemophilia and sickle cell services.
- Patients who are under the care of the palliative care team, but who have undergone a surgical procedure.
- The anaesthetist or pain consultant also has a responsibility to assist in training new members of ward staff.
- To conduct regular ward rounds where appropriate.
- Record and investigate all incidents (critical or otherwise) relating to acute pain management.
- Audit of the service against set guidelines and come up with recommendations to improve the quality of the service.
- Train and support ward staff.



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