Management of Acute Pain

Vaibhavi Baxi *

Introduction

A few years ago the prevalent attitude towards acute pain was widespread acceptance as inevitable and frequent indifference to its suboptimal management. However with the dedicated efforts of health care professionals worldwide, pain management is understood to be a fundamental human right and integral to the ethical, patient-centred and cost-effective practice of modern medicine.

Management of acute pain leads to earlier mobilisation, shortened hospital stay, reduced hospital costs, and increased patient satisfaction.1, 2

Definition of Pain

International Association of the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Acute Pain

Acute pain is temporarily related to injury and resolves during the appropriate healing period. Characteristics of acute pain may include the following:

1. Duration is short - less than 3 months
2. Pain of varying intensity, initially severe then subsiding as healing takes place
3. Reasons for pain - trauma, surgery, acute medical conditions or a physiological process
4. Responds well to conventional analgesia - NSAIDs, opioids, local anaesthetics, etc
5. Psychological problems such as depression.

Acute pain is also known as nociceptive pain and can be divided into visceral and somatic pain. The relief of acute pain should be on a high priority as acute pain may become chronic and persistent when neglected.

Pain can cause significant systemic problems and delay postoperative recovery (Table 1).

Physiology of Pain

Pain afferents do not have any specialised receptors; they use “free nerve endings”. They are polymodal, i.e. they respond to more than one kind of stimulus, e.g. chemical, thermal or mechanical stimuli. Free nerve endings are found in all parts of the body except

<table>
<thead>
<tr>
<th>System</th>
<th>Effects</th>
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<tbody>
<tr>
<td>Cardiovascular</td>
<td>↑ HR, ↑ BP, ↑ Myocardial O₂ demand</td>
</tr>
<tr>
<td></td>
<td>↓ Myocardial blood supply</td>
</tr>
<tr>
<td>Respiratory</td>
<td>↑ RR with Hypocapnia and Respiratory Alkalosis</td>
</tr>
<tr>
<td></td>
<td>Diaphragmatic splinting, Atelectasis</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Catabolic, anabolic changes, ↓ insulin production</td>
</tr>
<tr>
<td></td>
<td>Fluid retention</td>
</tr>
<tr>
<td>Metabolic</td>
<td>↑ Blood Sugar</td>
</tr>
<tr>
<td>GIT</td>
<td>Delayed gastric emptying, Nausea, ↓ GI motility, Ileus</td>
</tr>
<tr>
<td>Haemostasis</td>
<td>↑ Blood viscosity, Hypercoaguability, DVT risk</td>
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</tbody>
</table>

Fig. 1: Pain Pathway
the interior of the bones and the interior of the brain itself. In the cornea of the eye, only free nerve endings are found and abrasions of the cornea can be extremely painful. Most of these respond only to tissue damaging stimuli and are called nociceptors. Aδ fibres mediate the former or ‘fast’ pain, C-fibres signal the latter or ‘slow pain’. Although pain results from damage to these free nerve endings, in reality the pain is a result of substances released by damaged tissues: prostaglandins, histamine and peptides which activate receptors located on the free nerve endings as shown in Figure 1.

**Assessment and Measurement of Pain**

Pain is considered as ‘the fifth vital sign’ increases awareness and utilisation of pain assessment (JCAHO & NPC, 2001) which leads to improved acute pain management. Regular repeated measurement of pain helps in assessment of adequacy of analgesic therapy.

Visual Analogue Scale (VAS) Figure 2 consists of a 100 mm horizontal line with anchor points in the form of words ‘no pain’ at the left end and ‘worst pain imaginable’ at the right end. A reduction in pain intensity by 30% to 35% has been rated as clinically meaningful by patients with postoperative pain.

**Wong-Baker FACES Pain Rating Scale (Figure 3)**

Faces scale is often used in children where they are asked to indicate their pain by pointing to one of the faces.

**Safe and Effective Management of Acute Pain**

Treatment goals for acute pain can be summarised as:

- Early intervention, with prompt adjustments in the regimen for inadequately controlled pain
- Reduction of pain to acceptable levels
- Facilitation of recovery from underlying disease or injury.

Patient education in the form of booklets or short videos and specialist one-on-one education may increase his or carer knowledge about pain and promote positive attitudes towards pain relief.

**Therapeutic Strategies**

A. Pre-emptive Analgesia: Pre-emptive analgesia refers to the administration of one or more analgesic(s) prior to a noxious event (e.g., surgery) in an attempt to prevent peripheral and central sensitisation, minimising post-injury pain.

B. Multimodal Analgesia: “Multimodal analgesia” or “balanced analgesia” involves the use of more than one method or modality of controlling pain (e.g., drugs from two or more classes, drug plus non-drug treatment) to obtain additive beneficial effects; reduce side effects, or both e.g. tramadol paracetamol combination

C. Acute Pain Services (APS): This is a comprehensive and multidisciplinary service provided by trained APS nursing staff led by anaesthetist providing 24 hr cover and daily clinical input. Benefits of APS include better pain relief, low incidence of side effects, less postoperative morbidity, more patient satisfaction and early recognition of onset of neuropathic pain.

**Systemic Medications for Acute Pain Management:**

1. **Opioids**

   Opioids remain the mainstay of systemic analgesia for the treatment of moderate to severe acute pain (Table 2). The term “opioid” is used to designate all agents...
that act on opioid receptors, irrespective of their nature (natural or synthetic, peptide or non-peptide). These receptors have been subdivided into three main categories:

1. Mu receptors
2. Delta receptors
3. Kappa receptors

Common adverse effects of opioids are sedation, pruritus, nausea, vomiting, slowing of GI function, and decreased central CO2 responsiveness resulting in hypoventilation (respiratory depression), cognitive dysfunction and urinary retention.

Opioid Antagonist: Naloxone is used in the management of opioid overdose, or to relieve respiratory depression.

Patient Controlled Analgesia: PCA is a technique whereby small doses of analgesic drugs, usually opioids, (Table 3) are administered (usually IV, although can be subcutaneous) by patients themselves. It is mostly used for the control of postoperative pain. The PCA system allows on-demand bolus injections with the option of a background infusion. Over-dosage is avoided by limiting the size of the bolus and the total dose administered within a set period of time. A lock-out interval is also set. PCA has been shown to provide more consistent plasma drug levels when compared with standard intramuscular techniques, and less sedation. Drugs with relatively short half lives are usually used.

PCA (Figure 4) may also be used in conjunction with epidural analgesia (using plain bupivacaine infusions to avoid opioid over dosage). The pumps should be lockable and contain alarms which warn of excessive doses.

2. Paracetamol: Paracetamol (Acetaminophen) is an effective analgesic and antipyretic with negligible anti-inflammatory effect. It is well absorbed from the small intestine after oral administration with a bioavailability of between 63% and 89%. It can also be given rectally and intravenously. Paracetamol is also an effective adjunct to opioid analgesia. In the same doses, orally administered paracetamol is less effective and of slower onset than paracetamol given by IV injection. Paracetamol has fewer side effects than NSAIDs and can be used when the latter are contraindicated. Paracetamol should be used with caution in patients with active liver disease. However there is no evidence that patients who have depleted glutathione stores (e.g. cirrhosis, hepatitis C or HIV) are at increased risk of

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**Table 2: Commonly used Opioids**

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Equianalgesic Dose</th>
<th>Duration of effect (hr)</th>
<th>Side effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>15-30</td>
<td>3-4</td>
<td>respiratory depression sedation nausea/ oral, IV, IM, Subcutaneous routes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td></td>
<td>vomiting constipation, pin-point pupil, bronchoconstriction, itching</td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1-0.2</td>
<td>0.5-1(IV)</td>
<td>respiratory depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100mic</td>
<td>2-4 (TM)</td>
<td>highly potent. TD patches available to deliver 25, 50, 75 &amp; 100 mic/h</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>60-200</td>
<td>4-6</td>
<td>constipation</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.25</td>
<td>12-20</td>
<td>headache, drowsiness, nausea/vomiting mixed agonist-antagonist oral, sublingual, IV, IM, TD</td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>50-100</td>
<td>4-6</td>
<td>nausea/vomiting</td>
<td>atypical centrally acting analgesic. adjunct for moderate to severe pain.</td>
</tr>
<tr>
<td>Pentazocine</td>
<td>300</td>
<td>2-4</td>
<td>neuroexcitatory</td>
<td>synthetic opioid.</td>
</tr>
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</table>

(TM-Transmucosal, TD-Transdermal, IV- Intravenous, IM-Intramuscular)

**Table 3: Opioid Dose regimens for PCA**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bolus dose (mg)</th>
<th>Lock-out (minutes)</th>
</tr>
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<tbody>
<tr>
<td>Morphine (1mg/ml)</td>
<td>0.5-2.0</td>
<td>5-15</td>
</tr>
<tr>
<td>Fentanyl (0.01mg/ml)</td>
<td>0.02-0.1</td>
<td>3-10</td>
</tr>
</tbody>
</table>
liver dysfunction when exposed to therapeutic doses of paracetamol.\textsuperscript{10,11}

IV Paracetamol: Intravenous administration is more reliable and reaches peak concentrations faster compared with oral routes. The active ingredient is not considered water soluble at 1.43 g/100 cm\textsuperscript{3} in cold water. Hydrophilic ingredients like mannitol and disodium phosphate in intravenous preparations of paracetamol make it soluble. IV paracetamol reaches peak concentration as soon as infusion is complete. The analgesic effect starts within 5 minutes, peaks at 1 hour and lasts 4 to 6 hours.

Tramadol Paracetamol combination: A fixed dose combination of tramadol (37.5 mg) and paracetamol (325 mg) is effective in managing moderate to severe pain. The rationale of this combination is multimodal analgesia with tramadol and paracetamol acting on different sites of the pain pathway to provide analgesia. There are advantages of this combination which is USFDA and EMA approved, besides being approved by the Indian drug regulatory authority, namely CDSCO.\textsuperscript{12}

This combination ensures therapeutic efficacy at lower doses of individual components. The synergistic effect enhances analgesic efficacy, but due to reduced doses of individual components, it is relatively safe even in elderly patients. In one study in acute pain patients, the onset of pain relief was faster with the combination (17 minutes) as compared to the individual components. It is useful in post-operative pain and also in patients who are refractory to NSAID therapy, as an adjunct to NSAIDs. Different international organisations like WHO, The American Geriatrics Society, American College of Rheumatology and British Society for Rheumatology recommend the combination in moderate to severe pain.\textsuperscript{13,14}

One disadvantage of the combination is increased incidence of nausea and vomiting. Manufacturers have developed newer technology to address this problem. One such is the Soflet\textsuperscript{®} technology which provides a gelatine or non-animal film coating on the capsule. This masks the unpleasant odour and taste thereby enabling the patient to swallow easily and improve compliance.\textsuperscript{15}

3. NSAIDs (Non steroidal anti-inflammatory drugs): NSAIDs have a spectrum of analgesic,
anti-inflammatory and antipyretic effects and are effective analgesics. They are inadequate as a sole analgesic in the treatment of severe postoperative pain. When given in combination with opioids after surgery, NSAIDs result in better analgesia reduced opioid consumption and a lower incidence of Post-Operative Nausea and Vomiting (PONV) and sedation. In the perioperative period the main concerns are renal impairment, interference with platelet function, wound and bone healing, and peptic ulceration or bronchospasm in individuals at risk.

Innovative ways to manage adverse effects of NSAIDs: It is universally known that the commonest side effect of NSAIDs is gastro-intestinal disturbances like dyspepsia, vomiting, abdominal discomfort and sometimes serious side effects like bleeding and perforation. This limits the use of NSAIDs in clinical practice. The GI side effect of NSAIDs is due to inhibition of gastric mucosal protection by inhibiting prostaglandin synthesis from COX enzyme in the GI mucosa. However, another important cause is the topical disruption of physico-chemical barrier due to the acidic nature of the NSAID when it is present in the stomach. Local irritation of GI mucosa occur which causes short term damage.16

In order to provide GI safer NSAIDs, one innovative method is to complex them with cyclodextrin molecules. One such example is piroxicam-β-cyclodextrin, which forms an “inclusion complex” between piroxicam and the cyclodextrin molecule. Piroxicam sits inside the cyclodextrin ring and this makes the complex hydrophilic and more soluble in water (Figure 5).16

In the stomach, the drug dissolves quickly, releasing piroxicam. A quicker dissolution has several advantages – piroxicam gets quickly absorbed and its plasma concentration increases leading to a faster onset of action as compared to uncomplexed piroxicam. In one study, the onset of action of piroxicam-β-cyclodextrin was recorded as 15 minutes.17 A quicker dissolution and absorption leads to a shorter contact time with the GI mucosa which reduces GI irritation and makes the drug more GI tolerable. A series of endoscopy studies have shown superior safety profile
with piroxicam-β-cyclodextrin as compared to conventional NSAIDs. The complexation retains all anti-inflammatory and analgesic properties of the parent compound (Figure 6).16,18

4. NMDA receptor Antagonists: Ketamine primarily acts as a non-competitive antagonist of NMDA receptor/ion channel complex which are present peripherally and centrally within the nervous system. It plays a role of an adjuvant in the treatment of pain associated with central sensitisation with severe acute pain, neuropathic pain and ‘opioid-resistant’ pain.

5. Alpha 2 agonists: Systemic administration (oral, I.V., I.M.) of single dose of clonidine decreases perioperative opioid requirements in surgical patients. The addition of clonidine to morphine for PCA significantly improved postoperative analgesia with less nausea and vomiting compared with morphine alone.19 In the intensive care setting, IV dexmedetomidine infusions used for sedation of ventilated patients resulted in a 50% reduction in morphine requirements.20

6. Glucocorticoids: Surgical tissue trauma leads to the conversion of arachidonic acid to prostaglandins and leukotrienes. NSAIDs inhibit the formation of prostaglandins whereas glucocorticoids also inhibit the production of prostaglandins, leukotrienes and cytokines. Addition of glucocorticoid like dexamethasone reduces postoperative pain and analgesic requirement with the additional benefit of decreased PONV and fatigue.21,22

Regional and Local Analgesic Techniques and Drugs (Table 4): A variety of neuraxial and peripheral regional analgesic techniques may be employed for the effective treatment of postoperative pain. However one should evaluate the risks and benefits of these techniques on an individual basis in determining the appropriateness of neuraxial or peripheral regional techniques for each patient especially in the presence of various anticoagulants.

1. Epidural Analgesia: Epidural analgesia has become a widely used technique for the management of acute pain in adults and children, particularly after surgery and sometimes trauma, and in parturients. Epidural analgesia is provision of pain relief by single bolus or continuous administration of pharmacological agents into the epidural space directly or via an indwelling catheter. For all types of surgery, epidural analgesia provides better postoperative pain relief compared with parenteral (including PCA) opioid administration except epidural analgesia using a hydrophilic opioid only.23 The epidural group has a lower incidence of nausea/vomiting and sedation, but a higher incidence of pruritus, urinary retention and motor block.

Side effects of neuraxial analgesics include hypotension, motor blockade, nausea, vomiting, pruritus, urinary retention and respiratory depression.

Like intravenous PCA, Patient controlled epidural analgesia (PCEA) allows for individualisation of postoperative analgesic requirements and may have several advantages over Continuous Epidural Infusion (CEI), including lower drug use, greater patient satisfaction, and superior analgesia.24

2. Peripheral regional analgesia: A variety of wound infiltration and peripheral regional techniques (i.e., brachial plexus, lumbar plexus, femoral, sciatic-popliteal, and fascia-iliac and scalp nerve blocks) as a single injection or continuous infusion can be used to enhance postoperative analgesia.

3. Thoracic non epidural analgesia: Non-epidural regional analgesic techniques used for management of postoperative thoracic pain include paravertebral block, intercostal blocks, interpleural analgesia, and cryoanalgesia. Thoracic paravertebral is a valuable alternative to thoracic epidural analgesia, used for thoracic, breast, and upper abdominal surgery and for rib fracture pain.

4. Intra-articular analgesia: Local (intra-articular) administration of local anaesthetics and opioids may provide analgesia for up to 24 hours after surgery and decrease the incidence of chronic pain. Peripheral opioid receptors are found on the peripheral terminals of primary afferent nerves and are up-regulated during inflammation of peripheral tissues.

5. Wound Infiltration including wound catheters: Continuous infusion of local anaesthetic into the wound after surgeries like hepatectomy, mastectomy, abdominal hysterectomy, bone graft harvest from iliac crest etc leads to reductions in pain scores, opioid consumption, PONV and length of hospital stay and higher patient satisfaction. Also there was no difference in the incidence of wound infections.

B. Non Pharmacological Management

1. TENS: The mechanism by which TENS produces analgesia may be related to the modulation of nociceptive impulses in the spinal cord, release of endogenous encephalins, or a combination of these and other mechanisms. It may be a useful adjunct
to more traditional pharmacologic analgesic drugs in some acute pain settings.

2. **Acupuncture**: Acupuncture reduces postoperative pain as well as opioid-related adverse effects.

3. **Acupressure**: Acupressure is a technique derived from acupuncture, where physical pressure is applied to acupuncture points.

4. **Psychological interventions**: These may be divided into four broad categories: information provision (procedural or sensory); stress/tension reduction (relaxation and hypnotic strategies); attentional strategies; and cognitive-behavioural interventions. It should be emphasised that these are rarely ‘stand-alone’ interventions.

We have discussed a general approach to the practice and principles of acute postoperative pain management, but certain populations (e.g. paediatric patients, patients for ambulatory surgery, pregnant patient) that may have unique anatomic, physiologic, pharmacologic, affective, and cognitive issues. For a particular population the acute pain management should be tailored for its specific needs.

**Conclusion**

Postoperative pain management can be really effective if well planned, delivered in a consistent, evidence-based manner and based on patients’ assessment of their own pain whenever possible. Pain is the 5th vital sign and robust protocols, team work and regular evaluation are needed to effectively manage acute pain.

**References**


15. Soflet – Authorised user: *Geltec Private Limited


