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# Indian Journal of CRITICAL CARE MEDICINE

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# Postoperative pain and its management

Sona Chaturvedi, Amit Chaturvedi\*

## Abstract

Postoperative pain is both distressing and detrimental for the patient. The management of postoperative pain involves assessment of the pain in terms of intensity at rest and activity associated pain, treatment by pharmacological and non pharmacological means as well as monitoring induced side-effects. Besides being physically and emotionally disabling, the pain is associated with various physiological effects involving the increased perioperative stress response. The pain causes the patient to remain immobile, thus becoming vulnerable to DVT, pulmonary atelectasis, muscle wasting and urinary retention. Poor control of postoperative pain could be due to various reasons which may include uniformed prescribing without taking into consideration the individual patient's physical status, the surgery that has been performed or the site and intensity of pain. Besides, the poor compliance of orders in administrating the analgesics prescribed and the fact that optimal pain relief is not aimed for may also contribute to the inadequate management of the pain occurring in the postoperative period. Thus, despite all efforts, there continues to be inadequate pain relief in a large majority of patients. The introduction of multimodal analgesia including opioids and non-opioids, delivered through various routes, neuraxial use of local anesthetics, either alone or in combination with other drugs, nerve blocks, antihyperalgesics and techniques such as patient controlled analgesia and pre-emptive analgesia have greatly improved the efficacy of pain-control while minimizing the side-effects of any one modality. The recent recommendation of planning the pain services in an organized manner and implementation of Acute Pain Services (APS) has proven to be beneficial and rewarding.

**Key words:** Management, post operative pain

## Introduction

The Taxonomy Committee of International Association for 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".<sup>[1]</sup> Postoperative pain is considered a form of acute pain due to surgical trauma with an inflammatory reaction and initiation of an afferent neuronal barrage.

It is a combined constellation of several unpleasant sensory, emotional and mental experience precipitated by the surgical trauma and associated with autonomic, endocrine-metabolic, physiological and behavioral responses.<sup>[2]</sup>

Pain being a subjective phenomenon is perceived only by the sufferer. In no symptom are the patients more inconsistent and unreliable as they are while describing pain. The intensity of pain may not be constant even in a given individual but will wax and wane in a cyclical pattern. Women require less analgesia than men<sup>[3]</sup> probably due to difference in neuro-endocrine mechanism of pain relief. Neurotic patients suffer greater postoperative pain than less neurotic patients.<sup>[4]</sup> Smokers metabolise analgesics

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considerably faster than non-smokers<sup>[5]</sup> and need more as a result.

### Problems Associated with Postoperative Pain

Severe postoperative pain may have physiological consequences increasing the stress response to surgery, seen as a cascade of endocrine-metabolic and inflammatory events that ultimately may contribute to organ dysfunction, morbidity, increased hospital stay and mortality. The pain often causes the patient to remain immobile, thus becoming vulnerable to deep venous thrombosis, pulmonary atelectasis, muscle wasting and urinary retention. Besides, restlessness caused by severe pain may contribute to postoperative hypoxemia.<sup>[6]</sup>

The peripheral neural activation, together with central neuroplastic changes, associated with postoperative pain may in some patients continue into a chronic pain state.<sup>[7,8]</sup> Patients with moderate to severe pain during postoperative period and those having undergone operation with risk of nerve damage are more likely to develop chronic pain. Treatment of acute pain by pre-emptive analgesia may prove to be beneficial in avoiding this complication.

### Mechanism of Postoperative Pain

Surgical procedures are characterized by incisional damage to skin and various other tissues, application of thermal and chemical stimuli to wound and often prolonged traction and manipulation of somatic and visceral structures. Nociceptive pain is often regarded as the key feature of acute postoperative pain. Besides inflammatory, visceral and neuropathic pain mechanisms may contribute to the pain occurring during the postoperative period.<sup>[2]</sup>

Primary and secondary hyperalgesia have been demonstrated in both, the rat model<sup>[9]</sup> and the human model.<sup>[10]</sup>

### Assessment of Postoperative Pain

The aim of assessment is to determine the intensity, quality and duration of pain, to help decide on the choice of therapy and to evaluate the relative effectiveness of different therapies.

Approaches to the measurement and assessment of

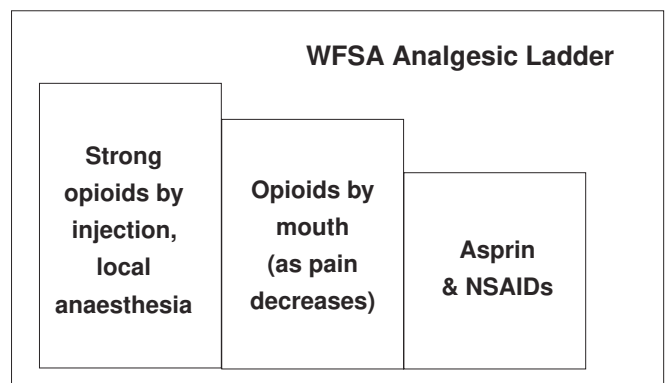
pain include verbal and numerical rating scales, visual analogue scale (VAS), behavioral observation scales and psychological responses. Of these the VAS is the most frequently used self rating score.

The most common VAS consists of a 10 cm horizontal or vertical line with the two end points labeled 'No pain' and 'Worst pain ever'. Patients are required to place a mark on the 10 cm line at a point that corresponds to the level of pain intensity they presently feel. The distance in centimeter from the low end of VAS to the patient's mark is used as a numerical index of the severity of pain. Advantages include ease and brevity of administration and scoring, its minimal intrusiveness, its greater sensitivity to detect intervention-based changes in pain and its conceptual simplicity.<sup>[11]</sup>

A simple code for pain scoring in the postoperative set up is:

1. Comfortable (awake or asleep)
2. Slight pain - only elicited by close questioning
3. Moderate pain - bothering the patient, but often controllable by lying still. The patient may ask for analgesia.
4. Severe pain - dominating the consciousness and calling out for urgent relief.<sup>[12]</sup>

The World Federation of Societies of Anesthesiologists (WFSA) Analgesic Ladder has been developed to treat acute pain. Initially, the pain can be expected to be severe and may need controlling with strong analgesics in combination with local anesthetic blocks and peripherally acting drugs. The oral route for the administration of drugs may be denied because of the nature of the surgery and drugs may have to be given by injection. Normally, postoperative pain should decrease with time and the need for drugs to be given by injection should cease.



The second rung on the postoperative pain ladder is the restoration of the use of the oral route to deliver analgesia. Strong opioids may no longer be required and adequate analgesia can be obtained by using combinations of peripherally acting agents and weak opioids. The final step is when the pain can be controlled by peripherally acting agents alone.<sup>[13]</sup>

### Pre-emptive Analgesia

The idea of pre-emptive analgesia is based on the observation that if afferent pain signals are prevented from reaching the central nociceptive neurons by preinjury administration of analgesics, sensitization of the central neurons will not take place or will be reduced.<sup>[14]</sup>

### Antihyperalgesics

In addition to pre-emptive analgesia, recent interest has focused on various antihyperalgesic drugs for postoperative pain. They act by preventing sensitization of the central nervous system with no effect on the nociceptive input<sup>[15]</sup> and may even reverse a sensitized system back to a physiological state.<sup>[16]</sup> Ketamine and dextromethorphan, both NMDA receptor antagonists have demonstrated some analgesic or antihyperalgesic potential for postoperative pain.<sup>[17,18]</sup> Clinical trials have also shown pain relieving and opioid sparing effects of pregabalin and gabapentin in patients with acute postoperative pain.<sup>[19]</sup>

### Management of Postoperative Pain

*1) Pharmacological measures:* Include administration of drugs like opioids as well as non-opioids by various routes including oral, intra-muscular, intra-venous, per-rectal, epidural, intrathecal, sublingual, intra-articular, subcutaneous, etc;<sup>[20]</sup>

Use of Opioids for Postoperative pain relief: Various factors may affect the absorption of opioids and the resulting clinical response. These include route of administration, presence of hepatic or renal disease, age of the patient, concurrent administration of other drugs, hypothermia, hypothyroidism, hypovolemia, hypotension, etc;

### Patient controlled analgesia (PCA)

Introduced in 1966, PCA has been used both, as a means of treating pain and a means of quantifying analgesic deficit.<sup>[21]</sup> It has been demonstrated to be

better than conventional intramuscular analgesia, having lower postoperative morbidity, faster recovery of minute ventilation, rapid ambulation and early discharge of the patient,<sup>[22]</sup> though certain other studies have failed to demonstrate a similar benefit.<sup>[23]</sup> It is shown to provide adequate pain relief in the postoperative period without appreciable respiratory depression.<sup>[20]</sup>

The patient can administer his own analgesia and so titrate the dose to his own end-point of pain relief using a small microprocessor - controlled pump. In theory, the plasma level of the analgesic will be relatively constant and side effects caused by fluctuations in plasma level will be eliminated. Patient compliance is critical to the effectiveness of PCA and so patients should be given a pre-operative demonstration as well as explanation of the entire procedure. Choice usually depends upon availability, personal preference and experience. Certain parameters need to be set including the size of the bolus dose, the minimum time period between doses (the lock-out period) and the maximum dose allowed. Some devices permit the use of a continuous background infusion. Morphine is the most commonly used drug, in the dose of 1-1.5 mg with a lock-out period of five to ten minutes.<sup>[13]</sup> However, regular review is needed in every case to ensure that pain relief is adequate. Besides being administered intravenously, PCA may also be given by subcutaneous and epidural routes.

### Intrathecal and epidural analgesia

This may be provided either by using opioids, local anesthetics or a combination of both. Intrathecal opioids are easy to administer and effective in producing analgesia without any demonstrable motor, sensory or autonomic deficit.<sup>[24]</sup> The intrathecal potency of opioids is inversely proportional to their lipid solubility,<sup>[25]</sup> with patients remaining comfortable for 24h or more after a single injection of intrathecal morphine.<sup>[13]</sup>

The epidural route may be used for administration of single bolus or as a continuous infusion of the drug. It has demonstrated advantageous physiological effects including efficient activity-dependent pain relief, improvement in protein economy, reduction in ileus as well as improvement in postoperative pulmonary function and decrease in cardiac demands.<sup>[26]</sup> Drug used may be either an opioid alone or in combination with a local anesthetic. The latter has shown better results in

relieving postoperative pain.

Side-effects encountered using these routes of delivery include nausea, vomiting, itching and urinary retention. Of most concern however, as with any opioid, is the possibility of respiratory depression. Other problems encountered with epidural infusions are that there is no end-point between ineffective at too low an infusion rate and systemic toxicity at too high an infusion rate. Besides, in slow infusions, "break-through" pain is a problem and needs treatment with an additional epidural bolus dose.<sup>[6]</sup>

### **Opioid analgesic agents**

Opioids act as agonists on those stereospecific opioid receptors occurring at presynaptic and postsynaptic sites within the CNS and in the peripheral tissues.<sup>[27]</sup> These opioid receptors are classified as  $\mu$ ,  $\delta$  and  $\kappa$  receptors.<sup>[28]</sup> Opioids mimic the actions of endogenous ligands by binding to opioid receptors, thus resulting in the activation of pain-modulating (antinociceptive) systems. Opioids administered by neuraxial routes act by diffusion across the dura to gain access to  $\mu$  opioid receptors on the substantia gelatinosa of the spinal cord, as well as by systemic absorption to produce effects similar to those that would follow intravenous administration of the opioid.<sup>[29]</sup>

**Morphine:** Morphine is the prototype opioid agonist which produces analgesia, euphoria, sedation and a diminished ability to concentrate. Given intravenously in the postoperative period, it provides pain relief in 15-30 min. Metabolism is mainly by conjugation with glucuronic acid in hepatic and extra hepatic sites, especially the kidneys.<sup>[29]</sup> Recommended analgesic doses are 0.15mg/kg IM, 0.03mg/kg IV. May also be administered as PCA by intravenous or subcutaneous infusion.<sup>[30]</sup>

**Pethidine:** Pethidine is one-tenth as potent as morphine with shorter duration of action, having agonist action at  $\mu$  and  $\kappa$  receptors. It undergoes hepatic metabolism.<sup>[31]</sup> Besides extensive use as a post-operative analgesic, pethidine is also useful for control of post-operative shivering.<sup>[32]</sup> In a dose of 0.5 mg/kg IV or 1.5 mg/kg IM, it produces effective analgesia in two to five minutes. It is also effective by the epidural route.<sup>[12]</sup>

**Fentanyl:** Is 75-125 times more potent than morphine

in its analgesic properties. Used in a wide range of doses from 1 to 2  $\mu$ g/kg IV to 2-20  $\mu$ g/kg IV or by transdermal or transmucosal routes. Duration of action is 30-60 min. It undergoes enterohepatic recirculation with rebound effects at three to five hours after injection.<sup>[29]</sup> Side-effects are similar to other opioids.

**Sufentanil, Alfentanil:** Analgesic potency of sufentanil is five to 10 times that of fentanyl, due to greater affinity of sufentanil to opioid receptors. The potency of alfentanil is less, about one-fifth to one-tenth and has one-third the duration of action of fentanyl. An advantage of alfentanil is the more rapid onset of action, making it useful in the post-operative set-up.

**Tramadol:** Is a centrally acting analgesic with moderate affinity for  $\mu$  receptors and weak  $\kappa$  and  $\delta$  opioid receptor affinity, but is five to 10 times less potent than morphine.<sup>[33]</sup> It may be administered by oral, intravenous or intramuscular routes in a dose of 3 mg/kg. Advantages over other opioids include absence of depression of ventilation<sup>[34]</sup> and a low potential for development of tolerance, dependence and abuse.

**Pentazocine:** Pentazocine, 10-30 mg IV or 50 mg orally, may be used for the relief of moderate pain. Side effects include sedation and dysphoria. Respiratory depression is dose related but has a ceiling effect.<sup>[29]</sup>

**Nalbuphine, Butorphanol:** Are agonist/antagonists acting at the  $\kappa$  receptor. Both have been used to provide postoperative analgesia by intermittent, continuous and PCA techniques. They exhibit a ceiling effect for analgesic activity and also for respiratory depression. They are alleged to have a lower abuse potential than conventional opioid agents.<sup>[13]</sup>

**Buprenorphine:** Is an agonist-antagonist opioid which is effective in relieving moderate to severe pain. Its affinity for  $\mu$  receptors is 50 times that of morphine. The recommended dose is 0.3 mg. It may be administered by intramuscular, intravenous, sublingual or epidural routes having duration of action upto eight hours.<sup>[29]</sup>

**Side effects:** Pruritis, urinary retention, depression of ventilation orthostatic hypotension, nausea, vomiting and physical dependence are the usual problems encountered with use of opioids.



## Non-opioid analgesics

**Paracetamol:** Use of oral paracetamol and intravenous propacetamol<sup>[35]</sup> is well documented in post-operative pain treatment. These probably act by both peripheral and central anti-inflammatory effects. Doses range from a minimum of 500 mg orally, four hourly to a maximum of 4 g daily.<sup>[13]</sup>

**NSAID's:** NSAID's are a heterogenous group of agents that mediate anti-inflammatory, analgesic, antipyretic and platelet inhibitory effects. NSAID's are more effective than paracetamol in the post-operative setting, but their usefulness may be limited due to their tendency to cause gastrointestinal and surgical site hemorrhage and renal failure, especially in high risk patients.<sup>[36]</sup> Intra-articular NSAID's may provide a better analgesic effect than that achieved by a similar oral dose.<sup>[37]</sup> Besides they can be used as topical applications, suppository and parenterally also. Various NSAID's in common use include Diclofenac (100 mg oral, rectal, intramuscular, topical), diflunisal (500 mg), indomethacin (100 mg oral or rectal), naproxen, piroxicam (40 mg). Ketorolac has been found to be as effective as morphine, but is associated with a similar incidence of vomiting.<sup>[38]</sup> 'Opioid sparing' effect of NSAID's is beneficial as it reduces the dose requirement of opioids, at the same time reducing their side-effects.<sup>[39]</sup> All NSAID's are to be avoided in severe renal failure, peptic ulceration, severe hepatic failure, fluid retention and ulcerative colitis.<sup>[12]</sup>

**Cyclooxygenase-2 inhibitors:** Coxibs seem to have a similar analgesic potency as compared to NSAID's,<sup>[40]</sup> but a superior safety profile with respect to the gastrointestinal tract<sup>[41]</sup> and platelet function.<sup>[42]</sup>

**Local anesthetics:** Continuous infusion of epidural local anesthetics results in effective pain relief and is recommended after major thoracic, abdominal and orthopedic surgery and may be a prerequisite for enhanced recovery in such procedures. Addition of opioids to epidural local anesthetics improves analgesia, but may be associated with side-effects like hypotension, urinary retention, motor weakness, respiratory depression, nausea, vomiting and pruritis.<sup>[43]</sup> Clonidine,<sup>[44]</sup> adrenaline<sup>[46,47]</sup> or ketamine<sup>[24]</sup> may be added to the local anesthetic in an effort to enhance the quality and/or duration of analgesia provided.

Local anesthetics may be administered in the surgical wound,<sup>[47]</sup> as continuous wound infusion,<sup>[48]</sup> as intraperitoneal instillation<sup>[49]</sup> or intra articular administration,<sup>[50]</sup> with variable results. They may also be used for peripheral nerve blocks like paravertebral, intercostals or intraperitoneal in order to provide postoperative pain relief. Infusion of the drug for peripheral nerve blockade may be efficient and safe.<sup>[51]</sup>

**Other pharmacological modalities:** Magnesium by blocking NMDA receptor may prevent central sensitization and thus provide post-operative pain relief.<sup>[52]</sup> Intrathecal and epidural administration of neostigmine is effective in preventing postoperative pain. Adenosine, has also demonstrated antinociceptive and antihyperalgesic properties in surgical patients.<sup>[36]</sup> A variety of other drugs like cannabinoids<sup>[53]</sup> and glucocorticoid<sup>[54]</sup> may also prove to have a role in treatment of postoperative pain.

*II) Non-pharmacological modalities:* Transcutaneous electrical nerve stimulation (TENS) applied with a relevant, strong, subnoxious intensity and adequate frequency in the wound area may reduce analgesic consumption in the postoperative period.<sup>[55]</sup> Acupuncture is another non-pharmacological means which may prove to be of value in acute pain management especially in the postoperative period.<sup>[56]</sup>

## Multimodal analgesia

The strategy of postoperative pain treatment is to maintain the nociceptive system in physiological mode. A combination of neural blockade with local anesthetics, anti-inflammatory drugs and hyperalgesics is recommended. The combination of epidural local anesthetics with opioids, opioids and NSAID's and paracetamol with NSAID's have been demonstrated to improve analgesia.<sup>[57,58]</sup>

## Organization of Pain Services

The solution to the problem of inadequate postoperative pain relief does not lie so much in development of new techniques, but rather in the establishment of a formal organization.<sup>[59]</sup>

The first Acute Pain Service (APS) was introduced in U.S and Germany in 1985. APS represents an instrument to improve pain relief, although the structure and cost-effectiveness need to be established.<sup>[60]</sup> In this respect,

Practice Guidelines for acute pain management in the perioperative setting have been developed by ASA Task Force on Pain Management.<sup>[61]</sup> These include:

1. Proactive planning
2. Education and training of hospital personnel
3. Education and participation of patients and families
4. Monitoring and documentation of perioperative pain management.
5. Availability of Anesthesiologists providing perioperative pain management.
6. Standardized institutional policies and procedures.
7. Use of PCA, epidural analgesia or regional anesthesia techniques.
8. Organizational characteristics related to perioperative pain management.
9. Pediatric perioperative pain management.
10. Geriatric perioperative pain management.
11. Pain management for ambulatory surgery.

### Conclusion

Intensity of postoperative pain in a surgical patient occurs because of pre-existing disease, the surgical procedure or a combination of disease related and procedure related sources. There are various variables which should be considered when selecting the postoperative analgesic regime for the patient. These include the degree of pain, the operation performed, patients perception of the pain, drug response in the patient, presence of any pre-existing disease and finally the availability of drugs and treatment available. The goal should be to make the patient "pain-free at rest". Multi-modal analgesia is recommended so as to achieve optimal pain relief with minimal side effects.

To reduce the incidence and severity of acute postoperative pain, increased awareness among both professionals and the general public is necessary, along with the establishment of acute pain management programs and aggressive public and patient education programs. The organizational issues include a demand for improved collaboration on the pain issue between anesthesiologists, the acute pain service, surgeons and surgical nurses to provide full benefit to the patients.

Future strategies should focus on the integration of the APS and multimodal rehabilitation techniques on outcome in specific procedures optimally performed as randomized, controlled clinical trials or in large scale multi-centre trials.

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