

# ACUTE POSTOPERATIVE PAIN MANAGEMENT

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## ***INTRODUCTION***

One of the most important concerns of the patients in postoperative period is postoperative pain. This phenomenon is a combination of sensation, emotions and thoughts presents as pain behaviour. Pain is commonly defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.<sup>1</sup> Pain, as a sensory experience, varies in its severity and life impact according to the individual's subjective meaning associated with a pain situation, the patient's emotional responses, attention given to the pain and other personal appraisals.<sup>2</sup>

Acute postoperative pain (APP) is defined as pain temporarily related to surgery that resolves during the appropriate healing period. Acute postoperative pain is a clinical condition that should be treated accurately and completely. Each patient should be evaluated individually in preoperative period and the method should be determined according to the severity of the pain. This method should be a non-invasive method that may control postoperative pain. Management of postoperative pain, a very difficult process, should begin in preoperative period, multimodal approach formed by newly developed drugs and regional techniques, preemptive analgesia methods may convert the difficult to easy.

Concerted deliberation on acute postoperative pain management is now towards preventing progressive degeneration into chronic pain. Ineffectively treated and persistent postoperative pain may lead to anxiety, sleep disorders, demoralization, disturbances in mental activity and social relations.<sup>3,4,5</sup> Prompt and adequate management of postoperative pain relieves suffering and enhances earlier mobilization, shortened hospital stay, reduced hospital costs, and increased patient satisfaction.<sup>6,7</sup> Pain control regimens, rather than being standardized, should be tailored to the needs of the individual patient, taking cognisance of the physical condition, psychological, medical, age, level of fear or anxiety, surgical procedure, personal preference and response to agents administered.

Adequate postoperative pain management is aimed at minimising side effects while providing adequate analgesia. This goal is best accomplished with multimodal and preemptive analgesia.<sup>8</sup>

Pain has been found to constitute one of the three causes of delay in discharge after ambulatory surgery. That an effective postoperative pain management cannot be achieved is a reality and unfortunately satisfaction is low both for the physicians and the patients.<sup>9</sup> In a study done, approximately 80% of the patients were reported to suffer from pain after surgery.<sup>10</sup> Many patients still suffer from pain despite focusing on pain management programs and development of novel postoperative pain management programs.

A multidisciplinary team approach (eg, acute pain service) is useful for formulating a plan for pain relief, particularly in complicated patients, such as those who have undergone extensive surgery, chronically use narcotics, or have medical comorbidities that could increase their risk of analgesia-related complications or side effects.

The primary aim of this clinical review is to introduce the surgical clinician to the various best practices models of acute postsurgical pain management.

### The physiology of surgical pain

Neurophysiological and pharmacological studies in recently developed animal models for postoperative pain have advanced our knowledge of the mechanisms of pain resulting from surgical incision and associated tissue injury. <sup>11, 12, 13, 14</sup>

Acute pain from whether superficial or deep surgical extirpation causes a wide range of pathophysiological responses, which are initiated when nociceptors are activated after tissue injury, resulting in a local inflammatory response and subsequent behavioural and physiological responses.<sup>15</sup> After tissue injury, sympatho-neural and neuro-endocrine activation (along with uncontrolled pain) can ultimately lead to various potentially detrimental responses such as tachycardia, hypertension, hyperglycaemia, immune-suppression, decreased regional blood flow or venous stasis, and platelet aggregation.<sup>15</sup> In high-risk patients (eg, presence of multiple co-morbidities, decreased physiological reserves) or those undergoing high-risk procedures, these pathophysiological responses can result in increased morbidity. Some analgesic agents or techniques, such as regional anaesthesia–analgesia with local anaesthetics, used for the treatment of acute postoperative pain can attenuate these

pathophysiological responses to a greater extent than that seen with systemic analgesics<sup>16</sup> and result in improvement of some patient outcomes.

The somato-sensory pain pathway has the ability to detect actual noxious and potentially tissue-damaging stimuli. The function involves other multiple interacting peripheral and central pathways. The neural processes underlying the encoding and processing of the information from a noxious stimulus is described as nociception.<sup>17</sup>

The detection of noxious stimuli requires the activation of nociceptors (sensory organs) and transduction into action potentials for conduction to the central nervous system. These nociceptive afferents are widely distributed throughout the body – skin, muscle, joints, viscera and meninges. The afferents comprise both medium-diameter lightly myelinated A-delta fibres and small-diameter, slow conducting unmyelinated C-fibres.

Incisional pain differs in its mechanism from other inflammatory or neuropathic pain states. Tissue damage from surgery leads massive to disruption of cell walls, degranulation of mast cells, secretion by inflammatory cells and subsequent induction of enzymes such as cyclo-oxygenase-2 (COX-2). An array of chemical mediators acts either directly via ligand-gated ion channels or via metabotropic receptors to activate and/or sensitise nociceptors. Some endogenous modulators of nociception such as proteinases<sup>18</sup>, pro-inflammatory cytokines (eg TNF $\alpha$ , IL-1 $\beta$ , IL-6)<sup>19</sup>, anti-inflammatory cytokines (e.g. IL-10)<sup>20</sup>, and chemokines (eg CCL3, CCL2, CX3CL1)<sup>21</sup>, also act as signalling molecules in pain pathways.

Following activation, intracellular kinase cause the phosphorylation of channels (such as voltage-gated sodium and transient receptor potential channels), alterations in channel kinetics and threshold, and sensitization of the nociceptor. The release of neuropeptides such as substance P and calcitonin gene-related peptide from the peripheral terminals also contributes to the recruitment of serum factors and inflammatory cells at the site of injury (neurogenic oedema). This increase in sensitivity within the area of injury due to peripheral mechanisms is termed peripheral sensitisation, and is manifest as primary hyperalgesia.<sup>22</sup> This could explain why non-steroidal anti-inflammatory drugs (NSAIDs) modulate peripheral pain by reducing prostaglandin E2 (PGE2) synthesis by locally induced COX-2. Changes in protein synthesis in the cell body of the dorsal root ganglion are also induced by inflammation and alter the expression and transport of ion channels and receptors, such as opioid receptors respectively, to the periphery.<sup>22</sup>

Sodium channels are essential in modulating neuronal excitability, signaling and conduction of neuronal action potential to the central nervous system. Local anaesthetic agents act on the rapidly inactivating fast sodium current found in all nerve fibres. These agents can also block sympathetic and motor neurons. Following surgical incision, the sodium channel kinetics change giving rise to hyper-excitability with subsequent reversible alteration in the configuration of these channels. Afferent pain signals are transmitted in the spinal cord to the brain. Most of these primary afferents contain excitatory amino acids (for example, glutamate, aspartate), peptides (eg substance P, calcitonin) and neurotrophic factors (eg brain-derived neurotrophic factor) which act as neurotransmitters and are released by different intensity stimuli.

Depolarisation of the primary afferent terminal gives rise to the release of glutamate which in turn activates postsynaptic ionotropic alpha-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate (AMPA) receptors and rapidly signals information relating to the location and intensity of the noxious stimuli

Systemic consequences of acute postoperative pain

Every system of the body is affected by unrelieved pain following surgery. The systems involved with gross physiological changes include:

**? *Cardiovascular effects***

- Increased heart rate.
- Increased blood pressure.
- Increased stroke volume.
- Increased myocardial oxygen demand, reduced myocardial oxygen supply and possible myocardial ischaemia.
- Reduced blood flow to viscera and skin causing delayed wound healing

**? *Respiratory effects***

- Stimulation of respiration causing initial hypocapnia and respiratory alkalosis.
- Diaphragmatic splinting and hypoventilation, atelectasis, hypoxia and ensuing hypercapnia.
- Development of chest infection

**? *Endocrine effects***

- Catabolic and anabolic changes.

- Decrease in insulin production.
- Reduction in testosterone level.
- Fluid retention

? ***Metabolic effects***

- Raised blood sugar levels

? ***Gastrointestinal effects***

- Delayed gastric emptying
- Nausea
- Reduced gastro-intestinal motility and ileus

? ***Haemostasis***

- Immobility
- Increased blood viscosity
- Hypercoagulability and risk of deep vein thrombosis

***Characteristics of acute postoperative pain***

- Duration is short lived - less than 3 months;
- Pain of varying intensity, initially severe then subsiding as healing takes place;
- Nervous system is usually intact;
- Reasons for pain can be pinpointed - pain is caused by trauma, surgery, acute medical conditions or a physiological process;
- Responds well to conventional analgesia - opioids, local anaesthetics, etc;
- Pain tends to subside as healing takes place;
- Psychological problems such as depression are short lived if present at all.

***Assessment of Postoperative Pain***

Various methods have been suggested to assess the severity of acute postoperative pain. Most often the severity of pain is under assessed and treatment given is not commensurate with the degree of pain. Although pain is a subjective phenomenon, the same degree of pain could vary from one patient to

another. Therefore, a more objective method of assessing pain is in line with adequate management and treatment.

***There are three types of pain measures. These include:***

1. Self-report
2. Observational measures
3. Physiological measures

Self-report measures can be useful in many ways. This type of measure involves rating the pain using a metric scale. Self-report is frequently seen as the gold standard of pain assessment because it is consistent with the definition of pain. However the drawback of this form of assessment is that it is exactly subjective in nature. The edge this form of measure has is that it relies on the patient's ability to communicate about pain.

Observational measures usually rely on a therapist, or someone well known to the patient, completing an observational measure of some aspect of pain experience, usually related to behaviour or activity performance. This type of measures can be useful to corroborate the self-report given by the patient. The observational measures have been shown to be most accurate for acute pain since pain behaviour tends to habituate as pain becomes more chronic.<sup>23</sup>

Pain can cause biological changes in heart rate, respiration, sweating, muscle tension and other changes associated with a stress response.<sup>24</sup> These biological changes can be used as an indirect measure of acute pain, but biological response to acute pain may stabilize over time as the body attempts to recover its homeostasis. Physiological measures are useful in situations where observational measures are more difficult. For example, observational measures can be used to measure pain in infants but physiological measures have provided important information about post-surgical pain in neonates.<sup>25</sup>

### ***Assessment of postoperative pain***

Assessment of pain before intervention is important to ensure that the therapist and the pain team have a complete picture of the patient's needs and areas of difficulty. During assessment, pain is frequently described in the form of self-report. The assessments are done either in the form of questionnaires, rating scales, visual analogue scales and drawings. Intensity of postoperative pain can be described in

terms of its intensity (i.e. how much is the pain), its quality (if it is aching, dull or sharp) and where it is located.

Visual analogue scale (VAS): This is a 10-cm line with 'stops' and 'anchors' at the ends of the line. This line can be vertical or horizontal. The patient is usually requested to mark on the line the point corresponding with the pain. The VAS is reproducible, sensitive, simple, and universal (i.e. understood in every language).

Numeric rating scales (NRS): The numeric rating scale is the most popular but more frequently used for the assessment of chronic pain.

Faces Pain Rating Scale – Revised (FPS-R): The Faces Pain Scale – Revised is a self-report measure of pain intensity developed for children adapted from the Faces Pain Scale in order to make it possible to score on the widely accepted 0-to-10 metric.<sup>26, 27</sup>

It shows a close linear relationship with visual analogue pain scales across the age range of 4-16 years. It is easy to administer and requires no equipment except for the photocopied faces. The absence of smiles and tears in this scale may be advantageous. It is particularly recommended for use with younger children.

### ***Treatment of acute postoperative pain***

Managing postoperative pain in the current healthcare environment can be difficult. Busy hospital wards, low staff numbers, limited time, inappropriate attitudes or focus on other imperatives, and inadequate knowledge all impede optimal postoperative pain management. This may be mitigated by producing an environment where pain management is considered a priority by introducing regular and accurate pain assessment, a multimodal treatment approach and a focus on responding to individual patient's needs. Many healthcare systems are also under pressure to reduce length of stay and improve patient satisfaction, both of which will be compromised if pain management is not adequate.

Multimodal Analgesia: Advancement in molecular science has led to development of multimodal analgesia for the treatment of postoperative pain. Multimodal (balanced) analgesia is achieved by combining different analgesics that act by different mechanisms at different sites in the nervous system, reducing the incidence of side effects owing to the lower doses of the individual drugs.<sup>28</sup> Controlling postoperative pain with unimodal approaches is almost impossible as it is a complex problem. Multimodal pain therapy is well known to result in early mobilization, early oral intake, early returning of colon functions, early discharge and short duration of hospital stay, lower pain scores with a successful postoperative pain control and reduction in perioperative stress response.

Pain management should be initiated as a preventive preoperative period and continued in the early postoperative period and extended into the post-discharge period if a maximum short-term and long term benefit from multimodal analgesic therapy is to be achieved.<sup>29, 30</sup>

Many options are now available for acute postoperative pain treatment. These include systemic analgesics (e.g, opioids, non-opioids) and regional analgesic techniques (neuroaxial and peripheral nerve blocks). A successful treatment of postoperative pain requires good multi-disciplinary and multi-professional cooperation.

Multidisciplinary team consists of the anaesthesiologist, pain nurse, specialist surgeon, and a pharmacist. In the ward the patient's physician and nurse, physiotherapist when needed are responsible for all care, in partnership with the pain team. The nurse, being the first point of contact is responsible to report the patient's intensity of pain to the physician and to treat the pain within the defined rules of the local guidelines.

Preemptive analgesia: This approach to pain relief is aimed at preventing spinal sensitization and neuroplasticity processes that could cause an increase in pain intensity and duration following surgery. Although the effects of different timing of administration of single agents have been studied, no one result has demonstrated differences in efficacy.<sup>31</sup>

Non-steroidal anti-inflammatory drugs (NSAIDs) have been found to be very effective in the management of postoperative pain<sup>32</sup> but their adverse effects and contraindications pose as major limitations in their use. One of the major concerns in the use of these agents is their effect on platelets. Other concerns are gastroduodenal erosive tendencies, renal impairment and bronchospasm in susceptible patients. Careful patient selection is therefore necessary. NSAIDs have been found to be great benefit in appropriately selected patients as they appear to improve analgesia and reduce the incidence of nausea, vomiting and sedation. The opioid sparing effect is considerable and may benefit patients in whom low opioid doses are preferred. Agents like diclofenac suppositories, and intravenous paracetamol have been used and found to give adequate pain relief

Opioids: Opioids analgesics play essential role in the acute treatment of moderate to severe pain in the early postoperative period. Some complications associated with these agents include, postoperative nausea and vomiting (PONV), sedation, nausea, pruritus, urine retention, ileus, constipation and respiratory depression.

Opioids have administered through various routes including intravenous, intramuscular, subcutaneous, trans-mucosal, neuraxial and transdermally. Of these routes, the intravenous injection is commonest. However when a good result is desired following visceral pain, an intrathecal injection can be administered but in small doses.<sup>33</sup>



Analgesia delivered by the patients or patient controlled analgesia (PCA) is known to provide superior postoperative analgesia and improves patient satisfaction. Patient controlled analgesia (PCA) optimizes delivery of analgesic opioids and minimizes the effects of pharmacokinetic and pharmacodynamics variability in individual patients. It can be programmed for several variables: demand (bolus) dose, lockout interval, continuous or basal infusion, and a 4-hour limit

Intravenous patient controlled analgesia (IV PCA): This is now widely used to deliver opioids to patients unable to take oral analgesics. It is generally preferred over other methods of injection.<sup>34</sup> Intravenous PCA is safe, associated with reduction of pulmonary complications such as atelectasis and enhances patient satisfaction. However there are some challenges associated with this method of analgesic administration. These include that:

- The patient must understand what the technique is all about
- The fear of opioid overdose or addiction by the patients must be allayed
- There could be under-usage of this method as a result of the mild side effects that could follow

The efficiency of this method will depend on effective communication, education and careful attention to reduce or avoid side effects.

#### Neuraxial and local anaesthesia

Local and regional anaesthesia have been found useful in the multimodal management of postoperative pain. Infiltrative techniques, infusions, preineural injections, subarachnoid and epidural injections have been used.

Wound infiltration has been found to be effective in some types of surgery and have been found to reduce pain scores, reduced the need for opioid use, nausea and vomiting and increase patient satisfaction.<sup>35</sup> Perineural analgesia infusions are also effective but require more skills in the correct placement of needles.

Subarachnoid blocks have been used also to institute postoperative pain relief. Various adjuvants have been used. The effects of this combination with bupivacaine extend into the postoperative period. These include fentanyl<sup>36</sup>, dexmedetomidine.<sup>37</sup> The introduction of intrathecal microcatheters has provided a new horizon in the postoperative pain management of patients. It makes provision for smaller doses of local anaesthetic with or without adjuncts to be administered over a given period. However the potential problems associated with this technique cannot be underscored.

The use of patient controlled epidural analgesia (PCEA) has been demonstrated to provide a superior analgesia.<sup>38</sup> Local anaesthetic combined with an opioid is thought to be the superior drug combination. Epidurals are often used in high risk patients with the evidence supporting their use. Studies have shown that epidurals may have positive effects on some cardiac and pulmonary outcomes. However, this technique is not without its complications. Complications such as delayed respiratory depression can also occur. As many of these patients are cared for on the general wards, staff training needs to include an awareness of these potential problems.

### ***Extended-release epidural morphine***

The aim of current postoperative pain research is to find a medication that gives long-lasting pain relief at the site of surgical focus. One drug which is a step toward this analgesic goal administered is the extended-release epidural morphine (EREM) called DepoDur<sup>®</sup>. DepoDur<sup>™</sup> has been found to have duration of action up to 48 hours<sup>39, 40</sup> with long-lasting analgesia in the absence of large systemic concentrations of opioids as well as better patient activity levels. EREM is formulated for a one-time dose, given epidurally at the lumbar level. It has been evaluated in various surgeries including knee arthroplasty and Caesarean section. Several studies have shown that EREM produces long-term pain relief.<sup>41, 42</sup>

Side effects of EREM have been treated with opioid antagonists. Twelve to 12.5 percent of patients who received EREM required opioid antagonists. It has been stated that pruritis<sup>39</sup> and respiratory depression<sup>40</sup> were the primary causes for antagonist administration.

### ***Patient-controlled regional analgesia***

One of the most significant changes in surgical practice during the last two decades has been the growth of ambulatory surgery.<sup>43</sup> Adequate postoperative analgesia is a prerequisite for successful ambulatory surgery. Sending patients home with perineural, incisional, and intra-articular catheters is a new and evolving area of postoperative pain management. Current evidence suggests that these techniques are effective, feasible, and safe in the home environment if appropriate patient selection routines and organization for follow-up are in place.<sup>44</sup>

Patient-controlled regional analgesia (PCRA) encompasses a variety of techniques that provide effective postoperative pain relief without systemic exposure to opioids.<sup>44</sup> Using PCRA, patients control the application of pre-programmed doses of local anaesthetics, most frequently ropivacaine or bupivacaine (occasionally in combination with an opioid), via an indwelling catheter, which can be placed in different regions of the body depending upon the type of surgery. Infusions are controlled either by a staff-

programmed electronic pump (similar to that used for IV PCA) or a disposable elastomeric pump. An elastomeric pump is a device that has a distensible bulb inside a protective bulb with a built-in filling port, delivery tube, and bacterial filter.<sup>45</sup> Analgesia can be delivered directly into a surgical incision (incisional PCRA), intra-articular (IA) tissue (IA PCRA), or perineural site (perineural PCRA).

Other agents such as ketamine and gabapentin have been used with varied success. While ketamine may have a preventative analgesic effect and may improve analgesia in patients not responding to opioids, gabapentin is still being investigated for its role in postoperative pain management. An increased risk of sedation, dizziness and vomiting are some of the limitations in the use of gabapentin. Transdermal patches impregnated with fentanyl or clonidine has been used for mild to moderate pain.

### ***The challenges***

Many challenges are likely to come into play during the management of postoperative pain. One of such challenges is the inaccurate pain assessment. The best form of assessment is “self-report”. This is so because pain is a subjective experience and only the patient can correctly assess his or her pain. The patient in pain should always be encouraged to ask for relief. Reluctance to ask for pain relief could be due to being regarded as “nuisance” or to avoid disrupting busy nurses or for fear of side effects.

The prescribed pain relief agent may not be regularly administered as a result of busy schedule of the ward nurse, lack of appropriate skills by the attending nurse or sheer negligence of duty. There is varying evidence surrounding the benefits of preoperative education. It is also part of quality of care to ensure that patients received the information they need to make decisions and to participate in their recovery. Therefore patient education is an important part of perioperative care; however information needs to be clear and given in different formats both verbal and written and it is possible that the timing of such information being given may also be important.

Patients with chronic illness such as dementia, mental disability, and hearing disability accurate pain assessment or self-report of pain may not be reliable. Patients who are opioid-dependent may pose special problem in assessment of pain and administration of pain relief. A multidisciplinary approach with appropriate teams such as drug dependency units, general practitioners and pain teams is essential.

### ***The way to go***

Improving postoperative pain management is a complex multidisciplinary task. It is of essence to have the right knowledge and attitudes, adequate training, the use of pain management protocols and a pain team. The provision of procedure specific protocols, new methods to predict postoperative pain and new drugs and delivery systems are ways to improving pain management in postoperative patients.

Hospitals and the government should be directly involved in the provision of pain relief in postoperative patients. Management of postoperative pain is a shared responsibility by the government, hospital, the managing team and the patient. The government provides the resources; the hospital and the pain team utilize such resources while the patients ask for the pain relief.

### **Conclusion**

The management of acute postoperative pain is evolving, and recognition of acute pain has progressed from considering it an afterthought or nuisance to realizing that improperly or inadequately treated postoperative pain can have a number of adverse effects, including debilitating chronic pain syndromes. Inadequately treated pain is also contributing to the calamitous rise in addiction to illegal substances and prescription medications. The time has come to take responsibility and meet the expectations of the patients.

While many clinicians have been moving towards aggressive pain-management practice, hospital infrastructure has not kept pace with this trend. It is often ill-equipped to adequately monitor breathing patterns and to alert personnel to the need for rapid intervention. In the 21st century, there is a great need to respond to this challenge with a combination of tools and technology, including improved clinical assessment and monitoring equipment that has proven to save lives in the peri-operative setting.

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