

Role of pre-emptive analgesia in post operative Pain management - a review of literature

Rubina Yasmin¹, AKM Akhtaruzzaman², Sayed Akhter Khan³

¹Department of Anaesthesiology & ICU, Dhaka Medical College Hospital, , Dhaka, ²Dept. of Anaesthesia, Analgesia & Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, ³Department of Surgery, Dhaka Medical College Hospital, Dhaka

Corresponding Author: E-mail: milli@bol-online.com

(*JBSA, 2010; 23(2): 62-66*)

Introduction

Pain is not just a sensory modality but also an experience. The 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.”¹

Peripheral tissue injury provokes modification in the responsiveness of the neural circuit. Peripheral sensitization, a reduction in the threshold of nociceptive afferent peripheral terminal and central sensitization, an actively dependent increase in the excitability of spinal neurons; contributes together to post injury pain hypersensitivity state.²

Damaged tissue again produces two phases of sensory input. First, one is associated with tissue damaging stimulus i.e. during surgery. Second one results from inflammatory reaction to damaged tissue. Surgery produces local tissue damage with consequent release of analgesic substances like prostaglandins, histamine, serotonin, bradykinin, 5-HT, substance P and generation of noxious stimuli.³

Postoperative pain, which is a form of acute pain caused by noxious stimulation due to injury, is typically associated with neuro-endocrine stress response that is proportional to pain intensity.⁴ Physical response to injury and stress include pulmonary, cardiovascular, gastrointestinal, urinary dysfunction, neuro-endocrine and metabolic changes.⁵ Thus postoperative pain management is not only humane but also a key aspect of postoperative care.

Post Operative Pain

Postoperative pain is an acute pain, which starts with the surgical trauma and usually ends with

tissue healing. When the patient first awakes after surgery, the period of first ‘fast’ pain is over and the pain of which the patient initially becomes aware is the poorly localized ‘second’ pain. The pain is most severe when the patient first awakes after surgery. It is important during the first 24 to 48 hours. As time passes the pain gradually decreases in intensity. There are various factors, which can affect postoperative pain.

- i) Site and type of surgery- In general, thoracic and upper abdominal surgery produces greater pain than lower abdominal surgery which in turn is associated with greater pain than peripheral surgery.
- ii) The type of pain differs with different type of surgery. Operations on joints are associated with sharp pain; in contrast abdominal surgery is associated with two types of pain: a continuous dull nauseating ache (which responds well to morphine) and sharper pain induced by coughing and movements (which responds poorly to morphine). There is some evidence that minimally invasive, laparoscopic surgery produces less postoperative pain than do traditional techniques.⁶
- ii) Age, gender and body weight- The analgesic requirements of males and females are identical for similar type of surgery.

Psychological factors- The patient’s personality affects pain perception and response to analgesic drugs. Thus, patients with a low anxiety and low neuroticism score on a personality scale exhibit less postoperative pain and require small doses of opioid than patients who rate highly on scales extent of patient’s anxiety also affects pain perception, increased anxiety results in a greater degree of perceived postoperative pain and increased opioid requirements.⁷

Pathophysiology of Post Injury Pain Hypersensitivity

An important conceptual breakthrough in our understanding of pain has been the recognition that the pain we experience in our everyday lives when exposed to noxious stimuli, physiologic pain is qualitatively quite different from the clinical pain experienced after frank tissue or nerve injury has occurred.

Physiologic pain has a high threshold, is well localized and transient, and has a stimulus-response relationship similar to that of other somatosensations. Its fundamental role is to operate as a protective system, warning of contact with potentially damaging stimuli.

Clinical pain can be divided into inflammatory and neuropathic pain; the former refers to pain associated with peripheral tissue damage e.g. that produced during surgery and the latter refers to damage to the nervous system.

Preventing peripheral sensitization has been assumed to be the major action of NSAIDs by virtue of the inhibition of prostaglandin production by the inhibition of the enzyme cyclo-oxygenase⁸. The second mechanism is a change in the excitability of neurons in the spinal cord, triggered by and outlasting nociceptive afferent inputs. This is the phenomenon of central sensitization⁹.

Clinical pain differs from physiologic pain by the presence of pathologic hypersensitivity. The specific involvement of central sensitization in generating abnormal hypersensitivity in humans has been demonstrated in three different circumstances: 1 in volunteers after the application of the chemical irritants capsaicin or mustard oil, where after these intense but short-lasting noxious stimuli, low-threshold Ab mechano-receptors begin to produce pain¹⁰, 2 in patients in whom a reduction in nociceptive reflex excitability due to central changes has been demonstrated after abdominal surgery¹¹ and 3 in patients with neuropathic mechanical allodynia, where A-fiber blocks eliminate touch-evoked pain¹².

Postoperative Pain Management

Since the beginning of twentieth century, surgeons were aware of the importance of acute pain relief, particularly with regard to the affect of patients responses to injury on postoperative morbidity and

mortality¹³. Recently anaesthesiologist have become increasingly involved in the provision of postoperative analgesia and development of pain management services¹⁴.

Postoperative pain control is generally best managed by anaesthesiologist because¹⁵, they offer regional anaesthetic techniques as well as pharmacologic expertise in analgesics; they have adequate knowledge about pain pathways and their interruption.

Management of postoperative pain by anaesthesiologist can be professionally rewarding. Expression of gratitude from patient free from pain can contribute to feeling of self esteem and job satisfaction. Additional contact with patients, nurses, other physicians and the administration in the postoperative period helps to define anaesthesiologists as valued consultants outside the operation theatre.

Prevention of Postoperative Pain

In addition to humanitarian reasons for improving acute postoperative pain treatment, there is now convincing evidence that unrelieved acute pain may result in harmful physiological and psychological effects. These adverse effects may result in significant morbidity and mortality¹⁵. Evidence of shortened hospital stay, decreased morbidity and mortality and increased patient satisfaction have been reported in association with effective relief of pain. Thus adequate and appropriate management of postoperative pain is a demand of time.

Recent editorials and reviews have emphasized the importance of preventing pain as a more effective treatment of postoperative pain and for prevention of persistent pain syndromes¹⁷. In a recent editorial, Armitage encouraged anaesthesiologist to make changes in thought and terminology so that pain management is preemptive rather than retrospective. He suggests abolishing the use of the term pain relief in the context of postoperative analgesia and recommends that analgesia techniques should be targeted at prevention of pain rather than relief of pain¹⁸.

The Need For a New Approach for The Treatment of Postoperative Pain

For the treatment of postoperative pain the conventional of prescribing intermittent doses of

analgesics in response to patients demand is often ineffective¹⁹. Breakthrough pain is accepted as normal by many patients, doctors and nurses after surgical procedures²⁰. This strategy is now beginning to be recognized as constituting sub-optimal management and more resources are being devoted to acute pain services, including the development of continuous epidural analgesics administration and patient controlled analgesia (PCA). One strategy for preventing abnormal sensitivity postoperatively could be to prevent or minimize the activation of central neurons by the barrage of afferent activity necessarily evoked during surgery by a preintraoperative treatment. This led to the concept of preemptive analgesia.

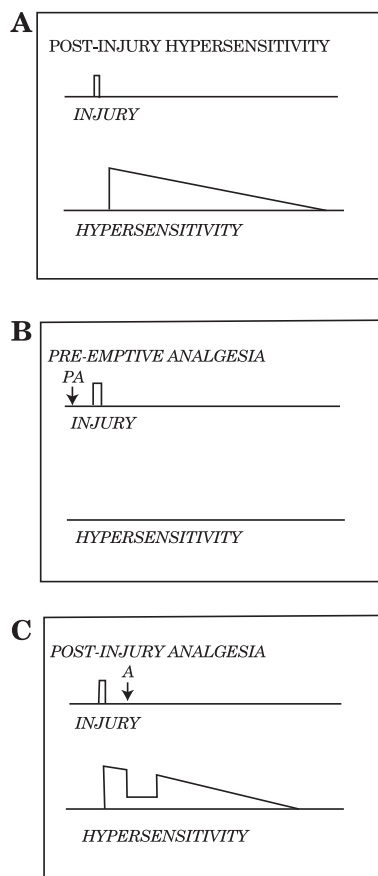


Fig 1 Models of preemptive analgesia

Models of Pre-emptive Analgesia

[A simple model of the rationale behind single treatment pre-emptive analgesia. Injury triggers central sensitization, leading to a prolonged hypersensitivity state. A pre-emptive analgesia (PA) prevents the induction of central sensitization pre-empting the post injury hypersensitivity.

Post injury analgesia (A) has a much diminished effect on established state of hyperexcitability.]

Figure-1 illustrates a simple model of post injury hypersensitivity. A transient injury initiates central sensitization as a result of excitability increases triggered in spinal neurons by the nociceptors activated by the injurious stimulus. This leads to a hypersensitivity state that outlasts the duration of the injury. Preemptive treatment, i.e., regional local anesthetics at the site of the injury, will prevent the establishment of the hypersensitivity by blocking the sensory input that induces the central sensitization. Post injury regional anesthesia will have a reduced effect because the central sensitization has already been established. This sort of analysis has provided the theoretical basis for a number of recent clinical trials that have investigated the efficacy of particular preemptive treatments for managing postoperative pain.

Pre-emptive analgesia treating postoperative pain:

Preemptive treatment could be directed at the periphery, at inputs along sensory axons and at central neurons by non-steroidal anti-inflammatory drugs (NSAIDs), local anaesthetics and opioids either alone or in combination. The underlying principle is that therapeutic intervention is made in advance of the pain rather than in reaction to it.

Pre-emptive analgesia is an antinociceptive treatment that prevents establishment of altered central processing of afferent input from sites of injury²¹. The most important conditions for establishment of effective pre-emptive analgesia are the establishment of an effective level of antinociception before injury and the continuation of this effective analgesic level well into the post injury period to prevent central sensitization during the inflammatory phase. Surgery offers the most promising setting for preemptive analgesia because the timing of noxious stimuli is known²².

Preemptive analgesia may damp down the development of both immediate and long term pain following surgery and adequate psychological preparation can improve coping abilities. The delivery of opioid analgesics can be improved using patient control analgesia (PCA)²³. The result of

the use of preemptive analgesia with different research workers is not always consistent, often conflicting even negative and contrary results were obtained. The concept of pre-emptive analgesia was formulated by Crile at the beginning of previous century on the basis of clinical observation²⁴. Later revival of this idea was associated with a series of animal studies started by Woolf^{25,26}.

Richmond-CE, in a randomized double blind study, they compared the effect of parenteral morphine when given before or after TAH in 60 patients. 10 mg of morphine were given I.M. 1 hour before operation, intravenously at induction of anaesthesia, intravenously at closure of the peritoneum (Iv, Post). They concluded that preemptive analgesia with intravenous morphine by preventing the establishment of central sensitization during surgery, reduces postoperative pain, analgesic requirements and secondary hyperalgesia²⁷.

Elhakim et al. were no significant differences between pre and postoperative lidocaine groups in pain scores during the observation period but use of preoperative lidocaine tended to be associated with a more rapid return to calm wakefulness.

Dahl-V; et al wanted to see the preemptive effect of pre-incisional versus post incisional infiltration of local anaesthetics on children undergoing hernioplasty. The results they published said- pre incisional group needed significantly less halothane during the procedure compared with the post incisional group ($p < 0.05$). The pre incisional group also had a tendency towards faster awakening after the end of anaesthesia and a significantly lower OPS pain score 30 mins. after the operation ($p < 0.03$). They concluded that perioperative infiltration with a local anaesthetic in children undergoing hernioplasty results in a smooth recovery with little need for opioids postoperatively.

Wong-CS; et al in 1997 showed that Epidural Ketamine plus morphine with lidocaine before surgical incision produced better pain relief and patient satisfaction than when after incision²⁸.

Fisher et al. a in prospective double blind randomized study on new regimen of preemptive analgesia for inguinal hernia repair; evaluation of postoperative pain consequently concluded that,

this regimen of preemptive analgesia is an effective method of reducing postoperative pain and analgesic consumption after inguinal hernia repair.

Thus we see although promising in experimental studies of post traumatic pain, the concept of preemptive analgesia is still controversial in a clinical setting. Some advocate extending the preemptive treatment well into postoperative period using balanced, multimodal analgesia which may prolong the initial advantage conferred by the preoperative blockade and possibly interfere with the development of long lasting pain.

The traditional management of postoperative pain comprises a standard dose of an opioid to be given on demand by a nurse when the patient's pain threshold has been exceeded, this leads to poor control of postoperative pain. So it is crucial to emphasize the importance of giving analgesics preemptively 'by the clock' instead of waiting for the patient to complain of pain.

References

1. Marskey H, Able Fessard DG, Bonica JJ et al, Pain terms. A list with definitions and notes on usage. Pain 1979; 6:249
2. Clifford J woolf, Mun-Sengchong. Pre-emptive analgesia – Treating postoperative pain by preventing the establishment of central sensitization Anaesthesia Analgesia 1993; 77: 362-79
3. Miller D Ronald, Anaesthesia, Third edition, Acute postoperative pain, page 2135-36
4. Cousins MJ. Acute Pain and the injury response; immediate and prolonged effects, Regional Anaesthesia 1989;14: 162-178
5. Miller D.Ronald, Anaesthesia, Third edition, Acute postoperative pain, Page-2137
6. I. Power, G. Smith; Postoperative pain, In Alan R. Aitkenhead, David J. Rowbotham, Graham Smith, Text book of Anaesthesia, 4th Edition 2001, page-544-545
7. I. Power, G. Smith; Postoperative pain, In Alan R. Aitkenhead, David J. Rowbotham, Graham Smith, Text book of Anaesthesia, 4th Edition 2001, page-545

8. Dahl JB, Kehlet H, Non-steroidal inflammatory drugs. Rationale for use in severe post-operative pain. *Br J Anaesth* 1991; 66:703-12.
9. Lamotte RH, Shaine CN, Simon DA, Tsai EFP, Neurogenic hyperalgesia: Psychological studies of underlying mechanism. *J Neurophysiology* 1991.
10. Torebjork HE, Lundberg LER, la Motte RH, Central changes in processing of mechanoreceptive input in capsaicin-induced secondary hyperalgesia in humans. *J. Physiology* 1992; 448: 765-80.
11. Dahl JB, Ericson CJ, Fugslang – Frederiksen A, Kehlet H. pain sensation and nociceptive reflex excitability in surgical patients and human volunteers. *Br J Anaesth* 1992; 69: 117-21.
12. Campbell JN, Raja SN, Meyer RA, Mackinnon SE. Myelinated afferent signal the hyperalgesia associated with nerve injury. *Pain* 1989;36:89-94.
13. Crile GW, Lower WE. Anoci –association, Philadelphia; WB Saunders, 1994; 222-225.
14. Ready LB, Oden R, Chadwick HS, et.al. Development of an anaesthesiology based postoperative pain service. *Anaesthesiology* 1988;68:100-6.
15. Miller D Ronald, *Anaesthesia*, Churchill Livingstone 3rd edition. Vol.2; Page-2142-43.
16. Yenger et.al. 1987; Kehlet 1988; Scott Kehlet 1988, Cousins 1989.
17. Wall PD; The Prevention of postoperative pain, *Pain* 1988; 33: 289-290.
18. Armitage EN. Postoperative pain – prevention or relief? *Br J Anaesth* 1989; 63: 136-137.
19. Kuhn A, Cooke K, Collins M, et.al. Perception of pain relief after surgery. *Br. Med. J.* 1990;300: 1687-90
20. Lavies N, Hart L, Rouseffell B, Roncimann W. Identification of patient, medical and nursing staff attitudes to post-operative opioid analgesia: stage 1 of a longitudinal study of postoperative pain, *Pain* 1992;18:313-9
21. Kelly, Dermot J, Ahmad, Mahmood, Brull, Sorin J. Preemptive Analgesia; recent advances & current trends. *Canadian Journal of Anaesthesia. D&C.* 2001; 48: 1091-1101
22. Allan Gottschalk, John Hopkins, David S Smith. *New concepts in Acute pain therapy; Pre-emptive analgesia; American Family physician*, 2001; 10: 1979-83
23. Justins –DM; Richandron – PH. Clinical management of acute pain. *Br Med Bull* 1991; 47: 561-83
24. Crile GW; The Kinetic theory of Shock and its presentation through anoci-association; *Lancet* 1913; 185: 7-16
25. Woolf CJ; Evidence for a central component of post-injury pain hypersensitivity. *Nature*, 1983; 308: 686-8
26. Clifford J. Woolf, pre-emptive analgesia – treating postoperative pain. *Anaesth, analgesia* 1993; 362-68
27. Richmond CE, Bromley LM, Woolf CJ. Preoperative morphine preempts postoperative pain, *ancet* 1993; 10: 13-5.
28. Wong CS, LU CC, Chheng CH, HO ST. Preemptive analgesia with ketamine, morphine and epidural lidocaine prior to total knee replacement. *Can J Anaesth* 1997; 44: 31-7