

Anesthetic Concerns in Patients Receiving Preoperative Opioids: a Review

Gupta N^{1*}, Gupta A², Garg R¹ and Kumar V¹

¹Department of Onco Anesthesia and Palliative Medicine, DRBRAIRCH, AIIMS, India

²Department of Anesthesia, Chacha Nehru Bal Chikitsalya, India

***Corresponding author:** Nishkarsh Gupta, Assistant Professor, Department of Onco Anesthesia and Palliative Medicine, DRBRAIRCH, AIIMS, New Delhi, Email: drnishkarsh@rediffmail.com

Mini review

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Introduction

Patients suffering from cancer or non cancer pain syndromes are frequently receiving opioids for pain management in the preoperative period [1,2]. Anesthesiologist commonly encounters patients on chronic opioids medication for surgery and has to manage behavioral, psychological and pharmacological aspects. It is important for anesthesiologist to know about effects and management of chronic opioids therapy because opioids are an important component of postoperative pain therapy, an adequate opioids dose in the perioperative period should be maintained to prevent opioids withdrawal and it can be challenging to revert to preoperative opioids regimen after surgery [1].

In one of the surveys, 67% of orthopedic patients and 25% of general surgical patients were receiving long term opioids treatment [3]. The patients with cancer on chronic opioids therapy (daily oral morphine dose 90 to 360 mg) often require 3-4 times morphine given via a continuous epidural infusion or intermittent intravenous bolus for breakthrough pain after surgery compared with opioids-naïve patients. Rapp *et al.* [4] have also reported a 3-fold greater postoperative opioid requirement in chronically opioids-consuming patients [4]. In addition, regular administration of strong opioids like morphine leads to side effects like nausea, constipation, sedation and respiratory depression. In addition these patients may have opioid induced dependence (physical/psychological), addiction and hyperalgesia and need to be managed carefully in the perioperative period [1,2].

A patient on chronic opioid therapy may develop behavioral changes like loss of control over use,

compulsive use, continued use despite causing harm and craving [2,5].

Patients may also be physically dependent on the drug and show symptoms on withdrawal due to fall in plasma levels and decreased receptor occupancy. This may be due to sudden Withdrawal of drug, rapid reduction of dose or administration of an antagonist. In the perioperative period if inability to maintain baseline opioid consumption may precipitate withdrawal.

In addition patients develop tolerance and may require greater dose of opioid to achieve the same analgesic effect [6,7]. The degree of tolerance depends upon duration and amount of opioid exposure and receptor kinetics. It may occur due to learned compensatory mechanisms in individuals (learned), altered distribution and metabolism of drug (pharmacokinetic) and decrease in number of opioid receptors (pharmacodynamic). Opioids are metabolized by cytochrome P450 which can be induced by barbiturates and antiepileptic drugs [6]. Chronic exposure of such drugs can increase opioid metabolism and cause tolerance.

Also, chronic administration of opioid may paradoxically increase sensitivity to painful and non-painful stimuli. This occurs due to neurochemical changes in the central nervous system by neuropeptides to restore equilibrium in response to increased anti-nociceptive activation by opioid administration [7]. This is typically seen after rapid dose escalation of opioids and responds to a reduction in opioid dose.

Prolonged opioid usage in preoperative period may affect the immune function, by inhibit Tcell and macrophage activity, and can result in adrenocortical

suppression. These may affect the surgical outcome and cancer recurrence and is discussed in detail in other part of this chapter [7,8].

Peri-operative Management

In patients on long-term opioids, it is essential to identify relevant problems and formulate an appropriate management plan. At present, no data or guidelines are available to predict individual postoperative opioid requirements based on preoperative opioid dose.

Key Factors in Pre-operative Assessment of patient on strong opioids

These patients may be anxious and need to be educated, counselled and reassured.

- A detailed history must be taken to get the correct preoperative opioid usage. Some patients may be abusing the opioid drugs and it may be difficult to ascertain the correct opioid doses.
- Baseline pain assessment should be done to monitor the signs of withdrawal.
- Patients requiring >30mg intravenous morphine equivalent per day for over 1 month may develop tolerance.
- Regular doses of opioid and other adjuvant analgesics need to be continued on morning of surgery.
- Patients requirements may increase up to 4 times the baseline in the postoperative period and analgesia may be required for a longer period.
- A dosing less than required may precipitate withdrawal and may be difficult to diagnose in the perioperative period.
- In case oral route is not possible, an alternative drug/ route (IV, transdermal or epidural) route may be utilised after calculating equivalent dosing
- No single anaesthetic technique can be prescribed to such patients. The anaesthetic technique need to be individualised depending on surgical and patient factors.
- Regional anaesthesia alone or with general anaesthesia improves tissue perfusion and reduces opioid requirement

- Even central opioid receptors are reduced in such patients and an increased dose of the opioids are required from central neuraxial route. Moreover, an additional oral/parenteral administration may be required for satisfactory pain relief [9,10].

Other Strategies

Patient controlled analgesia

The use of patient controlled analgesia (PCA) can be a good alternative for customized dosing above background opioid therapy in such patients. Depending upon pre-existing patient's requirement a large bolus on demand may be set and adjusted to effect on an individual basis [10,11]. This will allow autonomy to the patient and requirement can be reassessed to titrate the effect further.

Regional blocks

Analgesia can be supplemented by local anaesthetics with adjuvant given through peripheral/ central neuraxial blocks [11,12]. The common blocks that may be used in once surgeries are mentioned in the table.

S.no	Surgery	Block
1	Head and Neck	Maxillary and mandibular nerve block
2	Thyroid surgery	Superficial and deep cervical nerve block
3	Thoracic, breast	Epidural, par vertebral
4	Abdominal	Epidural, TAP block

Multimodal analgesia

In immediate postoperative period nociceptive pain has multiple mechanisms and addition of other analgesics may provide benefit [13].

- Opioid rotation:** patients exhibit inter individual variation in response to different opioids and instead of rapidly escalating the doses of opioids, switching to an alternative strong opioids in equianalgesic doses may be beneficial. This opioid rotation improves pain relief in up to 50% of patients.
- Ketamine:** is NMDA receptor antagonist and helps in reversing opioid tolerance. It may be given as a

continuous infusion (5-15 mg/hr) in the immediate pre-operative period and continued for 24-48 hours post-operatively [14,15]. Patients on Ketamine should be monitored for hallucinations (50% incidence) and other vital parameters on regular basis.

- c) Clonidine is an agonist at the Alpha-2 adrenoceptor. It augments the effects of opioid drugs, decreases opioid withdrawal reactions and reduces the neurohumeral stress response to surgery. It may be given by the intravenous or epidural route in the dose of 1-2 mcg/kg peri-operatively to enhance analgesia.
- d) Paracetamol and NSAID's are simple analgesics and have significant opioid sparing effects. In absence of any contra-indications, all patients should receive them in the immediate postoperative period [13].
- e) Gabapentin is an anticonvulsant that acts upon the $\alpha 2\delta$ subunit of calcium channels and at the GABAB receptor. Gabapentin in doses of either 600 or 900mg pre-operatively reduces morphine requirements and its side-effects such as nausea and vomiting in the post-operative period.

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