Editorial

Opioid-free anaesthesia: The conundrum and the solutions

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The widespread recognition of the need for pain management and the subsequent surge in opioid prescriptions, in the late 18th and early 19th century, led to a global opioid epidemic. This movement, which was also backed by the pharmaceutical industry, resulted in the opioid use disorder and a significant number of patient deaths due to opioid overdose.[1] This opioid crisis provoked the medical fraternity and anaesthesiologists to revisit pain management strategies which reduce or eliminate the use of opioids and still provide effective pain relief. In India, there is a non-availability of potent opioids at many places and opioids are generally not administered in the wards of tertiary care hospitals. In fact, the concept of opioid-free anaesthesia is advantageous in private practice in India.

'Opioid-Free Anaesthesia' (OFA) is a technique where the intra-operative use of systemic, neuraxial or intracavitary opioid is completely eliminated. In 'Opioid Sparing Anaesthesia' (OSA) techniques, small amount of opioids can be used as a component of multimodal regimen.[1,2] Restricting opioid use in anaesthesia has shown variable effectiveness in different surgeries and patient population.[3-6] Whereas on one hand, the opioid consumption is reduced intraoperatively, effective nociception and reduction in postoperative opioid consumption is still under investigation with OFA/OSA.[7] Number of alternate analgesics and analgesic adjuncts are usually employed to replace or reduce perioperative opioids. The merits of these alternate pain management tools have been questioned due to cost escalation and variable responses.[7,8]

The spectrum of OFA/OSA can be of prime utility in patients at high risk of opioid-related respiratory complications such as patients with obstructive sleep apnoea, patients posted for bariatric surgeries and patients with pulmonary limitations including obstructive airway diseases. OFA/OSA also offers particular advantages in opioid tolerant patients such as patients with chronic pain, cancer-related pain and patients suffering from opioid addiction.[9] It has also been observed that the chronic use of opioids as in cancer patients further compromises the immune system by decreasing the progenitor cells of lymphocytes and macrophages. They also suppress T cell–mediated immunity.[10] This immunomodulation by opioids also justifies the need of OFA/OSA in oncological illness.

The commonly used armamentarium of non-opioid analgesics includes local anaesthetics, clonidine, dexmedetomidine, ketamine, gabapentin, magnesium sulphate and dexamethasone. Although many of these have shown acceptable results in maintaining anti-nociception, their use is guided and limited by the associated side effects.[2] Nevertheless, these drugs in sub-anaesthetic doses or as an adjunct for OSA can

achieve the desired results. These drugs are not new in clinical pharmacology but their roles are now refined with the advancement of safe and effective monitoring and drug dispensing vehicles.

Dexmedetomidine is in clinical practice since 1999 [United States Food and Drug Administration (FDA) approved for short-term sedation in intensive care units]. This wonder drug labelled as an anti-anxiety, sedative-analgesic drug of the 21st century in both paediatric and adult anaesthesia, has replaced perioperative opioid utilisation to a large extent.[11] The spectrum has further widened to include labour analgesia, preeclampsia and neuraxial analgesia in the parturient, with negligible effects on foetal APGAR scores and well-being.[12] In children, dexmedetomidine is used perioperatively as a pre-medicant, analgesic and adjunct for airway procedures. It effectively prevents emergence agitation and postoperative nausea vomiting, a well-known complication of opioid-based anaesthesia.

Ketamine is another remarkable drug (the oldest OFA drug), which has resurfaced after a dark period. The traditional uses of ketamine were limited as an induction agent and as an analgesic for burns dressings. However, the resurgence of ketamine has limited the use of opioids in more than one way. Ketamine is now the preferred drug in many procedures like sedation for magnetic resonance imaging, premedication in children, procedural sedation and acute and chronic pain management.[13] The newly found revolutionary role in posttraumatic stress disorders and anti-depressant effect in chronic illnesses has further consolidated its place as a soldier in the opioid-free world.[14]

The blending of ketamine and dexmedetomidine as a combination has opened a new dimension in the field of OFA, the concept being that the weakness of one becomes the strength of the other. A combination of a small dose of ketamine and dexmedetomidine provides effective analgesia, moderate sedation and haemodynamic stability without postoperative hallucinations.[15] The risk of postoperative sore throat is decreased as well, as an additional advantage.[16]

Gabapentin although approved in 1993 (FDA approval for seizures), lately found for itself in the 21st century, a unique role in the management of postoperative pain, chronic pain and pain related to diabetic neuropathy.[17] Both the gabapentinoids, pregabalin and gabapentin, have been tried as preemptive analgesics and as a part of multi-modal analgesia regimens. In a randomised controlled trial being published in this issue of the Indian Journal of Anaesthesia (IJA), the authors have evaluated the postoperative morphine-sparing effect of oral premedicants such as tramadol and pregabalin when used as preemptive analgesics in breast-conserving cancer surgeries. They found that oral premedication with either tramadol 100 mg or pregabalin 75 mg reduced the 24 hours postoperative morphine requirement as compared to placebo. However, tramadol was associated with more side effects.[18]

Magnesium sulphate, another adjunct from the opioid-free tool kit, has been found promising in attenuating perioperative pain and in blunting somatic, autonomic and endocrine reflexes provoked by noxious stimuli. Many researchers also reported that it reduces the requirement for anaesthetics and/or muscle relaxants and can effectively reduce opioid consumption in the first 24 h postoperatively.

Dexamethasone reduces post-operative nausea vomiting, reduces postoperative pain and inflammation. It has an opioid sparing effect and also significantly improves QoR-40 scoring systems.[1] Dexamethasone has been shown to enhance and prolong regional analgesia when administered either perineurally or intravenously.

Regional anaesthesia and nerve blocks add another very significant dimension in OFA. Regional anaesthesia has become more effective with the advent of ultrasound.[19,20] The duration of analgesia of local anaesthetics in regional anaesthesia can be sufficiently prolonged by adjunct drugs such as clonidine, dexmedetomidine and dexamethasone, with minimal side effects. The prolongation of analgesia spares post-operative opioid use as well.[21-23] Regional anaesthesia reduces central sensitisation and improves long-term pain outcomes.[1]

Opioid misuse has always been a major concern. More harm is done with opioids than their utility due to addiction on continuous use. However, there are many ways by which anaesthesiologists, surgeons and intensivists can limit opioid exposure and minimise patient harm.[24] Enhanced recovery after surgery (ERAS) protocol forms a feasible guide to

implement OFA or OSA. It uses multimodal analgesia mainly involving non-opioid analgesics and regional anaesthetic techniques. The success of ERAS depends on the right combination of multimodal analgesia methods with minimal postoperative nausea, vomiting and early mobilisation in the postoperative period. Although ERAS is a well-accepted global initiative, the critical challenge in low and middle income countries is inadequate scientific evidences limiting its utility and the implementation of opioid-free protocols without escalating the cost of treatment.[25]

It is premature to conclude that opioids can be completely eliminated from anaesthesia practice, especially when they are the primary drug in intravenous patient controlled analgesia where fast onset of action and predictable duration give them a distinct advantage over OFA. The non-opioid analgesics are limited in their use by the spectrum of their side effects and effects on various organ systems. Haemodynamic instability and sedation with α-2 receptor agonists, muscle relaxation and respiratory depression with magnesium sulphate, hallucinations and delirium with ketamine, nephrotoxicity with non–steroidal inflammatory drugs (NSAIDs), hepatotoxicity with paracetamol, sedation with gabapentin, hyperglycaemia with dexamethasone, to name a few. NSAIDs and paracetamol are additionally limited by their maximum daily safe dose. The ideal pain management goal should be to provide maximal patient benefit by ensuring effective pain relief using multimodal pain management techniques and reduction in opioid use. Nevertheless, in a study published in a recent issue of the IJA, multimodal anaesthesia technique was used and it was observed that opioid-free anaesthesia along with fascial plane block provides better post-operative pain relief when compared to conventional opioid anaesthesia.[26]

There is a learning curve in the administration and monitoring of effective OFA. More evidence is required on the use of different drugs in OFA regimen and their indications in specific surgeries and the optimal timing of administration. Current barriers for an effective OFA are resistance to change, cost of opioid-free therapy, need for more research and evidence-based practice and lack of training along with well-defined guidelines. The journey of OFA/OSA has already begun and we can reach the finishing line only by detailed analysis of its benefits and limitations. The dictum must be remembered: *Change happens for good.* So, we have to anticipate the change, monitor the change and adapt to change with a zeal to change again for scientific advancement. Nevertheless, OFA/OSA is an exciting field for growth in research and the anaesthesia community!

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