EDITORIAL VIEW

What is new in postoperative analgesia after caesarean sections?

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SUMMARY

The rate of Caesarean sections is on an increase and with it an increased awareness among the mothers to remain pain free during and after the surgery. This has put anesthesiologists to explore possibilities and options other than the routine methods of surgical analgesia. The cons and pros of using opioids, NSAID's, nerve blocks and regional techniques, all have been scrutinized and the associated disadvantages and side effects discussed.

Key words: Caesarean section; Postoperative pain; Opioids; Adjuvant medications

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Caesarean section (CS) commonly induces moderate to severe pain for 48 hours.[1] The aims of postoperative pain treatment are to provide subjective comfort, inhibit nociceptive impulses and blunt the neuro-endocrine response to pain thus enhancing the restoration of function.[2]

CS patients have additional compelling reasons to provide adequate pain relief, as early mobilization is a key factor to prevent the risk of thrombo-embolic disease, which is increased during pregnancy. Besides these patients need to be pain free to care for their newborn and breastfeed them effectively.

Role of Opioids: Historically opioids are most commonly administered analgesia for postoperative CS pain management. They are used both systemically and neuraxially for postoperative analgesia. *Systemic administration* is mostly used after general anaesthesia and in places where there is unavailability of long acting preservative free opioids or lack of expertise in its usage. Systemic routes for opioids administration are intramuscular and intravenous, given either intermittently, on demand basis or by intravenous continuous method.

These methods do not take into account the very large variability of the responses of patients, and are all dependent upon the interpretation of nurses and prescription by physicians. Recently Landau[3] tried to individualize anaesthestic care during caesarean section by identifying some genetic polymorphisms. He concluded that "genetic test" might become a useful bedside screening tool to predict the development of chronic pain and to individualize postoperative pain therapy.

The limitation of individual patient's variability and fluctuating blood level of analgesic is overcome to some extent by the use of patient controlled intravenous analgesia (IV-PCA). Pain relief with IV-PCA has shown to be superior to conventional intramuscular opioids for women having had a caesarean section.[4] In one of our randomized controlled trial of intravenous patient controlled analgesia (IV-PCA) with continuous opioid infusion (in press) in post caesarean section patients, we found better pain score at 6, 12 and 24 hours postoperatively, less need for rescue analgesia and better pain satisfaction. Patients' own control over their pain management may have allowed them to obtain an opioid bolus at the initial feeling of pain, without having to wait for the nurses and doctors to provide analgesia. This has resulted in overall improved analgesia. Despite being less efficacious than neuraxial administration, patient satisfaction scores are highest with IV-PCA.[5,6]

It has been almost 32 years since *Neuraxial opioids* first underwent rigorous clinical study for use in

humans.[7] Several large reviews indicate that the neuraxial approach provide superior analgesia over systemic administration.[5] Preservative-free morphine is perhaps the most popular adjuvant administered either intrathecally or epidurally in many countries. It provides proven and significantly prolonged postoperative analgesia with a reduction in postoperative analgesic requirement. A meta-analysis of intrathecal opioid studies revealed that intrathecal morphine (0.1-0.2 mg) provided optimal analgesia with a median time to first request for supplemental analgesia of 27 hours (range 11-29 hours), in addition to reducing pain scores and the amount of supplemental analgesics needed for 24 hours postoperatively.[8]

Other opioids like fentanyl, sufentanil, diamorphine, hydromorphone, meperidine, buprenorphine and nalbuphine have been administered neuraxially for postoperative analgesia but more rarely.

Limitation to the use of opioids: Pain, pruritus, nausea/vomiting, sedation and respiratory depression are concerning issues that complicate postoperative opioid usage. The incidence of respiratory depression is not known but is probably low.[9,10] Nevertheless, frequent monitoring of vital signs and/or respiratory pattern is important to prevent such rare mishaps.

These limitations have led to the introduction of use of **multimodal analgesia** in the form of:

- Co-analgesic/ adjuvant drugs.
- Nerve block and wound infiltration

The goal is to obtain synergistic or additive analgesia with fewer side effects by combining lesser amounts of each drug with different mechanisms of action. The anti-inflammatory and antipyretic properties of non-steroidal anti-inflammatory drugs (NSAIDs) may reduce visceral pain originating from the uterus, complementing the somatic wound pain relief from the opioid. The addition of NSAIDs has been shown to potentiate opioid effect, decrease opioid consumption and reduce side effects when systemic or neuraxial opioids are administered for post cesarean delivery analgesia.[10,11] NSAIDs must be used with caution because of the potential problems with bleeding, platelet dysfunction and renal insufficiency although practice varies widely in this matter. A systematic review of 36 studies on 3362 patients comparing efficacy of adding acetaminophen (paracetamol) or its precursor, NSAIDs or their combinations to postoperative opioid pain management suggests acetaminophen is a useful alternative with low incidence of adverse effects and with mostly similar or slightly less efficacy (depending on types of surgery) compared to NSAIDs. However, the data on enhanced analgesic efficacy, if any, from adding acetaminophen to NSAIDs require further investigation especially on the potential increase of side effects from their combined use.[12] A randomized, double blind controlled trial[13] comparing the postoperative analgesic effects of IV acetaminophen with those of oral ibuprofen in patients receiving IV-PCA after CS showed equal analgesic profile to oral ibuprofen and therefore can be used in patients where NSAIDs are contraindicated.

A newer COX-2 inhibitor, (parecoxib) was compared with ketorolac combined with morphine on IV-PCA in post CS pain management.[14] It was found to have efficacy-equating ketorolac with PCA morphine for an opioid sparing effect. Preoperative gabapentin 600mg in the setting of multimodal analgesia reduces post CS pain and increase maternal satisfaction but 19% of the patient had severe sedation as compared to 0% in the controlled group but there was no difference in the Apgar score or umbilical artery pH.[15]

A number of clinical studies have examined the effects of other **adjuvant medications administered neuraxially** for enhancing postoperative analgesia, but each has been associated with various degrees of side effects. Use of neuraxial neostigmine is limited by its high incidence of prolonged motor blockade, nausea and vomiting even with spinal doses as low as 6.25 μg.[16] Clinical studies with the use of neuraxial clonidine (a Lipophilic α_2-adrenergic agonist), when combined with an opioid prolongs analgesia, reduce opioid consumption and decrease shivering, but hypotension, dose-dependent sedation, bradycardia, prolonged motor blockade and perioperative vomiting are common side effects occurring in similar frequency in women after cesarean delivery as in other post surgical populations.[17] Besides the high cost of clonidine in the US, it also carries an FDA "black box" warning against neuraxial use in obstetrical, postpartum and perioperative pain management because of its potential hemodynamic side effects.

Dexmedetomidine, also a α_2-adrenergic agonist approved only for intravenous use, has similar side effects as clonidine and there is limited information on neonatal effect and postpartum or post cesarean delivery usage. Clinical data are too limited in obstetrical and postpartum populations to offer meaningful clinical recommendations on some of the potentially useful agents currently under investigation such as the N-methyl-D-aspartate (NMDA) receptor antagonist dextromethorphan, the anticonvulsant gabapentin and the cycloxygenase inhibitor Ketorolac

given intrathecally.

The NICE guidelines for cesarean sections suggest that wound infiltration and/or ilioinguinal nerve block are viable alternatives to systemic analgesia.[18] Ranta et al. report the subfascial catheter administration of levobupivacaine following cesarean delivery to be a useful and safe component of multimodal pain management and a viable alternative to epidural analgesia.[19] The improvement in modern elastometric balloon pump design also enables the ease of application for wound analgesic infiltration technique without hindering ambulation or caring for the newborn. Ranta and her colleagues' results are encouraging and provide support for such an adjuvant modality in postoperative analgesia, especially in women undergoing general anesthesia for caesarean delivery.[19] The Cochrane database of 2009 indicates that local analgesia infiltration and abdominal nerve block as adjunct to regional analgesia and general anaesthesia are of benefit in caesarean section by reducing opioid consumption.[20]

Transversus Abdominis Plane (TAP) block was first described in 2001 by Dr Rafi[21] and was further developed and tested by McDonnell et al.[22] It involves peripheral block of the anterior abdominal wall. A meta-analysis[23] to study the efficacy of TAP block shows that it reduces the need for postoperative opioid, the time for first request for further analgesia, provides more effective pain relief and reduces opioid associated side effects. However there are conflicting results of TAP block in two studies done on post CS patients. [24,25] Both studies have used ultrasound-guided technique for TAP block. Costello et al[24] have used it, as part of multimodal analgesia along with long acting intrathecal opioid did not find any improved quality of analgesia for post CS patients. Similarly one study[26] comparing intrathecal morphine with TAP block showed superior analgesia with intrathecal morphine but more side effects compared to TAP block group. However Belavy et al[25] using TAP block as a part of multimodal analgesia with long acting opioid and using IV-PCA morphine postoperatively, showed improved pain score, higher patient satisfaction score and opioid-sparing effect and reduced use of antiemetic in women undergoing CS. Therefore TAP block can be a better option for patients not receiving long acting neuraxial opioids.

Have we reached the standard?: Noblet and Plaat have raised an interesting point about the unachievable standard suggested by the Royal College of Anaesthetists (RCoA).[27,28] The standard suggests that >90% of women should score their worst pain as <3 on VAS of 0-10. We did an audit in our unit and found that 39.8% of women had VAS score of >3. A literature search revealed that we are not the only one failing this target.[27,29,30] The result of these studies and our results showed a patient satisfaction of >90%. Therefore, this raises the question of the need to reconsider pain relief and its assessment in CS patient.

Developing countries face another challenge of limited supply of opioids, lack of long acting intrathecal preservative free narcotic and expertise for its use. In our observational study on the technique of anaesthesia (in press), we determined that general anaesthesia is still used in 49% of cases and in another study (in press) we determined that continuous opioid infusion was the most common method of postoperative analgesia after CS in our institution and pethidine was the most common opioid used. One study done in rural health district of South Africa[31] has shown pethidine (69%) as the most common opioid prescribed after CS and intramuscular route was the only route of administration.

CONCLUSION

Women having CS presents a unique set of problems to the anaesthetist and requires optimal pain management. We need to explore the possibility to establish standard pain relief methods; the choice should be determined by drug availability, resource limitations and financial consideration.

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