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Review Article

A Review of Modalities of Pain Relief Post Caesarean Section

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Abstract

Caesarean section (CS) is one of the most commonly performed surgical procedure and post-operative pain is an important issue for women. Pain is multifactorial, and the experience of pain is subjective, with significant inter-person variability. The provision of effective post-operative pain relief is vital to facilitate early ambulation, ensure infant care and bonding, effective breast feeding and for prevention of post-operative morbidity. An ideal method of pain relief after CS should be cost effective, safe for the mother, require minimal monitoring and use drugs that are not secreted into breast milk. Although several analgesic modalities and drugs have been introduced over the past few years, it is seen that we have still not achieved optimum post-operative analgesia. Drug availability, maternal co-morbid conditions, patient preferences and availability of medical expertise and trained support staff also play a role in choice of analgesic method. In developed countries, administration of opioid analgesics remains the gold standard for post-operative analgesia. However, the associated side effects have led to incorporation of non-opioid analgesics in post-CS analgesia regime. The various systemic and neuraxial analgesic options available will be discussed. In addition, newer drug applications of potential benefit will be reviewed.

Keywords: *Caesarean Section; Pain Management; Multimodal Analgesia*

Introduction

The incidence of Caesarean sections in India is rising [1]. The provision of effective post-operative pain relief is of key importance to facilitate early ambulation, ensure maternal and neonatal bonding, infant care, effective breast feeding and prevention of post-operative morbidity.

Compared with other major surgeries, deciding a plan for optimal anaesthesia and analgesia for caesarean sections involves distinct considerations:

- Operative anaesthesia is almost always neuraxial and is performed in un-sedated patients.
- Concerns for in-utero foetal drug transfer.
- Potential risk of transfer of analgesic drugs to breastfeeding neonates.
- Post-operative mobility of mothers to facilitate optimal neonatal care.

The various analgesia options for providing optimal post-operative pain relief for women undergoing uncomplicated caesarean section (CS) with neuraxial anaesthesia are summarized in this article. These options are suitable for most women.

Oral and intravenous analgesics

In developed countries, neuraxial opioids are the most common mode of pain relief post CS. However, in developing countries, oral and intravenous route still continue to be the foremost route of pain relief. The advantage of systemically administered analgesics is their ease of administration, low cost, and long history of use in postpartum women. There are diverse analgesic regimens for management of the post CS pain. Most practitioners prescribe a combination of two or more drugs, depending on the adequacy of pain relief.

The various options available are:

- Non-steroidal anti-inflammatory drugs (NSAIDS)
- Acetaminophen
- Combining acetaminophen and NSAIDs
- Opiods
- Dexamethasone
- Ketamine
- Gabapentinoids

Acetaminophen

One of the commonest drugs used for pain relief, acetaminophen can be administered either as monotherapy or as a part of multi modal approach. It provides effective analgesia with minimal side effects. Further it provides an opioid-sparing effect of approximately 20%. It can be given by oral and intravenous route. Drug transfer to breast milk is very low. In 2009, the US FDA has reduced the recommended maximum daily dose of acetaminophen from 4000 mg to 3250 mg [2].

Nonsteroidal anti-inflammatory drugs

NSAIDS are key in a multi modal approach. They are particularly useful against the visceral pain that arises from the uterine incision and involution following caesarean delivery [3]. NSAIDs not only reduce the inflammatory component of pain by inhibiting cyclooxygenase enzyme and preventing the central and peripheral prostaglandins generation but also effectively relieve the pain of uterine contractions in the postpartum period.

There is strong evidence that NSAIDs have an opioid sparing effect and they cause reduction in opioid induced nausea, vomiting and respiratory depression [4]. Lim., *et al.* demonstrated that a single dose of 100 mg diclofenac suppository is effective in reducing post CS epidural local anaesthetic/opioid requirements by approximately one third for the first 24 hr post-operatively [5].

The mode of administration can be oral, intravenous, intramuscular or rectal route. Intravenous formulations are used in patients not tolerating oral intake or experiencing nausea or vomiting.

Contraindications for the use of NSAIDs include [6]:

- Significant haemorrhage
- Pre-eclampsia (up to 24 hours after delivery)
- Renal impairment
- Thrombocytopaenia
- Asthmatics sensitive to NSAIDs.

Selective cyclooxygenase (COX) 2 inhibitors such as celecoxib are now available which have reduced risk of gastrointestinal and hematologic effects associated with non-selective NSAIDs.

Opioids

They can be given by oral, intravenous or neuraxial route. Oxycodone, hydrocodone, and tramadol are oral opioids commonly used for post CS pain relief. Oxycodone is a mu-opioid receptor agonist while tramadol is a weak mu opioid receptor agonist with centrally acting noradrenergic, serotonergic and GABAergic activity [7].

Oral or intravenous opioids are mainly reserved for treatment of breakthrough pain when pain relief from neuraxial opioids or non-opioid adjuncts is inadequate. As compared to oral opioids, intravenous route of administration do not provide superior analgesia and are associated with more side effects and limit mobility after caesarean delivery. Therefore, the use of oral opioids is generally preferred [8].

Dexamethasone

Glucocorticoids have analgesic and antiemetic properties in addition to anti-inflammatory effects. Doses between 1.25 and 20 mg have been described, however, the optimal dose has not been determined. Wu., *et al.* evaluated and compared different dosages of Dexamethasone in CS and concluded that patients who received Dexamethasone experienced less pain and emesis [9].

Dexamethasone may be associated with marginal rise in blood glucose at 24 hours post CS and should be avoided in diabetics. A single dose is not known to impair wound healing or increase risk of infection [10].

Gabapentinoids

Although commonly used in the management of chronic pain, gabapentinoids have been used for their analgesic and opioid-sparing effect in the acute postoperative period. They act by not only modulating GABA concentrations, but also interact with calcium channels, NMDA receptors, protein kinase C and inflammatory cytokines to modulate pain [11].

Given the potential risk of transfer to the foetus through the placenta and breastmilk, they are not routinely recommended in post CS pain relief.

Other drugs that are rarely used are ketamine, clonidine, midazolam, dexmedetomidine etc.

Neuraxial medications

Neuraxial opioids provide a high quality of post-caesarean delivery analgesia. The various options available are:

- Intrathecal administration
- Epidural administration
- Continuous and patient-controlled epidural infusions.

The American Society of Anaesthesiology's Obstetric Anaesthesia Practice Guidelines recommend routine use of neuraxial anaesthesia for caesarean delivery [12].

Neuraxial anaesthesia for CS is promoted because:

- Reduced maternal risk
- Improved foetal outcomes
- Superior postoperative analgesia with the use of neuraxial opioids.

Merits and demerits of spinal opioids is summarised in table 1.

Merits
• Greater spinal anaesthesia success rate
• Faster onset of surgical block than LA alone
• Improved intraoperative analgesia (enhances sensory block without increased motor block)
• Permits lower LA dose with faster recovery from spinal anaesthesia
• Postoperative analgesia beyond the duration of LA motor block
• Less nausea and/or vomiting during caesarean delivery
• Shorter time to extubation, significantly reduces MAC
Demerits
• Frequent pruritus
• Sedation (never with lipophilic opioids; Rarely with high doses)
• Rare respiratory depression (more likely in parturients; especially late onset respiratory depression)
• Rare urinary retention (more likely with Morphine)
• IT Fentanyl ï ?? cross tolerance to I.V Morphine

Table 1

Opioids administered in the subarachnoid space appear to act principally on mu receptors in the substantia gelatinosa of the dorsal horn by suppressing excitatory neuropeptide release from C fibres [13]. The degree of uptake from the cerebrospinal fluid by the dorsal horn is determined primarily by the physicochemical properties of the drug, mainly lipid solubility.

The mechanism of action after epidural injection is more complex, owing to the presence of a dural barrier, the role played by epidural fat as drug depot, and the vastly increased vascularity of the epidural compartment during pregnancy. As compared to intravenous opioids, neuraxial opioids provide greater analgesic efficacy at a lesser risk of respiratory depression.

Many opioids, including morphine, fentanyl, meperidine, sufentanil, nalbuphine and heroin have been used intrathecally for post CS analgesia.

Intrathecal morphine is the gold standard single-shot drug for post CS pain and it provides long-lasting analgesia for 14 to 36 hours. Morphine, in doses ranging from 0.075 mg to 0.5 mg can be given [14]. It is seen that higher doses do not provide a dose-dependent improvement in analgesia and are associated with increased side-effects [15].

A meta-analysis including 28 studies, which investigated intrathecal morphine versus placebo, demonstrated moderate increases in the frequency of pruritus, nausea, and vomiting in the morphine compared with placebo group [16].

Intrathecal hydromorphone can also be used for post-operative pain relief. As morphine is more hydrophilic, it has longer duration of analgesia after single-dose administration compared with hydromorphone. Comparisons of morphine and some lipophilic opioids are summarized in table 2.

Opioid	IT/iv potency ratio	Onset of IT analgesia (min)	Duration of analgesia (h)	Time of peak respiratory depression	Clinical dose range
Morphine	200-300:1	60 - 120	18 - 24	8 - 10h	0.1 - 0.5 mg
Fentanyl	10-20:1	< 10	1 - 4	5 - 20 min	6 - 30 mcg
Sufentanil	10-20:1	< 10	2 - 6	5 - 20 min	2.5 - 10 mcg

Table 2: *Comparison of intrathecal morphine with hydrophilic opioids (Fentanyl and Sufentanil) [17].*

IT: Intrathecal; iv: Intravenous.

Epidural morphine is especially suitable for post-operative pain relief in cases of emergency CS in labouring women with epidural catheter *in situ*. When using an epidural technique for CS, opioids can be administered either as a bolus or as continuous infusion for post CS pain relief. The optimal dose is 2 to 4 mg, with larger doses not providing superior analgesia [18].

In a dose response study by Palmer., *et al.* it was seen that quality of analgesia increases as the dose of epidural morphine is increased up to 3.75 mg, increasing the dose further to 5 mg did not improve analgesia [19].

Although both epidural and intrathecal morphine have similar analgesic efficacy and side effects, intra-thecal morphine is preferred as it requires lower opioid dose and less potential neonatal drug transfer. Developing countries face challenge of limited supply of opioids, lack of long acting intrathecal preservative free narcotic and expertise for its use.

Patient-controlled intravenous infusions

In patient controlled IV analgesia (IVPCA), a small bolus of opioid administered IV by a device. The device is programmable for the dose administered, a lockout interval, basal infusion of drug and the maximum dose of drug delivered. The benefit of PCA for the patient stems from prompt delivery of the analgesic, reducing the time between pain occurrence and drug administration [20].

Although they provide effective post CS pain relief, their use reduces maternal mobility, complicates anti-coagulation prophylaxis, increases nursing workload, and adds to cost.

Local anesthetics

The various routes that are used are:

- Wound infiltration
- Transversus abdominis plane (TAP) and quadratus lumborum blocks
- Others.

Wound infiltration

Local anaesthetics may be administered by direct application into the wound. This mode of anaesthesia is suitable as a supplemental adjunct for pain relief in women who undergo CS under general anaesthesia. Pain relief is often incomplete because they do not tackle uterine cramping or pain from peritoneal structures.

They are unsuitable for CS under spinal anaesthesia as single dose wound infiltration usually does not last beyond the duration of the neuraxial block, affects only somatic (not visceral) pain, and has variable efficacy. To overcome this drawback, catheter-based local anaesthetic instillation has been suggested to provide prolonged pain relief. The most common concentrations reported are 0.2 - 0.5% of bupivacaine, levobupivacaine or ropivacaine [21].

Transversus abdominis plane and quadratus lumborum blocks

The TAP block is a regional block performed by introducing local anaesthetic into the plane between the fascia of the transversus abdominis muscle and the internal oblique muscle (Figure 1). It blocks the abdominal wall neural afferents between T6 and L1 and thus relieve pain associated with an abdominal incision [22].

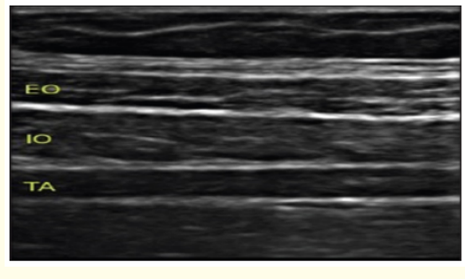

Figure 1: *Ultrasound image of transversus abdominus muscle.*

They are especially suitable for post CS pain relief in patients who undergo general or spinal anaesthesia without intrathecal or epidural morphine. They act on somatic incisional pain rather than visceral pain. The duration of sensory blockade for single-shot TAP block is limited to 6 to 12 hours. A recent systematic review and meta-analysis reviewed five randomized double-blind studies receiving TAP block for management of pain after CS concluded that TAP block was effective in reducing pain scores, morphine consumption and postoperative nausea and vomiting for 24h compared to the placebo group [23].

Breastfeeding considerations

Although adequate post CS pain relief is important as it promotes successful breastfeeding, there is a potential risk of transfer of analgesics to the breast-feeding infant. The following points should be considered before starting analgesics:

- Opioid-sparing multimodal analgesia is preferable as opioids are associated with breast milk transfer and may cause neonatal sedation [24].
- The amount of drug in breast milk parallels maternal blood levels.

Conclusion

Caesarean delivery rates are increasing worldwide, and effective pain relief is a key priority of women undergoing caesarean delivery. Pain management in postpartum women is unique in that initial anaesthesia is almost exclusively neuraxial, analgesic use is limited by concerns of foetal drug transfer, and post CS analgesics given to mother have the potential for transfer to the breastfeeding neonate. Further, optimal management post CS should address the goals of maternal mobility and rapid recovery. Multimodal analgesia should include neuraxial morphine in conjunction with nonopioid adjuncts such as scheduled NSAIDs and acetaminophen, with additional opioids reserved for severe breakthrough pain.

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