REVIEW ARTICLE

# MANAGEMENT OF POST CESAREAN PAIN

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**SUMMARY:**

Post cesarean pain relief is important. Good pain relief will improve mobility and reduces risk of thromboembolic disease. Pain and anxiety may impair the early interaction between mother and infant, it may also adversely decrease the ability of mother to effectively breast feed the baby. It is necessary that pain relief be safe and effective that it not interfere with mother's ability to move around and optimally care for her infant, and that it result in no adverse effects in breast feeding women.

This brief review will focus on commonly used strategies such as systemically administered analgesics and neuraxial techniques as well as new drug applications, for relieving pain after caesearean deliver.

**KEY WORDS :**

Post cesarean pain, neuraxial opioids, future applications.

## INTRODUCTION :

Women undergoing cesarean section should have access to high quality pain relief that is safe and effective. Post cesarean analgesia can be provided by variety of means. The most commonly used modalities are systemic administration of opioids, either by intramuscular(im)/ intravenous(iv)/ by iv patient controlled analgesia (PCA) and neuraxial injection of opioid as part of regional anaesthetic for cesarean delivery. These techniques have specific advantages/ disadvantages which will be discussed in this review.

## MANAGEMENT OF ACUTE POST OPERATIVE PAIN :

Management strategies for post operative pain are aimed at reducing a patient's pain to tolerable level. Though the traditional approach has been to begin pain therapy when surgery is complete, the concept of **pre-emptive analgesia**[2] has become increasingly popular.

**Pre emptive analgesia**[2,3], an evolving concept involves introduction of an analgesic regimen before onset of noxious stimuli, with the goal of preventing sensitization of nervous system to subsequent stimuli that can amplify pain. Surgery offers the most promising setting for preemptive analgesia because the

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timing of insult is known. The most effective preemptive analgesic regimens are those that are capable of limiting sensitisation of nervous system throughout entire perioperative period. Bang et al[4] in there study showed that preemptive analgesia with iv nalbuphine 10mg decreased postoperative pain and analgesic requirement.

Just as "**balanced anaesthetic technique**" are used to meet the intraoperative anaesthetic needs of patients by making use of several agents, balanced analgesia uses several modalities of pain management to provide a pain and stress free state, thereby promoting good postoperative outcome[5].

**Multimodal technique** of pain management involves administration of two or more drugs that act by different mechanism via a single route (eg. epidural opioids, local anaesthetics + clonidine) for providing superior analgesic efficacy with equivalent or reduced adverse effects [6, 7, 8, 9, 10, 11].

Effective pain relief does not necessarily make the patient completely insensible to the fact that surgery was performed, rather it allows a degree of comfort that promotes physical recovery and a sense of well-being.

The goals of **new methods of drug administration** include the following:

1. The precise, controlled delivery of the prescribed dose.
2. A rapid onset of action.
3. The avoidance of first pass hepatic metabolism.
4. The maintenance of steady state concentration of drugs.
5. An improved side effect profile.
6. Improved patient compliance.

**WFSA (World Federation of Societies of Anaesthesiologists) ANALGESIC LADDER :**

The WHO analgesic ladder was introduced to improve pain control in patients with cancer pain. However, it has lessons for management of acute pain as it employs logical strategy to pain management. WFSA analgesic ladder has been developed to treat acute pain[16].

**Strong opioids (by injection), →→→opioids(by mouth)→→→ NSAID/aspirin.**

**+ Local anaesthetics (as pain decreases) peripherally acting drugs**

Initially, the pain can be expected to be severe and may need controlling with strong analgesics in combination with local anaesthetic blocks and peripherally acting drugs. Post operative pain decreases with time and the need for drugs to be given by injection should cease. The second rung on the post operative pain ladder is the restoration of the oral route to deliver analgesia. Strong opioid may no longer be required and adequate analgesia can be obtained by using combination of peripheraly acting agents and weak opioids. The final step is when the pain can be controlled by peripherally acting agents alone[16].

**SYSTEMIC OPIOIDS:** were the main stay of pain management in the past and still continue to be a popular technique. Usually administered by im/iv/subcutaneous/transdermal route. The prescription should include and indicate the agent, dose, frequency and route of administration.

**WEAK OPIOIDS :**

**CODEINE :** is a weak opioid, markedly less active than morphine. The molecule is devoid of analgesic activity. Codeine-6-glucuronide and morphine which is formed as a result of metabolism *account for most of the analgesic activity.* It is effective against milld-moderate pain. Dose: **15-60 mg, 4th hourly with maximum of 300mg daily**[16].

**DEXTROPROPOXYPHENE:** is structurally related to methadone but is relatively poor analgesic. It is often marketed in combination with paracetemol. Dose: **30-60mg 4th hrly with a maximum of 300mg daily[16].**

If pain doesn't respond to weak opioid, use of stronger drug or combination is advised.

Combination of weak opioid and peripherally acting drugs[16]:

**Paracetemol 500mg+codeine8mg(2tab at a time,maximum of 8tab/day).**

If insufficient use,

**Paracetemol 1g+codeine30-60mg(4-6th hrly, maximum of 4doses)[16].**

**STRONG OPIOIDS :**

Severe pain requires the use of strong opioids. Early administration will achieve effective analgesic concentrations and make it easier to maintain theurepetic level of the drug in the blood. Once a satisfactory level of pain relief has been achieved this can be sustained by regular administration of opioid[17].

**Fentanyl** is a strong opioid increasingly used in treating acute pain because of its lack of active metabolites and fast onset of action. Only **3%** fentanyl is secreted in breast milk. It is therefore safe in post operative period[18,19].

**Morphine** is the opioid most widely used in the management of acute pain. It is metabolized into morphine-6-glucuronide and morphine-3-glucuronide in the liver. Morphine-6-glucuronide is u agonist and more potent than morphine while morphine-3-glucuronide has low affinity to opioid receptors and has no analgesic activity[18,20].

Morphine administered im/iv & continuous epidural infusion has proved to be safe in the postoperative period. Only **6%** of administered dose is transferred in **breast milk.** As oral bioavailability in infants is around **25%**, only small amounts reach the infant[18,21,22].

**Pethidine** is a synthetic opioid still widely used despite its multiple disadvantages. It induces more nausea and vomiting than morphine when used parenterally[18,21]. **Norpethidne,** which is a metabolite of pethidine, accumulates in breast milk with repeated use of pethidine. Infants of mothers exposed to PCA-iv pethidine have been found to be less alert and oriented on day 3&4 after caesarean section[23]. Hence, pethidine is not recommended for repeated use in the postoperative period following caesarean section[1].

**Tramadol** is an atypical centrally acting analgesic because of its combined effects as an opioid agonist(mainly its metabolite, **O-desmethyl tramadol**) and a serotonin and noradrenaline reuptake inhibitor. It is listed as a weak opioid by the WHO[18,21]. The risk of respiratory depression is significantly lower at equianalgesic doses and does not depress the hypoxic ventilatory response. Nausea and vomiting are the most common side effects[24].

**ROUTES OF ADMINISTRATION OF OPIOIDS:**

**Intravenous route:** is preferred because of ease of administration, low cost and long history of safe use in postpartum women. It produces prompt and predictable blood levels, it allows precise titration of analgesic requirements to the need of the patient[25].

**TABLE 1[26]**

| Drug | Iv bolus | Iv infusion |
|---|---|---|
| Morphine | 0.01-0.2 mg/kg | 20-30ug/kg/hr |
| Pethidine | 0.1-1 mg/kg | 200-300ug/kg/hr |
| Fentanyl | 1-5 ug/kg | 0.5-2 ug/kg/hr |
| Tramadol | 0.5-1 mg/kg | 100-200 ug/kg/hr |

**Intravenous Patient controlled analgesia (PCA):** became popular when it was realised that individual requirements for opioids varied considerably[27]. PCA allows patient to

receive drugs on demand. A PCA pump administer's drug usually intravenously when the patient pushes the button, the physician has the control of determining **the intermittent injection dose**(the dose received when patient pushes the button), **the lock out interval**(minimal length of time that must elapse between consecutive doses), a limit to how much the drug may be injected in a limited time(1-4hrs), a **bolus dose** to be administered by a nurse through the machine and a **basal rate**.

When prescribing PCA for patients recovering from CS, it is best to use PCA alone without a basal infusion of opioid. A continuous basal infusion should be added only if pain relief is inadequate despite appropriate PCA use. This scheme may need to be modified and basal infusion included for patient's who are opioid dependent[1,28,29,30,31].

**TABLE 2[1,28]:**

| Drug(conc) | Demand dose | Lock out interval | Continuous basal infusion |
|---|---|---|---|
| Morphine (1mg/ml) | 1-2 mg | 6-10 min | 0-2 mg/hr |
| Pethidine (10mg/ml) | 10-20mg | 6-10 min | 0-20 mg/hr |
| Fentanyl (10ug/ml) | 20-50 ug | 5-10 min | 0-60 ug/hr |
| Buprenorphine (300ug/ml) | 30-100 ug | 8-20 min | |
| Sufentanil | 4-6 ug | 5-10 min | 0-8 ug/hr |
| Tramadol | 10-20 mg | 6-10 min | 0-20mg/hr |

**Advantages** : iv PCA reduces the peaks and valleys in blood drug concentration and pain relief observed in CS patients is better as **patient-nurse-injection loop** is bypassed. These patients have the highest satisfaction scores when compared to intramuscular/epidural opioid usage[32,33,34,35,36,37].

**Limitation**: The most significant limitations to the use of iv PCA in post partum women relate to the device itself and patient's ability to use it correctly. It requires **patient education** and implies that the patient will understand and follow through with directions required to use demand mode iv PCA effectively. Some devices are **cumbersome** and women may find it difficult to ambulate and care for their infant. Nonetheless, IV PCA has emerged as a popular modality for post caesarean delivery pain[1].

The equipment is **expensive** and the technique may allow breakthrough pain on an intermittent basis because when the patient is asleep, administration ceases. This can be overcome by a slow background infusion that is supplemented by a patient controlled additional dose. The use of a basal (background) infusion did not improve pain relief but resulted in an increased total dose of opioid and an increased severity of side effects[28,29,30,31].

**Subcutaneous/intramuscular route:** opioids can be given **intermittently** or in **continuous** infusion through a small cannula or butterfly needle placed in subcutaneous tissue of upper arm. Like intramuscular route it also produces unpredictable blood levels if peripheral perfusion is poor[38]. Late absorption of the drug depot can occur once perfusion is restored resulting in very high plasma levels of the drug. However, in presence of normal tissue perfusion, the subcutaneous route has the advantage of producing stable plasma levels[1].

**Limitations**: repeated injections which can be uncomfortable to the patients, large inter individual

variations in drug pharmacokinetics and drug requirements. There are **peaks and troughs** in blood opioid concentration[38]. At peaks opioid adverse effects will be seen and at troughs inadequate analgesia is seen.

**Transdermal route:** Used to administer drugs like scopolamine, nitroglycerine, clonidine, estradiol, nicotine and fentanyl[1,39].

**Transdermal fentanyl patches** are available with different delivery rates ranging from **25-100ug/hr**. These have a slow onset and offset of action and absorption continues for upto 72hrs while the patch is in place[40,41,42,43].

**Adverse effects**: potential for ongoing transdermal absorption of drug after removal of the patch, this results in a slow decline in plasma concentrations of fentanyl and norfentanyl.

### Intrathecal (IT) opioids:

Neuraxial opioids are popular mode for CS pain for a number of reasons[1]:

- As most women undergoing CS will do so under spinal/epidural/both. It is easy enough to add small dose of opioid to prolong the analgesia.
- Commonly used opioids like morphine, fentanyl, buprenorphine have long history of safe and effective use.
- Finally adverse effects are well described and although not infrequent, can be described as nuisance side effects.

### Mechanism of action of intrathecal opioids[44]:

Opioids administered in subarachnoid space appear to act principally on **mu receptors in substantia gelatinosa of dorsal horn** by suppressing excitatory neuropeptide release from C fibres. The degree of uptake from CSF by dorsal horn is determined by physiochemical properties of the drug and in particular, lipid solubility[45,46]. Lipid soluble drugs enjoy greater direct diffusion into neural tissue as well as greater delivery to the dorsal horn by spinal segmental arteries.

Fentanyl is highly lipid soluble. It has relatively rapid uptake into lipid rich dorsal horn and so has swift onset of action. The large uptake of highly lipid soluble opioids by spinal cord results in small CSF concentrations and decreased potential for the drug to diffuse to higher spinal levels. For this reason, analgesic effect of fentanyl is thought to be segmental.

Morphine is highly ionised, hydrophillic and doesnot penetrate lipid rich tissue, it lingers in CSF and this is responsible for its prolonged duration of action. Morphine spreads rostrally within CSF by bulk flow. This rostral spread is responsible for delayed respiratory depression.

**TABLE 3[1]:**

| Drug | Dose (mg/ug) | Onset (min) | Peak effect (min) | Duration (hrs) |
|---|---|---|---|---|
| Morphine | 0.1-0.25 mg | 30 | 60 | 12-24 |
| Meperidine | 10mg | 10 | 10 | 2-3 |
| Fentanyl | 10-20ug | 5 | 10 | 2-4 |
| Sufentanil | 5-10ug | 10 | 15 | 4-5 |

### Epidural opioids :

Mechanism after epidural injection is more complex, owing to

- The presence of dural barrier,
- Epidural fat(acts as a drug depot) and
- Vastly improved vascularity of epidural compartment during pregnancy.

### Mechanism of action of hydrophillic drugs(morphine)[44]:

When hydrophillic drug such as morphine is injected it moves slowly across arachnoid granulations and speed of onset of analgesia is correspondingly slow. So large amount of ionised morphine accumulates in CSF that not only leads to

rostral diffusion but also a long duration of analgesia. Vascular absorption of morphine by epidural venous plexus is relatively rapid. However plasma levels correlate poorly with the analgesic effect because there is predominant spinal mechanism of analgesia after epidural opioid administration[48]. In case of hydrophillic drug uptake by epidural fat is probably not significant in reducing systemic absorption.

**Mechanism of action of lipophillic drugs(fentanyl/sufentanil)[44]:**

After epidural injection, unionised drug diffuses rapidly into the epidural veins, segmental arteries and across both arachnoid granulations and dural cuff into CSF. Actual mechanism of action of epidural fentanyl is controversial, it acts at both supraspinal(via systemic delivery) and spinal sites in addition to drug difusing to spinal receptors from CSF[49]. Blood concentration depends on large part on **"flow dynamics"**[45] within epidural venous plexus and spinal arteries. Example in pregnancy like *aortocaval compression, where inferior vena caval* blood flow is impaired. Decreased blood flow from the pelvis and lower extremity can redistribute to azygous system via epidural plexus markedly enhancing flow and drug delivery to systemic circulation during pregnancy[45].

**TABLE 4[1]:**

| Drug | Dose | Onset (min) | Peak effect (min) | Duration (hrs) |
|---|---|---|---|---|
| Morphine | 2-4mg | 45-60 | 60-120 | 12-24 |
| Fentanyl | 50-100 ug | 5 | 20 | 2-3 |
| Sufentanil | 25-50 ug | 5 | 15-20 | 2-4 |
| Meperidine | 50 mg | 15 | 30 | 4-6 |
| Butorphanol | 2-4 mg | 15 | 40 | 2-4 |
| Morphine + Fentanyl | 3mg+50ug | 10 | 15 | 12-24 |
| Morphine + Sufentanil | 3mg+25ug | 5 | 15 | 12-24 |
| Continuous Fentanyl | 100ug bolus 40-75ug/hr | 10 | 20 | - |
| Continuous Sufentanil | 25ug bolus 20-25ug/hr | 5 | 15 | - |

Opioids can either be administered alone or in a combination with 0.0625%-0.125% bupivacaine. When opioids are being administered by the epidural or subarachnoid route, one must avoid the concurrent systemic use of other opioids or sedatives. Patients should be closely monitored for systemic effects of opioids such as decreased respiratory rate or excessive sedation. When combined with local anaesthetics, one should in addition monitor haemodynamic and motor blockade[1].

The epidural route of administration is **complicated** by several anatomic and physiologic factors, including the following:

1. Drug penetration of dura and pia mater.
2. Absorption by the epidural fat.
3. Consequences of vascular uptake and redistribution of drug to supraspinal sites.

Advantages of **Patient controlled epidural analgesia** Vs **Epidural bolus doses/infusion**[1]:

- ✓ Patient control and autonomy.
- ✓ Increased patient satisfaction.
- ✓ Decreased anxiety.
- ✓ Reduced opioid requirement.

Advantages of **Patient controlled epidural analgesia** Vs **Intravenous PCA**[1]:

- ✓ Increased efficacy of analgesia.
- ✓ Increased patient satisfaction.
- ✓ Reduced opioid requirement.
- ✓ Decreased sedation.

**OPIOIDS IN BREAST MILK AND EFFECT ON NEWBORN:**

The effect depends on extent of systemic absorption after oral administration to the infant, infant's ability to excrete the drug or its metabolites. The effect of maternal medication can be minimised by giving attention to following principles[1]:

- ✓ Avoiding drugs with long plasma half life.
- ✓ Whenever possible, delay drug administration untill just after an episode of breast feed. If infant feeds when mother's blood level of drug level is high, more drug is transferred to breast milk[1].
- ✓ When possible, choosing drugs that have least potential for excretion into breast milk and accumulation in neonate.
- ✓ Observing the neonate for abnormal signs/symptoms like change in sleep/ feeding pattern, decreased muscle tone, irratibility.

**American Academy of Pediatric Committee**[50], on drugs has compiled and categorised list of drugs that are transferred through human breast milk:

- Category 1 : drugs that are contraindicated while breast feeding.
- Category 2 : drugs that require temporary interuption of breast feeding.
- Category 3 : drugs that are compatible with breast feeding.

**TABLE 5** [1, 50, 51, 52, 53, 54, 55]

| Drug | Category | Milk/Plasma ratio | Newborn tolerance/comment |
|---|---|---|---|
| Morphine | 3 | 0.23-5 | Possible accumulation. |
| Methadone | 3 | 0.83 | Abrupt cessation ppts withdrawal symptoms. |
| Fentanyl | 3 | >1 | Well tolerated. |
| Codeine | 3 | 2.5 | Possible accumulation. |
| Butorphanol | 3 | 0.7-1.9 | No adverse effects reported. |
| Nalbuphine | - | No data | No data. |
| Pentazocine | - | Minimal excr | No data. |
| Acetaminophen | 3 | 1.9 | Well tolerated. |
| Aspirin | 3 | 0.08 | Can precipitate reye's syndrome in infants. |
| Ibuprofen | 3 | 0.01 | Well tolerated. |
| Ketorolac | 3 | 0.025-0.03 | Usage controversial. |

## ADVERSE EFFECTS OF OPIOIDS:

Opioid administration may result in annoying side effects and complications like pruritis, nausea and vomiting, urinary retention and most feared of all respiratory depression.

**PRURITIS:** The incidence of pruritis ranges from **40-80%** of parturients treated with epidural and intrathecal morphine, hydromorphone or methadone. It is most severe **3-6hrs** after intraspinal morphine administration[56,57]. Changes in spinal efferent outflow may indirectly release small amounts of histamine in tissues adjacent to peripheral nerve endings. Mild pruritis involves face and chest or may even occur more frequently however patients may not mention it unless questioned directly[58].

*Treatment :*

- **Mild** pruritis is relieved by **cold compresses**[1,6].
- **Moderate** pruritis is treated by **1 or 2 doses of 25mg diphenhydramine**[1,6].
- **Severe pruritis** is treated by **small iv doses of naloxone(0.04-0.08mg)** which typically relieves pruritis without reversing analgesia. **Iv infusion of naloxone 50-100ug/hr** may be necessary as side effects of intraspinal opioids may outlast the effect of bolus naloxone[59].
- Other drugs that have been used are: 10-20mg of propofol[60,61], iv nalbuphine 3mg[62,63], ondansetron 8mg to relieve pruritis with variable results.

**NAUSEA AND VOMITING:** depending on the agent used and dose given, **20-60 percent** develop nausea and vomiting. Some but not all require treatment. Nausea may result from rostral spread of drug in CSF to the brainstem or vascular uptake and delivery of drug to Chemoreceptor Trigger Zone[64,65,66].

*Treatment :*

- **Metoclopramide 10mg iv bd** is a good choice[1].
- **Scopolamine transdermal patch (1.5mg released over 72hr period)** before CS has been used for patients with strong history of hyperemesis gravidarum/ motion sickness[1,27,67]
- **Ondansetron 2-4mg, 4-6hrly** can be used in cases of intractable nausea[5].
- **Iv boluses of naloxone 40-80ug** followed by **infusion of 50-100ug/hr** are used for intractable nausea[1].
- **Iv dexamethasone 8mg and droperidol 1.25mg** have been used and found effective in treating nausea[68].
- **Acupressure** is performed by placing flexible strap with spherical plastic bead at a point on the anterior surface of right forearm 4-5cm proximal to transverse crease of wrist and 1-1.3cm deeep to skin between tendons of flexor carpi radialis and palmaris longus[1].

## URINARY RETENTION :

Intraspinal opioid induced urinary retention may result from inhibition of sacral parasympathetic outflow, which results in relaxation of bladder detrusor muscle and an inability to relax the sphincter. This effect may be relieved with a large **iv dose 0.8mg naloxone.** Unfortunately, a reversal of analgesia may also occur[6,69].

## RESPIRATORY DEPRESSION :

This is most feared complication of opioid administration. **Mild respiratory depression** occurs **30-90 min** after epidural morphine, this results from systemic absorption of morphine from epidural space[6]. **Delayed respiratory depression** results from rostral spread of morphine in CSF, it usually occurs **6-10hrs** later[28]. After reaching the fourth ventricle, the drug rapidly equilibrates with intracranial CSF and interacts with medullary

respiratory centers to reduce ventilatory response to carbon dioxide.

**Risk factors** include advanced age, obesity, preoperative administration of magnessium sulphate and pre existing lung pathology[6]. In CS women are young, healthy without any co morbid condition and progesterone is present in increased concentration which is respiratory stimulant[70]. So risk of opioid induced respiratory depression is less. Thus most anaesthesiologists do not administer prophylactic naloxone to CS patients[71].

Epidural 3-4mg morphine or IT morphine 0.1-0.25mg morphine results in very low risk of clinically significant respiratory depression in obstetric patients. Single epidural/IT lipophillic opioid is rarely associated with respiratory depression.The rare patient who displays signs of somnolence, hypoventilation and arterial desaturation should receive supplemental **oxygen and iv bolus naloxone 40-80ug. Continuous IV infusion of naloxone (1ug/kg/hr)** prevents delayed respiratory depression in high risk surgical patients without affecting the quality of analgesia. Such therapy should be continued as long as 8-12 hrs in patients who have received neuraxial morphine[1].

**NON STEROIDAL ANTI INFLAMMATORY DRUGS (NSAID):**

NSAID such as acetaminophen, ibuprofen, ketorolac, diclofenac and COX-2 inhibitors are popular drugs used for this purpose. These drugs are administered by the oral/rectal/im routes to supplement an opioid based analgesia. They are often administered along with premedication in the technique termed **preemptive analgesia.** While traditional NSAID's such as acetaminophen, ibuprofen, ketorolac and diclofenac inhibit both COX-1 and COX-2 forms of the cyclo-oxygenase enzyme, newer NSAID's inhibit inducible form of the enzyme, the COX-2 enzyme which is released following surgical trauma, sepsis and hypoxia[26,72].

**Paracetemol (acetaminophen)** has analgesic and antipyretic properties, it is weak analgesic. Therefore it is only suitable for treatment of mild pain or it may be combined with other analgesics to provide superior analgesia and reduce opioid requirements. Action of paracetamol is due to inhibition of the COX-3 iso enzyme and central cyclo-oxygenase (COX-2) & reduction of prostanoid release in the central nervous system. Probably it also acts on the opioidergic system & NMDA receptors[26,72].

It is used **orally** in doses of **10-15mg/kg every 4-6hrs** with a maximum dose not exceeding 100mg/kg/day. The oral dose of acetaminophen in adult is 650-975mg once every 4-6hrs. Single oral dose in excess of 100mg/kg can result in severe liver damage and acute tubular necrosis.The drug can also be given **rectally** in an **initial dose of 35-40mg/kg followed by 20mg/kg every 6hrs**[26,72].

**Diclofenac** can be given by rectal or IM routes as adjuncts to opioid medications. While rectal suppositories are available in strength of **12.5,25,50 &100mg.** The intramuscular preparation is available as **75mg/3ml ampoule.**

**Oral COX-1 inhibitors (ex: ibuprofen)** have been widely used for providing analgesia after caesarean and vaginal delivery. **Ketorolac**, an injectable COX-1 inhibitor is used postoperatively when patients are unable to tolerate oral agents. Some physicians are reluctant to administer COX-1 NSAIDS for routine postpartum analgesia because of concern that these agents might inhibit platelet function and cause increased post partum bleeding. **Oral ibuprofen** in a dose of **6-10mg/kg 6$^{th}$ hrly** is known to produce 30% reduction in opioid requirement[26].

NSAIDS exert an anti inflammatory effect at the incision site, and they also may relieve discomfort of uterine cramping after vaginal delivery. Pain after caesarean delivery may have at least **two components**: post operative (**somatic**) pain from wound itself and **visceral** pain arising from uterus.

Although somatic pain may be relieved by opioids, visceral pain may be more difficult to treat. NSAID's are effective for relieving pain related to menstrual cramping and as a result, there has been interest in the use of NSAID's to treat a component of pain after caesarean delivery[26].

Unfortunately, NSAID's alone are insufficient to effectively treat post caesarean delivery pain. However, inclusion of NSAID's in a multimodal approach to pain relief after caesarean delivery has been very successful both in improving the quality of analgesia resulting from systemic or neuraxially administered opioids and reducing side effects[6,7,8,9,10,11].

NSAID's such as ketorolac and ibuprofen are secreted into breast milk, although at small concentrations, and are generally regarded as safe by the American academy of paediatricians for use in breast feeding women[44].

However, ketorolac has a "**black box**" warning by the food and drug administration and its manufacturer stated that use of ketorolac is contraindicated during labor and delivery because it may adversely affect fetal circulation and inhibit uterine contractions and in nursing mothers because of the potential adverse effect of prostaglandin inhibitor drugs on the neonate[44].

Disadvantages are, it cannot be used when patients are suffering from nausea and vomiting & gradual onset of pain relief.

## CYCLO-OXYGENASE-2 INHIBITORS:

Oral COX-2 selective NSAIDS ex rofecoxib, celecoxib, valdecoxib are finding their way into obstetric clinical practice. **Parecoxib 20mg** compares favorably with **ketorolac 30mg** and morphine 4mg in patients recovering from lower abdominal gynaecological surgery.

COX-2 inhibitors selectively act on COX-2 enzyme and spare COX-1. Thus it carries all benefits of NSAID's without any side effects caused by inhibition of COX-1. Analgesic efficacy of COX-2 inhibitor is similar to NSAID's. Risk of gastric ulceration and platelet dysfunction is minimal. COX-2 inhibition may transiently decrease urine sodium excretion and induce mild to moderate elevation of blood pressure[18,20].

COX-2 inhibitors such as **rofecoxib** and **valdecoxib** are available for oral administration. **Parecoxib** a prodrug of valdecoxib is the only injectable COX-2 inhibitor available. It is administered in dose of **40mg IV bd**. First dose is given immediately after surgery.

COX-2 inhibitors have been found to have a negative influence on bone growth. They are not to be used for more than 3-5days following surgery.

**TABLE 6[26]:**

| Drug | Route | Dosage (mg) | Onset (min) | Duration (hrs) |
|---|---|---|---|---|
| Celecoxib | Oral | 200-400 | 30-50 | 4-8 |
| Valdecoxib | Oral | 20-40 | 30-40 | 6-12 |
| Rofecoxib | Oral | 20-50 | 30-50 | 12-24 |
| Etoricoxib | Oral | 60-90 | 20-30 | 24 |
| Parecoxib | Im/iv | 20-40 | 10-15 | 6-12 |

## ANALGESIC ADJUNCTS :

NMDA antagonists; ketamine, dextromethorphan, magnesium and adenosine have been tried as an analgesic adjuncts for post operative pain management. These have been shown to inhibit the receptor gated calcium currents that amplify neuronal firing.

**Alpha-2 agonists**: low dose clonidine has proved to be a useful analgesic adjunct when given neuraxially **(150ug intrathecally,2-3ug/kg epidurally and in combination with peripheral nerve block 0.5ug/kg)**. Higher doses are associated with adverse effects such as sedation, bradycardia and hypotension and should be avoided.

Dexmedetomidine is the other alpha-2 agonist that has recently been approved for use. Unfortunately,there is little experience with routine use of the drug in post partum women. At this time, it is not approved for neuraxial use[72].

**Neostigmine : intrathecal** administration of **25-100ug**. This has been associated with high incidence of nausea, vomiting, bradycardia, hypotension, sweating, agitation and distress[72].

**Gabapentin and Pregablin** : they are structural analogues of gamma aminobutyric acid and are used for treatment of persistent neuropathic pain. **Preoperative use of gabapentin 1200mg** reduces postoperative requirement of opioid and movement related pain. The main side effects are dizziness and somnolence[72].

**Glucocorticoids:** they block COX-2 and lipoxygenase enzyme and thus reduce and thus reduce inflammatory response and pain associated with surgery. Preoperative dexamethasone (4-8mg iv) not only reduces post operative pain but also nausea and vomiting[72].

## FUTURE APPLICATIONS:

1. **Mini dose epidural (1-2mg) or intrathecal (0.05-0.1mg) morphine, combined with an alpha 2 adrenergic agonist** and perhaps small doses of iv ketorolac. This combination of agents would provide multimodal analgesia while minimising dose dependent side effects[1].
2. **Continuous intrathecal administration of a lipophillic opioids** - The use of this technique depends on reapproval of small gauge microcatheters by the FDA[1].
3. **Intrathecal administration of a lipophilic opioid sequestrated in albumin, lipid solvents or liposomes.** These substances function as drug depends that permit slow, sustained release of the drug, there by extending the duration of activity[1].
4. **Lipid encapsulated morphine: Depo-Foam™** is a lipid based vehicle consisting of aqueous chambers that package (encapsulate) the active drug, such as morphine **(DepoDur™)**[1], resulting in sustained release and prolonged analgesia when the drug is administered epidurally. Nonetheless, encapsulated morphine given as single epidural injection may be useful single drug regimen for providing prolonged (upto 48hr) analgesia.
5. **Penetration enhancers (sodium glycocholate)** may be added to facilitate the absorption of drugs transdermally[73].
6. **Chemical enhancers :** may be used to facilitate absorption of the drug. Constant electricity **(ionotophoresis)** is also used to diminish the skin barrier[74].
7. **Drug carriers (liposomes)** may facilitate the administration and release of drugs in specific locations.

## NON PHARMACOLOGICAL METHODS:

1. **CRYOANALGESIA :** intense cooliing of peripheral nerves to temperatures below -5 to -20?°C causes disintegration of axons and breakdown of myelin sheaths without disrupting the perineurium/epineurium. This results in an interuption of nerve conduction for several weeks. The typical cyroprobe uses system to deliver compressed $N_2O/CO_2$ through a small orifice at its tip to produce intense cooling[75].
2. **ELECTROANALGESIC TECHNIQUE:** these include **TENS** (Transcutaneous Electrical Nerve Stimulation) ; **ALTENS**(Acupuncture Like TENS) ; **percutaneous neuromodulation therapy; transcutaneous acupoint electrical stimulation.**TENS is simple, non invasive technique for providing post operative analgesia. It produces pain relief through modulation of nociceptive impulses in spinal

cord. Immediately after wound closure, sterile adhesive electrodes are applied to skin on either side of incision. The wound is dressed and electrodes connected to stimulator. The stimulator delivers an asymmetric, biphasic waveform with **current strength of 12-20 mA, stimulus frequency of 10-100hz and pulse width of 60-150usec**. This should result in vibrating, tingling, soothing sensation that is in itself not painful. The settings on stimulator are then fine tuned to produce maximum benefit[75].

3. **ACUPUNCTURE.**
4. **HYPNOSIS.**
5. **MEDITATION.**
6. **HERBAL MEDICINE.**

**CONCLUSION :**

Despite the availability of several guidelines for the management of acute post operative cesearean pain, the day to day pain treatment is still not optimal. One of reasons being, general guidelines are not user friendly that is they provide general information on analgesics. It may be more rational to develop patient-procedure-specific pain treatment guidelines. Women undergoing cesearean delivery should have access to high quality pain relief that is safe and effective. The choice is frequently influenced by factors such as use of regional anaesthesia or patient preference. This review is not comprehensive but is intended to summarise current thought about the practical management of postoperative pain in an understandable and accessible fashion.

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