Neuraxial techniques of labour analgesia

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ABSTRACT

In recent years, many neuraxial techniques have been introduced to initiate and maintain labour analgesia, with low-dose mixtures of local anaesthetics and opioids, which have improved the quality of analgesia and made it safer for both mother and neonate. An independent search of the databases of PubMed, Medline, and Cochrane controlled trial data was conducted by two researchers, and randomized controlled trials that compared different methods of neuraxial analgesia and the different techniques of maintaining labor analgesia were retrieved and analyzed. The advantages, disadvantages, and indications of each technique along with the doses of intrathecal and epidural drugs are discussed. The myths and controversies involving neuraxial labor analgesia and the current consensus on their effect on the maternal and foetal outcomes are also outlined.

Key words: Computer-integrated patient-controlled epidural analgesia, continuous spinal analgesia, neuraxial labour analgesia, programmed intermittent bolus

INTRODUCTION

Many modalities have been introduced by obstetric anaesthesiologists to provide pain relief during labour, but neuraxial analgesia has been considered incomparable due to its proven efficacy and flexibility with maternal satisfaction. Some of the non-neuraxial methods which have gained popularity among labouring parturients who do not opt for epidural analgesia are parental opioids and nitrous oxide. Women vary in their needs and desire for pain relief during labour, with some aiming for non-neuraxial or neuraxial methods for labor analgesia. However, the fact needs to be emphasized that most non-neuraxial methods do not provide complete pain relief, but they do allow a woman to cope with her labour pain. We can further influence our patient's experiences by understanding that satisfaction during labour is not directly correlated with pain or pain relief. Regardless of the woman's analgesic choices, unmet expectations are an important source of dissatisfaction. In this review, we will focus on the pharmacological agents used for neuraxial analgesia and the different techniques of neuraxial analgesia for pain relief during labour.

STAGES OF LABOUR

Labour has been divided into three stages. The first stage occurs from onset of cervical change to 10 cm dilatation. It can be divided into latent and accelerative phases. The latent phase can last up to 8 h, without the need of intervention, whereas the active phase is associated with faster rate of cervical dilatation and usually begins at 2–4 cm dilatation and the duration varies from 2 to 6 h. The second stage of labour occurs from full cervical dilatation (10 cm) to delivery of the baby. Normally, the second stage lasts for 2 h (approximately 3 h with regional anaesthesia) in primipara and 1 h (approximately 2 h with regional anaesthesia) in a multipara. The third stage occurs from delivery of the baby to separation and expulsion of placenta and membranes.

PAIN PATHWAYS

Labour pain is associated with regular, painful uterine contractions that increases in frequency and intensity as labour progresses and has both a visceral and somatic component. Uterine contractions and cervical dilatation result in visceral pain. These pain impulses...
are transmitted by afferent, slow-conducting, A-delta and C fibers that accompany the sympathetic nerves and enter the spinal cord at the T10 to L1 level. As labor progresses, the descent of foetal head and subsequent pressure on the pelvic floor, vagina, and perineum generates somatic pain, which is transmitted by the pudendal nerve (S2–4) [Figure 1a] Supraspinal pain pathways [Figure 1b] start with the ascending pathways projecting to the pons and the medulla, thereby activating centers of cardiorespiratory control and descending pathways as well as the thalamus, which in turn sends projections to the anterior cingulate, motor, somatosensory, and limbic regions with projections to the cortex, resulting in the sensory–emotional experience of pain.

**Methods of pain relief during labour**
Effective and safe analgesia during labour is yet to gain wide acceptance and is riddled with myths and controversies, which makes it more challenging. The commonly used methods of labour analgesia are listed in Table 1.

**Pharmacology of drugs used for neuraxial analgesia**
The ideal local anaesthetic for labour analgesia should produce a reliable sensory block, no motor block, without tachyphylaxis, and inadvertent overdose or accidental intravenous administration should have a good safety profile. The doses and concentrations of local anaesthetics and adjuvants that are routinely used for labour analgesia are given in Table 2.

Single-enantiomer compounds (e.g., ropivacaine, levobupivacaine) have definite advantages over the racemic mixtures of two stereoisomers such as bupivacaine, which has a poor safety profile in terms of cardiovascular and central nervous system toxicity. Ropivacaine and L-bupivacaine are the propyl homologues of bupivacaine and have lower lipid solubility, slightly higher plasma clearance, shorter elimination half-life, and a similar degree of protein binding. Bupivacaine is found to dissociate more slowly from the inactive and resting sodium channel configurations for which it has a greater affinity. This renders cardiac tissues susceptible to arrhythmias since recovery from action potentials is delayed.

Ropivacaine, a propyl homologue of bupivacaine (pure S-enantiomer), is levorotatory (left-isomer), and although it possesses a relatively low potency, it has a greater safety profile. However, it appears that the drugs are not equipotent. The minimal local analgesic concentration (MLAC) ratio of ropivacaine to bupivacaine is 0.6 and the motor blocking potency is 0.66, suggesting that ropivacaine does not have a superior sensory–motor differential block when compared with bupivacaine. Since ropivacaine is less lipophilic than bupivacaine, it has a selective action on the sensory fibers (A δ and C) as it is less likely to penetrate large myelinated (A α) motor fibers. In equipotent doses (0.15% ropivacaine vs 0.1% bupivacaine), the incidence of motor block is found to be same.[3]

Levobupivacaine is a single-enantiomer local anaesthetic and a levorotatory stereoisomer of bupivacaine. Unlike ropivacaine, it is equipotent to bupivacaine with an MLAC ratio of 0.98.[3] It is less cardiotoxic than bupivacaine, with approximately
a 50% greater safety margin in animal trials. When low-dose techniques are used, toxicity concerns may seem irrelevant, but the total amount of local anaesthetic used may be high during protracted labour and large boluses may be required for operative delivery. Various epidural analgesic potency studies suggest a spectrum of relative potencies of 0.7:0.9:1.0 for ropivacaine:levo bupivacaine:bupivacaine. However, there does not appear to be any clinical advantage of one drug over the other two drugs for epidural labour analgesia.

Chloroprocaine and lignocaine are also used in obstetrics in some parts of the world but are not considered ideal for labour analgesia. Chloroprocaine is an ester local anaesthetic with an extremely rapid onset of action and is used to extend labour epidurals for operative delivery. Although placental transmission is minimized as it undergoes ester hydrolysis, its duration of action is too short for labour analgesia. Lignocaine is not popular for labour analgesia, as repeated doses can cause tachyphylaxis. It is only

| Table 1: Methods of labour analgesia |
|-------------------------------------|
| **Nonpharmacological**              |
| Continuous emotional support        |
| Relaxation/breathing techniques      |
| TENS                                |
| Bio-feedback and physical therapies |
| Hydrotherapy                        |
| Intradermal water injection         |
| Hypnosis                            |
| Acupuncture/acupressure             |
| Miscellaneous: aromatherapy, music, massage, therapeutic use of heat and cold |
| **Pharmacological**                 |
| Systemic                            |
| Inhalational methods                |
| Entonox                             |
| Volatile anesthetic agents: sevoflurane, isoflurane, desflurane, enflurane   |
| Systemic analgesics                 |
| Opioids: pethidine, meperidine, morphine, diamorphine fentanyl, sufentanil remifentanil, alfentanil |
| Nonopioid analgesics                |
| Agonist-antagonist analgesics (nalbuphine, buprenorphine, butorphenol)        |
| Sedatives, tranquillizers (barbituates, benzodiazepines, phenothiazone derivatives) |
| Dissociative or amnesic drugs (ketamine)                                    |
| **Regional**                        |
| Lumbar epidural analgesia           |
| CSEA                                |
| Single shot spinal analgesia        |
| CSA                                 |
| Dural puncture epidural technique   |
| Maintenance of LA                  |
| Intermittent top ups                |
| Continuous epidural infusion        |
| PCEA                                |
| CI-PCEA                             |
| PIEB                                |
| Alternative regional anesthetic block |
| Lumbar sympathetic block            |
| Pudendal block                      |
| Paracervical block                  |

| Table 2: Example of common epidural/intrathecal drug regimes |
|-------------------------------------------------------------|
| **Drug regimes**                                            |
| Lumbar epidural (LDM/top ups)                               |
| PCEA                                                         |
| CSEA                                                        |
| CSA                                                         |
| **Initial bolus dose**                                      |
| 10-15 mL LDM                                                |
| 5-10 mL LDM                                                 |
| Intrathecal                                                 |
| 0.5% B (1-2.5 mg) + F (10-25 µg) or S (2.5-10 µg)           |
| Intrathecal bolus dose                                      |
| 0.5% B (1.75-2.5 mg) + F (15-20 µg) or S (5 µg)             |
| **Maintenance**                                             |
| Intermittent bolus (top ups, without background infusion)   |
| 10-15 mL LDM                                                |
| 8-12 mL LDM (as required by parturient)                     |
| Epidural 5-10 mL LDM                                        |
| Intrathecal bolus dose                                      |
| 0.5% B (1.75-2.5 mg) + F (15-20 µg/1-2 h) S (5 µg SOS)      |
| **Continuous basal infusion (LDI)**                         |
| 5-8 mL/h LDM                                               |
| Bolus*LDM can be given as required                         |
| 5-8 mL/h LDM                                               |
| Bolus dose: 5-8 mL (as required by parturient)              |
| Intrathecal bolus infusion                                 |
| B (0.05%-0.125%) + F 2.5 µg/mL at 0.5-3 mL/h (titrated to a T8-10 sensory level) or S (2.5-5 µg/h) as required |
| **Lock out time (dose interval)**                          |
| 10-20 min                                                  |
| 10-20 min                                                  |
| **Concentration of other local anaesthetic used**           |
| 0.08%-0.2%                                                  |
| 0.05%-0.125%                                                |
| **Dose of opioids**                                         |
| Intrathecal                                                 |
| Fentanyl                                                   |
| 5-25 µg                                                    |
| Sufentanil                                                  |
| 2.5-15 µg                                                   |
| Morphine                                                   |
| 0.1-0.2 mg                                                  |
| Diamorphine                                                |
| 0.2-0.4 mg                                                  |
| Epidural                                                   |
| 50-100 µg (1.5-3 µg/mL)                                    |
| 25-50 µg (0.2-0.4 µg/mL)                                   |
| 7.5-10 mg                                                  |
| 2-3 mg                                                     |

B – Bupivacaine; S – Sufentanil; F – Fentanyl; CSEA – Combined spinal epidural analgesia; CSA – Continuous spinal analgesia; PCEA – Patient-controlled epidural analgesia; LDI – Low-dose infusion; LDM – Low-dose mixture; *LDM: bupivacaine (0.0625%-0.125%) 10-15 mL/fentanyl (1.5-3 µg/mL) or sufentanil (0.2-0.4 µg/mL)
used for topping up epidurals when profound sensory and motor block is required for operative delivery.[5,6]

Adjuvants
Administration of local amide anaesthetics in combination with opioids is routinely used for relief of labour pain. Synthetic opioids such as the lipid-soluble sufentanil and fentanyl can increase the potency of local amide anaesthetics such as bupivacaine, levobupivacaine, and ropivacaine by modifying their minimum potencies. Other adjuvants which have been used along with local anaesthetics and opioids are alpha-2 agonists such as clonidine, cholinesterase inhibitors such as neostigmine,[7,8] and vasoconstrictors such as epinephrine, though due to concerns about their safety profile, they are not routinely recommended for obstetric analgesia. No adjuvant studied till date prolongs the duration of fentanyl or sufentanil/bupivacaine analgesia long enough to avoid the use of maintenance epidural analgesia for most parturients, and no adjuvant reduces or eliminates the side effects associated with the analgesic drugs used clinically.[5,6]

Neuraxial techniques for labour analgesia[5,9,10]
A thorough maternal history and physical examination should be done to identify obstetric and anaesthetic risk factors in all mothers undergoing labour analgesia. Examination of the back for any anatomical deformity, obesity, and local oedema which may conceal spinal orientation making neuraxial access difficult, should be confirmed. The foetal status should be assessed and an informed consent should be obtained. Indications and contraindications for neuraxial LA are listed in Table 3. Oral intake of moderate amounts of clear liquid may be allowed for uncomplicated patients but solid foods should be restricted. Intravenous infusion should be started and all the resuscitative equipments and drugs should be kept ready. Parturient should be well-informed, prepared, and counseled during the antenatal classes along with her partner.[1] Advantages and disadvantages of each technique are discussed in Table 4.

Test dose
An ideal test dose should be able to detect both accidental intravascular and subarachnoid injections of local anaesthetics. The choice of drugs for the test dose is controversial. A typical test dose is 3 mL of either 1.5% lignocaine with epinephrine 1:200,000 (i.e., lignocaine 45 mg and epinephrine 15 µg) or bupivacaine 7.5–12.5 mg with epinephrine. However, many anaesthesiologists have argued for a “no test dose” technique (considering the concentration of local anesthetic used to maintain labor epidural analgesia has been decreased to 0.0625%–0.125%), in which “every dose is a test dose” and signs and symptoms of intravascular injection are sought every time a bolus of local anesthetic is administered.

LUMBAR EPIDURAL ANALGESIA
Lumbar epidural analgesia aims to produce a selective sensory block from T10 to L1 while at the same time sparing the motor supply to the lower limbs (L2–L5), and it is called the “mobile epidural or walking epidural.” Decreasing the concentration of local anesthetics by addition of opioid, most commonly fentanyl (2 µg/mL) with epidural bupivacaine (0.0625%–0.125%), results in sparing of motor fibers.
The low-dose mixtures (LDMs) of local anesthetics and opioids also act as test doses to detect intravascular or intrathecal placement of epidural catheters.\[^{11}\]

### MAINTENANCE OF LUMBAR EPIDURAL ANALGESIA

#### Intermittent bolus technique

Epidural analgesia was routinely maintained by the intermittent administration of bolus doses of local anesthetic when analgesia began to wane, before the introduction of infusion pumps. On recurrence of pain, analgesia was usually reestablished with a bolus injection of 8–12 mL of a local anesthetic/opioid solution.\[^{9,10}\] Improved analgesia and higher maternal satisfaction with manual bolus doses versus continuous infusion through multiorifice catheters is observed as flow occurs through all the catheter ports, leading to greater spread of infusate, but it has several limitations. Pain relief is constantly interrupted by regression of analgesia, requires frequent provider intervention with assessment and recording of the sensory level, and the intensity of motor blockade before and after each bolus injection of local anaesthetic.\[^{11,12}\] As after several injections, blockade of the sacral segments, intense motor blockade, or both may develop.\[^{13}\]

#### Continuous infusion into epidural space

It provides adequate and smoother analgesia and haemodynamic stability with titrated doses of local anaesthetics and opioid by infusion devices and can be adjusted to individualize analgesia.\[^{14}\] There are no peaks and valleys of local anaesthetic concentration as in intermittent technique but it requires larger doses of local anaesthetics, which may impair the ability to bear down during second stage of labor, resulting in increased rate of instrumental deliveries. A recent systemic review and meta-analysis\[^{15}\] concluded that there was a reduction in motor blockade and rate of assisted delivery with programmed intermittent boluses when compared with continuous infusions in the epidural space.

#### Patient-controlled epidural analgesia

This technique allows the parturient to control the dose of local anaesthetics according to the severity of pain and hence improving maternal satisfaction with the psychological advantage of being in control of her own therapy. There is reduction in clinician intervention, amount of local anaesthetics and opioid requirement, and incidence of motor block when compared with continuous epidural infusion (CEI).\[^{16,17}\] Disadvantages of patient-controlled epidural analgesia (PCEA) technique include...
requirement of a dedicated infusion pump and proper education of the parturient in its use.

**Programmed intermittent epidural bolus or automated mandatory epidural boluses**

It is a relatively new innovative protocol used for the maintenance of labour analgesia, where a preset volume of epidural mixture is administered as a bolus at a timed interval by a drug delivery pump. It has been suggested to be a superior mode for the maintenance of labour epidural analgesia compared with a conventional continuous epidural infusion (CEI). In programmed intermittent epidural bolus (PIEB), instead of background infusion, the hourly total amount of local anesthetic solution normally used in a CEI is administered as intermittent boluses of LDMs (e.g., two 5 mL boluses within 30 min instead of a 10 mL/h epidural infusion). This provides similar analgesia, higher maternal satisfaction, less need for unscheduled rescue boluses, and reduced consumption of bupivacaine with less motor blockade when compared with a CEI. PIEB has also been combined with PCEA, which results in reduced consumption of local anaesthetics and less PCEA demand boluses, when compared with PCEA with standard continuous background infusion, though the analgesic efficacy is the same. The infusion solution, patient-controlled bolus volume, lockout interval, background infusion rate, and maximum allowable dose per hour can be manipulated by the anaesthesia providers.

**Computer-integrated patient-controlled epidural analgesia**

It is an advanced and novel epidural analgesia delivery system with preset algorithm which is programmed to analyze the dose of LA and to increase or decrease the basal infusion rate based on previous hour demand requirement. It converts a continuous infusion pump into a computer-integrated PCEA (CIPCEA) which is more responsive to the parturients’ needs. This interactive program records the history of the analgesic requirements over the past hour, and according to the number of demand boluses, it increases the magnitude of its basal infusion proportionally. The basal infusion is adjusted to 5, 10, or 15 mL/h if the parturient required one, two, or three demand boluses, respectively, in the last hour and decreases the basal infusion by increments of 5 mL/h if there were no bolus demands in the preceding hour. The CIPCEA regimen is associated with a significant reduction in the incidence of breakthrough pain without increasing local anaesthetic consumption or incidence of side effects.

**COMBINED SPINAL EPIDURAL ANALGESIA**

CSE (needle through needle) has added advantages of both spinal (rapid onset and dense block) and epidural (prolonged duration of block and postoperative analgesia) blocks. Walking epidural was first coined to describe low-dose CSE opioid analgesia, because motor function was not impaired and ambulation of parturient was maintained. CSE may be chosen in more advanced labour when compared with epidural analgesia, because the spinal component provides rapid pain relief. In the case of a short time interval between CSE placement and delivery, spinal analgesia may still be effective, and potential shortcoming of epidural component might pass unnoticed.

**SINGLE-SHOT SPINAL ANALGESIA**

This is one of the easiest techniques with success rate of 98% in parturients with severe restlessness due to pain during the later stages of labour, especially in resource-limited situations. Low-dose combination (fentanyl 25 µg, bupivacaine 2.5 mg, and morphine 250 µg) in one injection provides up to 4 h of ambulatory pain control. However, since labour is unpredictable and the process of labour is unique to parturients, a second spinal block (fentanyl 25 µg + bupivacaine 2.5mg) may be required, when the effect of the first dose wears off.

**DURAL PUNCTURE EPIDURAL TECHNIQUE**

Dural puncture epidural (DPE) is a technical modification of the CSE in which the dura is perforated with a Whitacre spinal needle (CSE technique), but direct administration of medications into the subarachnoid space is not done. A conduit for translocation of epidural drugs from the epidural to the subarachnoid space occurs following insertion of the epidural catheter and appropriate administration of medications into the epidural space. The size of the dural puncture, the distance between the puncture location and epidural drug administration, and the pressure gradient between the two compartments determine the extent of drugs reaching the subarachnoid space. In addition, the volume and concentration of the local anaesthetic solution, the diffusion capacity of the drug, and the pressure of an
epidural bolus injection may also play an important role. DPE technique may thus provide a faster onset of labour analgesia giving a better quality, reliable, and consistent block compared with the epidural technique with less maternal and foetal side effects compared with the CSE technique.\[24,25\]

**CONTINUOUS SPINAL ANALGESIA**

This technique is indicated in parturients in whom epidural catheter placement is difficult due to morbid obesity or anatomical deformities or as a salvage technique after an unintentional dural puncture, while attempting epidural. There are concerns about cauda equina syndrome with the spinal microcatheters, their very small internal diameter severely limiting the flow rate of local anesthetic injected through them, resulting in laminar flow of local anesthetic within the cerebrospinal fluid, exposing some nerve roots to very high concentrations of local anesthetic. Thus, for continuous spinal analgesia (CSA), paediatric epidural catheters size 24G placed through 20G epidural needles or 20G epidural catheters placed through 18G epidural needles may be used. Special precautions to label these catheters need to be ensured, to avoid the possibility that it may be mistaken for an epidural catheter. This technique is not popular because of more technical difficulties and catheter failures when compared with epidural analgesia; however, these risks should be weighed against the many advantages of the technique in specific, challenging patient populations.\[26\]

**Practical tips to salvage an inadequate block**

Ensure that the epidural blocks are successful because each rescue maneuver takes 30 min to be effective [Figure 2]. If visual analog score (VAS) for pain assessment is <4 on a VAS of 0–10, it means the analgesia is satisfactory and parturient can cope with the pain, whereas if it is >4 she requires additional analgesia. Therefore, an aggressive response in terms of drug supplementation or catheter replacement is required, as none of the drugs gives immediate pain relief. Pan et al. 2004\[27\] reviewed 12,590 neuraxial anesthetics and found an overall failure rate of 12% (epidurals 14% and CSE 10%) and incidence of epidural catheter misplacement as 6%.

**Complications of regional analgesia in labour are listed in Table 5**

**Myths and controversies**

1. Progress and outcomes: high-quality evidence exists, which states that early or late initiation of LA has similar effects on all measured outcomes of labour.\[28-30\] Epidural analgesia with low dose mixtures (LDM) is not associated with

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*Figure 2: Practical tips to salvage an inadequate block*
significant prolongation of duration of stage II of labour (<15 min). There is no association between risk of caesarean delivery and neuraxial labour analgesia versus non-neuraxial analgesia; however, an increased risk for instrumental vaginal delivery was observed in the neuraxial group versus systemic analgesia group. Recent impact trials and meta-analysis have concluded that the incidence of instrumental vaginal delivery is much lower with the low-dose local anaesthetic opioid mixtures. Maternal foetal factors and obstetric management are the most important determinants of caesarean delivery rate. The early onset of severe pain and the requirement of high doses of analgesic agents predict higher risks for abnormal labour, foetal heart rate abnormalities, and operative delivery. These findings may explain the observed association between neuraxial analgesia and operative delivery.

2. The discontinuation of epidural analgesia during the second stage of labour does not seem to be an acceptable practice and labouring women should not be deprived of using epidural labour analgesia at any stage of their labour.

3. After childbirth, there are no differences in the incidence of long-term low back pain, disability, or movement restriction between women who receive epidural pain relief and women who receive other forms of pain relief.

4. Breastfeeding success and epidural labour analgesia with fentanyl, when analyzed at 6 weeks postpartum, was not influenced by epidural fentanyl concentration. Multiple factors such as intention of mother to breastfeed, social support, need of mother to return to work, doses of oxytocin, and maternal fever influence breastfeeding success.

5. Epidural analgesia is causally related to maternal fever and the most likely cause is sterile inflammation. Causal association with neonatal sepsis is controversial as also its association with neonatal brain injury.

6. Epidural analgesia can be used during trial of labor for vaginal birth after previous caesarean delivery (VBAC) and adequate pain relief may encourage more women to attempt VBAC; epidural analgesia is not expected to mask signs of uterine rupture.

**FUTURE POTENTIAL**

Research must continue to improve obstetric outcomes in women who choose neuraxial analgesia, and analgesia techniques should be tailored to the needs of the individual parturients. Protocol refinement with ultra-low-dose (≤0.1%) local anesthetic-opioid solutions with PCEA and PIEB allowing more flexibility through cost-effective smart pumps and ultrasound-guided neuraxial blocks in difficult cases can further minimize the adverse effects on progress and outcome of labour, along with improving analgesia, patient satisfaction, and reducing motor block.

**SUMMARY**

Maintenance regimens, especially PIEB, automated mandatory bolus (AMB), PCEA, and CIPCEA techniques, remain a subject of extensive research as also the newer neuraxial techniques (CSA and DPE) whose optimization seems to be essential in tailoring efficient analgesia to the individual patient’s need. Modern neuraxial analgesia, especially the LDM of local anaesthetics and opioids, has minimal adverse obstetric outcomes. Further research is required not only to improve the women’s experience of labour but also to ensure the avoidance of any negative effect on the process of birth.

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**Conflicts of interest**

There are no conflicts of interest.

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