

Recent advances in labour analgesia

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ABSTRACT

Pain of labour is said to be one of the most intense on the pain scale. Experience of labour varies among women, and even among different pregnancies in the same woman depending on various factors. Offering of analgesia to labouring women has become the standard of care across the globe. Since the earliest days when labour analgesia was initiated, multiple non pharmacological methods have been described. Different forms of exercises performed antenatally also have shown some benefit in labouring women. However pharmacological methods are more efficacious with higher chance of success compared to nonpharmacological methods. Systemic analgesics include administration of opioids and inhaled anaesthetics. Of special mention in recent times is the advantageous use of remifentanyl for alleviating pain of labour. Inhaled anaesthetics are being less favoured due to their effects like amnesia. Neuraxial blockade remains to be the gold standard form of labour analgesia. Of the various methods, the most commonly followed forms include epidural analgesia and combined spinal epidural analgesia. Various new technological advances have been made to make administering analgesia via epidural easier, such as computer integrated patient controlled epidural analgesia and programmed intermittent epidural boluses which have been detailed in the review. Other newer technologies such as virtual reality are also described as newer forms of painless labour. Despite multiple options that are available, it must be borne in mind that each labouring woman and every birth is special. Hence, these options need to be tailored to suit every woman's needs during childbirth.

Key words: Labour, pain pathways, analgesia, epidural

INTRODUCTION

Labour is one of the most memorable albeit painful experiences in a woman's life. The pain felt during childbirth is often rated the most intense on the pain scale comparable to that of traumatic amputation of a limb¹. Experience of labour pain varies among women, and even among different pregnancies in the same woman depending on various physical, psychological and social factors^{2,3}.

Pain is usually a good thing, with its manifestation thought to direct patient and physician to underlying disease; but, labour pain can have deleterious effects. Labour pain activates the sympathetic nervous system, causing maternal hyperventilation, shift of the oxygen dissociation curve to the left and foetal hypoxia. Other factors which contribute to foetal hypoxia include increased catecholamines and strong uterine contractions, both of which reduce uterine blood flow⁴.

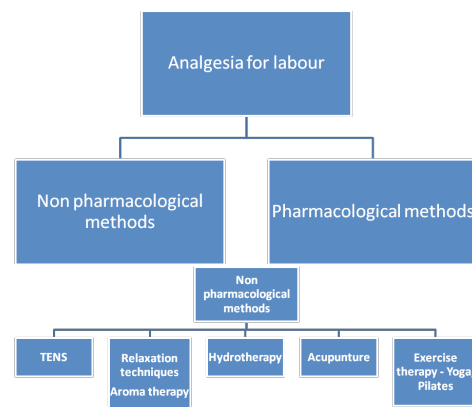


Figure 1. Flow diagram showing the non-pharmacological methods of labour analgesia.

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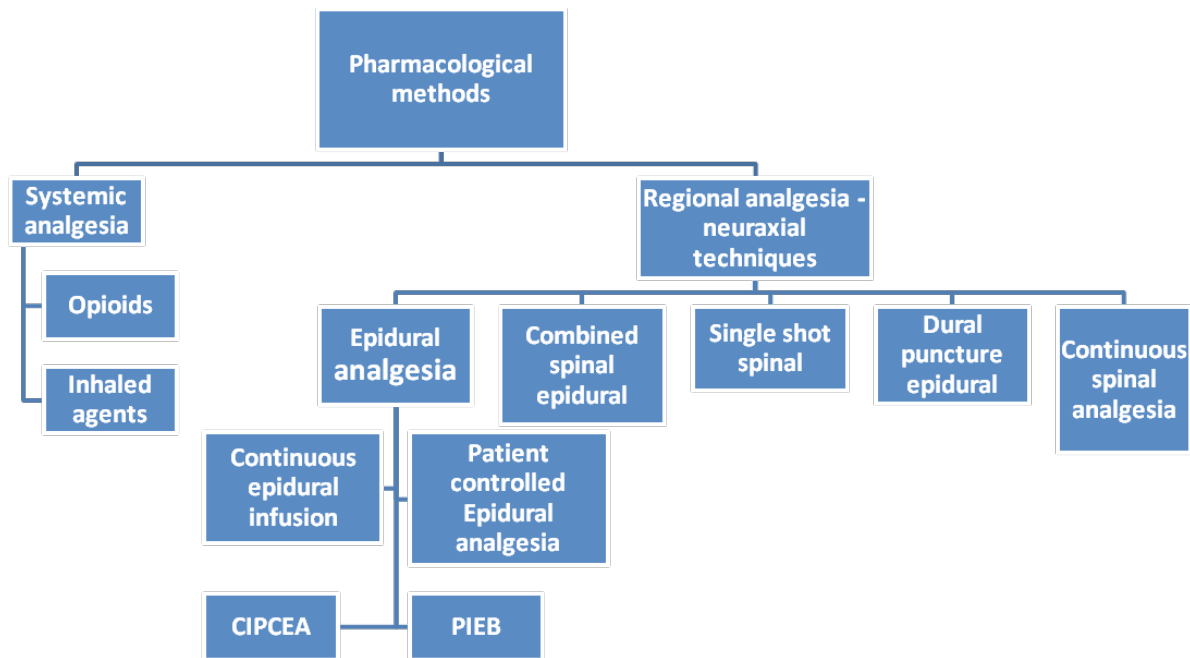


Figure 2. Flow diagram showing the pharmacological methods of labour analgesia.

Maternal effects include increased anxiety, which can lead to post partum vulnerability and depression⁵. It is for all these reasons, that modern anaesthesia practice is used for offering of effective analgesia to labouring mothers and at the same time, aims to minimally interfere with the process of childbirth. It has been observed that provision of labour analgesia has the potential to improve foetal acidosis and improve cardiovascular and pulmonary function in the mother⁶⁻⁹.

Most women require analgesia during labour. Few methods are non – pharmacological which help women to cope with the pain of labour¹⁰. In this review article, we shall briefly discuss non-pharmacological methods, pharmacological methods and recent advances in labour analgesia.

STAGES OF LABOUR AND PAIN PATHWAYS

Labour is divided into three stages, with the first stage – comprising of the latent and active phases, second stage and ending with the third stage. The early or latent phase of labour is when uterine contractions begin, resulting in cervical dilatation of up to four centimetres. Active first stage of labour then takes over, resulting in full dilatation and effacement of cervix causing the foetus to descend into mid – pelvis. Second stage of labour is that phase spanning from full cervical dilatation to delivery of the foetus, culminating in the third stage, where the placenta is delivered.

Knowledge of origin of labour pain is important to achieve appropriate analgesia. Pain in the first stage arises from uterine contractions and cervical dilatation, giving rise to intense visceral, cramping pain. This occurs due to activation of uterine mechanoreceptors and ischemia of tissues during contractions. At this stage, pain sensation is carried to the spinal cord via the white rami communicantes of T10 to L1 nerves and is carried forward to reach supra-spinal centres of pain. In the second stage of labour, pain is more intense with the presenting part distending the vagina and perineal tissues superadded with uterine contractions. Vaginal distension causes somatic pain, carried by nociceptors to the spinal cord by three sacral nerves i.e. S 2-4 (Pudendal nerve).

INITIATION OF LABOUR ANALGESIA

For many initial years, it was thought that early introduction of labour analgesia, before cervical dilatation of four centimetres (cm), in the form of neuraxial analgesia was associated with increased rates of Caesarean delivery. However, many impact studies¹¹⁻¹⁵ and a large meta-analysis¹⁶ has proven that there is no association with neuraxial analgesia and increased rate of caesarean sections.

Initial recommendations by the American College of Obstetricians and Gynaecology (ACOG) for many years stated that women delay requesting epidural analgesia

“when feasible, until the cervix is dilated to 4-5 cm.” Further, randomized trials conducted^{17,18} also dismissed concerns regarding association of early neuraxial analgesia with instrumental vaginal deliveries. A meta-analysis of 37,000 patients found no increase in instrumental vaginal deliveries when epidural analgesia was used. Following these studies, the ACOG in 2007 revised their initial statement, stating that maternal request at any stage of labour was an indication sufficient for providing labour analgesia¹⁹. However, there is confusion regarding the dose of epidural used which may predispose to instrumentation during labour. The COMET trial in 2001 reported higher incidence of vaginal operative delivery in women who received 0.25% bupivacaine top – ups compared to low dose or opioid top ups²⁰.

FORMS OF LABOUR ANALGESIA

Labour analgesia is provided by various methods – consisting broadly of non – pharmacological and pharmacological methods. Some of the non – pharmacological methods include:

- Transcutaneous electrical nerve stimulation – TENS therapy
- Relaxation techniques
- Aromatherapy
- Hydrotherapy
- Temperature modulation – heat / cold therapy
- Acupuncture
- Audio analgesia / Electro analgesia
- Exercise and antenatal Yoga

In a recent Cochrane review of pain management options for women in labour, most of the non-pharmacological techniques were found to decrease pain in isolated studies, but had insufficient evidence to make judgements on whether or not they were effective means to provide labour analgesia¹⁰.

Use of birth ball exercises was shown to reduce labour pain, probably explained by the gate control theory. A systematic review of three studies showed significant reduction of pain scores during labour in women who practiced these exercises. However, notes on analgesic consumption or request for other forms of analgesia were

not mentioned. Similarly Yoga also had beneficial effect on maternal comfort during childbirth, but lacks sufficient high quality evidence^{21,22}.

Of interest, is hydrotherapy or immersion of the pregnant abdomen in warm water baths of up to 37.5 degrees Celsius. It was found to reduce the requests for neuraxial analgesia when initiated in the first stage of labour, however did not have any effects on opioid requirement, duration of labour or foetal outcomes²³.

PHARMACOLOGICAL METHODS OF LABOUR ANALGESIA

Pharmacological methods to reduce pain in labour can be subdivided into

- Systemic analgesia
- Opioids
- Inhaled agents
- Regional analgesia

SYSTEMIC ANALGESIA – OPIOIDS

Opioids have been used parenterally for labour analgesia and include the use of pethidine, morphine, fentanyl, sufentanyl, remifentanyl and partial agonists like nalbuphine and butorphanol. Of these agents, pethidine has been most widely used²⁴.

Pethidine, however has an active metabolite normeperidine which was shown to cause neonatal respiratory depression for up to three days after birth. A Cochrane review of 7000 parturients revealed that parenteral opioids provide moderate relief of pain in labour but the effect was not well sustained²⁴. Maternal adverse effects such as drowsiness, nausea and vomiting were noted commonly, but clear cut evidence on neonatal depression could not be established despite these effects reported in observational studies²⁵.

PATIENT CONTROLLED ANALGESIA (PCA)

PCA in labour is a recent addition and can be used whenever regional techniques are contraindicated or unavailable. Drugs amenable for use in PCA include fentanyl and more recently, remifentanyl. Fentanyl has the advantage of having a short half life with no active metabolites and can be given as boluses or patient controlled analgesia (PCA). Usual doses used are 25 to 50 micrograms with analgesic effect lasting up to 60 minutes²⁶. Remifentanyl, considered

as the “ideal” opioid for labour analgesia is an ultra – short acting opioid due to its rapid metabolism by blood and tissue esterase. Countries which use remifentanyl have formulated guidelines for use in labour²⁷.

Remifentanyl is used in PCA at doses of 25 to 50 microgram/kg with a lock out interval of 2 minutes. Remifentanyl in labour is more efficacious and safer than pethidine²⁸. Postpartum conditions of neonates born to mothers who were given remifentanyl had a better safety profile than those whose mothers received fentanyl²⁹. Despite its high safety profile, maternal and foetal monitoring is essential with use of remifentanyl during childbirth.

SYSTEMIC ANALGESIA – INHALED AGENTS

Agents used for labour analgesia include Entonox and Flurane derivatives. Entonox which is a commercial preparation of 50% nitrous oxide and 50% oxygen has been in use for a long time for providing analgesia during labour. Entonox is available in cylinders and delivered through additional apparatus consisting of pressure reducing valves. Recently, Entonox cylinder is now available in modern cylinders with integral valves and higher capacities, making them more patient friendly. However Entonox provides only mild to moderate pain relief with its effect only better than placebo. Also, it needs to be inhaled about 30 seconds before a contraction starts so as to have the peak effect, thus making it difficult to use in second stage of labour, where the mother needs to push. Its use was also associated with higher incidence of maternal nausea, vomiting and drowsiness. Owing to these factors combined with concerns of environmental pollution, clinical use of Entonox has declined³⁰.

FLURANE DERIVATIVES

Methoxyflurane, Isoflurane, Enflurane and Sevoflurane have all been described for use in pain relief for labour. These agents provide better analgesia compared to Entonox in the first stage of labour and lesser side effects³¹. Of all these agents, most recent advance was seen in the use of sevoflurane for labour analgesia.

PATIENT CONTROLLED INHALATION ANALGESIA – SEVOFLURANE

Is the drug used for patient controlled inhalational analgesia in labour. Administered in a concentration 0.8% with oxygen via specialised apparatus, sevoflurane has benefits due to its rapid onset and offset which is of value particularly during birthing³². However, concerns

regarding maternal amnesia and environmental pollution limit its use in practice³³.

REGIONAL TECHNIQUES FOR LABOUR ANALGESIA – NEURAXIAL ANALGESIA

Is considered the “gold standard” method of providing labour analgesia because of its high efficacy. Various methods of providing neuraxial analgesia include

- Epidural analgesia
- Combined Spinal Epidural (CSE)
- Single – shot spinal
- Dural Puncture Epidural (DPE)
- Continuous spinal analgesia

Neuraxial analgesia is performed to relieve labour pain and at the same time, provide for an epidural catheter for surgical anaesthesia, should operative delivery become necessary. Neuraxial blockade must cover appropriate segments when required, so that T10 – L1 roots are blocked during first stage and sacral roots in the second stage. Further, neuraxial analgesia can be initiated at any stage of labour, regardless of parity or cervical dilatation. Because of such a wide margin of safety, the joint statement regarding timing of labour analgesia was issued by the ACOG and American Society of Anesthesiologists (ASA).

NEURAXIAL TECHNIQUES

EPIDURAL ANALGESIA AND CSE

Among all the neuraxial techniques, epidural analgesia and Combined Spinal Epidural (CSE) are the most commonly used. The main advantage of epidural techniques over spinal analgesia is its versatility to provide surgical anaesthesia when the need arises.

The choice between conventional epidural and CSE is often dictated by clinical situation, institutional protocols, available equipment and practitioner preference. The advantage of CSE over epidural is the faster onset of analgesia with CSE, especially that of sacral segments. This feature is especially of value in parous patients with faster progress of labour into second stage³⁴. Technically, both techniques are easily performed, with minimal complications and equivalent foetal outcomes. The incidence of catheter related complications and unilateral block was found to be reduced with CSE³⁵.

RECENT ADVANCES IN OBSTETRIC EPIDURAL ANALGESIA

- Pre – procedural ultrasound – allows accurate interspace for needle placement and ensures success of procedure and ease of performance³⁶. Also helps in estimating distance between skin and epidural space, making the procedure simpler in obese women.
- Epidural catheters and kits – flexible wire reinforced catheters are now available which aid in easier threading and lesser complications such as kinking, intravascular threading and knotting.
- Test dose – standard test dosing with 3ml of 1.5% lidocaine plus 5mcg/ml of epinephrine is best avoided in obstetrics. The best way to test the catheter is to use small volumes of Local Anaesthetic (LA) of about 5 ml and waiting for a few minutes before the next aliquot is given. Every injection must be preceded by careful aspiration. Epinephrine in test dose for obstetrics is best avoided as inadvertent vascular injection may have serious consequences such as hypertension and uteroplacental insufficiency.
- Newer adjuvants – α_2 agonist clonidine and cholinesterase inhibitor neostigmine added as adjuvants have been tested in labour analgesia³⁷⁻³⁸. These drugs were used both intrathecally and epidurally and were found to significantly prolong the duration of labour analgesia when combined with bupivacaine. However, incidence of hypotension was found to be higher with the use of clonidine and has not been approved for use in obstetric patients.

INITIATION AND MAINTENANCE OF LABOUR EPIDURAL

Starting with small incremental doses, 10 – 20 mL of LA plus opioid mixture is used to initiate analgesia. When higher volumes are used, it is preferable to use lower concentration of LA such as – 0.0625% - 0.1% bupivacaine or 0.08 – 0.1% ropivacaine with 2 mcg/mL fentanyl. Alternatively, lower volumes of a more concentrated drug such as 5 - 10 ml of 0.125% bupivacaine may be used.

Maintenance of labour analgesia with epidural is often necessary when the woman progresses to second stage where sacral analgesia is required. Maintenance is achieved by continuous or intermittent administration of a drug

mixture similar to that used for initiation. Some commonly used regimens for maintenance include:

- Anaesthetist administered top – ups
- Low dose infusions
- Low dose top ups

MODES OF DRUG ADMINISTRATION FOR LABOUR EPIDURAL

- Continuous Epidural Infusion techniques (CEI) – epidural infusion pumps are used for this mode. Advantages include reduced workload, reduced fluctuations in pain and better hemodynamic stability over boluses.
- Patient Controlled Epidural Analgesia (PCEA) – system where patient self – administers an epidural bolus when the need arises. PCEA pumps are available with settings for continuous background infusion with provision for intermittent boluses with a lock out of 10 to 15 minutes.
- New pump technologies
 - a. CIPCEA – Computer Integrated PCEA is a mode in which the computer modifies the background infusion rate based on the patient’s bolus requirements in the previous hour³⁹.
 - b. PIEB – Programmed Intermittent Epidural Bolus is a novel technology which allows the infusor to deliver boluses at a predetermined interval. PIEB offers better analgesia when combined with multi-orifice catheters than with single orifice catheters⁴⁰. Advantages of this technique include fewer rescue doses, improved maternal satisfaction and lesser total Local Anaesthetic (LA) consumption over CEI.

SINGLE SHOT SPINAL ANALGESIA

Single dose of intrathecal drug placement is done without placement of an epidural catheter. This technique allows for rapid onset of analgesia but is limited by short duration of action. All these features make it suitable for second stage of labour when parturient progress fast or when epidural placement is not possible. Intrathecal fentanyl 5 – 25 mcg or sufentanyl 1.5 – 2.5 mcg is given as a single bolus^{41,42}.

DURAL PUNCTURE EPIDURAL (DPE)

In this method, intentiona by thr l puncture of the dura is made, without injection of LA or opioid into the thecal sac, followed eading of the epidural catheter for continuous analgesia. The advantage of this technique is that it allows for intrathecal transfer of injectate from the epidural space via the dural hole, allowing for more rapid onset and symmetrical analgesia. A study found that parturients who received DPE has lesser pain scores and reduced one – sided analgesia⁴³.

CONTINUOUS SPINAL ANALGESIA

Although rarely used in modern practice due to associated incidence of Post Dural Puncture Headache (PDPH), it is still preferred in some patients with morbid obesity and known airway difficulties due to its ability to rapidly convert to surgical anaesthesia. It also may be used in patients with accidental dural puncture, by using smaller gauge micro-catheters. However, the US Food and drugs Administration (FDA) has restricted the use of micro – catheters due to its association with cauda equina syndrome.

NEWER TECHNOLOGIES – DISTRACTION ANALGESIA AND VIRTUAL REALITY

This technology is based on the fact that pain perception requires cognitive attention and capacity to focus on pain signals. A “distractive helmet” is worn by the patient; it blocks external noises, and provides computer generated scenes in order to cause pleasant sensations. This theory has been supported by evidence in the form of functional MRI images showing significant reduction in pain related brain activity⁴⁴. High quality evidence and number of studies is lacking to prove the benefit of this modality of pain treatment.

CONCLUSION

Despite the various options available, neuraxial techniques remain to be the gold standard form of providing labour analgesia, due to their high efficacy. Pharmacological options may be a reasonable second choice in select patients when feasible. Non pharmacological methods may still be used in order to provide psychological support and help women cope with labour pain and associate it with good memories, although they lack scientific evidence. Other newer technologies discussed have shown to reduce pain in labour, but their safety and associated obstetric outcomes remain to be known, making way for the need of extensive research in these fields. There can never be

definitive regimens and clear cut doses that can be fixed, as childbirth is unique in its own right and analgesic requirements have to be tailor made to every situation.

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