# PAIN RELIEF IN LABOUR - REVIEW ARTICLE

Professor A Rudra, Calcutta National Memorial Hospital, India

## Introduction

Giving birth is a painful process. This applies to all social and ethnic groups and has probably been so since mankind walked upright. It is very difficult to measure pain which is recognised via the signals carried through the nervous system and the woman's intellectual response to the stimulus.

## Physiology of pain in labour

Labour pain is the result of many complex interactions, physiological and psychological, excitatory as well as inhibitory. Pain during the first stage of labour is due to distention of the lower uterine segment, mechanical dilatation of the cervix and lastly due to stretching of excitatory nociceptive afferents resulting from the contraction of the uterine muscles[1]. The severity of pain parallels with the duration and intensity of contraction[2].

In the second stage additional factors, such as traction and pressure on the parietal peritoneum, uterine ligaments, urethra, bladder, rectum, lumbosacral plexus, fascia and muscles of the pelvic floor increase the intensity of pain.

## Neural pathway of pain

The uterus and cervix are supplied by afferents accompanying sympathetic nerves in the uterine and cervical plexuses, the inferior, middle and superior hypogastric plexuses and the aortic plexus. The small unmyelinated 'C' visceral fibres[3] transmit nociception through lumbar and lower thoracic sympathetic chains to the posterior nerve roots of the 10th, 11th and 12th thoracic and also to 1st lumbar nerves to synapse in the dorsal horn[4]. The chemical mediators involved are bradykinin, leukotrienes, prostaglandins, serotonin, substance P and lactic acid[5]. As the labour progresses severe pain is referred to the dermatomes supplied by T10 and L1.

In the second stage, the direct pressure by the presenting part on the lumbosacral plexus causes neuropathic pain. Stretching of the vagina and perineum results in stimulation of the pudendal nerve (S2,3,4) via fine, myelinated, rapidly transmitting 'A delta' fibres[3]. From these areas, the impulses pass to dorsal horn cells and finally to the brain via the spino-thalamic tract.

## The stress response to pain in labour

Segmental and supra-segmental reflex-responses from the pain of labour may affect respiratory, cardiovascular, gastro-intestinal, urinary and neuro-endocrine functions.

**Respiratory** - Pain in labour initiates hyperventilation leading to maternal hypocarbia, respiratory alkalosis and subsequent compensatory metabolic acidosis. The oxygen dissociation curve is shifted to the left and thus reduces tissue oxygen transfer, which is already compromised by the increased oxygen consumption associated with labour[6].

**Cardiovascular** - Labour results in a progressive increase in maternal cardiac output, primarily due to an increase in stroke volume, and, to a lesser extent, maternal heart rate. The greatest increase in cardiac output occurs immediately after delivery, from the increased venous return associated with relief of venocaval compression and the autotransfusion resulting from uterine involution.

**Hormonal** - Stimulation of pain results in the release of beta-endorphine and ACTH from the anterior pituitary. Associated anxiety also initiates further pituitary response[7].

Pain also stimulates the increased release of both adrenaline and noradrenaline from the adrenal medulla which may lead to a progressive rise in peripheral resistance and cardiac output. Excessive, sympathetic activity may result in incoordinate uterine action, prolonged labour and abnormal fetal heart-rate patterns. Activation of the autonomic nervous system also delays gastric emptying and reduces intestinal peristalsis.

**Metabolic - Maternal**: During labour, glucagon, growth hormone, renin and ADH level increases while insulin and testosterone level decreases[7]. Circulating free fatty acids and lactate also increase with a peak level at the time of delivery. **Fetal** : Maternal catecholamines secreted as a result of labour pain may cause fetal acidosis due to low placental blood flow[8].

## Severity of labour pain

The severity of labour pain varies greatly among women in labour. If women are asked during or shortly after birth to score their labour pain most rate it as severe while few mention little or no pain[9,10]. Using the McGill pain questionnaire, Melzack et al in Montreal, Canada, found that labour pain usually rated a high score particularly among primiparae, those with a history of dysmenorrhoea and those belonging to low socio-economic status[9].

Principles of pain relief

The essentials of obstetric pain relief are:

- Simplicity
- Safety
- Preservation of fetal homeostasis

Women who are given any form of analgesia should be monitored closely. After spinal or epidural anaesthesia they should be monitored with frequent measurements of blood pressure, level of consciousness and maternal oxygen saturation by pulse oximetry.

## Role of the Anaesthesiologist

Anaesthesiologists do have a role antenatally. They should be ready to answer the mothers' questions about the methods of

analgesia. It is important that women with serious underlying chronic disease should be assessed antenatally by the anaesthesiologist to adopt a management plan before the onset of labour. Good communication between obstetrician, physician, haematologist and any other relevant specialist can help the anaesthesiologist in the management of high-risk pregnancy.

**History of pain relief**

Ancient methods of pain relief included various plant-derived sedatives, acupuncture and physical methods such as binding.

- In 1847 James Young Simpson administered the first obstetric general anaesthetic using ether.
- In 1853 John Snow delivered Queen Victoria's eighth child under chloroform.
- In 1881 Stanislav Klikovitch described the use of nitrous oxide for labour in Russia.
- In 1902 morphine and hyoscine was first used in labour. Pethidine was first used in 1940.
- In 1931 Eugen Bogdan Aburel, Romanian obstetrician, described continous caudal plus lumboaortic plexus blocks in labour.
- In 1945 Curtis Mendelson described the syndrome of acid aspiration under general anaesthesia for caesarean section.
- In 1949 Cleland described continuous lumbar epidural block in labour.
- In 1958 Ferdinand Lamaze published his book suggesting that pain was a conditioned reflex triggered by uterine contractions, and that psychoprophylaxis could reduce pain.
- In 1961 Brian Sellick described cricoid pressure as a means of preventing gastric aspiration.

**Psychological methods of pain relief**

Methods of psychological analgesia can be divided into three broad categories :

- Natural child birth - the Read method.
- Psychoprophylaxis - the Lamaze technique.
- Hypnosis

Each technique claims the elimination of pain without any harm to the mother, the baby or to the progress of labour and without the need for chemical analgesia. All require adequate antenatal preparation. Still most women experience severe labour pain[9]. Furthermore, psychological analgesia can place increased demand on the staff.

**Support during labour**

A friendly atmosphere in the labour room is preferable to help a woman to cope with pain. Homely surroundings help to allay anxiety and reduce the need for pharmacological analgesia.

- **Hypnosis**. Hypnosis (hypnos, sleep) can produce analgesia and amnesia during labour and delivery for some selected patients. Only about 25% of women however are suitable as deep trance hypnotic subjects. And the technique relies on extensive preparation.
- **Bio-feedback**. This is borderline between psychological and physical methods of analgesia. Relaxation is a major component of psychological preparation for child-birth and is claimed to relieve pain, reduce anxiety and speed labour.

**Physical methods of pain relief**

- **Transcutenous Electrical Nerve Stimulation (TENS)**. TENS was introduced to relieve pain in childbirth in the early 1980s. Since then the use of TENS in labour has become increasingly popular as it is simple to use and is non-invasive. The mode of action depends on the two principal theories. One that A-fibres are stimulated by the electrical stimulation preventing the transmission of afferent noxious stimulus originating from C-fibres, the other that the electrical stimulus increases endorphines and enkephalins within the system. TENS electrodes are applied over the dermatomes supplied by T10 to L1. The TENS machine then gives a low background stimulus which can be augmented at the time of each contraction. It has been observed in clinical practice that TENS may provide limited pain relief during the first stage of labour. Meta-analysis of randomised controlled trials of TENS in labour does not, however, confirm its efficacy.
- **Acupuncture**. Mentioned in the literature in 581 B. C. and widely practiced in China. Acupuncture is not used for childbirth in China, however, and there are no acupuncture points described for pain relief in labour.
- **Water (bath or shower)**. A bath or shower is relaxing and should be encouraged. There has been enthusiasm in some quarters to extend this to the delivery of the baby under water and many maternity units have the facility to offer water birth. However, while its use during the first stage of labour is not discouraged, very few units would encourage the use of the birthing pool for the delivery of the baby. At present there is little evidence to support the use of immersion in water during labour[11].

**Inhalational analgesia**

Several inhalational agents, both gaseous and volatile, have been used successfully in labour. The earliest to be used were ether, chloroform[12] and cyclopropane,[13] followed by trichloroethylene and methoxyflurane.[14] Enflurane, isoflurane and desflurane[15] are more recent additions.

Analgesia during labour can be provided by the inhalational anaesthetic agents in subanaesthetic concentrations thus relieving pain whilst maintaining maternal consciousness and avoiding regurgitation or aspiration of stomach contents. In fact, the competence of the upper oesophageal sphincter is well maintained under light general anaesthesia, although lost under mild sedation with barbiturate or diazepam[16]. Inhalational agents readily cross the placenta and the concentration in foetal blood soon approaches that of the mother but, since these agents are excreted almost entirely through the lungs, they are readily excreted from the newborn.

The efficacy of inhalational analgesia depends on the analgesic strength of the agent and on how quickly it reaches analgesic concentration after the start of inspiration. A rapid offset with complete elimination between contractions would prevent

accumulation completely. Nitrous oxide is the best match in current use.

Various portable machines exist for administration of nitrous oxide blended with oxygen through an on-demand valve. Nitrous oxide concentrations can be varied from 0 to 75% in oxygen. For self-administration, a concentration above 50% nitrous oxide should not be allowed. Entonox, which is a mixture of 50% nitrous oxide and 50% oxygen is most commonly used.

- **Ether** has several side effects including potent emetic effects with an unpleasant pungent odour, irritant to the respiratory tract and explosive. Chloroform has a pleasant odour, is non-irritant, more potent and faster acting than ether but has undesirable, dose-related side effects, namely arrhythmias and liver damage.

- **Methoxyflurane and trichloroethyline** have been used for analgesia in labour, but have been withdrawn for other, non-obstetric, reasons.

- **Enflurane and isoflurane** have been given via a draw-over vaporiser in subanaesthetic concentrations to relieve pain in labour. The usual concentrations, in oxygen, of enflurane and isoflurane for self administration are 0.3-1% and 0.2-0.7%. Such concentrations will not change uterine contractility or responsiveness to oxytocin. The neonate is not affected by these analgesic concentrations of these inhalational agents. Enflurane, however, causes long-term drowsiness so was never popular. Both the agents are expensive and since neither shows a significant advantage over entonox in terms of analgesia they are unlikely to be widely used on their own.

- **Desflurane** is the newest volatile agent to be applied in labour. The chief advantage of this agent is rapid onset and offset of action, however it is expensive and since it has not been shown to provide superior analgesia to entonox, it is unlikely to become a popular agent for labour analgesia.

**Systemic opioid analgesia**

Opioids have been used for anaesthesia in labour for hundreds of years. However, it was not until the early twentieth century that techniques deliberately employing the analgesic effects of the opioids gained major attention. Unfortunately, dosage and effect are limited by maternal and neonatal side-effects, so that only moderate pain relief could be obtained with these drugs.

- **Pethidine** has become the most commonly used and widely investigated systemic opioid in labour. It is principally a mu-agonist but of a low potency. Administered as hydrochloride in a dose of 75-100mg intramuscularly it reduces labour pain by about 25%. Delayed gastric emptying is a prominent feature. Respiratory depression is not usually observed in women who receive pethidine, because contractions continue to be painful and to provoke hyperventilation. However hypoxic episodes have been observed probably associated with significant underventilation between contractions. The major metabolite, nor-pethidine, is itself active, and has convulsant properties. Thus, pethidine may be inadvisable for use in fulminating preeclampsia or eclampsia, particularly in repeated doses.

- **Morphine** fell from favour in the first half of the twentieth century, in part because of its association with "twilight sleep" and in part because of its addictive side effects.

- **Meptazinol** is a mixed opioid agonist/antagonist, act primarily at the kappa receptor. It is given in a dose of 100-150mg intramuscularly every 2-4 hours. In high doses it has dysphoric side effects and also produce nausea and vomiting. The antagonist properties of meptazinol may cause withdrawal in parturients dependent on mu-agonists. It has a reduced potential to cause respiratory depression.

- **Buprenorphine** is a partial agonist acting selectively at mu-receptors. It is about 20 times as potent as morphine and has a high affinity for opioid receptors and slow dissociation from them. It has a capacity for self-antagonism, which tend to produce a biphasic time course of action. This may be observed for both analgesia and respiratory depression. It appears to have a long duration of action and though side effects are rare, when nausea and respiratory depression do occur they can be exceedingly persistent and difficult to reverse.

- **Nalbuphine** is a synthetic mixed mu-agonist/antagonist and a kappa-agonist. For analgesia in labour it is given in doses of 10-20mg intramuscularly. Maternal or foetal respiratory depression is less likely with nalbuphine due to the ceiling effect. The chief disadvantages of this drug are sedation and dysphoria.

- **Fentanyl** primarily acts on mu-receptors and is approximately 80-100 times as potent as morphine. It has a rapid onset action and shorter duration of action. The peak analgesic effect occurs within 5 minutes and the duration of effect is about 30 minutes after 1 mcg/kg administered intravenously. Fentanyl is principally bound to albumin which favours its transplacental transfer. For analgesia in labour 50-100mcg/hour is required, given in increments of 10mcg IV.

- **Tramadol** is a weak mu-agonist that has been prescribed in labour in doses of 50-100mg 4 hourly. The incidence of nausea is more common with tramadol than with pethidine or morphine[17].

- **Butorphanol** is a synthetic narcotic given as a 1-2 mg dose which lasts 3 to 4 hours. Neonatal respiratory depression is reported to be less than with pethidine[18].

**Patient-controlled analgesia**

Patient-controlled analgesia with intravenous administration of opioid analgesics was assessed for obstetric pain as early as 1970[19]. The patient's ability to control the analgesic administration may produce pharmacological as well as psychological benefits.

**Perineal infiltration, pudendal nerve block and paracervical nerve block**

Perineal infiltration with local anaesthetic solution is of no value for analgesia during labour, but is employed prior to episiotomy just before delivery of the baby.

Pudendal block is a relatively simple, safe and effective method of providing analgesia for spontaneous delivery, normally performed by the obstetrician. Pudendal block may not provide adequate analgesia for forceps delivery or when delivery requires extensive manipulation. 10ml of local anaesthetic solution (lignocaine 10mg/ml) containing adrenaline is injected, after appropriate aspiration.

Paracervical block serves to relieve the pain of uterine contractions, but because the pudendal nerves are not blocked, additional analgesia is required for delivery. Usually lignocaine is injected at 3 and 9 o'clock. Because these anaesthetics are relatively short acting, paracervical block may have to be repeated during labour. This technique has fallen out of favour because of the high incidence of foetal bradycardia and neonatal depression.

**Epidural and subarachnoid administration of local anaesthetics & opioids for labour analgesia**

Epidural anaesthesia is now widely recognized as the most effective form of pain relief technique for labour. Local anaesthetics alone were used for many years, but are now generally administered in lower concentrations in combination with opioids to provide effective, synergistic analgesia whilst reducing some of the unwanted side effects of local anaesthetics, such as motor block.

**Local anaesthetics**.

Bupivacaine has high protein binding and a long duration of effect. It is the most frequently used local anaesthetic for obstetric epidural analgesia. 10 ml of 0.25% bupivacaine (25mg) epidurally will normally provide good analgesia for approximately 90-120 minutes although repeated boluses may produce an increasing motor block. A spinal bolus of 2.5mg bupivacaine (1 ml of 0.25% bupivacaine, often diluted with 1 ml of 0.9% saline) will produce rapid onset of good analgesia for labour but this may only last 30 to 60 minutes.

- **Lignocaine** has a relatively short duration of action due to low lipid-solubility.

- It was suggested that ropivacaine produces less motor block than bupivacaine[20], but this may result simply from its relatively lower potency.

**Opioids**

Good analgesia can be achieved in labour with low doses of a combination of opioid and local anaesthetic. Side effects from neuraxial opioid administration include nausea, pruritus, urinary retention and respiratory depression. The respiratory depression may be delayed, particularly when less lipid soluble opioids are used such as diamorphine. Close observation of women who have received neuraxial opioids is important.

- A spinal dose of 15mcg of **fentanyl** added to local anaesthetic will improve the quality of analgesia. An epidural loading dose of 50mcg fentanyl will similarly enhance the effect of local anaesthetic. Continuous epidural infusion of up to 12ml per hour of 0.1% bupivacaine with 2mcg fentanyl per ml generally provides excellent pain relief in labour.

- Spinal **sufentanil**, in a dose of 10mcg, can be used to provide labour analgesia for over one hour.

- A single spinal dose of 100 to 300mcg of **diamorphine** added to local anaesthetic provides prolonged analgesia for up to 24 hours. 5 mg of diamorphine added to the epidural loading dose reduces the subsequent requirement of bupivacaine infusion[21]. Without this loading dose an infusion of up to 12 ml per hour of 0.1% bupivacaine with 50mcg diamorphine per ml gives excellent pain relief.

- Epidural **pethidine** produces good analgesia due to its partial local anaesthetic effect. 50mg administered 2 to 3 hourly.

**Patient-controlled epidural analgesia and combined spinal-epidural analgesia in labour**

- Patient-controlled epidural analgesia (PCEA)[22] allows immediate access to more epidural solution and creates flexibility, allowing self-titration of solution to acceptable analgesic endpoint throughout labour. As well as the psychological benefits of self-administration, staff workload should be less and reduced drug delivery might minimize side-effects and risks. The disadvantages of the technique include the delayed feedback loop associated with the slow onset of epidural solution and concerns about equipment, safety, monitoring and education.

- Combined spinal-epidural analgesia (CSEA) have evolved in an attempt to optimize the advantages of each separate technique. The advantages of this technique over epidural analgesia alone include more rapid onset of pain relief and good perineal analgesia despite much smaller drug doses. Motor block and its unwanted sequelae are reduced, thus improving maternal satisfaction. The disadvantages are an increased risk of complications due to two procedures as opposed to one.

**Non-narcotic analgesic techniques for labour**

- **Alpha 2-adrenergic agents**. These drugs have been used as it has been recognized that alpha 2-adrenoceptors can be found in the dorsal horn of the spinal cord and that their activation could produce analgesia.

- The **addition of adrenaline** to local anaesthetic solution intensifies and prolongs the neural blockade.

- **Clonidine** is a more selective alpha 2-agonist than adrenaline. It potentiates the action of spinal opioids. Clonidine does not enhance motor blockade. It does not lead to respiratory depression, pruritis or nausea. It can, however, produce hypotension, bradycardia and sedation after its administration epidurally.

- **N-methyl-D-asparate receptor antagonists**. Receptors for NMDA are thought to play a role in various physiological systems among which their role in enhancing pain transmission ('wind-up') is now well appreciated. Because wind-up and hyperalgesia is primarily a spinal cord phenomenon, it appears to be logical to administer NMDA antagonists spinally.

- **Ketamine** has been shown to have analgesic properties in various models. As this drug administered epidurally or intrathecally may not produce respiratory depression, urinary retention or pruritis, its clinical usefulness may be great. Spinal administration of ketamine does not cause motor blockade and arterial blood pressure and heart rate remained unaltered. Drowsiness, dizziness, horizontal nystagmus and dysphoria, however, are the major drawbacks. Recent studies suggest that ketamine may be a useful drug when used in combination.

- **Midazolam** has been demonstrated to have a direct spinal action. Recent studies have focussed on the mechanism of anti-nociception produced by midazolam. The initial step is interaction between midazolam and GABA leading to an increase in chloride flux into the neurone. Through an unknown process, anti-

nociception is then produced by activating a system which involves delta-opioid receptors[23]. A study in obstetric anaesthesia has shown that 1mg of intrathecal midazolam injected with bupivacaine at Caesarean delivery reduces post-operative morphine requirements[24].

**Effects of pain-relief on labour, mother and foetus/neonate**

Pharmacological pain relief in labour is frequently used. Maternal choice of pharmacological methods for analgesia in labour includes not only preferences for the route of drug delivery but also their efficacy and side effects for herself and her baby.

**Effect of epidural analgesia on labour.**

Epidural block induced prior to well-established labour may be followed by desultory labour. The precise role played by epidural analgesia in this phenomenon is not clear, because this sequence of events is also seen in its absence[25]. During the second stage of labour, epidural analgesia that provides effective pain relief, is likely to reduce appreciably maternal expulsive efforts. As a consequence, an epidural block could lead to delay or, less frequently, failure of descent of the presenting part and spontaneous rotation to the occiput anterior position, and hence an increased incidence of operative vaginal delivery as well as Caesarean delivery. However, mothers with high-risk, prolonged or difficult labours are more likely to request epidural analgesia. It is therefore difficult to prove whether the increased rate of interventional delivery seen in mothers with epidurals is the result of causation rather than association.

**Effects on mother**

- **Parenteral Opioids**. The inadequacy of analgesia associated with parenteral opioids is more likely to lead to hyperventilation. This will lead to a lowered maternal $PaCO_2$ that may produce a reduction in utero-placental blood flow. Relative overdose of opioids may lead to hypotension, which is further aggravated by posture and venocaval occlusion. Parenteral opioids cause delayed gastric emptying, which may already have been impeded by labour itself. Furthermore, opioids administered during labour cause nausea and vomiting, from a central action.

- **Paracervical block**. Minor effects such as vertigo, tinnitus and 'aura' have been reported[26]. Transient paraesthesia, numbness and anaesthesia of the leg can occur due to spread of anaesthetic solution to the sacral plexus[27]. Women may be sedated due to partial intravascular injection.

- **Pudendal block**. Unintentional overdosage or intravascular injection can induce dysrrhythmias and cardiovascular collapse. The needle used to place the pudendal block is a source of potential complication as it may unintentionally pierce and damage either the rectum, vagina or foetus. Haematoma in the ischaeorectal and paravaginal spaces have been described following pudendal block. The needle may serve as a vector, introducing bacteria into previously sterile spaces; abscess and periosteal infections have been reported in association with pudendal blocks[27,28].

- **Spinal opioids**. Nausea, vomiting, pruritus and urinary retention can occur with any mu-agonist given by the epidural or subarachnoid route. Respiratory depression (usually delayed) after subarachnoid and epidural opioid administration is a potentially serious complication. Post dural puncture headache severe enough to keep the patient bed-ridden is undesirable as she needs to take care of the neonate and to be mobilized to prevent thrombo-embolic complications.

- **Epidural analgesia with local analgesic**. Epidural analgesia in labour may be associated with maternal pyrexia and shivering not attributed to infection. The rise in temperature may be secondary to both vascular and thermoregulatory modifications induced by epidural analgesia[29].

**Effects on foetus/neonate**

- **Opioids**. The immature respiratory centre is more sensitive to the opioid analgesics. Thus, the analgesics cause respiratory depression after crossing the placenta. Opioid analgesics do not tend to have any primary effect on the cardiovascular system of the neonate but may cause bradycardia secondary to opioid-induced respiratory depression.

- **Paracervical block**.Transient foetal bradycardia is associated with this technique in a significant number of cases due to direct effects of the local anaesthetic on the foetus as a result of vascular constriction or uterine hyperactivity. Other pharmacological effects of local anaesthetics on the foetal heart are lengthening of the atrioventricular and intraventricular conduction times[30].

- **Spinal opioids**. Drugs administered to the women are transported rapidly to the uterus and cross the placenta. All commercially available opioids have low molecular weights and rapidly cross the placenta by diffusion.

  - **Morphine** - risk of neonatal depression with epidural morphine appears to increase with higher doses and shorter interval between dosing and delivery time because of higher maternal blood levels of morphine[31].
  - **Fentanyl** - neonatal depression has only been reported with very high repeated epidural doses[32].
  - **Alfentanil** - has been associated with neonatal depression[33].
  - **Butorphanol** - may be associated with low amplitude, high frequency sinusoidal like foetal heart rate pattern[34].

**Drug interactions**

Information on drug interactions specific to labour and delivery is both limited and complex.

- **Oxytocin**: tetracaine and chloroprocaine antagonize the uterotonic actions of oxytocins.

- **Nifedipine**: hypotensive effects of inhaled anaesthetics will probably be enhanced by this agent secondary to the peripheral vasodilating effect.

- **Epidural hydromorphone** in conjuction with intravenous droperidol cause profound respiratory depression to the parturient.

- **Chloroprocaine** administered into the epidural space decreases the subsequent effectiveness of both fentanyl[35] and morphine[36].

## Conclusion

Antenatal fear of pain in labour is common for many women. The measurement of pain in labour, albeit difficult, and its relief by analgesics or alternative methods, are central to care. Much time, effort and expense is expended in the control of pain. The experience of pain in labour, however, remains an overwhelmingly common experience despite the use of analgesia.

### References


1. Bonica JJ, Chadwick HS. Labour pain. In Wall PD and Melzack R (eds.) Textbook of pain. 1989, pp. 482-489. New York: Churchill Livingstone.

2. Gibb DMF, Arulkumaran E, Lun KC and Rathan SS. Characteristics of uterine activity in nulliparous labour. British Journal Obstetric and Gynaecology 1984;**91**:220-227.

3. Ward ME. Acute pain and the obstetric patient : recent developments in analgesia for labour and delivery. International Anaesthesiology Clinics 1997;**35**:83-103.

4. Bonica JJ. Peripheral mechanisms and pathways of parturition pain. British Journal of Anaesthesia 1979; 51 (Supplement): S3-S9.

5. Brownridge P. The nature and consequences childbirth pain. European Journal of Obstetric, Gynaecology and reproductive Biology 1995;**59**:S9-S15

6. Mahomed K, Gulmezoglu AM, Nikodem VC et al. Labour experience, maternal mood and cortisol and catecholamine levels in low-risk primiparous women. Journal of Psychosomatic Obstetrics and Gynaecology 1995;**16**:181-186.

7. Bonica JJ. The nature of pain in parturition. In Vanzundert A and Ostheimer GW (eds.) Pain relief and anaesthesia in obstetrics. 1996; pp. 19-52. New York: Churchill Livingstone.

8. Irestedt L, Lagercrantz H and Belfrage P. Causes and consequences of maternal and fetal sympatho-adrenal activation during parturition. Acta Obstetrica et Gynecologica Scandinavica 1995; 118 (Supplement): S111-S115.

9. Melzack R, Taenzer P, Feldman P, Finch RA. Labour is still painful after prepared childbirth training. Canadian Medical Association Journal 1981;**125**:357-63.

10. Kangas-Saarela T, Kangas-Karki T. Pain and pain relief in labour: parturients' experiences. International Journal Obstetric Anaesthesia 1994;**3**:67-74.

11. Nikoderm VC. Immersion in water during pregnancy, labour and birth (Cochrane Review). In the Cochrane Library, Issue 3 Oxford: Update Software 1998.

12. Moya F. Use of chloroform inhaler in obstetrics. NY State Journal of Medicine 1961;**61**:421-9

13. Shnider SM, Moya F, Thorndike V, Bossers A, Morishima H, James LS. Clinical and biochemical studies of cyclopropane analgesia in obstetrics. Anaesthesiology 1963;**24**:11-17.

14. Major V, Rosen M Mushin WW. Methoxyflurane as an obstetric analgesic: a comparison with trichloroethylene. British Medical Journal 1996; ii: 1554-61.

15. Abboud TK, Swart F, Zhu J, Donavan MM, Pares DaSilva E, Yakal K. Desflurane analgesia for vaginal delivery. Acta Anaesthesia Scandinavica 1995;**39**:259-61.

16. Vanner RG. Mechanisms of regurgitation and its prevention with cricoid pressure. International Journal of Obstetric Anaesthesia 1993;**2**:207-15.

17. Prasertsawat PO, Herabutiya Y, Chaturachinda K. Obstetric analgesia: comparison between tramadol, morphine and pethidine. Current Therapeutic Research 1986;**40**:1022-8.

18. Quilligan EJ, Keejan KA, Donahue MG. Double blind comparison of intravenously injected butorphanol and meperidine in parturients. International Journal of Obstetrics 1980;**18**:363-6.

19. Ferrante FM, Ostheimer GW, Covino BG (eds.). Patient-controlled analgesia. Boston, MA: Blackwell. 1980.

20. Zaric D, Nydahl PA, Philipson L et al. The effect of continuous lumbar epidural infusion of ropivacaine (0.1%, 0.2% and 0.3%) and 0-25% bupivacaine on sensory and motor block in volunteers. Regional Anaesthesia 1996;**21**:14-25.

21. McGrady EM, Brownhill DK, Davis AG. Epidural diamorphine and bupivacaine in labour. Anaesthesia 1989;**44**: 400-3.

22. Gambling DR, Yu P, Cole C et al. A comparative study of patient-controled epidural analgesia (PCEA) and continuous infusion epidural analgesia (CIEA) during labour. Canadian Journal of Anaesthesia 1988;**35**:249-54.

23. Goodchild CS, Guo Z, Musgrave A and Gent JP. Antinociception by intrathecal midazolam involves endogenous neurotransmitters acting at spinal cord delta opioid receptors. British Journal of Anaesthesia 1996;77:758-63.

24. Valentine JMJ, Lyons G and Bellamy MC. The modifying effects of intrathecal midazolam and diamorphine on postoperative pain. European Journal of Anaesthesiology 1996; **13**:589-93.

25. Akamatsu TJ, Bonica JJ. Spinal and extradural analgesia for parturition.Clinical Obstetric Gynecology 1974;**17**:183-86.

26. Flower CE. Conduction anaesthesia in obstetrics. In: Flowers CE (ed.) Obstetric analgesia and anaesthesia. Harper & Row, New York, page 104.

27. Svancarek W, Chirino O, Schaefer GJ. Retropsoas and subgluteal abscess following paracervical and pudendal anaesthesia. Journal American Medical Association 1977;**237**: 892-94.

28. Qvigstad E, Jerne F. Severe infection following pudendal anaesthesia. International Journal Gynecology and Obstetrics 1980;**18**:385-87.

29. Fusi L, Steer PJ, Maresh MJA, Beard RW. Maternal pyrexia associated with the use of epidural analgesia in labour. Lancet 1989;**1**:1250.

30. Anderson KE, Gennser G, Nilsen E. Influence of mepivacaine on isolated human foetal hearts at normal and low pH. Acta Physiologica Scandinavica 1970;**80**:37-40.

31. Sevarine FB, Johnson MD, Lema MJ et al. The effect of epidural morphine on neonate. Anesthesia Analgesia 1989;**68**: 530-33.

32. Hughes SC. Intraspinal narcotics in obstetrics. Clinical Perinatology 1982;**1**:167.

33. Weintraul SJ, Naulty JS. Acute abstinence syndrome after epidural injection of alfentanil. Anaesthesia Analgesia 1985;**64**: 452-53.

34. Hug CC. Pharmacokinetics of new synthetic narcotic analgesics. In Estafanous FG (ed.) Opioids in anaesthesia. Butterworths, Boston, Page 52.

35. Naulty SJ, Herting L, Hunt CO et al. Duration of analgesia of epidural fentanyl following caesarean delivery - effects of local anaesthetic drug selection. Anesthesiology 1988;**65**:A183.

36. Koteo DM, Thigpen JW, Shnider SM et al. Postoperative morphine analgesia after various local anaesthetics. Anaesthesiology 1983;**59**: A413.