Original Article

A prospective randomized controlled study comparing efficacy of 0.2% ropivacaine, 0.125% levo-bupivacaine and 0.5% lignocaine in epidural labour analgesia

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Abstract

Background: Lumbar epidural analgesia offers a safe and effective method of pain relief during labour. Low doses of local anesthetic or opioid combinations are administered (usually by infusion) to provide a continuous T10-L1 sensory block during the first stage of labor. **Aim:** To compare the efficacy of epidural labour analgesia using 0.125% levo-bupivacaine with 2mcg/ml fentanyl, 0.2% Ropivacaine with 2mcg/ml fentanyl and 0.5% lignocaine with 2mcg/ml fentanyl. **Materials and Methods:** Sixty parturients who were admitted to the antenatal ward and who requested pain relief during labor and who fulfilled the recruitment criteria were selected for the study. **Results:** 0.125% Levo-bupivacaine with 2mcg/ml fentanyl stands better than other two agents in providing satisfactory labour analgesia with very minimal side effects.
Key Words: ropivacaine, levo-bupivacaine, lignocaine.

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INTRODUCTION

Labour is an extremely painful process. Among the current methods of obstetric analgesia, regional analgesia (the most widespread technique being epidural analgesia) offers the best effectiveness/safety ratio1. Epidural anaesthesia is an effective means of providing analgesia during labour. The increased availability of epidural analgesia and the favourable experiences of women who have had painless labour with epidural block have reshaped the expectations of pregnant women entering labor[1]. Compared with other forms of pain relief, epidural analgesia is associated with the highest level of maternal satisfaction[2]. The use of either an intermittent bolus or a continuous infusion of local anaesthetic (with or without an opioid) is considered to provide similar analgesic efficacy and no measurable outcome differences[2, 3,4]. The addition of an opioid to the local anaesthetic epidural bolus or infusion has become a highly popular technique, and the combination is believed to influence the duration and quality of labour analgesia. The efficacy and duration of epidural opioid alone is considered inferior to epidural local anaesthetic, but the benefits of an opioid should outweigh the side effects such as nausea, pruritus, and sedation. An epidural opioid- local anaesthetic combination may enhance the duration and quality of pain relief at less intense motor blockade and contribute to the good progress of labour and vaginal delivery. Fentanyl does not cross placental barrier. So it is used safely. It produces walking epidural with full muscle

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power and the patient can co-operate during second and third stage of labour.

ANATOMY OF THE EPIDURAL SPACE THE EPIDURAL SPACE

The epidural (extradural, peridural) space is that part of the vertebral canal external to the duramater and its contents. It lies between the duramater and the periosteum lining the canal, and corresponds to the very restricted space within the skull between the two layers of the cranial duramater enclosing the venous sinuses.

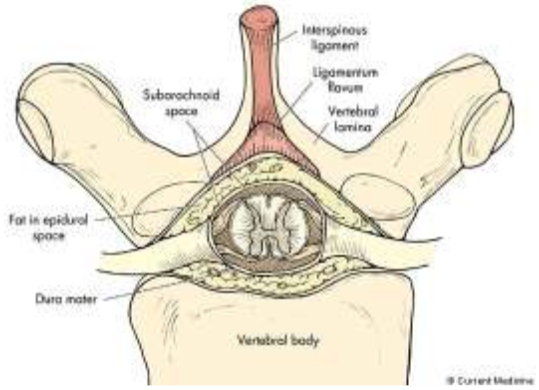


Figure 1: Epidural space

BOUNDARIES

Anteriorly: By vertebral bodies and posterior longitudinal ligaments

Posteriorly: Vertebral arches and ligamentum flavum

Superiorly: Fusion of dura with periosteum at foramen magnum

Inferiorly: Sacrococcygeal ligament at sacral hiatus

PRESSURE AND VOLUMES OF THE EPIDURAL SPACE

Substantial differences have been observed between the actions of epidural and subarachnoid injections of local anaesthetics in the pregnant and non-pregnant patient. In many respects the changes are thought to be due to the mechanical effects of the pregnancy as the actual size of the space available is reduced. The return of blood from the lower part of the body is mainly via the inferior vena cava; the epidural veins are also involved and they become dilated. This reduces the space available for the injection of fluid into the epidural space. For the same reason, the subarachnoid space is also reduced. As these veins are an alternate method of returning lower limb blood flow, their use is maximized if there is an obstruction to vena cava return as can happen in pregnancy.

There are three effects from this

The volume of local anaesthetic required to provide an extensive block is reduced in pregnancy. There is an increased risk of puncture of the distended veins by either the spinal or epidural needles or the catheter. Distension is likely to be maximum in the sitting position and pressure in the epidural space is increased, particularly in the sitting position. During a contraction, as the blood expelled from the contracting uterus passes to the epidural venous plexus, the pressure in the epidural space may rise by 4-10 cms H20. It is for this reason that injections of local anesthetics should be withheld during a contraction, as the spread may be unpredictable and probably excessive. Epidural space is also increased.

Physiology of pain in labour

Pain as described by the International Association for Study of Pain (ISAP) is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or as described in terms of such damage"[5].

Pain in the first stage of labour

During the first stage of labor, pain impulses arise primarily from the uterus. Uterine contractions may result in myometrial ischemia, which ultimately causes the release of bradykinin, histamine, and serotonin. In addition, stretching and distention of the lower uterine segment and cervix may stimulate mechanoreceptors. These noxious impulses follow the sensory nerve fibers that accompany sympathetic nerve endings; they travel through the paracervical region and the hypogastric plexus to enter the lumbar sympathetic chain[6].

Pain in The Second Stage of Labour

The pain caused by the distension of the pelvic structure and perineum following descent of the presenting part is added to the pain of uterine contractions, although once cervical dilatation is complete the pain induced by uterine contractions may become less severe[1]. The uterine pain continues to be referred to T10-L1, while the pain produced by stretching or pressure exerted on intrapelvic structures, including the peritoneum, bladder, urethra and rectum is referred to sacral segments. Pressure on the roots of the lumbosacral plexus may manifest itself, as pain felt low in the back or in the thighs. Pain produced by stretching of the perineum is transmitted by the pudendal nerve (S2,3,4) and in part by the posterior cutaneous nerve of the thigh(S2,3), the genitofemoral nerve (L1,2) and theilio-inguinal nerve (L1)[1, 6]

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-endocrinefunctions.

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[7].

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-endorphin and ACTH from the anterior pituitary. Associated anxiety also initiates further pituitary response[8]. 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[8]. 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[9].

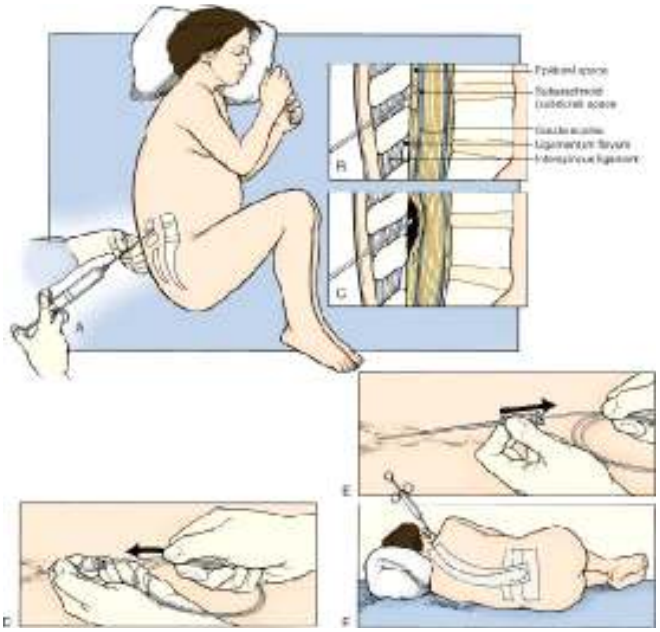


Figure 2: Technique of lumbar epidural puncture by the midline approach

A, This side view shows left hand held against patient's back, with thumb and index finger grasping hub. Attempts to inject solution while point of needle is in the interspinous ligament meet resistance. B, Point of needle is in the ligamentum flavum, which offers marked resistance and makes it almost impossible to inject solution. C, Entrance of the needle's point into epidural space is discerned by sudden lack of resistance to injection of saline. Force of injected solution pushes dura-arachnoid away from point of needle. D, Catheter is introduced through needle. Note that hub of needle is pulled caudad toward the patient, increasing the angle between the shaft of the needle and the epidural space. Also note technique of holding the tubing: It is wound around the right hand. E, Needle is withdrawn over tubing and held steady with the right hand. F, Catheter is immobilized with adhesive tape. Note the large loop made by the catheter to decrease risk of kinking at the point where the tube exits from the skin.

PHARMACOLOGY OF ROPIVACAINE

Ropivacaine is an amide local anaesthetic produced in three concentrations (2, 7.5 and 10 mg/ml). It is unique in that membrane separation synthesis yields an enantiomerically homogeneous solution that is more than 99% pure S-(-) isomer. Ropivacaine is highly plasma protein binding (94%) and the lipid solubility lies somewhere between that of lidocaine and bupivacaine. The duration of action and onset time are similar to those of bupivacaine. The analgesic potency of ropivacaine is 0.60 (0.47-0.75) relative to bupivacaine. Claims for reduced motor block must be considered with differences

in analgesic potency in mind. Ropivacaine is extensively metabolised by the cytochrome P450 system in the liver to 3 and 4-hydroxy-ropivacaine, both of which have some local anaesthetic activity.

PHARMACOLOGY OF LEVO-BUPIVACAINE

Levobupivacaine is the S(-) enantiomer of bupivacaine. It is prepared as a sterile, colourless solution (pH 4.0-6.5) containing levobupivacaine hydrochloride equivalent to 2.5 mg/ml, 5.0 mg/ml and 7.5 mg/mL of levobupivacaine. The pKa of 8.1 for levobupivacaine is the same as that of bupivacaine. Protein binding is more than 97%, mainly to alpha-1-acid glycoprotein. It is extensively metabolised, with no unchanged levobupivacaine detected in the urine or faeces. In vitro studies showed that cytochromes CYP3A4 and CYP1A2 mediate the metabolism of levobupivacaine to desbutyl levobupivacaine and 3-hydroxy levobupivacaine, respectively. The 3-hydroxy levobupivacaine appears to undergo further transformation to glucuronide and sulphate conjugates.

PHARMACOLOGY OF LIGNOCAINE

Lidocaine is a common local anaesthetic and has Class 1b anti-arrhythmic properties. It is an amide-type local anaesthetic. It is 70% protein bound to alpha-1-acid glycoprotein. Lidocaine has a more rapid onset of action and longer duration of action than ester-type local anaesthetics such as procaine. It is approximately 90% metabolised in the liver by N-dealkylation (cytochrome CYP1A2 and CYP3A4) to the pharmacologically active metabolites monoethylglycinexylidide and glycinexylidide. The elimination half-life of lidocaine is approximately 1.5–2 hours. This may be prolonged in patients with hepatic impairment or congestive heart failure. Lidocaine 2% may be used to top up an epidural. 20 ml is often combined with epinephrine 1 ml of 1:200,000 and an opiate. After a test dose, 5-8 ml may be given every 2-3 minutes. Lidocaine is more likely than bupivacaine, prilocaine or procaine to induce transient neurological symptoms (TNS) when used for spinal anaesthesia. These symptoms have been described as pain and dysesthesia in the buttocks, thighs or calves, occurring after the recovery from spinal anaesthesia, usually within 24 hours and resolving within 72 hours.

STRUCTURE and PHARMACOLOGY OF FENTANYL

Fentanyl is a synthetic phenylpiperidine - derivative opiate agonist. Fentanyl citrate is N-(1-Phenethyl-4- piperidyl) propionanilide citrate (1:1). Fentanyl is a highly lipophilic compound that is freely soluble in organic solvents and sparingly soluble in water (1:40). The molecular weight of the free base is 336.5 (the citrate salt is 528.6). The pKa of the tertiary nitrogens are 7.3 and 8.4.

MATERIALS AND METHODS

Study Centre

Meenakshi Medical College Hospital and Research Institute, Enathur, Kanchipuram.

Study Design

Randomised, Prospective, Comparative study.

Study Period

December 2013 to September 2015.

Study Population

Sixty parturients who were admitted to the antenatal ward and who requested pain relief during labor and who fulfilled the recruitment criteria were selected for the study. The procedure was explained to them in detail and written consent was obtained from them.

Inclusion Criteria

- ASA Status I and II
- Age group from 18 to 35 years
- Primigravida
- Adequate gynaecoid pelvis
- Cervical dilatation less than 4 cm

Exclusion Criteria

- Patient refusal
- Patients with pregnancy induced hypertension, heart disease, anaemia and other complications of pregnancy
- Cervical dilatation greater than 4 cm
- Patients who received systemic opioids within 4 hours of epidural request
- Coagulopathy
- Patients with clinically significant renal, hepatic, cardiovascular, haematopoetic, pulmonary, gastrointestinal, nervous or endocrine disorders.
- Patients unwilling or unable to comply with the study procedures

Study Procedures

- After obtaining approval from the Institutional Ethics Committee and written informed consent, 60 women fulfilling the inclusion criteria who required epidural analgesia in labour were studied.
- IV access was secured but no IV fluid load was given. The patients were shifted to the operation theatre for insertion of the epidural catheter in aseptic manner. An epidural catheter was sited at the second lumbar interspace using a standard midline technique with an 18-gauge Tuohy needle. Patients entered in to the study in a randomized order to receive one of the study treatments.

Equipment

The needles used for both groups were of Portex-Smith make (18G Tuohy epidural needle and 20G epidural catheter)

Procedure

With the patient in left lateral position, under aseptic precaution L2-L3 interspace was identified and skin infiltration was done with 1.5 ml of 2% lignocaine. Using a 18G Tuohy needle and 'loss of resistance to air' technique the epidural space was identified. After confirmation by negative aspiration test 20G epidural catheter was inserted in L2-L3 interspace and 6cms kept inside the epidural space. The catheter was fixed firmly to the back. The patient was turned to supine position. After solution given in divided doses. A standard epidural test dose itself will result in augmentation of motor blockade. Further, addition of epinephrine to confirm intravascular placement is not reliable in active labor. Hence test doses were done away with. Rather the bolus dose itself was given in divided doses with 5 mins interval checking for motor block after the first dose.

PROCEDURE FOR GROUP R – 0.2% Ropivacaine

IV access

Monitors

Technique:

An epidural catheter was sited at the second lumbar interspace using a standard midline approach with loss of resistance technique 10ml of 0.2% Ropivacaine with 2mcg/ml fentanyl and with 5 ml topup doses of 0.2% Ropivacaine 2mcg/ml fentanyl every one hour

PROCEDURE FOR GROUP B – 0.125% levo-bupivacaine

IV access

Monitors

Technique:

An epidural catheter was sited at the second lumbar interspace using a standard midline approach with loss of resistance technique 10ml of 0.125% of levo-bupivacaine with 2mcg/ml fentanyl and with 5 ml topup doses of 0.125% levo-bupivacaine with 2mcg/ml fentanyl every one hour

PROCEDURE FOR GROUP L – 0.5% Lignocaine

IV access

Monitors

Technique:

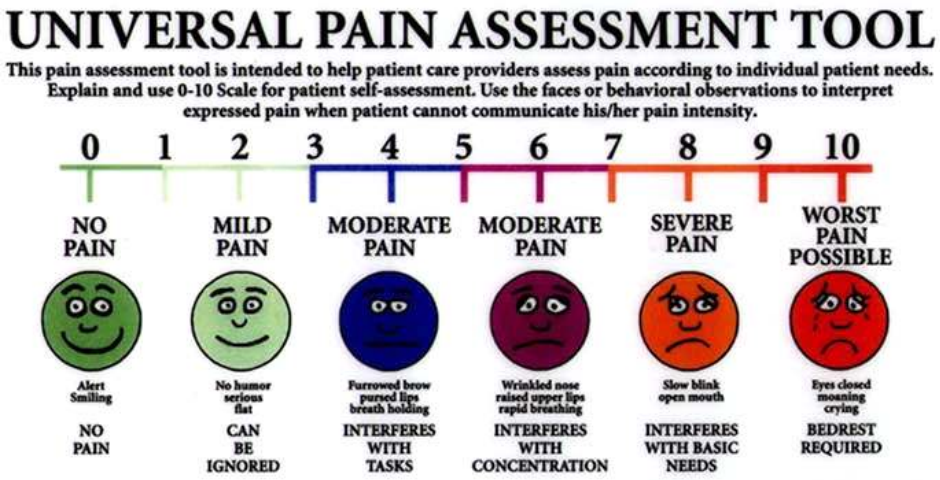
An epidural catheter was sited at the second lumbar interspace using a standard midline approach with loss of resistance technique

10ml of 0.5% of Lignocaine with 2mcg/ml fentanyl and with 5 ml top up doses of 0.5% Lignocaine 2mcg/ml fentanyl every one hour

PARAMETERS THAT WERE COMPARED

Time of onset of analgesia is noted

Analgesia was measured using Verbal Pain Descriptor Scale (VDS) on a 10 cm line (0 being no pain and 10 being most severe pain). Measurements were performed every 5 minutes until analgesia was established and at 30 min and 1 hr after the initial dose. Thereafter 1 hourly VPD were recorded until delivery



- Pulse rate and Blood pressure recorded every 5 min for 30 minutes and there after every one hour Motor Power was assessed using a modified Bromage score 30 mins after each top-up and at each request to get out of bed (score 0 = no weakness, able straight leg raise against resistance, 1 = not able to straight leg raise, able to flex knee, 2 = unable to flex knee, able to flex ankle, 3 = unable to move lower limb.
- complications like dural puncture, venous puncture, pruritus, nausea, vomiting, rigor, drowsiness, urinary retention, hypotension and respiratory depression were monitored for vigilantly.

Statistical report

Data were analysed using IBMSPSS version 21. Statistical significance was assessed using p at 0.05 cut off or 95% confidence interval.

RESULTS

A total of 180 patients were screened for the study. 60 patients who fulfilled the inclusion criteria were enrolled for the study and were divided in to three groups -

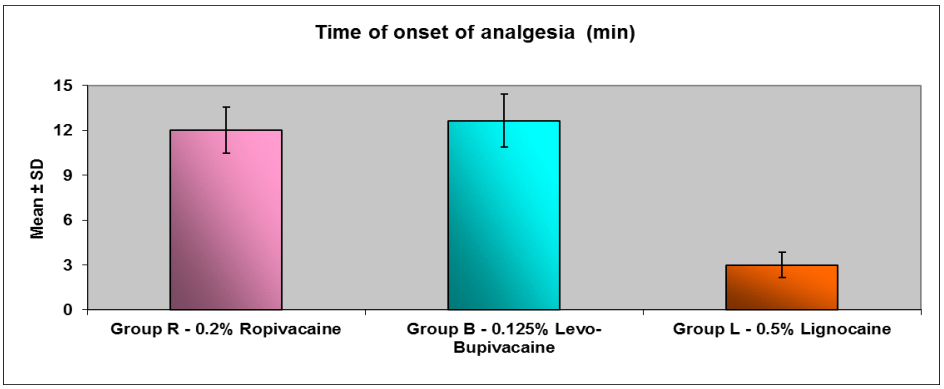
GROUP R: 20 patients
GROUP B: 20 patients
GROUP L: 20 patients (control)

Patients were randomly allocated to groups R or B or L to receive respective drugs allotted to the group.

DATA COLLECTION

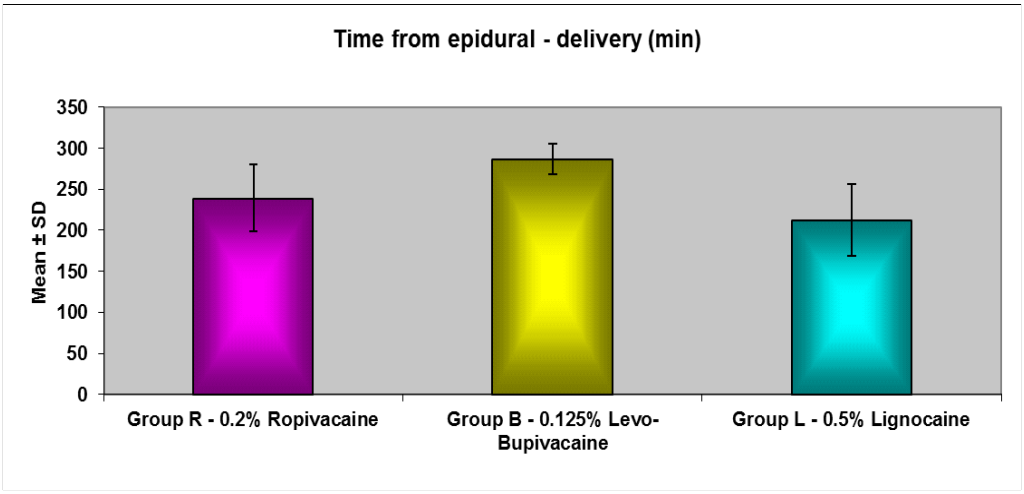
- Time of Onset of analgesia (min)
- Hemodynamic stability (systolic BP, diastolic BP, pulse rate)
- Quality of analgesia (Verbal Pain description scale - VDS)
- Motor block (Bromage score - BS)
- Duration of labour
- Time from epidural to delivery
- Mode of delivery
- Fetal outcome (APGAR score)
- Maternal satisfaction

STATISTICAL ANALYSIS



*** p < 0.001 S

Using ANOVA test, there is statistically significant difference among the 3 groups at p < 0.001 Mean of Group R is 12, Group B is 12.65 and Group L is 3 and there is difference.



***p<0.001 S

Using ANOVA test, there is statistically significant difference among the 3 groups at p < 0.001 Mean of Group R is 239.06, Group B is 286.83 and Group L is 212.53

DISCUSSION

0.5% Lignocaine with 2 mcg/ml fentanyl is quicker in onset when compared to Ropivacaine with fentanyl and Levo-bupivacaine with fentanyl. If we want quicker action we can go for Lignocaine as it is a time tested drug and no untoward effects 0.125%Levo-bupivacaine with 2mcg/ml fentanyl produces satisfactory analgesia and reasonably prolonged duration of analgesia 0.2% Ropivacaine stands in between Levo-bupivacaine and Lignocaine as duration is concerned. Patient satisfaction is rather uniform in all.

SUMMARY AND CONCLUSION

We found 0.125% Levo-bupivacaine with 2mcg/ml fentanyl stands better than other two agents in providing satisfactory labour analgesia, and provides satisfactory outcome for patient with very minimal side effects, anaesthetist as well as surgeon. We advice Levo-bupivacaine for epidural labour analgesia.

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