Dissertation on

"A COMPARATIVE STUDY ON LOW DOSE INTRATHECAL ROPIVACAINE ALONE WITH ROPIVACAINE AND SUFENTANIL IN LABOR ANALGESIA"

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CERTIFICATE

This is to certify that the dissertation **" A COMPARATIVE STUDY ON LOW DOSE INTRATHECAL ROPIVACAINE ALONE WITH ROPIVACAINE AND SUFENTANIL IN LABOR ANALGESIA"** presented herein by **Dr.S. Prithiviraj,** is an original work done in the Department of Anesthesiology, Government Stanley Medical College and Hospital, Chennai, in partial fulfillment of regulations of the Tamilnadu Dr.M.G.R.Medical University for the award of degree of M.D. (Anesthesiology) Branch X, under my guidance and supervision during the academic period 2004-2007.

Prof.Dr.D.R. Gunasekaran, M.S.,
DEAN,
Government Stanley Medical
College & Hospital,
Chennai - 600001

Prof.Dr.R. Meenakshi, M.D., D.A.,
PROFESSOR AND HOD
Dept of Anesthesiology,
Government Stanley Medical
College & Hospital,
Chennai - 600 001.

DECLARATION

I, **Dr.S. PRITHIVIRAJ** solemnly declare that this dissertation, titled **"A COMPARATIVE STUDY ON LOW DOSE INTRATHECAL ROPIVACAINE ALONE WITH ROPIVACAINE AND SUFENTANIL IN LABOR ANALGESIA"** is a bonafied record of work done by me in the Department of Anesthesiology, Stanley Medical College and Hospital, Chennai, under the guidance of **Prof. R. Meenakshi, M.D., D.A.,** Professor and H.O.D., Department of Anesthesiology, Government Stanley Medical College & Hospital, Chennai - 600 001.

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Date: **Dr. S. PRITHIVIRAJ**

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INTRODUCTION

“For all the happiness Mankind can gain is not in pleasure but in rest from pain “

JOHN DRYDEN

Pain derived from the Latin word “poena” which means punishment. In ancient times, Pain was considered as punishment from god.

Labor is an extremely painful process. Being a natural process, women have accepted labor pain as a normal one. Traditionally a number of techniques have been employed to provide labor analgesia. Epidural analgesia, either continuous or intermittent boluses, is considered to be the gold standard in labor analgesia due to the long duration of labor. Traditionally only high doses of local anaesthetics were used. Though they provide excellent pain relief, they produce an unacceptable high level of motor blockade which impairs the parturient’s ability to bear down during labor, resulting in prolonged labor. Lower doses of local anaesthetics by themselves are inadequate. The technique of spinal analgesia in labor pain relief was a setback due to the shorter duration of analgesia. The newer technique of combined spinal-epidural analgesia is a major breakthrough in labor analgesia.

Current obstetric practice aiming to provide effective pain relief, led Collins and colleagues to popularize the combined spinal-epidural technique for labor analgesia. These

techniques involved an initial intrathecal injection of a local anaesthetic with an opioid (Fentanyl) to establish analgesia and subsequent epidural injections to maintain analgesia. The doses of drugs involved were such that ambulation was possible.

The discovery of opioid receptors in spinal analgesia provides an interesting option. Opioid agonists selectively block pain impulses but leave the motor system unaffected. The doses for central neuraxial blockade are also very little when compared to parenteral routes and does not result in significant respiratory depression both to the mother and the fetus. Since opioids and local anaesthetics act at different sites, their combination provides a synergistic effect permitting to use lesser concentration of both. When used in such low doses the individual side effects are minimized while maximizing the desired effects.

Ropivacaine, a newer local anaesthetics which has been shown to cause less intense motor blockade and less cardiotoxic is rapidly evolving as local anaesthetic of choice in labor analgesia as well as in post operative analgesia. The aim of this study was to compare the analgesic and the motor sparing effect of low dose intrathecal Ropivacaine 3mg with or without sufentanil 10µg as a part of CSE labor analgesia. Efficacy, Duration of analgesia, sensory blockade and fetal effects were studied in detail.

AIM

To compare the effect of low dose intrathecal Ropivacaine alone with Ropivacaine and Sufentanil in providing labor analgesia.

The parameters that were analysed include:

- The analgesic and the motor sparing effect of low dose intrathecal Ropivacaine alone and with sufentanil in labor analgesia.

- Maternal and fetal outcomes.

- Safety and patient comfort.

HISTORY

Throughout history women suffered with pain until the advent of using ether for labor analgesia by Dr.James Young Simpson of Edinburgh on 19th January 1847, which opened up the interesting avenue of pain relief for labor. At that time it was a highly controversial issue.

Labor analgesia became popular when John Snow administered chloroform anesthesia to Queen Victoria for the birth of her 8th child Prince Leopold in 1853 and 9th child Princess Beatrice in 1857. Kinkovich of St.Petersburg used Nitrous Oxide in Obstetric analgesia in 1880.Guedel designed an apparatus for the self-administration of nitrous oxide in labor in 1910.

Dennis Jackson and Striker used Trichloroethylene in 1934. Freedman inhaler was developed in 1943 to facilitate administration of analgesic concentrations of Trichloroethylene to women in labor.

Methoxyflurane was used for labor in 1959 and in 1970. Even midwives were permitted to use 0.35% Methoxyflurane.

Tunstall tried Entonox in 1962.Inhalation anesthesia for labor is not much used now except Entonox. Following the demonstration of spinal analgesia by August Bier in 1899 this was also tried for labor but without much success.

Stoeckel of Marburg described extradural sacral block in 1909 using Procaine. This was followed by Schlimpert and Schneider who used 50ml of 1% Procaine.

Eugen Bagden in 1930 and J.G.P.Clealand of University of Oregon in 1933 provided important contributions to the understanding of the anatomical pathways and physiology of labor pain.

Fidel Pages of Spain performed the first lumbar epidural block in 1921 and Dogliotti of Turin developed the technique in 1930. Refinements in the needle by Tuohy and in the catheter quality made continuous epidural analgesia a popular technique. The flexibility introduced by the continuous epidural technique with regard to the duration was especially very suitable for labor because of the longer duration required for successful labor analgesia. The CSE technique combines the advantages of both spinal and epidural analgesia.

The discovery of opioid receptors in the central nervous system by Snyder in 1973 and Pert in 1976 was soon followed by flurry of activity. A number of opioids have been used successfully both Intrathecally and extradurally. Highly lipophilic opioids like Fentanyl, Sufentanil and Alfentanil are more suitable than less lipophilic drugs like morphine. Opioids provide excellent pain relief when used Intrathecally or extradurally without affecting the motor system – a property that is much desired in an agent used for labor analgesia.

ANATOMY OF THE EPIDURAL AND SUBARACHNOID 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 dura and the periosteum lining the canal, and corresponds to the very restricted space within the skull between the two layers of the cranial dura mater enclosing the venous sinuses**.**

BOUNDARIES

By vertebral bodies Anteriorly: 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

The epidural space extends from the Foramen magnum to sacral hiatus. Except in the lower sacral region it is annular in shape, and narrow. The anterior and posterior nerve roots with their dural coverings pass across the very narrow space to unite in the intervertebral foramen to form the segmental nerves. The rest of the epidural space is occupied by numerous small veins and by fatty areolar tissue, which is continuous around the nerves through the intervertebral foramina with the fat in the paravertebral spaces. The upward spread of drugs is limited by the attachment of dura to the circumference of the foramen magnum.

The amount of fat in the areolar tissue of the space depends on the obesity of the subject. It is greatest in the median plane posteriorly where the summit of the vertebral arch is commonly separated from the rounded posterior aspect of the dura by approximately 5 to 6 mm, and antero-laterally where it is continuous with the pads of fat surrounding the spinal nerves in the intervertebral foramina. Between the postero-lateral walls of the lumbar vertebral canal and the dura, the space is narrower, and the fat less evident. Anteriorly in a thin subject, the space is only potential, since here the dura lies close to the posterior longitudinal ligament on the posterior aspect of the vertebral bodies.

The spread of the local analgesic solution injected into the epidural space is not accurately predictable, because of the resistance offered by the fatty areolar tissue and the numerous foramina through which the fluid can leak. A dorso-median fold of dura mater was demonstrated in a few cases, which sometimes divides the epidural space into a ventral and two dorso-lateral compartments, not necessarily freely communicating with each other. The median thickness of the space might be only 2 mm. These observations explain the occasional patchy analgesia and inadvertent dural puncture when the midline approach is used.

The space occupied by the venous plexus varies with the amount of the venous distention and is related to the intrathoracic pressure.

SUBARACHNOID SPACE

The subarachnoid space is lined externally by the arachnoid, internally by the piamater, and innumerable cobweb like trabeculae run between the two membranes, though sparsely in the cisterns, the cranial and spinal nerves traverse it. It houses the main blood vessels of the central nervous system, and extends along the smaller arteries and capillaries in to the substance of the brain and the spinal

cord. Here the cerebrospinal fluid takes the place of the tissue fluid (lymph) found in other regions of the body.

In the cervical and thoracic regions the space is annular and the distance between the arachnoid and pia covering the cord, even in an adult is only about 3mm, so that a spinal tap here is fraught with the danger of injuring the cord with the needle. The cord commonly ends at the lower end of the first lumbar vertebra so that below this level the subarachnoid space is no longer annular but it is practically circular in section and has a diameter of about 15mm. Lumbar puncture should be carried out in the lower lumbar region. The fact that the cord terminates above this level renders it immune to injury, the constituent nerve roots of the cauda equina escape damage on account of their limited mobility, and the absence of the cord greatly increases the cross sectional area of the sub arachnoid space, the ultimate target at which the needle is aiming.

PRESSURE AND VOLUMES OF THE EPIDURAL SPACE

Substantial differences have been observed between the actions of epidural and subarachnoid injections of local anesthetics 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 also increased.

For the above reasons 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 H_2O. 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.

Although the engorgement of the epidural veins would appear to be increased in the sitting position, there is little evidence to suggest that the lateral position is associated with a decrease in complication rates such as dural puncture or reduced incidence of venous puncture.

PHYSIOLOGY OF PAIN IN LABOR

Pain as described by the International association for study of pain (IASP) is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or as described in terms of such damage”.

PATHWAYS AND MECHANISM

Bonica has modified the description of peripheral pain pathways proposed by Cleland in 1993.

PAIN IN THE FIRST STAGE OF LABOR

Uterine contractions cause stretching, tearing and distortion and possibly ischemia of the uterine tissues, whilst simultaneously dilating the cervix and stretching the lower uterine segment. The intensity of the pain increases progressively with the raising strength of the contractions. In early labor only the nerve roots of T11 and T12 are involved, but as the intensity of contractions increases, T10 and L1 are recruited.

Backache is a frequent complaint during labor and may be caused by two mechanisms. Pain originating in the uterus or cervix may be referred to the cutaneous branches of the posterior divisions of T10-L1. Pressure on peri uterine tissues often, in association with fetal malposition or an unusual shape of the sacrum, refer to the L5-S1 segments.

PAIN IN THE SECOND STAGE OF LABOR

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. 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 the ilio-inguinal nerve (L1).

CLINICAL IMPLICATIONS

During the first stage of labor, a block limited to the T11-T12 segments at the beginning and later extending to involve T10 and L1 will usually be sufficient to provide excellent pain relief whilst avoiding neural blockade of the sacral segments. Premature sacral blockade can result in the loss of the stimulating effect upon contractions of Ferguson’s reflex and the loss of pelvic muscle tone, which aids the rotation of the presenting part.

Later in the first stage and during the early part of the second stage, pain is often experienced in lower lumbar and upper sacral segments, so that the block will have to be extended if analgesia is to be guaranteed.

Complete block of the sacral segments need to be performed only when perineal pain becomes established.

Epidural block will interrupt the preganglionic sympathetic fibers and leave the postganglionic fibers intact.

RELAY OF PAIN

Pain from the peripheral nociceptive field is transmitted to the cortex by the afferents arising from the dorsal root ganglion i.e., the first order neurons. The majorities of these first order neurons passes to the contralateral side as the spinothalamic tract and gives afferents to the medullar centre, reticular activating system, and hypothalamus and reach the post central gyrus in the cortex. The efferent impulses reach the segmental area through the corticospinal and rubrospinal tracts.

Some of the first order neurons communicate through the intern uncial neurons and give efferent impulses to the peripheral nociceptive areas from the segmental autonomic reflexes.

Labor and vaginal delivery produces tissue damage, and like tissue injury from any cause, result in pain and local segmental, suprasegmental and cortical responses.

Pain relief during labor provides excellent satisfaction for the mother in labor. Lumbar epidural analgesia is far superior to parenteral and inhalational approaches, as the mother remains alert throughout and the analgesia can be extended to relieve both uterine pain and pain related to distension of the lower birth canal, thus providing analgesia for instrumental delivery or caesarean sections if there is any indication. Regional analgesia minimizes or completely avoids the problems of maternal aspiration, as well as neonatal drug depression due to general anesthesia.

CONSEQUENCES OF PAIN IN LABOR

Pain is a noxious and unpleasant stimulus, which produces fear and anxiety. It was once thought that fear, anxiety and ignorance exacerbated labor pain. But the opposite may also be true.

The maternal and fetal consequences of unrelieved pain in labor has been stressed on many an occasion. Unrelieved pain in labor causes increased plasma cortisol and catecholamine levels. This may be responsible for the decrease in the utero-placental blood flow. Effective pain relief reduces plasma noradrenalin levels, prevents the rise of 11-hydroxycorticosteroid in the first and second stages. It also prevents metabolic acidosis by reducing the rate of rise of lactate, pyruvate and decreases maternal oxygen consumption by up to 14%. Effective epidural analgesia prevents the pain induced hyperventilation and hypocapnia, which can be severe enough to produce tetany in painful labor. The respiratory alkalosis further impairs feto-maternal gas exchange by shifting the oxygen dissociation curve to the left and the fall of fetal PaO_2.

PHYSIOLOGICAL CONSIDERATIONS DURING LABOR

RESPIRATORY SYSTEM

During labor, particularly in the late first stage and second stage, the pain from episodic uterine contractions produce corresponding increases in maternal minute ventilation (as much as 300% over that of non pregnant women) and oxygen consumption. Maternal hypocarbia ($PaCO_2$ <=20mmHg) and alkalemia (pH 7.55) results. Hypocarbia can lead to hypoventilation between uterine contractions, resulting in intermittent hypoxemia (particularly in obese patients or those who have received parenteral opioids). Epidural analgesia eliminates these pain-induced increases in oxygen consumption and minute ventilation and the accompanying hyperventilation-hypoventilation cycle. Pain, which causes the pregnant woman to hyperventilate, shifts the oxygen dissociation curve to the left. This increases the maternal oxygen affinity and makes the unloading of oxygen to the fetus less favorable.

During pregnancy, capillary engorgement of the mucosa occurs throughout the respiratory tract, potentially causing edema in the nasopharynx, oropharynx, larynx and trachea. Therefore, manipulation of the upper airway requires extreme care. Regional analgesia abolishes the requirement of airway manipulation and hence avoids the dangers involved in general anesthesia.

CARDIOVASCULAR CHANGES

The cardiovascular system is progressively stressed during pregnancy and parturition. Many of the changes appear during the first trimester of pregnancy (increases in cardiac output of 22% and decrease in systemic vascular resistance by 30% at 8 weeks gestation). The changes continue into the second and early third trimester of pregnancy, when cardiac output increases to approximately 30-40% of non-pregnant values. The increase in cardiac output during pregnancy is primarily a result of increase in stroke volume (by about 30%) with a more modest increase in heart rate (10-15 beats/min). Arterial blood pressure does not change during normal pregnancy because of a decrease in peripheral vascular resistance.

Clinical examination of a pregnant woman may reveal a wide, loud split first sound and a soft ejection systolic murmur, caused by the increased blood flow and vasodilatation. The elevated diaphragm usually alters the position of the heart at term, so that the point of maximum impulse is felt a little to the left. The axis on the ECG is also shifted to left. ECG may show non-specific ST, T and Q wave changes and benign arrhythmias.

The pain and apprehension of labor adds to cardiac work during pregnancy and increases stroke volume and cardiac output by 45% over prelabor values. Blood pressure increases during painful labor. Additional stresses are imposed by uterine contractions, which cause, in effect an auto transfusion. With each uterine contraction, blood from the body of the uterus is pushed into the central circulation and blood volume and cardiac output increase by 10-25%. After delivery also the same auto transfusion occurs. In addition to increase in central blood volume, obstruction of the venacava is relieved. As a result there is a marked increase (up to 80% of pre labor values) in stroke volume and cardiac output in the immediate post partum. Patients with limited cardiac reserve may experience cardiac failure at this time.

Despite the increase in blood volume and cardiac output, the parturient at term is susceptible to hypotension in supine position. When the patient is supine, the gravid uterus partially or completely compresses the aorta and inferior vena cava, leading to decreased venous return, decreased cardiac output, hypotension and reduced uterine blood flow. Up to 10% of pregnant patients near term develop signs of shock (hypotension, pallor, sweating, nausea, vomiting, changes in cerebration) when they assume this position.

Compensatory mechanisms include increased sympathetic tone and collateral routes (paravertebral veins to azygos vein) to improve venous return during obstruction of the vena cava. Caval compression also increases uterine venous back pressure, which further decreases uterine blood flow. Compression of the aorta is not associated with maternal symptoms but does cause arterial hypotension in the lower extremities and uterine arteries, which can further decrease uterine blood flow and impair utero-placental perfusion.

During labor the patient should be positioned either on her side or with a left tilt. During delivery the operating or the delivery table can be tilted laterally to the left or a small pillow or foam rubber wedge can be used to elevate the patient's right buttock and back to about 10-15 cms.

The pregnant woman at term is in a hypercoagulable state owing to increase in factors VII, VIII, X and plasma fibrinogen. Estimation of blood loss at delivery varies but may be around 500ml for an uncomplicated vaginal delivery. Blood loss during caesarean section varies widely with 500 to 1400 ml, being reported.

HEPATIC CHANGES

Total protein concentration and the albumin- globulin concentration ratio decrease. Although plasma cholinesterase activity is reduced during pregnancy and in the immediate post partum period, moderate doses of Succinylcholine are usually metabolized easily.

GASTRO INTESTINAL CHANGES

During pregnancy, the secretion of gastric acid increases. During late pregnancy, gastric emptying is slowed as a result of displacement of pylorus by the enlarged uterus. Pain, anxiety and use of opioid analgesia during labor contribute to impaired gastric emptying. Intra-gastric pressure is increased and lower esophageal sphincter tone is decreased during pregnancy. All these changes increase the risk of regurgitation and aspiration during either during general anaesthesia or during the state of impaired consciousness from any other cause.

CENTRAL NERVOUS SYSTEM CHANGES

Pregnancy reduces anesthetic requirements both during regional and general anesthesia. During spinal or epidural anesthesia, less local anesthetic is required to produce a given level of anesthesia. This was thought to be due to the mechanical effects of increased intra-abdominal pressure, causing epidural venous engorgement and a reduction of both the epidural and subarachnoid spaces. Reduced MAC is seen during early pregnancy and immediate post partum period.

RENAL CHANGES

Renal blood flow and glomerular filtration rate increase rapidly during pregnancy, reflecting changes in cardiac output. During the third trimester, they slowly return to normal. Creatinine clearance usually increases and therefore the upper limits of normal for blood urea nitrogen and serum creatinine are lower in the pregnant woman.

UTERINE BLOOD FLOW

Uterine blood flow in the parturient at term is approximately 700ml/min and is determined by the following relationship:

$$\text{Uterine blood flow} = \frac{\text{(uterine arterial pressure) - (uterine venous pressure)}}{\text{(Uterine vascular resistance)}}$$

There is auto regulation of uterine blood flow. The vessels are maximally dilated during pregnancy. As such in the absence of aortic compression, uterine arterial pressure directly reflects maternal blood pressure and cardiac output. Uterine blood flow decreases during maternal hypotension (sympathetic block, hypovolemia, hemorrhage, compression of the inferior vena cava), in circumstances in which uterine venous pressure is increased (compression of the inferior venacava, abruption placenta), and with increases in uterine vascular resistance (maternal hypertensive disorders, α agonists, uterine hypercontracitility). Due to increased maternal mean arterial pressure and a concomitant decrease in uterine blood flow there are deleterious effects on the fetus.

After epidural analgesia uterine blood flow increases, mean arterial pressure stabilizes and placental blood flow is increased by either a reduction in extrinsic vascular tone (uterine tone) or a decrease in intrinsic vascular resistance (placental vasodilatation).

EFFECTS OF LABOR PAIN ON THE FOETUS

During uterine contractions there is intermittent reduction of the intervillous blood flow and during a peak of contraction, there may be a temporary decrease in the placental gas exchange. This is worsened by maternal hyperventilation due to severe pain.

Respiratory alkalosis in the mother results in the following:

- A shift of the mother's oxygen dissociation curve to the left, diminishing transfer of oxygen form mother to the fetus.
- Maternal hypoxia during uterine relaxation.
- Umbilical vasoconstriction causing a diminution of umbilical blood flow.
- A reduction in uterine blood flow due to elevations in noradrenalin levels.
- Fetal hypoxia

Normally maternal blood receives acid metabolites and carbon dioxide from fetal blood and the pH decreases so that there is shift in the maternal oxyhaemoglobin dissociation to the right maintaining

increased oxygen delivery to the fetus. At the same time in fetal blood, the pH increases leading to a shift in fetal oxygen dissociation curve to the left. This effect is known as the double Bohr Effect. In prolonged labor maternal hyperventilation leads to alkalosis and with diminishing maternal $PaCO_2$, the Bohr Effect may be attenuated and cause hypoxia in conditions of fetal stress. Thus maternal hyperventilation as a result of pain decreases fetal oxygenation, presumably by shifting the maternal oxygen dissociation curve to the left and by reducing umbilical blood flow.

EFFECTS OF MATERNAL ANALGESIA

Maternal hyperventilation is reduced as a result of adequate pain relief. The periods of hyperventilation during contractions followed by hypoventilation during relaxation are avoided and $PaCO_2$ remains in the near normal range. Hypoxia consequent to hypoventilation in between contraction is also avoided. Epidural analgesia, by blocking impulses as well as sympathetic efferents reduces the release of catecholamines, cortisol and ACTH, reducing the stress response.

Analgesia also reduces the marked rise in cardiac output and blood pressure due to pain. These may be especially beneficial to the parturient with cardiac disease, PIH and pulmonary hypertension. Maternal and fetal acidosis is also reduced.

EFFECTS ON THE FOETUS

The benefits of pain relief, best achieved by regional techniques, are likely to be of value to all infants but are especially important to the fetus at risk. Epidural analgesia increases intervillous blood flow by vasodilatation and may attenuate the pre-existent vasoconstriction in PIH.

METHODS OF LABOR PAIN RELIEF

A. Non pharmacological Methods:

- Psycho prophylaxis
- Hypnosis

- Aromatherapy
- Reflexotherapy
- Music and magnets
- Breathing Excercises
- Acupuncture
- TENS

None of the above methods are effective in providing complete pain relief.

B. Pharmacological Methods:

a.Systemic:

- Narcotic analgesia
- Sedatives
- Ketamine
- Inhalational agents-Entonox, Isoflurane, Sevoflurane.

b.Regional:

- Epidural block
- Subarachnoid block
- Combined spinal –epidural
- Lumbar Sympathetic block
- Paracervical block
- Pudendal block

PHARMACOLOGY OF ROPIVACAINE

GENERIC NAME : Ropivacaine HCl Injection

CHEMICAL NAME S-(-)-1-propyl-2',6'-pipecoloxylidide hydrochloride monohydrate

PHYSICAL PROPERTIES

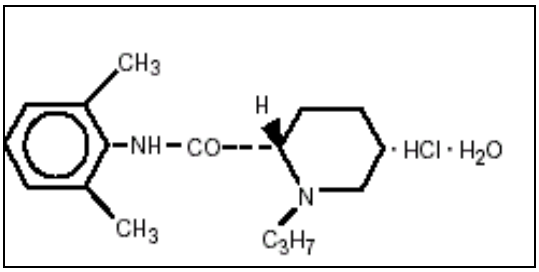
The drug substance is a white crystalline powder, with a chemical formula of

C17H26N2O•HCl•H2O, molecular weight of 328.89. At 25°C Ropivacaine HCl has a solubility of 53.8 mg/mL (0.164 mol/L) in water, a distribution ratio between n-octanol and phosphate buffer at pH 7.4 of 141 and a pKa of 8.07 in 0.1 M KCl solution [12]. The pKa of Ropivacaine is approximately the same as Bupivacaine (8.1) and is similar to that of mepivacaine (7.7). However, Ropivacaine has an intermediate degree of lipid solubility compared to Bupivacaine and mepivacaine. The solubility of Ropivacaine is limited at pH above 6. Thus, care must be taken as precipitation may occur if Ropivacaine is mixed with alkaline solutions.

CHEMICAL PROPERTIES

Ropivacaine HCl Injection is a member of the amino amide class of local anesthetics. It is chemically described as S-(-)-1- propyl-2', 6'-pipecoloxylidide hydrochloride monohydrate . Ropivacaine is structurally similar to Bupivacaine and mepivacaine. However, it differs from these drugs in that they are racemic preparations, while Ropivacaine is available as the S-(-) enantiomer. The drug substance has a chemical formula of C17H26N2O•HCl•H2O, molecular weight of 328.89, and the following structural formula:

STRUCTURAL FORMULA OF ROPIVACAINE



PHARMACOLOGICAL ClASSIFICATION

Ropivacaine HCl Injection is a member of the amino amide class of local anesthetics. It is a homologue of Bupivacaine and mepivacaine. Systemic absorption of local anesthetics can produce effects on the central nervous and cardiovascular systems. At blood concentrations achieved with therapeutic doses, changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are minimal. However, toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrioventricular block, ventricular arrhythmias, and to cardiac arrest, sometimes resulting in fatalities. In addition, myocardial contractility is depressed and peripheral vasodilation occurs, leading to decreased cardiac output and arterial blood pressure [21, 22, 23, 24, 26] . Following systemic absorption, local anesthetics can produce central nervous system stimulation, depression, or both. Apparent central stimulation is usually manifested as restlessness, tremors, and shivering, progressing to convulsions, followed by depression and coma, progressing ultimately to respiratory arrest [24,25,26].

Mechanism of action

Ropivacaine is a member of the amino amide class of local anesthetics and is supplied as the pure S-(-)-enantiomer. Local anesthetics block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, slowing the propagation of the nerve impulse, and reducing the rate of rise of the action potential.

PHARMACOKINETICS

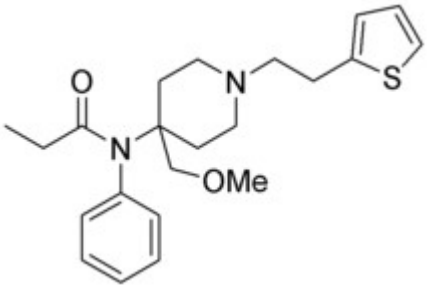
Elimination: The kidney is the main excretory organ for most local anesthetic metabolites. In total, 86% of the Ropivacaine dose is excreted in the urine after intravenous administration, of which only 1% relates to unchanged drug

PHARMACOLOGY OF SUFENTANIL

Generic Name : Sufentanil citrate.

Chemical Name : N-[4-(methoxymethyl)-1-(2-thiopen-2-ylethyl)-4 - piperidyl] - N – phenyl - propanamide

Chemical Formula : C22H30N2O2S



Sufentanil, a Synthetic opioid of phenyl piperidine derivative is 5 - 10 times more potent than fentanyl with μ agonistic action.

Physical Properties : Mol. weight - 386.552 gm/mol

Melting point – 97ºC (207ºF)

pH - 3.5-6.0

Preparations : Sufentanil citrate 0.05 mg/ml in Preservative free acqueous solution.

Pharmacodynamics:

Cardiovascular System:

- Infrequent Bradycardia
- Preservation of Myocardial Oxygen balance
- At higher doses, 25 µg/kg it attenuates the sympathetic response.
- Infrequent hypotension and that too transient period.

This transient decrease in MAP is occasionally been accompanied by short lasting reduction in cerebral perfusion pressure.

Respiratory System:

- Dose dependent respiratory depression due to direct action on medullary respiratory centre.
- Hypoxic drive decreased.
- Delayed Respiratory depression can occur even during the postoperative period.

Respiratory depression can be nullified by the opioid antagonist naloxone.

Central Nervous system:

- Hypnosis and anesthesia can be produced at 8µg/kg dosage.

- Adequate reduction in intracranial volume at doses of 20µg/kg in craniotomy patients.
- EEG shows decreased cerebral blood flow and cerebral O2 utilization.

Endocrine System:

Attenuation of Sympathetic hormones mainly Noradrenaline .

Pharmacokinetics:

Pharmacokinetics studied using three compartment models.

Distribution time	- 0.72 min.
Redistribution time	- 13.7 min.
Half Life	- 265 min.
Elimination half life	- 148 min.
Biotransformation	- Liver and small intestine.
Metabolic pathway	- O-Oxidative demethylation and N- dealkylation
Plasma protein binding	- 93 ± 1%.
Clearance	- 12.7 ± 2.5 ml/min/kg.
Volume distribution	- 1.7 ± 0.6 lit/kg.
Excretion	- 2 - 6% unchanged in urine. 80% excreted within 24hours.

Epidural and Intrathecal Sufentanil:

Mechanism of action: Spinal opioid µ1 receptor agonist.

Sufentanil can be used epidurally for postoperative and labor analgesia. Following epidural Sufentanil, peak plasma concentration is attained in 10 min and is 4 – 6 times lower than those of IV administration. Peak concentration in CSF attains within 5-90 min after epidural injection. Decay of Sufentanil in CSF is biphasic with an average terminal half life of 165 min compared to 265 min in plasma. Placental transfer occurs with fetal concentration far below maternal plasma concentration but equilibrates rapidly.

Side Effects:

- Nausea/Vomiting
- Pruritis
- Hypotension
- Respiratory depression
- Urinary retention
- Motor blockade
- Chest wall rigidity

REVIEW OF LITERATURE

1. Levin A et al, Anesth Analg. 1998 Sep: 87(3): 624 -7

The authors did a study comparing two doses of intrathecal Ropivacaine and Sufentanil for combined Spinal – Epidural analgesia in parturients. Ropivacaine and it produces less motor block in equi - analgesic doses than Bupivacaine. They compared two different doses of intrathecal Ropivacaine (2mg Ropivacaine with 10µg sufentanil) with a standard dose of 2.5 mg intrathecal Bupivacaine 10µg sufentanil. They concluded that Ropivacaine when combined with sufentanil intrathecally is effective for providing CSE labor analgesia but offers no added advantage over Bupivacaine in the studied doses.

2. Soni AK, et al, Can I Anesth 2001 Jul - Aug; 4-8 (7) 677-680.

The authors evaluated the motor sparing effects of low dose Ropivacaine with or without sufentanil. 36 term parturients were randomly assigned to receive 3mg of intrathecal Ropivacaine or 3mg of intrathecal Ropivacaine with 10µg of sufentanil by CSE technique. Patients were evaluated for hypotension, linear analogue score for labor pain, motor power, sensory level, duration of analgesia and neonatal Apgar scores. The following day patients were assessed for satisfaction, headache and neurologic deficit.

The mean duration of analgesia was 41.4 ± 4.9 min and 95.0 ± 6.1 min for Ropivacaine and Ropivacaine with sufentanil respectively. No other significant difference was made out.

They concluded “Low dose Ropivacaine provides effective analgesia during labor via the intrathecal route. It can be mixed with sufentanil to improve the quality and duration of analgesia. Fetal outcome remains favourable. It may provide minimal or no motor block, to

facilitate ambulation".

3. McClellan KJ et al, Drugs. 2000 Nov; 60(5):1065-93.

Ropivacaine: An update of its use in regional anaesthesia.

Ropivacaine is a long acting, enantiomerically pure (S – enantiomer) amide local anaesthetic with a high pKa and low lipid solubility which blocks nerve fibres involved in pain transmission (A – delta and C – fibres) to a greater degree than those controlling motor function (A- beta fibers) . The drug was less cardiotoxic than equal concentrations of racemic Bupivacaine but more so than lignocaine and had a significantly higher threshold for CNS toxicity than racemic Bupivacaine in healthy volunteers. Extensive clinical data have shown that epidural Ropivacaine 0.2% is effective for initiation and maintenance of labor analgesia and provides excellent postoperative pain relief following abdominal and orthopaedic surgeries. In conclusion, Ropivacaine, a well tolerated regional anaesthetic with an efficacy broadly similar to that of Bupivacaine has reduced CNS and cardiotoxic potential with lower propensity for motor block.

4. Malinovsky JM et al, Anesth Analg. 2000 Dec; 91(6):1457-60.

Intrathecal anaesthesia: Ropivacaine versus Bupivacaine.

The authors compared intrathecal Ropivacaine to Bupivacaine in patients scheduled for TURP Surgeries. They have chosen in a ratio of 3:2 potency of isobaric Ropivacaine (15mg) and isobaric Bupivacaine (10mg) in 100 patients and tested for sensory level, motor blockade and hemodynamic effects. They concluded that 15 mg Ropivacaine intrathecally provided similar motor and hemodynamic effects but less potent anaesthesia than 10 mg of intrathecal

Bupivacaine for endoscopic urological surgeries.

5. Van Kleef JW et al, Anesth Analg 1998:87:624-7.

Spinal anaesthesia with Ropivacaine.

The authors did a double blind study on the efficacy and safety of 0.5% and 0.75% Ropivacaine (3ml) in patients undergoing minor lower limb and lower abdominal surgeries. They concluded that less intense motor block and lesser duration of motor block with 0.5% Ropivacaine and equated the anaesthetic properties of 0.75% Ropivacaine with those of 0.5% Bupivacaine

6. Malinovsky et al Anesthesiology Aug 2002; 97(2): 429-35.

The authors did a study in experimental models regarding the relationship between doses of intrathecal Ropivacaine and side effects and local neurotoxic effects. Seven days after intrathecal injections, Spinal cord and nerves were sampled for histopathology. In conclusion, Ropivacaine induced dose dependent spinal anaesthesia produce no neurotoxicologic lesion in experimental models.

7. McNamee et al, BJA 2002; 89(5): 702 – 6.

The authors did a prospective double blind study in patients undergoing Total hip Replacement surgeries. They concluded that Ropivacaine produces less intense motor block and less duration of motor block, thus establishing the motor sparing effect of Ropivacaine.

8. Camorcia M et al, Anesth Analg 2004 Jun; 98(6): 1779 – 82.

The authors did the study in patients undergoing elective LSCS using various dilutions of intrathecal local anaesthetic solutions determine less motor block and this may be considered in ambulant laboring patients.

9. Viscomi CM, Rathmell JP, Pace NL; Anesth Analg 1998 Jan; 86(1): 219- 20.

The authors did a prospective cohort observational study comparing the duration of intrathecal labor analgesia after intrathecal injections made in early labor (3-5 cm cervical dilatation) and those made in more advanced labor (7-10 cm cervical dilatation). Forty one parturients (18 in early labor and 23 in advanced labor) received intrathecal sufentanil (10 micro grams) and Bupivacaine (2.5 mg) as part of a combined spinal – epidural technique. They found the duration of spinal analgesia was significantly less when intrathecal injection was made in advanced labor (120 ± 26 min) compared with early labor (163 ± 57 min), $P < 0.01$. They concluded that cervical dilatation and stage of labor significantly impact the effective duration of intrathecal Bupivacaine/ sufentanil labor analgesia.

10. Dresner M et al, BJA 2000; 85: 826 - 9.

Did a study comparing 0.2% Ropivacaine with 2µg/ml Fentanyl and 0.1% Bupivacaine with 2µg/ml Fentanyl for CSE. They found Ropivacaine group was more likely to be pain free in the first stage (51% Vs 33.7%; $p = 0.01$). There were no significant differences in patients assessment of motor block or mode of delivery between the groups. Pain relief and patient satisfaction were better in Ropivacaine group but did not reach statistical significance.

11. Sia AT et al, Can J Anesth.1998 Jul; 45: 620 – 5.

The authors compared the combination of intrathecal sufentanil with Bupivacaine and intrathecal sufentanil alone for labor analgesia and found that adding Bupivacaine resulted in higher incidence of hypotension, reduced ability to ambulate and higher sensory blockade. They decided that quality of analgesia was excellent even without Bupivacaine and Bupivacaine resulted in higher side effects.

12. Camann WR et al, Anesthesiology – 1992 Nov; 77(5): 884 – 7.

A Comparison of intrathecal, epidural and intravenous sufentanil for labor analgesia.

Twenty four women in active labor were divided into 3 group receiving sufentanil either intrathecally, epidurally or intravenously using combined spinal – epidural analgesia. In conclusion, the duration of analgesia was significantly prolonged in intrathecal route (1-2 hrs) than epidurally (mean 30 mins) or intravenously (mean 34 min). Also the intrathecal route showed rapid and significant decrease in visual analogue scale scores. However the side effects were limited to pruritis only.

13. Campbell DC et al, Anesth Analg. 1995 Aug; 81(2): 305 - 9.

The addition of local anaesthetic, Bupivacaine to intrathecal sufentanil for labor analgesia.

Fifty two parturients were taken and allocated to three groups to receive either 2.5 mg Bupivacaine or 10 microgram sufentanil or 2.5 mg Bupivacaine with 10 micro gram sufentanil. In conclusion, the quality and duration of labor analgesia were much superior in the Bupivacaine with sufentanil group. Thus addition of 2.5 mg Bupivacaine prolongs the duration

of labor analgesia without any adverse maternal or fetal effects.

14. Sia AT et Al, Anesth Analg 1999 Feb; 88(2): 362- 6.

Combination of intrathecal sufentanil 10 micro gram plus Bupivacaine 2.5 mg for labor analgesia: Is half the dose enough?

The author compared two different doses of intrathecal sufentanil 10 µg and 5 µg with Bupivacaine 2.5 mg for labor analgesia using combined spinal – epidural technique. They concluded that half the recommended dose of 10 µg of sufentanil with Bupivacaine 2.5 mg adequately relieves the labor pain. However they added further that the larger dose produced faster pain relief which was long lasting than the reduced dose without adversely affecting the maternal and fetal outcome.

15. Savoia G et al, Minerva Anesthesiol. 2001 Sep; 67(9 Suppl 1): 206-16.

The authors evaluated relevant trials on perioperative sufentanil in order to design an optimal strategy for administration. 24 Trials were found eligible. It was possible to compare the use of IV and epidural sufentanil alone or in combination with local anaesthetics, clonidine, Ketamine and adrenaline. They concluded “Efficacy of sufentanil resulted the same or better than other analgesics used commonly despite context – sensitive half – life advantage. Its association with local anaesthetics or other adjuvant drugs prolong its action and sometimes decreases the side effect. Sufentanil can be used at very low doses with local anaesthetics or adjuvant drugs via epidural, intravenous or intrathecal route for perioperative analgesia”.

16. Nelson KE et al, Anesthesiology. 2002 May; 96(5): 1070 – 3.

The authors made a comparative study on intrathecal sufentanil and Fentanyl for labor analgesia using CSE technique. They concluded that the relative potency of intrathecal sufentanil to Fentanyl for labor analgesia is 4.4: 1 and the duration of analgesia was also significantly prolonged with the sufentanil group without any statistically significant difference in the side effects between the two.

17. Pickering et al, Anesthesiology 1999; 91: 436 - 41.

The author performed computerized posturographic testing on 44 women in labor after institution of regional analgesia and compared them with a control group of 44 pregnant women. The authors were unable to find any functional impairment of balance after CSE ambulatory analgesia in women in labor who had no clinical evidence of motor block.

18. D' Angelo R et al, Anesth Analg. 1999 Mar; 88: 573 – 6.

Studied the effects of spinal clonidine in prolonging CSE duration using Bupivacaine and sufentanil. Analgesia was significantly prolonged in the clonidine added group. They concluded that spinal clonidine significantly prolongs labor analgesia from spinal sufentanil and Bupivacaine without producing serious adverse side effects.

19. Landau R et al, Semin Perinatol. 2002 Apr; 26: 109 – 21.

The authors reviewed various studies comparing Epidural and CSE. They concluded "CSE should be considered a major breakthrough in the management of labor analgesia". The

advantages of CSE include more rapid onset, reduced total drug dosage, minimal or no motor blockade and increased patient satisfaction. CSE has also been associated with more rapid cervical dilatation when compared to epidural analgesia in nulliparous women in early labor.

20. Kartawiadi L et al, Reg Anesth. 1996 May- Jun; 21: 191 - 6.

Conducted a comparative study in 63 laboring parturients between epidural group (0.125% Bupivacaine, 10 µg sufentanil, 12.5 µg epinephrine – 10ml doses) and CSE using 1 mg Bupivacaine , 5µg sufentanil and 25µg epinephrine. CSE provided longer analgesia, more rapid onset and better satisfaction.

21. Rawal N et al, Anesthesiol clin N. America 2000 Jan; 18:267-9.

Concluded that CSE technique by **'needle through needle technique '**resulted in better epidural catheter siting. He also concluded that the concern about epidural catheter entering through the small dural hole was unfounded.

22. Calimaran AL et al, Anesth Analg 2003 Apr; 96:1167-72.

The authors conducted a study to test the effect of standard epidural test dose (3ml lignocaine 1.5% with epinephrine 1:200000) on motor block in CSE labor analgesia. They concluded that a standard lignocaine epidural test dose injected immediately after initiating combined spinal epidural labor analgesia with Bupivacaine 2.5mg and Fentanyl 25µg may interfere with the ability to perform simple test of motor function and ambulation.

MATERIALS AND METHODOLOGY

This is a prospective randomized controlled study. Prior approval was obtained from the ethics committee of **STANLEY MEDICAL COLLEGE AND HOSPITAL and RSRM Lying –in hospital** for the study. Forty parturients who were admitted to the labor ward and who requested pain relief during labor were selected for the study. The procedure was explained to them in detail and written consent was obtained from them.

Inclusion Criteria:

1. Patients in early active labor (Cervical dilatation 3-5 cms) [9]
2. Patients belonging to ASA I.
3. Only primigravida patients with singleton pregnancy were included in the study.
4. Vertex presentation.

Exclusion Criteria:

1. Patients with medical or systemic disorders.
2. Patients with obstetric complications (PIH, GDM, Eclampsia, etc.)
3. Presentation other than vertex
4. Any contraindications for Central Neuraxial Blockade.
5. Patients who have already received parenteral opioids or systemic analgesics.
6. Patients with known allergy to local anaesthetics.

The patients were randomly divided into two groups of twenty each.

Group R (Ropivacaine):

Received 3mg Ropivacaine 0.2 %(1.5ml) intrathecally followed by epidural drugs (0.0625% Bupivacaine with Fentanyl 1.5 µg/ml) as 10ml top-ups, during the entire period of labor. The top-ups were given only when the patient requested for additional pain relief.

Group RS (Ropivacaine with Sufentanil):

Received 3mg Ropivacaine 0.2% (1.5ml) along with Sufentanil as preservative free solution 10µg (0.2ml) intrathecally, followed by epidural top-ups as 10ml solutions(0.0625% Bupivacaine with Fentanyl 1.5 µg/ml).

Since the study period ended when the patient requested for further analgesia by epidural route after initial intrathecal injection, both the groups received same drugs via the epidural route for the purpose of standardization. A standard epidural test dose itself will result in augmentation of motor blockade[31]. Further, the addition of epinephrine to confirm intravascular placement is not reliable in active labor. Hence the test doses were put away with, rather the first bolus dose was given in two divided doses with 5 mins interval.

The procedure was clearly explained to the patient. The visual analog scale was shown to them and interpretation of the scale explained in detail. The patients were shifted to the operation theatre for performing CSE technique in aseptic manner.

Anaesthesia machine was checked and all emergency airway equipments like Laryngoscopes, different blades of different sizes, endotracheal tubes of appropriate sizes,

LMAs, oropharyngeal airways were kept ready. An emergency drug tray containing all the emergency drugs was also kept ready.

IV access was secured with an 18G venflon. All patients included in the study were preloaded with 10ml/kg of Lactated Ringer's solution. Patient's vital parameters like heart rate, blood pressure, SPO2, respiratory rate, and fetal heart rate were continuously monitored during the procedure. The baseline values were recorded. The drugs to be administered intrathecally were prepared and stored in a sterile container.

Equipments:

The needles used for both groups were 17G Tuohy needle,19G epidural catheter and 26G pencil point long spinal needle (CSE cure by Portex).

Procedure:

With the patient in left lateral position, under strict aseptic precaution L2-3 interspace was identified and skin infiltration was done with 1.5 ml of 2% lignocaine. Using 17G Tuhoy needle, epidural space identified by '**loss of resistance to air'** technique.

Intrathecal injection was performed using long spinal needle (pencil point 26G Whitacare) through epidural needle (**needle through needle technique**)[32] at rate of 0.2ml per second. Immediately following this, 19G epidural catheter was inserted and kept 3cms inside the epidural space. The catheter was secured firmly to the back. The patient was turned to supine position. Epidural drugs were not given till patients first request for analgesia.

With catheter in place, patients were shifted to labor ward after 20 mins of observation in operation theatre, where they were closely monitored till delivery. A single operator was involved in all cases and intravenous/intrathecal placement of epidural catheter was ruled out by aspiration for blood /CSF.

The study period commenced with the intrathecal injection and ended at the patients first request for analgesia.

The following parameters were observed:

1. HR,BP,SPO2,Respiratory rate at 0,5,10,15,30,45,60,90 and 120 mins.
2. Time of onset of analgesia – time of intrathecal injection to patients perception of first painless contraction..
3. Level of sensory blockade with loss of sensation to cold using surgical spirit.
4. Motor blockade by modified Bromage scale.

Grade	Level of motor blockade	Clinical assessment
0	Nil	Free movement of legs and feet
1	Partial	Just able to flex the knees , free movements of feet
2	Almost complete	Unable to flex knees , free movements of feet possible
3	Complete	Unable to move both legs and feet

5. Duration of analgesia – defined between commencement of intrathecal injection to the patients first request for analgesia.

6. Visual analog pain scale (VAS)

7. Hourly cervical dilatation

8. Mode of delivery, duration of labor

9. Fetal heart rate and APGAR at 1 and 5 mins.

10. Patient comfort, satisfaction

[4- Excellent, 3 – Good, 2 –Fair, 1- poor]

11. Side effects –Hypotension, nausea/vomiting, pruritis, respiratory depression, urinary retention, etc.

The patients were informed to ask for additional pain relief even when they felt mild discomfort / pain. The routine obstetric practice was allowed to continue. In our institution, injection Oxytocin infusion was used to accelerate labor. Artificial rupture of membranes done if indicated .During the entire labor, patients were positioned supine with left side tilt. Ambulation was allowed after assessing their motor power. The following tests were done in sequence to assess their motor power.

- Straight leg raising
- Sit at edge of cot unsupported.
- Stand for a minute without support.
- Perform a deep knee bend test.
- Take three unassisted steps.

RESULTS

The study was conducted in Government RSRM Lying-in Hospital during 2006. Forty patients in active labour (Cervical dilatation 3-5 cms)[9] who requested analgesia were chosen and randomly assigned to either of the two groups :

R-Group (Ropivacaine) : Recieved intrathecal Ropivacaine 3mg as part of CSE, followed by epidural top-ups with bupivacaine 0.0625% and fentanyl 1.5μg/ml.

RS-Group (Ropivacaine with Sufentanil) : Recieved intrathecal Ropivacaine 3mg with Sufentanil 10 μg as part of CSE, followed by epidural top-ups with bupivacaine 0.0625% and fentanyl 1.5μg/ml for standardization.

The study commenced at the intrathecal injection and completed with the patients first request for analgesia. The above stated period alone was taken for statistical analysis, using students t-test, Chi-Square tests, fischer tests. Since some of the cases end earlier, the datas were taken for analysis upto 45 mins duration, though all the parameters were monitored till the delivery of the baby.

Demographic Profile and Obstetric Parameters

	R-Group (mean ± S.D)	**RS-Group (mean ± S.D)**	**P- Value**
AGE(years)	21.75 ± 2.31	21.9 ± 2.17	0.83
HEIGHT(cms)	156.55 ± 4.65	157.4 ± 2.98	0.49
WEIGHT(kgs)	59.0 ± 2.83	60.10 ± 4.02	0.32
GEST-AGE(wks)	39.05 ± 0.69	38.75 ± 0.72	0.18
CERV-DIL(cms)	3.92 ± 0.72	3.92 ± 0.72	1.00

The physical characteristics like Age, Height, Weight, Gestational age, Cervical dilatations were compared between the two groups. For all the above parameters, the p-value >0.05 (not significant)

VAS Score

Time (min)	R-Group (mean ± S.D)	RS-Group (mean ± S.D)	T-Test P- Value
0	7.7 ± 0.57	7.75 ± 0.64	> 0.05
5	2.35 ± 0.49	2.45 ± 0.51	> 0.05
10	1.2 ± 0.41	1.3 ± 0.46	> 0.05
15	1.15 ± 0.37	1.05 ± 0.22	> 0.05
30	2.5 ± 1.24	1.00 ± 0.00	0.000
45	3.79 ± 1.25	2.7 ± 0.57	0.000

The visual analog scale for pain scoring was taken over the period of time. P-value using student T-test was not significant until 15 mins, but differs statistically significant by 30 mins onwards implying prolonged duration of analgesia in the RS-group.

Onset of Analgesia

R-Group (mean ± S.D)(mins)	RS – Group (mean ± S.D)(mins)	P. Value
2.45 ± 0.51	2.7 ± 0.57	0.153

The onset of analgesia between the groups was not statistically significant.

Sensory Level

Group	5min	10min	15min	30min	45 min
R – Group (median)	T9	T8	T8	T9	T10
RS – Group (median)	T9-10	T8	T8	T8	T8

The median sensory level over the period of time was tabulated above for both the groups. The descend of sensory level in the R-group by 30 and 45 min showed shorter duration than in the RS-group.

Motor Level

The motor level by modified Bromage scale showed nil motor blockade in both the groups over various time period which was not statistically significant.

Duration of Analgesia

R-Group (mean ± S.D) (min)	RS – Group (mean ± S.D) (min)	P. Value
47.6 ± 10.04	93.25 ± 10.72	0.000

The duration of analgesia was statistically significant (P-0.000) with RS-group 93.25

± 10.72 min over R- group 47.6 ± 10.04 min.

Duration of Labor

	I Stage	II Stage	III Stage	Total Duration
R-Group (mean±S.D)(mins)	189.75 ± 22.45	54.5 ± 9.61	14.45 ± 2.86	258.7 ± 29.7
R-Group (mean±S.D)(mins)	192.75 ± 26.92	52.65 ± 5.76	14.85 ± 2.96	260.25 ± 28.12
P – Value	0.704	0.465	0.666	0.866

They show no statistical significance using the T- test.

Hemodynamic variables

Systolic Blood Pressure :

Time (min)	R-Group (mean±S.D)(mmHg)	RS-Group (mean±S.D)(mmHg)	P- Value T-Test
0	125.4 ± 4.36	126.5 ± 5.35	0.480
5	115.7 ± 4.65	117.2 ± 4.37	0.300
10	112.8 ± 4.51	112.0 ± 4.21	0.565
15	112.7 ± 5.08	111.9 ± 4.52	0.602

30	116.8 ± 5.75	112.0 ± 4.21	0.005
45	124.29 ± 5.92	114.7 ± 4.60	0.000

The systolic pressure showed statistical significance only by 30 min and 45 min again due to regression of sensory level in the R-group.

Diastolic Blood Pressure :

Time	R-Group (mean±S.D)(mmHg)	RS-Group (mean±S.D)(mmHg)	P- Value T-Test
0	80.9 ± 4.61	81.6 ± 4.19	0.618
5	75.5 ± 3.83	77.4 ± 4.68	0.168
10	73.1 ± 3.34	74.3 ± 4.27	0.328
15	73.6 ± 3.82	73.9 ± 3.75	0.803
30	78.5 ± 4.98	74.8 ± 4.37	0.017
45	83.14 ± 3.74	75.2 ± 3.69	0.000

Again by 30 min and 45 min, the diastolic blood Pressure showed statistical significance due to regression of sensory level in R-group.

Maternal Heart Rate :

Time	R-Group (mean±S.D)(bpm)	RS-Group (mean±S.D)(bpm)	P- Value T-Test
0	106.05 ± 8.76	106.85 ± 10.29	>0.05
5	88.85 ± 5.32	89.0 ± 4.13	>0.05
10	80.65 ± 5.62	81.65 ± 3.12	>0.05
15	78.3 ± 5.51	78.75 ± 3.56	>0.05
30	83.65 ± 7.66	79.15 ± 5.16	<0.05
45	89.64 ± 7.01	78.55 ± 6.24	<0.05

The heart rate between the groups varied significantly by 30 min and 45 min.

Fetal Heart Rate :

Time	R-Group (mean±S.D)(bpm)	RS-Group (mean±S.D)(bpm)	P- Value T-Test
0	151.25 ± 11.18	151.95 ± 10.6	0.840
5	146.8 ± 7.45	145.95 ± 5.49	0.684
10	146.45 ± 8.86	145.4 ± 7.63	0.130
15	149.45 ± 7.78	142.3 ± 7.05	0.004
30	152.9 ± 8.60	149.3 ± 8.85	0.200
45	152.64 ± 6.76	148.95 ± 6.68	0.124

Though, the fetal heart rate was not statistically significant between the groups except at 15 min, it was well within the acceptable range of fetal heart rate of 120-160 beats per minute.

Fetal outcome

	R-Group (mean ± S.D)	**RS-Group (mean ± S.D)**	**P- Value T-Test**
APGAR 1	6.85 ± 0.37	6.8 ± 0.41	0.687
APGAR 5	9.00 ± 0.00	8.95 ± 0.22	0.330

No statistical significance in the APGAR score between the groups at 1 min and 5 min.

Number of Epidural top-ups

R-Group (mean ± S.D) (Min)	**RS – Group (mean ± S.D) (Min)**	**P. Value T-Test**
3.60 ± 0.68	2.55 ± 0.60	0.000

The number of epidural top-ups showed statistical significance as the duration of analgesia in the RS-group is prolonged causing less analgesic requirements.

Comfort scale

	Poor	Fair	Good	Excellent
R-Group	0	1	8	11
RS-Group	0	1	9	10

Chi-Square value = 0.948

Almost all the parturients were very much satisfied with the pain relief measures.

Complications

	RS – Group (n)	RS – Group (n)
Hypotension	0	0
Nausea / vomiting	0	1
Pruritis	0	2
Urinary Retention	3	3
PDPH	0	0
Resp. Depression	0	0
Sedation	0	0
Other complications	0	0

By applying pearson Chi-square test, no statistical significance of any complications occurred between the groups. These complications were only minor and easily managed by reassuring the patients.

DISCUSSIONS

A number of methods exist to provide pain relief to the laboring parturients. Among all the regional techniques epidural is considered the gold standard for labor analgesia until a major breakthrough brought was about by Collins[28] and collegues as combined spinal – epidural technique.

Most of the parturients had reported the pain relief was rapid and the quality of analgesia was superior. These findings were quite consistently similar in the studies carried out by Kartawiadi et al[29], van de Velde et al[30].

In this study, I compared a mixture of intrathecal Ropivacaine and Sufentanil with Ropivacaine alone. Ropivacaine was physically compatible with Sufentanil. When used alone, intrathecal Ropivacaine provided shorter duration of analgesia as compared to a similar dose mixed with Sufentanil. At this dose, maternal hemodynamic instability was minimal and adverse fetal effects were absent.

Ropivacaine is a local anaesthetic with lower cardiotoxic potential[21,22,23,24,26] and higher threshold for neurtoxicological symptoms[24,25,26] than racemic bupivacaine. The majority of published data on ropivacaine are on its use in the epidural space (MC Crae et al[18], Datta S et al[19]). There is little data available for its intrathecal use. Various studies show that at equal drug concentrations intrathecal Ropivacaine is less potent and produces a

shorter duration and lesser intensity of motor block[15,16,17]. Iida et al [23] using an closed spinal window technique in a canine model showed that Ropivacaine vasoconstricts, in a dose dependent fashion,the pial arterioles and venules as compared to bupivacaine. Kristensen et al [24] recently reported its relative safety when using ropivacaine in a rat model. Using clinically relavant doses, they suggested it can be administered in the intrathecal space without significantly lowering the spinal cord blood flow.

van Kleef et al [14] first reported its intrathecal use in patients undergoing lower abdominal surgery by comparing 3 ml of 0.5% Ropivacaine with 0.75% Ropivacaine. They found the less intense motor block and lesser duration of block with 0.5% Ropivacaine and equated the anaesthetic properties of 0.75% Ropivacaine with those of 0.5% Bupivacaine. Levin et al [10], described the use of the small dose of intrathecal Ropivacaine mixed with Sufentanil for labor analgesia. Comparing it with a bupivacaine sufentanil mixture they found no difference in the duration of analgesia, side effects and motor block.

In our study, the onset of analgesia was no indifferent between the two groups (2.45 mins ± 0.5 in the R-group vs 2.70 mins ± 0.57 in the RS-group). The duration of analgesia in the RS-group was significantly prolonged than the R-Group (mean 93.25 mins ± 10.72 mins and mean 47.60 mins ± 10.04 mins respectively) showing the additive effect of intrathecal Sufentanil for labor analgesia[1,2,3,4,11] The VAS score was also compared and the mean VAS score at 30 min and 45 min were found to be statistically significant which was well correlated with the duration of analgesia between the two groups, as the R-group

patients started feeling discomfort and pain, with request for first analgesic dose much earlier than the RS-group patients.

The sensory level between the two groups taken as median showed significant difference only by 30 mins onwards as the R-group patients requested for the first analgesic dose earlier than the RS-group again correlating with the difference in duration of analgesia between the two groups. When compared to R-group, more number of patients in the RS-group reached a sensory level of T6 (7 in RS-group vs 5 in R-group) over various period of time. The difference in volumes between the two groups may have influenced the level of sensory blockade, but it seems unlikely. Using equidose hyperbaric and isobaric intrathecal bupivacaine, Malinovsky et al [27], reported that volume had no significant influence on either cephalad spread or duration of sensory blockade.

In both the groups, the motor blockade by modified Bromage scale was nil and at any time, all the patients could be able to do the SLR test. This signifies the motor sparing effect of Ropivacaine[15,16,17.]

Regarding the hemodynamic parameters, no patients in both the groups had significant fall in BP (both systolic and diastolic) after the initiation of intrathecal labor analgesia upto 30 mins. There was a statistical difference in the hemodynamic parameters by 30 and 45 mins which was secondary to the prolonged pain relief in the RS-group[8].

The duration of labour in both the groups were no indifferent and the fetal outcome was also favourable in both the groups by comparing the APGAR at 1 and 5 mins between

the groups. The fetal heart rate was statistically significant by 15 mins between the two groups(mean 149.45±7.78bpm in R-group vs mean 142.3±7.05bpm in RS-group) but was well within the acceptable range of 120-160 beats per minute[7].

With regard to the mode of delivery, only one patient in the R-group underwent LSCS. The indication for which was persistent occipito transverse lie, not of any fetal distress or others. Anaesthesia was provided using the epidural catheter. All others in the study delivered by labor natural with episiotomy.

The number of epidural top-ups between the two groups showed statistical significance (mean 3.60 ± 0.68 in R- group vs mean 2.5 ± 0.60 in the RS-group) thus implying the lesser analgesic requirement in the RS-group which may be considered advantageous.

Regarding the complications, no patients had significant hypotension in both the groups. Two patients had pruritis [5,6] one patient had nausea and vomiting (one episode) in the RS-group and three patients in each group had urinary retention. Just reassurance was more than sufficient in all these cases. No patients had PDPH in both the groups.

During the follow-up period, no patients developed any neurological complications in both the groups. Regarding the patient comfort, almost all patients showed good to excellent in their satisfaction except one who had the scale of fair.

Roux et al [33] and others have indicated that CSE was technically difficult and were

not able to place the epidural catheter after intrathecal drug placement. In our study, no such difficulty was encountered. There were no incidence of intravenous or intrathecal catheter placement.

SUMMARY

In my study, parturients in both the groups had effective pain relief and gave more satisfaction because of the earlier onset of analgesia thus Ropivacaine, a useful local anaesthetic in labor analgesia.

Motor blockade was nil in both the groups, making Ropivacaine, an effective drug in central neuraxial analgesia, especially in settings where ambulation should be retained, such as analgesia during labor or outpatient anaesthesia.

The duration of analgesia was prolonged(mean 93.25 mins in RS-group vs mean 47.6 mins in R-group) when sufentanil is added intrathecally as an additive providing better pain relief, although no statistical difference between the groups in patients satisfaction.

Maternal and fetal outcomes were also favourable.

Complications were only few, minor and easily manageable with just reassurance. The technique doesnot pose any additional difficulty.

CONCLUSION

In my study, I conclude low dose intrathecal Ropivacaine(3 mg as 0.2% solution) provides effective and rapid pain relief ,and doesnot impair the motor function. Thus ambulation is made easy in CSE labour analgesia, without imposing any significant impact on the hemodynamics, mode of delivery, duration of labor or fetal outcome. Hence low dose intrathecal Ropivacaine is a safe drug in CSE labor analgesia. And when combined with sufentanil the quality and duration of intrathecal analgesia is much better(almost twice the duration) with minimal side effects.

Low dose intrathecal Ropivacaine with Sufentanil provides safe and satisfactory labor analgesia and can be used in all parturients who request labor pain relief.

Providing pain relief to laboring parturients will surely be a gratifying experience for the anaesthesiologists.

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Identification:

Name: Age: I.P.No: Unit:

Preop Assessment:

ASA: Vitals: PR - BP- FHR- VAS- Cervix: Presenting part:

Events:

Start of procedure (skin infiltration): Pain free contraction:
Epidural catheter placement: VAS<1:
Intrathecal drug administration: I stage:
End of procedure (Pt placed supine): II stage:
Onset of sensory loss: Time of delivery:

Variable	Basal	0 min	2 min	5 min	10 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min
PR												
BP												
VAS												
Sensory level												
Bromage scale												
FHR												
Cervix												

Epidural Topups

Time								Total
Volume								

Obstetric Intervention:
Oxytocin acceleration - Membrane rupture- other drugs:

Delivery - LN / LN with epi / Instrumental / Caesarian

Total duration of labor (I+II stage):

Baby Apgar: 1 min- 5min-

Patient Comfort – Excellent / good / fair / poor__

Side effects: - Hypotension / Bradycardia / Nausea / Vomiting / Shivering / Pruritus / Resp dep / Urinary retention / others