

Dissertation on

**"A COMPARATIVE STUDY OF INTRATHECAL  
ROPIVACAINE WITH FENTANYL VERSUS  
BUPIVACAINE WITH FENTANYL FOR LABOUR  
ANALGESIA"**

Submitted to the

**TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY**

in partial fulfillment of the requirements  
for the award of degree of

**MD (BRANCH X)  
ANAESTHESIOLOGY**



**STANLEY MEDICAL COLLEGE  
THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY  
CHENNAI, TAMILNADU**

September 2006

## **CERTIFICATE**

This is to certify that the dissertation "**A COMPARATIVE STUDY OF INTRATHECAL ROPIVACAINE WITH FENTANYL VERSUS BUPIVACAINE WITH FENTANYL FOR LABOUR ANALGESIA**" presented herein by **Dr.K.S.Karthikeyan**, 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 2003-2006.

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## **DECLARATION**

I **Dr.K.S.KARTHIKEYAN** solemnly declare that this dissertation, titled "**A COMPARATIVE STUDY OF INTRATHECAL ROPIVACAINE WITH FENTANLY VERSUS BUPIVACAINE WITH FENTANYL FOR LABOUR 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.J.Ranganathan, M.D., D.A.**, Professor and H.O.D., Department of Anesthesiology, Government Stanley Medical College & Hospital, Chennai - 600 001.

This dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the University regulations for the award of degree of M.D. (Anesthesiology), Branch X, examination to be held in September 2006.

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## ACKNOWLEDGEMENT

I wish to express my sincere thanks to **Prof.Dr.M.Vasantha, M.D.**, Dean, Government Stanley Medical College, Chennai for having kindly permitted me to utilize the facilities of the hospital for the conduct of the study.

My heart felt thanks to **Prof.Dr.J.Ranganathan, M.D, D.A.**, Head of the Department of Anesthesiology Stanley Medical College Chennai, for his motivation, valuable suggestions, constant supervision and for providing all necessary arrangements for conducting the study.

I thank **Dr.Deivambigai, M.D, D.G.O.**, Superintendent of Government RSRM hospital and her faculty for their kind cooperation and permitting me to use the hospital facilities for the study.

I express my sincere thanks to **Dr.R.Meenakshi, M.D., D.A.**, Additional Professor of Anesthesiology for her constant encouragement and guidance in carrying out this study

I express my sincere thanks to **Dr.C.R.Kanniya Kumari, M.D., D.A.**, Additional Professor of Anesthesiology for her valuable insights in doing this study.

I am greatly indebted to **Dr.S.Nellai kumar, M.D., D.A.**, Additional Professor of Anesthesiology for his guidance, support and excellent encouragement in carrying out this study.

I wish to thank **Dr.Naseer Ahamed, M.D., D.A.**, who is the Chief Anesthesiologist of Government RSRM hospital when this study was conducted for his encouragement and support.

I thank **Dr.V.Nagasamy M.D., D.A.**, lecturer in Anesthesiology for his guidance in carrying out this study.

I wish to express my gratitude to **Dr.R.S.Vijayalakshmi, M.D, D.A.**, Registrar in Anesthesiology for all her invaluable ideas and consistent support.

I thank all **Assistant Professors of Anesthesiology**, Dept of Anesthesiology, Stanley Medical College and Government RSRM Lying in Hospital for their keen interest and support without which this study would not have been possible.

I also thank the **theatre personnel** Government RSRM hospital for their willing cooperation and assistance. I finally wish to thank all the **patients** and their relatives of Govt. RSRM hospital Chennai whose willingness and patience made this study possible.

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## INTRODUCTION

Labor is an extremely painful process. Traditionally a number of techniques have been employed to provide labor analgesia. Epidural analgesia is considered to be the gold standard in labor analgesia. Continuous epidural analgesia is ideal to provide analgesia because of the long duration of labor. Traditionally only high doses of local anesthetics were used. Though they provide excellent pain relief, they produce an unacceptably high level of motor blockade which impairs the parturient's ability to *bear down* during labor, resulting in prolonged labor. Lower doses of Bupivacaine (0.04% -0.125%) by themselves are inadequate.

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

Current obstetric practice aims to provide effective pain relief while Efforts to improve epidural analgesia led to Collins and colleagues<sup>1</sup> popularizing the combined spinal-epidural technique (CSE) for analgesia in labor. This technique involved an initial Intrathecal injection of opioids (Fentanyl) and Bupivacaine to establish analgesia, and subsequent epidural injections to maintain the analgesia. The doses of drugs involved were such that ambulation in labor was possible. However after the initial Intrathecal injection, motor blockade was present for up to 20 min. Recent research has shown that, in the absence of motor weakness there is no functional impairment of balance in laboring women and therefore ambulation is safe<sup>30</sup>.

Ropivacaine is a newer local anaesthetic, which has been shown to cause less motor weakness and less cardio toxicity and is rapidly evolving as local anaesthetic of choice in Labor analgesia as well as in post operative analgesia<sup>37, 38, 39, 40</sup>. The aim of this study was to compare Intrathecal injection of Fentanyl 0.025 mg and Bupivacaine 2.5 mg, with an Intrathecal injection of Fentanyl 0.025 mg and Ropivacaine 2.5 mg as a part of CSE in labor analgesia. Efficacy, sensory and motor blockade and fetal effects were studied in detail.

The CSE technique was selected so that the analgesia will be maintained by Epidural route in both the groups even though the study stops short with the comparison of Intrathecal injection of Bupivacaine and Fentanyl with Ropivacaine and Fentanyl.

## AIM

To compare Intrathecal Bupivacaine and Ropivacaine with Fentanyl in labor analgesia with regard to:

1. Efficacy of pain relief
2. Effect on fetal and maternal outcomes
3. Patient comfort and the ease of ambulation during labor.
4. Safety

# HISTORY

Throughout history women suffered with pain until the advent of using ether for labor analgesia by Dr. James Young Simpson of Edinburgh on 19<sup>th</sup> 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 8<sup>th</sup> child Prince Leopold in 1853 and 9<sup>th</sup> 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.

Stoekel 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**

**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

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<sub>2</sub>O. 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 (ISAP) 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 worrisome.

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. 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 fetomaternal gas exchange by shifting the oxygen dissociation curve to the left and the fall of fetal PaO<sub>2</sub>.

## PHYSIOLOGICAL CONSIDERATIONS

### 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<sub>2</sub> <=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 cerebation) 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:

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

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,  $\alpha$  agonists, uterine hypercontractility). 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 from 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<sub>2</sub>, 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<sub>2</sub> 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.

# PHARMACOLOGY OF BUPIVACAINE

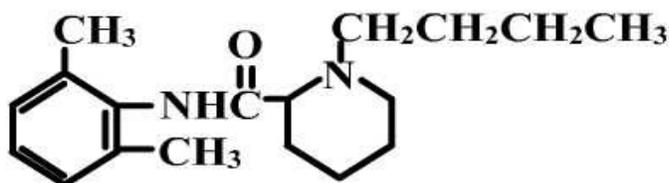
## HISTORY

It is an amide linked local anesthetic synthesized by B.A.F Ekenstam in 1957 and introduced into clinical practice by Talivuo in 1963.

## STRUCTURE

An amino amide local anesthetic having aromatic moiety (benzene ring), which offers lipophilicity at one end of the molecule. It is linked by an amide to a tertiary amine, which is hydrophilic on the other end of the molecule.

## MOLECULAR FORMULA



It displays stereoisomerism: marketed as a racemic mixture containing optically active enantiomers, R and S. S-enantiomer has been noted to have a slightly longer duration of action and lower systemic toxicity when compared to its R-type.

## MECHANISM OF ACTION

The base form is in equilibrium with cationic form outside the axoplasmic membrane. Base form diffuses inside the cell and recalibrates with cationic form. It then reaches the local anesthetic receptor in the Na<sup>+</sup> channel by reversing channel pore while it is in an open state. It prevents Na<sup>+</sup> ions moving intracellularly.

In addition to this simple sodium channel blockade, it also affects second messenger system such as adenylate cyclase and guanylate cyclase and also inhibits synaptic transmission by modification of post synaptic receptor (or) presynaptic calcium channel blockade in epidural / subarachnoid blockade.

## PHYSIOCHEMICAL PROPERTIES

<b>Property</b>	<b>Value</b>
Molecular weight	288
Potency ratio	15
Toxicity ratio	10
pKa(25.C)	8.16
<b>Protein binding in %</b>	
Maternal	95
Fetal	66
<b>% non ionized at</b>	
pH 7.4	17
pH 7.2	11
<b>Partition co-efficient</b>	
(25.C, pH 7.4)	346
Anesthetic index	3.0-4.0

## **PHARMACOKINETICS OF EPIDURAL BUPIVACAINE**

The uptake of local anesthetic into blood vessels in the area where it has been deposited and its subsequent transfer into systemic circulation is referred to as systemic absorption.

### **ABSORPTION**

A biphasic absorption pattern has been found for epidural Bupivacaine. The rapid initial absorption following epidural administration is most likely related to high concentration gradient between the drug in the solution and in the blood. In addition profound increases in epidural blood flow observed during epidural administration of Bupivacaine may contribute to its fast initial absorption rate.

Later on, after the local anaesthetic has been taken up into local tissues such as epidural fat, absorption will become dependent on tissue blood partitioning, resulting in marked slowing of absorption. Estimated total fraction of the dose ultimately absorbed into general circulation is 0.94 with mean absorption time 8.6 hours.

Absorption of local anesthetic is directly related to the amount of drug injected, vascularity, site

injected and tissue binding of local anesthetic at injection site. Bupivacaine will produce lower  $C_{max}$  than less potent and less lipid soluble agents.

## DISTRIBUTION

Distribution of local anesthetic has special emphasis in the pregnant patient, because one of the organs that will be exposed to the absorbed drug is fetoplacental unit.

## PHARMACOKINETICS OF BUPIVACAINE

Elimination half-life $t_{1/2\beta}$	-	162 minutes
Volume of distribution VDSS	-	73 lit
Clearance (lit/min)	-	0.6
Hepatic extraction	-	0.4

## BIODEGRADATION AND ELIMINATION

Liver is the site of metabolism. Two major factors controlling the clearance of the amide-linked local anesthetic are hepatic blood flow and hepatic function. The principal pathways are N-dealkylation, aromatic hydroxylation and amide hydrolysis.

## CLINICAL CHARACTERISTICS OF BUPIVACAINE

Property	Value
Penetrance	Moderate
Duration	6-8 hrs
Infiltration	0.05%
Field block	0.1%
Pudendal / paracervical	0.125%
Epidural analgesia	0.125 – 0.25%
Extradural motor	0.5 – 0.75%
Maximal dose	2mg/kg body weight

## ADVERSE EFFECT AND COMPLICATIONS

### Central Nervous System Toxicity

Potentially toxic blood level can occur when a drug is injected intravenously, intra arterially or a large dose of drug is given into highly vascular area. Risk of CNS toxicity is more because

Bupivacaine is a highly protein bound drug. Pregnancy is associated with 30% reduction in protein binding. This allows for higher brain level of Bupivacaine for a given dose of drug.

## Symptoms

Slow speech, jerky movements, tremors, hallucination, and seizure.

## Cardiovascular Toxicity<sup>41, 42</sup>

1. Dose dependant depression of contractility
2. Dose dependent depression of conduction and velocity in all conducting tissues. Progressive prolongation of ventricular conduction.
3. Predisposition to reentry phenomenon followed by sudden onset of ventricular fibrillation.
4. More affinity for cardiolipin

Toxic plasma concentration is 4-5 µg/ml.

## PHARMACOLOGY OF ROPIVACAINE

**GENERIC NAME :** Ropivacaine HCl Injection

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

## PHYSICAL PROPERTIES

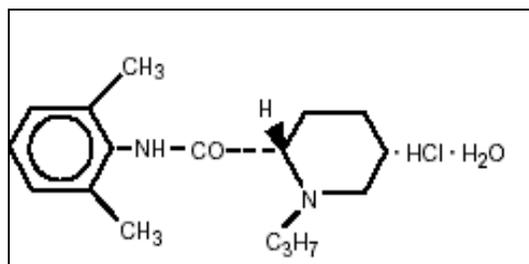
The drug substance is a white crystalline powder, with a chemical formula of  $C_{17}H_{26}N_2O \cdot HCl \cdot H_2O$ , molecular weight of 328.89. At 25°C Ropivacaine HCl has a solubility of 53.8 mg/mL (0.164 mol/L) in water, a distribution ratio between n-octanol and phosphate buffer at pH 7.4 of 141 and a pKa of 8.07 in 0.1 M KCl solution<sup>43,44</sup>. 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'-pipercoloxylidide hydrochloride monohydrate<sup>36</sup>. 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  $C_{17}H_{26}N_2O \cdot HCl \cdot H_2O$ , molecular weight of 328.89, and the following structural formula:

## STRUCTURAL FORMULA OF ROPIVACINE



## 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<sup>37, 38, 39, 40, 41, 42</sup>. 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.

### **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.

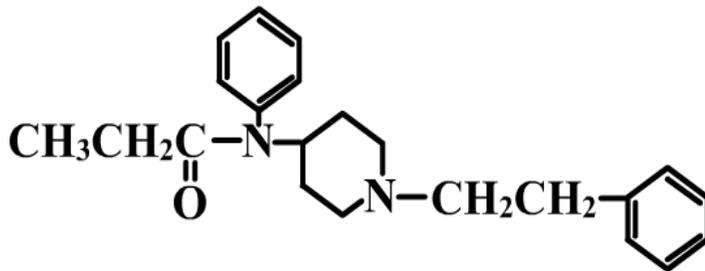
### **PHARMACOKINETICS**

**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 FENTANYL

## STRUCTURE

4 anilino piperidines that are structurally related to pethidine.



Fentanyl is a synthetic opioid with morphine like actions. Act at  $\mu$  receptors as a agonist. It is more specific, shorter acting and 80-100 times more potent than morphine.

## *PHARMACODYNAMICS OF FENTANYL*

### CARDIOVASCULAR SYSTEM

**Bradycardia** – vagal stimulation in high doses.

No effect on cardiac contractility

Hypotension in large doses due to bradycardia, venodilation and suppression of central sympathetic out flow.

### RESPIRATORY SYSTEM

Dose dependent respiratory depression through direct action on medullary respiratory centre.  
Effects are:

- Apnoeic threshold increased.

- Hypoxic drive decreased
- Delayed respiratory depression.

## CENTRAL NERVOUS SYSTEM

Analgesia, euphoria, sedation, hyponosis, miosis, nausea, vomiting.

**Gastrointestinal tract:** Delays gastric emptying produces biliary colic.

**Endocrine system:** Attenuation of stress response

## PHARMACOKINETICS / PHYSIOCHEMICAL PROPERTIES

Property	Value
pKa	8.4
% unionized at pH 7.4	<10
Percentage bound to plasma protein	84
t $\frac{1}{2}$ $\mu$	1 – 2 mins
t $\frac{1}{2}$ $\alpha$	10 – 30 mins
t $\frac{1}{2}$ $\beta$	2 – 4 hour
Vd <sub>cc</sub> L/kg	0.5 – 1.0 L /Kg
Vd <sub>ss</sub> L/kg	3 -5 L/kg
Clearance	10 – 20 ml/kg/mt
Hepatic extraction ratio	0.8 – 1.0

## CLINICAL PROPERTIES

Minimal CSF spread, Rapid onset, Short duration, Low CSF solubility, Rapid analgesia, Decreased side effects, Ideal for PCEA.

## DISADVANTAGES

Systemic absorption, Brief single dose analgesia.

When applied intraspinally these opioids should be injected as close as possible to the spinal segments where the previous nociceptive afferent, carrying the nociceptive impulses from the involved

dermatomes enter the spinal cord.

## **PHARMACOLOGY OF EPIDURAL FENTANYL**

**Dose** = 50 -200  $\mu$ g

**Onset** = 5 – 15 minutes

**Duration** = 2 – 4 hours after single dose

## **SIDE EFFECTS**

Pruritis, sedation, nausea and vomiting, urinary retention, apnoea and seizures, chest wall rigidity.

# REVIEW OF LITERATURE

## CES viz., Epidural Analgesia for Labor pain:

1. Collins RE, Davies DW, Aveling W, Lancet 1995 Jun 3; 345(8962): 1413-6:<sup>1</sup>

The authors carried out a randomized observational study to assess maternal satisfaction with the standard and combined techniques among 197 women in labor. Overall satisfaction was greater in the combined spinal-epidural group than in the standard epidural group. Good analgesia was achieved in both groups, but the combined spinal-epidural had faster onset of analgesia and more of this group were satisfied with analgesia at 20 min (92/98 vs 68/99,  $p < 0.0001$ ). 12 women in the combined spinal-epidural group had leg weakness (as shown by an inability to raise the straight legs) at 20 min, but this initial motor block had resolved in most of these mothers by 1 h. In the standard epidural group 32 had leg weakness at 20 min ( $p = 0.001$ ), and the proportion of mothers with weakness increased in this group during labor. Overall, women seem to **prefer the low-dose combined spinal-epidural technique to standard epidurals**, perhaps because of the faster onset, less motor block, and feelings of greater self-control

2. Landau R et al, Semin Perinatol 2002 Apr 26; 109-21:<sup>2</sup>

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

## Safety of Intrathecal Ropivacaine

3. Malinovsky et al, Anesthesiology. 97(2): 429-435, August 2002 <sup>5</sup>

The authors experimentally determined the relationship between doses of Intrathecal Ropivacaine and spinal effects and local neurotoxic effects. Seven days after the last Intrathecal injection spinal cord and nerves were sampled for histopathologic study. No neurological clinical lesion was observed in rabbits receiving saline or Ropivacaine within the 7 days after the last Intrathecal injection, and histopathologic study revealed no sign of neurotoxicity in these groups. In contrast, Intrathecal Lidocaine induced clinical and histopathologic changes. They concluded that Ropivacaine induced dose-dependent spinal anesthesia, and did not induce any neurotoxicologic lesion in this experimental animal model.

## Motor sparing with Ropivacaine

4. McNamee et al, British Journal of Anaesthesia 2002; 89(5): 702-6 <sup>13</sup>

The aim of this study was to compare the safety and efficacy of Intrathecal plain Ropivacaine 17.5 mg and plain Bupivacaine 17.5 mg in patients undergoing primary total hip arthroplasty. 66 ASA I-III patients (43 male, 23 female; aged 33-78 years) were included in this randomized, double blind study. The group R received 0.5% Ropivacaine and group B received 0.5% Bupivacaine; both drugs were

injected over 10 s. The results showed no difference in the median time of onset of sensory block between both groups. However, the Bupivacaine group (3.5 h) had a significantly longer median duration of sensory block than the Ropivacaine group (3.0 h). No significant differences were observed in the onset of motor block between both groups to achieve a Bromage score of 1, 2 and 3. However, the Ropivacaine group had a significantly **shorter median duration of complete motor block** than the Bupivacaine group. Furthermore, **the degree of motor block after surgery was lower in the Ropivacaine patients** compared with patients receiving Bupivacaine. The authors conclude that "Intrathecal administration of both 17.5 mg plain Ropivacaine or 17.5 mg plain Bupivacaine was well tolerated and an adequate block for total hip arthroplasty was achieved in all patients. A more rapid postoperative recovery of sensory and motor function was seen in the Ropivacaine group compared with the Bupivacaine group".

**5. Lee YY, Ngan Kee WD, Muchhal K, Chan CK. 1: Acta Anaesthesiol Scand. 2005 Nov; 49(10): 1477-82<sup>15</sup>**

This was a prospective randomized double-blind study conducted in 34 ASA I-III patients scheduled for urological surgery were randomly assigned to receive Intrathecal injection of either plain Ropivacaine 10 mg with Fentanyl 15 µg (Ropivacaine group) or plain Bupivacaine 10 mg with Fentanyl 15 µg (Bupivacaine group) using a combined spinal-epidural technique. All patients achieved sensory block to the T10 dermatome or higher at 15 min after Intrathecal injection. One patient in the Ropivacaine group was excluded because of unexpectedly prolonged surgery.

The primary outcome, the duration of motor block, was shorter in the Ropivacaine group (median, 126 min; interquartile range, 93-162 min) compared with the Bupivacaine group (median, 189 min; interquartile range, 157-234 min; difference between medians, 71 min; 95% confidence interval, 28-109 min; P = 0.003). The duration of complete motor block was also shorter in the Ropivacaine group compared with the Bupivacaine group. There was no difference in the onset time of motor block. The characteristics of sensory block and the haemodynamic changes were similar between the groups. They concluded that plain Ropivacaine 10 mg plus Fentanyl 15 µg provided similar sensory anaesthesia, **but with a shorter duration of motor block**, compared with plain Bupivacaine 10 mg plus Fentanyl 15 µg when used for spinal anaesthesia in urological surgery.

**6. Camorcia M, Capogna G, Lyons G, Columb MO, Anesth Analg. 2004 Jun; 98(6): 1779-82<sup>16</sup>**

This study established the median effective dose (ED (50)) for motor block of Intrathecal 1% and 0.1% Ropivacaine and determined the effects of the concentration of the solution injected on the motor block obtained. Study was done in 54 parturients undergoing elective Cesarean delivery under combined spinal-epidural technique. Parturients were randomized to receive Intrathecal Ropivacaine either 1% or 0.1%. The initial dose was chosen to be 4 mg, with subsequent doses being determined by the response of the previous patient (testing interval, 1 mg). The occurrence of any motor block in either lower limb within 5 min from the Intrathecal injection of the study solution was considered effective. They concluded that The ED (50) of spinal Ropivacaine to produce motor block in pregnant patients was significantly influenced by the concentration of the local anesthetic, with dose requirements being increased by 50% for the smaller concentration. The minimum local anesthetic dose for motor block with 0.1% Ropivacaine is 50% larger than the 1% concentration with a relative efficacy ratio of 1.5. They suggested **that more diluted local anesthetic solutions determine less motor block, and this may be considered in ambulant laboring parturients.**

**7. Wille M. Acta Anaesthesiol Belg. 2004; 55(3): 251<sup>17</sup>**

In their review, they concluded, "In order to further improve and understand safety issues as well as the

clinical use of spinal anesthesia, new local anesthetics and analgesic additives are being investigated for different applications.

As practice of medicine focuses increasingly on outpatient care, spinal anesthetics should provide short-acting and adequate anesthesia without compromising early ambulation and discharge from the day surgery unit. A review of the current literature suggests that **Ropivacaine could have potential in this area**".

## Potency of Ropivacaine

### 8. Capogna G et al. *Br J Anaesth* 1999; 82; 371–3<sup>22</sup>

Double blind sequential allocation to compare the minimum local analgesic concentrations (MLAC) of epidural Bupivacaine and Ropivacaine for women in the first stage of labor. The test bolus was 20 ml of local anaesthetic solution. The concentration was determined by the response of the previous woman to a higher or lower concentration of local anaesthetic, according to up-down sequential allocation. Efficacy was assessed using a 100-mm visual analogue pain score (VAPS). The test solution had to achieve a VAPS of 10 mm or less to be judged effective. For Bupivacaine, MLAC was 0.093 (95% CI 0.076-0.110)% w/v, and for Ropivacaine, 0.156 (95% CI 0.136-0.176)%w/v (P < 0.0001, 95% CI difference 0.036-0.090). The analgesic potency of Ropivacaine was 0.60 (0.47-0.75) relative to Bupivacaine.

### 9. Terrance W. Breen, MD; David C. Campbell, MD; Jean E. Kronberg, MD; Robert T. Nunn, MD; Gordon H. Fick, PhD 1. *Br J Anaesth* 1999; 82:371-3<sup>23</sup>

The authors did a study to determine the relative potencies of Ropivacaine and Bupivacaine by allowing patients to titrate their analgesia using PCEA. Patients received 30% of their analgesia via the background infusion and controlled 70% (PCEA or by requesting top-ups). Therefore, this study shows that when patients are responsible for delivering their own analgesia they require almost identical amounts of Ropivacaine and Bupivacaine. MLAC studies have shown that at the ED<sub>50</sub> dose, Ropivacaine is less potent than Bupivacaine. As the effective analgesia doses are the same, the dose-response curves must be different. Further studies are needed to determine the ED<sub>90</sub> or ED<sub>95</sub> doses of Ropivacaine and Bupivacaine are clinically equipotent when providing labor epidural analgesia. **"Therefore, outcome studies using the same concentrations of Ropivacaine and Bupivacaine are valid and will yield important information."**

### 10. Sia AT, Goy RW, Lim Y, Ocampo CE *Anesthesiology*. 2005 Mar; 102(3): 651-6<sup>24</sup>

In this double-blind study, 100 parturients in early labor were randomized to receive either Intrathecal Ropivacaine or LevoBupivacaine. For each drug, the patients were assigned to receive one of the five doses studied, namely 1, 1.5, 2, 2.5, or 3 mg. Effective analgesia was defined as a pain score (0-100 visual analog scale) of less than 10 within 15 min of injection, lasting for 45 min or more after the induction of analgesia. The duration of analgesia rendered by the two drugs at 2.5 and 3 mg was also compared. In their study LevoBupivacaine was found to be 1.31 (95% confidence interval, 1.04-2.01) times more potent than Ropivacaine. At doses of 2.5 mg or greater, there was no significant difference in duration of analgesia between levoBupivacaine (median, 63.5 min; range, 46-123 min) and

Ropivacaine (median, 59.0 min; range, 47-93 min;  $P = 0.18$ ). They detected no difference in the incidence of hypotension, nausea and vomiting, motor block, or abnormal fetal heart tracing between the two drugs.

They concluded that MED of Intrathecal Ropivacaine for labor analgesia was significantly greater than levoBupivacaine experimentally, but this significance was reduced when the comparison was based on molar potency. **There was no difference in the duration of analgesia or adverse effects between the two drugs at higher doses (2.5 mg or greater).**

## **Intrathecal Ropivacaine with Fentanyl for Labor Analgesia**

**11. D. Hughes, D. Hill and J. P. H. Fee, British Journal of Anaesthesia, 2001, Vol. 87, No. 5 733-737** <sup>25</sup>

The authors compared Ropivacaine 2.5 mg in the Intrathecal injection with a standard Bupivacaine CSE in a double-blind study. Forty women were randomized to receive either Bupivacaine 2.5 mg or Ropivacaine 2.5 mg intrathecally, both with Fentanyl 0.025 mg. There were no significant differences between the groups regarding the onset, duration or quality of analgesia or the level of sensory block attained. Forty per cent of the women (8/20) receiving Bupivacaine developed detectable motor block compared with only 5% (1/20) in the Ropivacaine group ( $P < 0.05$ ). Vibration sense was impaired in one woman in each group. Adverse effects did not differ between groups. They concluded that Intrathecal Ropivacaine 2.5 mg in combination with Fentanyl 0.025 mg as part of a CSE technique provides rapid and safe analgesia for labour as effective as that achieved with Bupivacaine 2.5 mg and **with significantly less motor block.**

**12. Craig M. Palmer, M.D.; Wallace M. Nogami, M.D.; Diane Alves, R.N. Anesthesiology 1999; 91:84-89. Anesthesiology 1999; 90:944-950: Br J Anaesth 1999; 82:371** <sup>26</sup>

Studied 49 ASA I and II nulliparous term parturients in active labor, patients were randomized to one of three groups to receive either Fentanyl 25  $\mu$ g (I,  $n=16$ ); Fentanyl 25  $\mu$ g and Ropivacaine 2 mg (II,  $n=17$ ); or Fentanyl 25  $\mu$ g and Ropivacaine 4 mg (III,  $n=16$ ) Intrathecally as part of a combined spinal epidural technique Duration of analgesia in both Ropivacaine groups (II & III) was longer than the plain Fentanyl group (I)(ANOVA,  $p < 0.05$ ), but groups II and III were not different from each other (I: 74 +/- 5 minutes; II: 97 +/- 8 minutes; III: 107 +/- 7 minutes, mean +/- SEM). Onset of analgesia was similar among all three groups, with no differences noted (two-way ANOVA,  $p=N.S.$ ). No patient in any group developed clinically detectable weakness (modified Bromage score  $< 6$ ). Pruritus scores at 20 minutes were not different among groups (range 30 - 33, scale 0 - 100, ANOVA  $p=N.S.$ ). They concluded that addition of Ropivacaine, 2 or 4 mg, to Fentanyl 25  $\mu$ g significantly prolonged the duration of analgesia, similar to the addition of Bupivacaine to Fentanyl<sup>1</sup>. Unlike Bupivacaine however, Ropivacaine did not speed the onset of analgesia or decrease the severity of pruritus. Based on relative potency studies of the two local anesthetics, the 2 and 4 mg doses of Ropivacaine were chosen for study as roughly equipotent to Bupivacaine 1.25 and 2.5 mg, respectively. Assuming these doses are equipotent, there appears to be little difference between the local anesthetics as adjuncts to Intrathecal Fentanyl for labor analgesia.

**13. Levin A, Datta S, Camann WR. Anesth Analg. 1998 Sep;87(3):624-7** <sup>27</sup>

The authors compared two doses of Intrathecal Ropivacaine combined with Sufentanil with a standard dose of Intrathecal Bupivacaine plus Sufentanil for labor analgesia using a combined spinal-epidural (CSE) technique. In a prospective, randomized, double-blind fashion, 48 patients requesting labor analgesia received either 2.5 mg of Intrathecal Bupivacaine plus Sufentanil 10 µg (B), 2 mg of Intrathecal Ropivacaine plus Sufentanil 10 µg (R2), or 4 mg of Intrathecal Ropivacaine plus Sufentanil 10 µg (R4). Duration of analgesia and side effects, such as motor block, pruritus, hypotension, ephedrine requirements and fetal bradycardia, were recorded.

Duration of analgesia (mean +/- SD) was 79+/-30 min for R2, 98+/-19 min for R4, and 92+/-38 min for B (P = not significant). No differences in motor block or side effects were detected among the groups. They concluded that Ropivacaine, when combined with Sufentanil, is effective for providing CSE labor analgesia and offers no advantage over Bupivacaine in the studied doses. In this study, they compared a standard dose of Intrathecal Bupivacaine with Sufentanil for combined spinal epidural analgesia with two doses of the new local anesthetic Ropivacaine. Both local anesthetics provided similar labor analgesia duration with equivalent side effect profiles in the doses studied.

**14. M. K. Shah, A. T. H. Sia and J. L. Chong, Anaesthesia  
Volume 55 Page 1008 - October 2000<sup>29</sup>**

Sixty patients in early labor were randomly allocated to one of three groups. The control group received Intrathecal Fentanyl 25 µg; the Ropivacaine group received Intrathecal Fentanyl 25 µg and Ropivacaine 2.5 mg while the Bupivacaine group received Intrathecal Fentanyl 25 µg and Bupivacaine 2.5 mg. The incidence of pruritus was 100% in controls, compared with 85% in the Ropivacaine group (not significant) and 75% in the Bupivacaine group (p = 0.003). The severity of pruritus was significantly less in the Ropivacaine (p = 0.006) and Bupivacaine (p = 0.001) groups. Most patients developed pruritus by 30 min. Pruritus above the abdomen was not reduced in patients receiving local anesthetics. There were no significant differences in the mean pain visual analogue score, systolic blood pressure, maternal heart rate and upper level of reduced pin-prick sensation in the first 30 min. Intrathecal Ropivacaine and, more so, Intrathecal Bupivacaine reduce the incidence and severity of pruritus from Intrathecal Fentanyl for labor analgesia.

## **Balance function after CSE for Labor analgesia**

**15. Pickering AE, Parry MG, Ousta B, Fernando R. Anesthesiology. 1999 Aug; 91(2): 436-41<sup>30</sup>**

The authors undertook a prospective controlled observational study using computerized dynamic posturography to examine balance function in pregnant women after combined spinal-epidural analgesia.

The authors performed posturographic testing on 44 women in labor after institution of regional analgesia and compared them with a control group of 44 pregnant women. A separate group of six women were tested both before and after combined spinal-epidural analgesia. Neurologic examination after regional analgesia showed two parturients (4%) to have motor weakness (excluded from posturography). Four women (9%) had clinical dorsal column sensory loss; these women all completed posturography. The spinal-epidural analgesia group showed a small, statistically significant reduction in one of six posturographic sensory-organization tests; however, this difference was functionally minor. There were no other differences in posturography between the control and spinal-epidural groups. Similar results were found in the paired study, in which there was minimal change in balance

function after spinal-epidural analgesia.

This is the first study to objectively examine the effect of spinal-epidural analgesia on balance function. Using computerized dynamic posturography the authors were **unable to find any functional impairment of balance function after spinal-epidural ambulatory analgesia in women in labor who had no clinical evidence of motor block.**

## **Effect of Epidural test dose on motor blockade**

### **16. Calimaran AI et al, Anaesth Analg 2003 Apr 96: 1167-72<sup>33</sup>**

The authors conducted a study to test the effect of standard epidural test dose (3ml lignocaine 1.5% with epinephrine 1:200,000) on motor block in CSE labor analgesia. Homodynamic variables, proprioception, straight leg rising, and the modified Bromage score was analyzed in 110 parturients who completed the study protocol and were not different between groups. Vibratory sense the ability to perform a partial deep knee bend and to step up on stool and the subjective ability to walk were impaired in large number of parturients in the lignocaine epinephrine group at 30 min ( $p < 0.05$ ). They concluded that a standard lignocaine epinephrine epidural test dose injected immediately after the initiation of combined spinal epidural labor analgesia with Bupivacaine 2.5 mg and Fentanyl 25  $\mu$ g may **interfere with the ability to perform simple tests of motor function and ambulation.**

## **Effect of addition of epinephrine to Intrathecal Fentanyl**

### **17. Goodman SR et al, Reg Anes Pain Med 2002 Jul – Aug 27:374-9<sup>34</sup>**

The authors did a study to find the efficacy of epinephrine in prolonging Fentanyl induced labor analgesia. They used four groups divided to receive Fentanyl 35  $\mu$ g with either saline (F); Bupivacaine 2.5 mg+ Saline (FB); Bupivacaine 2.5mg + Epinephrine 100  $\mu$ g (FBE); or Epinephrine 100  $\mu$ g +saline (FE). The study showed that Intrathecal Bupivacaine significantly prolonged Fentanyl analgesia with or without epinephrine ( $p = 0.018$ ), but **epinephrine did not significantly prolong the duration of Fentanyl alone or with Bupivacaine.**

## **Needle through needle technique for CSE**

### **18. Rawal N et al, Anesthesiolo Clinic North America 2000 Jun 18:267-9<sup>35</sup>**

Concluded that CSE technique by “needle through needle technique” resulted in better epidural catheter sitting. He also concluded that the concern about epidural catheter entering through small dural hole is unfounded.

## MATERIALS AND METHODS

This is a prospective, randomized, double blinded, control study. Prior approval was obtained from the ethical committee of **GOVERNMENT STANLEY MEDICAL COLLEGE AND HOSPITAL** and **RSRM lying in hospital** for the study. Fifty parturients who were admitted to the antenatal ward and who requested pain relief during labor were selected for the study. The procedure and complications of regional analgesia was explained to them in detail and written consent was obtained from them.

### **Inclusion criteria:**

- 1 Patients in established labor (cervical dilatation 3-5cms).
- 2 Patients belonging to ASA I.
- 3 Only primigravida patients with singleton pregnancy, in full term labor were included in the study.

### **Exclusion criteria:**

1. PIH, DM, bleeding disorder or other systemic disorders.
2. Patients who have already received any Opioid drugs or systemic analgesics within prior 24 hours.
3. Any contraindication for central neuraxial techniques.
4. Patients with known allergy to local anaesthetic or other drugs.
5. Patient refusal for regional technique.

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

**Group I (Bupivacaine):** Received 2.5mg Bupivacaine with 0.025mg Fentanyl (total volume 1 ml) Intrathecally, followed by epidural drugs (0.1% Bupivacaine with 2µg/ml Fentanyl) as 5 ml top-ups. At the start of second stage of labor a top-up of 10 ml bolus was used. The top-ups were given only when the patient requested additional pain relief.

**Group II (Ropivacaine):** Received 2.5mg Ropivacaine with 0.025mg Fentanyl (total volume 1 ml) Intrathecally, followed by epidural drugs (0.1% Bupivacaine with 2µg/ml

Fentanyl) as 5 ml top-ups. At the start of second stage of labor a top-up of 10 ml bolus was used. The top-ups were given only when the patient requested additional pain relief.

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. Further, the addition of epinephrine to confirm intravascular placement is not reliable in active labor. Hence the test doses were done away with. Rather the bolus itself was given in two divided doses with 5 mins interval for motor block after the first dose.

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 insertion of the epidural catheter in aseptic manner.

Anaesthesia machine was checked and all emergency airway equipments like Laryngoscopes, blades of different sizes, endotracheal tubes, 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 1000ml 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 base line values were recorded. The drugs to be administered Intrathecally were prepared and stored in a sterile container.

## **Equipment**

The needles used for both groups were 16 G Tuohy needle, 18 G epidural catheter and 26 G pencil point long spinal needle (CSE cure by Portex)

## **Procedure**

With the patient in left lateral position, under strict aseptic precaution L2-L3 interspace was identified and skin infiltration was done with 1.5ml of 2% lignocaine. Using a 17G Tuohy needle and

**'loss of resistance to air'** technique the epidural space was identified.

Intrathecal injection was performed using long spinal needle (25G Whitaker) through epidural needle (needle through needle technique) over 10 sec. Immediately following this 19G epidural catheter was inserted and 3 cms kept inside the epidural space. The catheter was tapped firmly to the back. The patient was turned to supine position. Epidural top-ups were not given till patient complained of pain or discomfort.

With the catheter in place patients were shifted to the labor ward after 20 minutes of observation in operation theatre, where they were closely monitored till delivery. A single operator was involved in all cases and position of epidural catheter was checked by aspiration for blood/CSF. Both the patient and observer were blinded to the contents of Intrathecal injection, the same two observers being involved in all cases. **The study period commenced after the Intrathecal injection and ended at the request for further analgesia by epidural bolus.**

The following parameters were observed

1. HR, BP, SPO<sub>2</sub>, FHR, Respiratory rate at 0, 5, 15, 30, 60 mins and fifteen minutes thereafter.
2. Time of onset of analgesia – time of Intrathecal injection to the time of perception of first painless contraction.
3. Level of sensory blockade with loss of sensation to pin prick.
4. Duration of analgesia – defined as interval between Intrathecal injection and request for first epidural top up.
5. Visual analog pain scale (VAS)
6. Motor block 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 movement of feet
2	Almost complete	Unable to flex knees, free movement Of feet possible
3	Complete	Unable to move both legs and feet

7. Hourly cervical dilatation.
8. Mode of delivery, duration of labor.

9. Birth weight of baby and Apgar score at 1 and 5 mins.
10. Patient comfort, satisfaction (4- Excellent, 3- Good, 2- Fair, 1- Poor)
11. Side effects – Hypotension, nausea & vomiting, Pruritus, 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 obstetricians give Inj.Oxytocin infusion for most of the patients to accelerate labor. Artificial rupture was done if indicated. During the entire labor the mothers were positioned supine with left side tilt. If the patients were willing they were allowed to ambulate after assessing their motor power. The following tests were done sequentially 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 2005-20065. Fifty patients in active labor (Cervix dilation 3-4 cms) who requested analgesia were chosen and randomly assigned to either of the two groups.

The patients were randomized into two groups Group 1 and Group 2 of 25 each all the patients had delivery via naturalis .The trial numbers were 25 in each group.

**Group 1:** Intrathecal Bupivacaine with Fentanyl.

**Group 2:** Intrathecal Ropivacaine with Fentanyl.

The following are the observations made during the study.

## *Physical Characteristics*

Physical characteristics like age, height and weight were comparable in both the groups.

## **Age distribution**

The age distributions in both groups are as shown in the table below. The distribution is similar in both groups and there is no statistical difference between the two groups.

**TABLE I Age distribution**

<i>Parameters</i>	<i>Group I (Bupivacaine)</i>	<i>Group II (Ropivacaine)</i>
<b>No. Of cases studied</b>	25	25
<b>Mean</b>	21.88	21.66
<b>Standard deviation</b>	2.108	1.952

T- test value = 0.35, P – value = 0.75 - Not significant, Student T – test

## *Weight Distribution*

The distributions of weight in both the groups are shown in Table II. The values are similar in both groups and are statistically comparable. The Student T test done on the values revealed no statistical significance.

**Table II Weight distribution**

<i>Parameters</i>	<i>Group I (Bupivacaine)</i>	<i>Group II (Ropivacaine)</i>
No. Of cases studied	25	25
Mean	64.32	64.84
Standard deviation	7.353	7.454

T- test value = 0.25, P – value = 0.81 - Not significant, Student T – test

***Height Distribution***

The distribution of height in both the groups is shown in Table III. The values are similar in both groups and are statistically comparable. The Student T test done on the values revealed no statistical significance.

**Table III Height distribution**

<i>Parameters</i>	<i>Group I (Bupivacaine)</i>	<i>Group II (Ropivacaine)</i>
No. Of cases studied	25	25
Mean	158.24	159.32
Standard deviation	7.259	7.111

T- test value = 0.64, P – value = 0.94, Student T – test

***Mode of Delivery***

One patient in the Bupivacaine group delivered by outlet forceps delivery. All others were delivered by Labor Natural with episiotomy. The indication for forceps delivery was maternal exhaustion. The baby was found to have cord around the neck during forceps delivery.

**Table IV Mode of Delivery**

<i>Mode of Delivery</i>	<i>Group I (Bupivacaine)</i>	<i>Group II (Ropivacaine)</i>
Labor Natural	24	25
Outlet Forceps	1	0

*Chi-square – 1.02, P-value 0.31*

## ***Duration of Labor***

The total duration of labor in both groups is comparable. The duration of individual stages of labor are comparable in both groups. Students T- test was done on duration on total and each stage. The P-values are all > 0.05 implying that the differences were not statistically significant.

**Table V Duration of Individual stages of labor**

<b>Stage of Labor</b>	<b>Group I (Bupivacaine)</b>		<b>Group II (Ropivacaine)</b>		<b>T – test</b>	<b>P- value</b>
	<b>Mean (Mins)</b>	<b>SD</b>	<b>Mean (Mins)</b>	<b>SD</b>		
<b>First Stage</b>	146.40	28.994	142.60	34.191	0.42	0.64
<b>Second Stage</b>	53.20	12.819	51.00	10.607	0.66	0.51
<b>Third Stage</b>	15.20	5.299	17.40	4.813	1.53	0.13

**Table VI Total duration of labour**

<b>Parameters</b>	<b>Group I (Bupivacaine)</b>	<b>Group II (Ropivacaine)</b>
<b>Mean (hours)</b>	3.55	3.48
<b>Standard deviation</b>	0.68	0.66

**T- test value = 0.69, P – value = 0.71, Student T – test**

## **Duration of Analgesia with First Dose**

The duration of analgesia after giving the first dose was compared for both the drugs .The duration was similar in both groups.

**Table VII Duration of analgesia with first dose**

Parameters	Group I (Bupivacaine)		Group II (Ropivacaine)		T – test	P- value
	Mean (Mins)	SD	Mean (Mins)	SD		
Duration of Analgesia	89.24	6.27	97.20	7.14	0.37	0.72

The student t–test done on these variables show no statistical difference between the two groups.

***Number of Top-ups given***

*There was no difference in the requirement of epidural top up in both the groups.*

**Table VIII Number of top-ups**

Parameters	Group I (Bupi)	Group II (Ropi)
Mean	2.04	1.92
Standard Deviation	0.455	0.572

Chi- square 0.82, P-value 0.42.

A Chi-square test done on these values showed no significant statistical difference between both the groups.

***Total dose of Epidural drugs used***

**Table IX Total dose of Epidural drugs used**

Drug	Group I (Bupivacaine)		Group II (Ropivacaine)		T – test	P- value
	Mean	SD	Mean	SD		

<b>Epidural Fentanyl</b>	30.40µg	4.546	29.20	5.715	0.82	0.42
<b>Epidural Bupivacaine</b>	15.20mg	2.273	14.60	2.858	0.82	0.42

The total dose of Epidural Fentanyl and Epidural Bupivacaine used were similar in both groups and there was no statistical difference between the groups.

### ***Motor Blockade***

This was assessed using the Modified Bromage Scale.

**92% (n = 23)** of the patients in the Ropivacaine group had no motor blockade (Bromage Scale 0) compared to **48% (n = 12)** in Bupivacaine group. These patients felt very comfortable during ambulation.

Only **8% (n=2)** in Ropivacaine Group when compared to **52% (n=12+1)** in Bupivacaine Group had mild to moderate Motor Blockade (Bromage Scale 1 & 2), which made ambulation uncomfortable.

**Table X Motor block**

<b>Bromage Scale (MAX BLOCK)</b>	<b>Group I (Bupivacine)</b>		<b>Group II (Ropivacaine)</b>	
	<b>N</b>	<b>%</b>	<b>N</b>	<b>%</b>
<b>0</b>	12	48	23	92
<b>1</b>	12	48	2	8
<b>2</b>	1	4	0	0

**Chi-square 11.6, P – value 0.01.**

A Chi –square test showed **significant statistical difference** with regard to motor blockade between the two groups.

This clearly shows that Intrathecal Ropivacaine causes significantly less Motor Blockade when compared with Intrathecal Bupivacaine.

## Sensory level

Patients in both groups had a mean sensory level of T8. The maximum was only T6 and minimum level was T10.

**Table XI Sensory level**

Sensory Level	Group I (Bupivacaine)		Group II (Ropivacaine)	
	N	%	N	%
T 6	2	8	1	4
T 7	3	12	5	20
T 8	13	52	11	44
T 9	2	8	4	16
T 10	5	20	4	16

**Chi square - 0.00, P value 1.00**

A Chi square analysis showed no statistical difference between the two groups in terms of sensory level of blockade.

## VAS SCALE

The pain perceived by the patients was assessed by showing them a VAS scale which contained pictures of faces depicting pain on one end and smiling face on the other end. The other side had a scale marked from 0 to 100. The scale had a slider, which the patients move to point below the image, which they felt expressed their perceived pain.

The VAS score was assessed at 0, 5, 15, 30,45,60,90,120 and 180 minutes. Since the study period ended when the patient requested for first epidural top up, the Vas score till that time was taken for statistical analysis. The initial VAS score ranged between 80 and 100 for all the patients. Both groups had a rapid onset of pain relief and their VAS score fell to < 5 within 5 min in both groups.

**Table XII VAS SCORES**

VAS Score (Time mins)	Bupivacaine Group			Ropivacaine Group		
	Mean	S.D	t- test	Mean	S.D	t- test
VAS 0	90.2000	6.37050	.195	92.4000	5.42371	.195
VAS 5	1.2000	2.98608	.271	.4000	2.00000	.272
VAS 15	2.6000	4.35890	.875	2.8000	4.58258	.875
VAS 30	2.0000	5.81881	.64	5.8000	6.72062	.65
VAS 60	4.4000	5.06623	.625	5.2000	6.37050	.625
VAS 90	4.2857	6.46206	.754	5.0000	6.72593	.753

No significant statistical difference between the two groups was noted.

## Haemodynamic variables

All haemodynamics variables were recorded at 0mins(base line), 5mins, 15 mins, 30 mins, 45 mins, 60 mins and thereafter every 15 minutes. The variables till the time when the patient received first epidural top up was taken for statistical analysis.

***PULSE RATE***

There was not much variation in the pulse rate recordings between the two groups.

**Table XIII Pulse rate**

MHR (at min)	Group			
	Bupivacaine		Ropivacaine	
	Mean	SD	Mean	SD
<b>0</b>	91.92	5.57	88.88	6.58
<b>2</b>	90.92	5.77	89.92	6.74
<b>5</b>	92.20	4.86	90.20	7.20
<b>15</b>	91.92	5.71	90.24	6.60
<b>30</b>	89.92	5.42	90.32	8.03
<b>45</b>	89.76	5.36	90.16	6.91
<b>60</b>	89.40	5.55	89.76	6.63
<b>90</b>	76.72	4.86	78.96	5.86

**Table XIV Repeated Measures of ANOVA**

MHR	F	Sig
<b>Within Group</b>	74.39	.001
<b>Between Group</b>	.16	0.69

The two-way ANOVA test done on the pulse rate recordings showed no statistical difference between the two groups. There was significant variation within the groups with time.

***SYSTOLIC BLOOD PRESSURE***

No statistically significant difference was noted between the groups with regards to the systolic blood pressure. 2 patients had hypotension (defined as systolic blood pressure less than 90 mm Hg) in Bupivacaine group and were treated with a single dose of 6mg Ephedrine IV. Both patients responded well to Ephedrine and did not require further boluses

**Table XV Systolic blood pressure**

SBP (at min)	Group			
	Bupivacaine		Ropivacaine	
	Mean	SD	Mean	SD
0	114.24	8.33	117.44	8.05
2	115.60	7.51	117.44	9.19
5	118.08	9.46	116.68	10.92
15	120.16	9.61	116.80	9.35
30	121.76	8.63	115.68	7.52
45	120.72	7.93	114.56	7.49
60	122.08	7.54	113.44	7.15
90	113.92	7.18	109.36	8.30

Table XVI Repeated Measures of ANOVA

SBP	F	Sig
Within Group	5.57	.001
Between Group	3.87	.07

The two-way ANOVA test done on the recordings showed no statistical difference between the two groups. There was significant variation within the groups with time.

#### DIASTOLIC BLOOD PRESSURE

The two groups had no significant difference in the diastolic blood pressure as was seen in the systolic blood pressure. The two-way ANOVA test showed no statistical difference between the two groups. There was significant variation within the groups with time.

Table XVII Diastolic blood pressure

DBP (at min)	Group			
	Bupivacaine		Ropivacaine	
	Mean	SD	Mean	SD
0	75.68	6.75	74.80	6.48
2	76.40	5.94	73.20	7.55
5	74.32	6.80	74.08	7.86
15	74.40	5.74	74.64	5.91
30	71.84	15.04	73.44	5.64
45	75.28	6.43	73.52	5.04
60	74.16	6.30	75.12	3.96
90	77.84	7.26	78.40	4.76

**Table XVIII Repeated Measures of ANOVA**

DBP	F	Sig
<b>Within Group</b>	2.85	0.007
<b>Between Group</b>	0.10	0.75

**FETAL HEART RATE**

There was not much variation between the two groups and the ANOVA test did not show any statistical significance between the two groups though there was variation within both groups with time.

**Table XIX Fetal heart rate**

FHR (at min)	Group			
	Bupivacaine		Ropivacaine	
	Mean	SD	Mean	SD
<b>0</b>	147.96	5.14	147.80	7.26
<b>2</b>	147.00	4.75	148.64	6.63
<b>5</b>	147.64	5.54	148.72	6.58
<b>15</b>	148.60	5.22	150.24	6.80
<b>30</b>	147.28	6.46	149.80	5.94
<b>45</b>	148.40	5.51	150.28	6.99
<b>60</b>	148.48	3.89	149.16	7.19
<b>90</b>	142.40	5.65	143.40	6.70

**Table XX Repeated Measures of ANOVA**

FHR	F	Sig
<b>Within Group</b>	9.76	.01
<b>Between Group</b>	1.18	0.28

**PATIENT COMFORT LEVEL**

This was assessed by asking the patient how they felt at the end of the delivery. Majority of the patients (80%) in Ropivacaine group had excellent pain relief whereas in the Bupivacaine group 72% had good pain relief and 28% had excellent relief. This was assessed on a scale as follows

**Table XXI Patient comfort level**

Comfort level	Group I (Bupivacaine)		Group II (Ropivacaine)	
	N	%	N	%
<b>1 – Poor</b>	0	0	0	0
<b>2 – Fair</b>	0	0	0	0

<b>3 – Good</b>	7	28	5	20
<b>4 – Excellent</b>	18	72	20	80

Chi – square = 0.44, P value = 0.51.

### **APGAR SCORE**

APGAR score estimated at one and five minutes are tabulated below

**Table XXII One minute APGAR**

APGAR 1	Group I (Bupivacaine)		Group II (Ropivacaine)	
	N	%	N	%
5	10	40	7	28
6	4	16	5	20
7	5	20	5	20
8	6	24	8	32
9	0	0	0	0
10	0	0	0	0

$\chi^2 = 0.93$ ,  $p=0.82$ , P value by Chi square test did not show statistical difference.

**Table XXIII Five minute APGAR**

APGAR 5	Group I (Bupivacaine)		Group II (Ropivacaine)	
	N	%	N	%
5	0	0	0	0
6	0	0	0	0
7	3	12	6	24
8	16	64	12	48
9	6	24	7	28
10	0	0	0	0

$\chi^2 = 1.65$ ,  $p=0.44$  P value by Chi Square did not show any statistical significance

**Table XXIV Complications**

Complication	Group I (Bupivacaine)	Group II (Ropivacaine)
Hypotension	2	0
Pruritis	2	3
Respiratory depression	0	0
Vomiting	1	2
Urinary retention	2	3

Intravenous Catheter Placement	0	0
Post dural puncture headache	0	0
Neurological complications	0	0

Hypotension (SBP < 90 mmHg or < 30% of baseline) was present in two cases in Bupivacaine group. Both cases responded to 6 mg of Ephedrine IV. Pruritus was also present in both groups 2 in the Bupivacaine and 3 in the Ropivacaine group. It was only mild and reassurance was all that was needed. One patient each in Bupivacaine group and 2 patients in Ropivacaine group had vomiting (one episode). 5 patients had urinary retention two in Bupivacaine and 3 in Ropivacaine group. Their bladder was emptied by simple catheterization. Both the groups had no incidence of intravascular catheter placement, PDPH or any neurological complications.

## DISCUSSION

Of all the methods of pain relief that can be used in Labor, neuraxial blockade (Epidural, Spinal, Combined spinal epidural, Continuous spinal) provides the most effective and least depressant analgesia. Out of these, studies by Collins et al<sup>1</sup>, Landau et al<sup>2</sup>, Norris et al<sup>3</sup> and Dressner et al<sup>4</sup> has shown that CSE combines the advantages of a Spinal analgesia (rapid onset, reliable analgesia and less motor blockade) with the additional flexibility of renewal with epidural catheter.

Collis and colleagues<sup>1</sup> reviewed a series of 300 women receiving CSE analgesia and found 51.3% of the women were able to bear weight and were fully ambulant. Although others were sufficiently mobile to sit in a chair or to be mobile in their bed, almost 13% experienced severe motor weakness that rendered them immobile in the first stage of labor. Thus this finding implies that though CSE decreases the degree of motor blockade there is still scope for improvement. So in our study we tried to further decrease the incidence of motor blockade in CSE.

Ropivacaine is a local anesthetic with lower cardio toxic potential than racemic Bupivacaine<sup>38,39,40,41,42</sup>. Intrathecal Ropivacaine does not produce any signs of neurotoxicity following administration to rats and Rabbits<sup>8,9,5</sup>. In dogs intrathecal Ropivacaine has been shown to produce effective local anaesthesia with an equipotent sensory block but shorter duration of motor block than intrathecal bupivacaine<sup>10</sup>. In humans, Ropivacaine has been shown to be effective in providing intrathecal anaesthesia for patients undergoing total hip replacement<sup>13</sup>, Knee arthroscopy<sup>6</sup>, transurethral resection of the prostate<sup>21</sup>, and lower abdominal or limb surgeries<sup>7,14</sup>. Ropivacaine has been reported to cause significantly less motor blockade than Bupivacaine when administered by the Intrathecal route<sup>13,14,15,16,17,18,19,20,21</sup>. Hence we decided to investigate its potential for motor sparing when used Intrathecally for labour analgesia

Capogna et al<sup>22</sup> did a double blind sequential allocation to compare the minimum local analgesic concentrations (MLAC) of epidural Bupivacaine and Ropivacaine for women in the first stage of labor. They inferred that the analgesic potency of Ropivacaine was 0.60 (0.47-0.75) relative to Bupivacaine. In another interesting study by Terrance et al<sup>23</sup>, the authors tried to determine the relative potencies of Ropivacaine and Bupivacaine by allowing patients to titrate their analgesia using PCEA. Patients received 30% of their analgesia via the background infusion and controlled 70% (PCEA or by

requesting top-ups). The study showed that when patients are responsible for delivering their own analgesia they require almost identical amounts of Ropivacaine and Bupivacaine. The authors concluded, “**Outcome studies using the same concentrations of Ropivacaine and Bupivacaine are valid and will yield important information.**” In our study we compared equal doses of both local anesthetics.

Little has been published on the use of Ropivacaine for Intrathecal labor analgesia<sup>25,26,27,28,29,30,31,32</sup>. D. Huges and colleagues<sup>25</sup> compared similar doses of Intrathecal Ropivacaine (2.5 mg) with Intrathecal Bupivacaine (2.5 mg) both with 25 micro g Fentanyl for Labor analgesia and concluded that Intrathecal Ropivacaine 2.5 mg in combination with Fentanyl 0.025 mg as part of a CSE technique provides rapid and safe analgesia for labour as effective as that achieved with Bupivacaine 2.5 mg and with **significantly less motor block**.

W. Levin and colleagues<sup>27</sup> compared two doses of Ropivacaine (2 and 4 mg) with Bupivacaine 2.5 mg in a CSE technique and found no difference in duration or quality of analgesia. They also reported no motor block in any of the women, including those receiving Intrathecal Bupivacaine. The Opioid used in conjunction with the local anaesthetic was Sufentanil.

In our study we compared equal doses of local anaesthetic (2.5 mg in both groups) and combined this with Fentanyl 0.025 mg in a total of 50 patients (25 in each group). We chose motor power retention as a major end-point.

There as no difference in the demographic variables between both the groups.

Our most significant finding was the difference in detectable motor block between the two groups. Only two patients (8%) in the Ropivacaine group developed leg weakness (all Bromage scale 1) compared with thirteen patients in the Bupivacaine group (52%) (including Bromage scale 1 and 2). All other patients had a Bromage scale of 0 and were ambulant without any difficulty (92% in Ropivacaine group and 48% in Bupivacaine group). This difference was statistically significant ( $P=0.01$ ). These results are similar to that inferred by Huges et al<sup>25</sup> who reported 4% incidence of detectable motor blockade in Ropivacaine group versus 40% in Bupivacaine group. As mobility has been a major consideration in the development and popularity of CSE analgesia in labor, this finding may have important clinical implications. Further dose-finding studies would be required to know that this difference is due to an intrinsic property of Ropivacaine or to a difference in potency between Ropivacaine and Bupivacaine.

Both groups were comparable with regard to the onset, duration and quality of analgesia and level of sensory blockade. This was similar to those observed in other studies<sup>25,26,27</sup>. While both drugs provided adequate and good pain relief, the lesser degree of motor blockade and consequent ease in ambulation in the Ropivacaine group had good psychological impact on the patients.

In our study both groups needed similar number of epidural topups. There was not much difference in the overall comfort level between the two groups which was assessed by asking how the patients felt at the end of the delivery.

The total duration of labor and the duration of individual stages of labor were comparable in both groups and this was similar to other studies<sup>25,26,27,29,31,32</sup>. Students T- test was done on the Total duration and on the duration of each stages. The P-values are all  $> 0.05$  implying that the differences

are not statistically significant.

One patient in the Bupivacaine group was delivered by outlet forceps delivery. All others were delivered by labor natural with episiotomy. The indication for forceps delivery was maternal exhaustion. The baby was found to have cord around neck during forceps delivery. The Apgar score observed at 1 mt and 5 th mt showed no significant neonatal depression.

The blood pressures (both systolic and diastolic) and pulse rate recorded during the analgesia in both the groups were not stastically different with minor episodes of hypotension, which responded to IV ephedrine. Pruritus was also present in both groups, two in the Bupivacaine and three in the Ropivacaine group. It was only mild and reassurance was all that was needed. One patient in Bupivacaine and two patients in Ropivacaine group had vomiting (one episode). 5 patients had urinary retention (2 in Bupivacaine group and 3 in Ropivacaine group). Their bladder was emptied by simple catheterization. No incidences of PDPH or neurological complications were noted in either group. Although previous studies have linked intrathecal Ropivacaine with an increased incidence of post-dural puncture headache<sup>7</sup> and low back pain<sup>28</sup>, no patient in the present study reported symptoms in keeping with these two complications. This is in agreement with the findings of others<sup>5,6,13</sup>.

## SUMMARY

In our study both the drugs (Intrathecal Ropivacaine and Bupivacaine with Fentanyl) provided good pain relief while the incidence of motor blockade was significantly less in Ropivacaine group when compared with Bupivacaine group.

The two drugs did not influence the outcome of labor such as the duration of labor or the type of delivery. There was no adverse fetal outcome in both the groups. Sensory blockade levels were similar in both the groups.

Both the drugs had lesser impact on the haemodynamics. Complications were only few, were minor and easily manageable.

## CONCLUSION

In our study we conclude that Intrathecal Ropivacaine 2.5mg in combination with Fentanyl 25 micrograms as a part of CSE technique provides rapid and safe analgesia for labor as effective as that achieved by Bupivacaine 2.5mg with significantly less motor blockade. So it is an ideal drug to use for labour analgesia.

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## Proforma - Ropivacaine/Bupivacaine in CSE for labor analgesia

### 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	120 min	180 min	240 min
PR												
BP												
VAS												
Sensory level												
Bromage scale												
FHR												
Cervix												

### Epidural Topups

Time									Total
Volum e									

### 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