"A COMPARATIVE EVALUATION OF HEMODYNAMIC EFFECTS BETWEEN HYPERBARIC ROPIVACAINE AND HYPERBARIC LEVOBUPIVACAINE IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA; A ONE YEAR RANDOMIZED CONTROLLED TRIAL"

By

REG NO: BA0121011

Dissertation

SUBMITTED TO THE
KLE ACADEMY OF HIGHER EDUCATION & RESEARCH
(DEEMED-TO-BE-UNIVERSITY), BELAGAVI, KARNATAKA

In Partial Fulfillment of the requirements for the degree of

M.D.

In ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI, KARNATAKA

DECEMBER 2024/ JANUARY 2025

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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"A COMPARATIVE EVALUATION OF HEMODYNAMIC EFFECTS BETWEEN HYPERBARIC ROPIVACAINE AND HYPERBARIC LOVEBUPIVACAINE IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA; A ONE YEAR RANDOMIZED CONTROLLED TRIAL ."** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

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LIST OF ABBREVATION

ASA	-	American Society of Anaesthesiologists
HR	-	Heart Rate (bpm)
SBP	-	Systolic Blood Pressure (mm Hg)
DBP	-	Diastolic Blood Pressure (mm Hg)
SpO_2	-	Saturation of peripheral oxygen (%)
L	-	Lumbar sensory dermatomal level
min.	-	minutes
kgs.	-	kilograms
cms.	-	centimeters

ABSTRACT

TITLE : "A COMPARATIVE EVALUATION OF HEMODYNAMIC EFFECTS BETWEEN HYPERBARIC ROPIVACAINE AND HYPERBARIC LEVOBUPIVACAINE IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA; A ONE YEAR RANDOMIZED CONTROLLED TRIAL"

KEYWORDS: Spinal anaesthesia, Ropivacaine, levobupivacaine, hemodynamic.

CONTEXT:

Spinal anaesthesia is the most popular method for anaesthesia in lower segment cesarean section surgeries. There are fewer direct studies contrasting hyperbaric ropivacaine and hyperbaric levobupivacaine, hence we took this study.

AIMS:

Comparison of onset of action of sensory and motor block and the duration of action of hyperbaric levobupivacaine and hyperbaric ropivacaine and to compare hemodynamic effects of drugs.

SETTING AND DESIGN: A ONE-YEAR RANDOMIZED CONTROLLED TRIAL.

MATERIALS AND METHODS:

This "one-year randomized controlled trial was conducted in the Department of Anaesthesiology, KLES Dr Prabhakar Kore Charitable Hospital Belagavi, from

March 2023 to April 2024 in 150 participants undergoing elective lower segment cesarean section under spinal anesthesia"

Group R received 2.2ml of 0.75% Hyperbaric Ropivacaine . Group L received 2.2ml of 0.5% Hyperbaric Levobupivacaine. The onset and duration of sensory-motor block and hemodynamic variables (HR, SBP, DPB, MAP, SPO_2) was assessed.

RESULT:

The haemodynamic parameters including " SBP, DBP, MAP and SPO_2" are comparable and had no statistical significance in 0.75% ropivacaine group and 0.5% levobupivacaine group during the course of the procedure although HR showed variation during the procedure "0.5% hyperbaric levobupivacaine is significantly more potent than 0.75% hyperbaric ropivacaine in terms of duration of sensory block (165.59 ±8.46 minutes vs 145.17 ± 8.09 minutes with p-value of <0.001) and motor block (161.33 ± 8.07 minutes vs 140.32 ± 8.35 minutes with p-value of <0.001) in patients undergoing lower segment cesarean section under spinal anaesthesia", while the "onset of sensory and motor blockade is earlier in 0.5% hyperbaric levobupivacaine compared to 0.75% hyperbaric ropivacaine" (1.11±0.54 minutes vs 1.56±0.67 minutes with p-value<0.001 for sensory onset) (1.16 ±0.53 minutes vs 2.01 ±0.85 minutes with p-value<0.001 for motor onset) .

CONCLUSION:

"The haemodynamic parameters while using hyperbaric ropivacaine and hyperbaric levobupivacaine were comparable while levobupivacaine is significantly more potent than ropivacaine in terms of onset and duration of sensory and motor block in patients undergoing lower segment cesarean section under spinal anaesthesia".

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INTRODUCTION

Caesarean section is the most commonly performed obstetric surgical procedure and can be done under spinal (intrathecal), epidural or general anaesthesia. The most popular method however for lower segment cesarean section procedures is spinal anesthesia[1].

According to the National Family Health study (NFHS-4) conducted in India, considering a five year time period prior to the study, 17% of live babies were delivered by cesarean section. Furthermore, according to the abovementioned study, 45% of cesarean section deliveries were done after the onset of labor pains. In India, the cesarean section rate was 8.5% in NFHS-3, but data from NFHS-4 indicates that it is now 17.2%[2].

The most common anesthetic technique used for lower segment caesarean sections (LSCS) is spinal anesthesia. The subarachnoid space, or the area surrounding the spinal cord, is where the local anesthetic agent is administered as part of the anesthetic procedure.. This achieves a quick and dense anesthesia for the surgery. Spinal anesthesia has a high success rate, a defined end goal, and is faster and easier to administer than epidural technique[3]. Block production is quick, dense, and consistent, particularly when working with hyperbaric local anaesthetic solutions. There is minimal chance of drug toxicity to the fetus even in cases where there might be transfer across the placenta[4].

It is the preferred choice whenever possible. Thus spinal anaesthesia helps avoid the disadvantages of general anaesthesia, such as the need for additional intravenous analgesics, the need for aiway intervention, postoperative nausea and vomiting and utilization of multiple drugs [5].

When it comes to spinal anesthesia during lower segment cesarean sections, bupivacaine is the most often utilized local anesthetic [6].But in contrast to other local anesthetics, it has been found to have significant negative effects on the nervous system and cardiovascular system.[4] The prolonged duration of action of bupivacaine has made it the preferred local anaesthetic agent in obstetric and regional anaesthesia for the past three decades. Bupivacaine has quite a few cardiotoxic properties along with the potential to develop local anaesthetic toxicity which can cause mild symptoms to seizures, cardiovascular instability, and sudden cardiac death. [5]Unexpected heart attacks without the onset of neurological manifestations, difficult resuscitations, and increased risk of maternal deaths (76 percent of recorded fatalities) have all been shown to be worrying adverse events.

Toxic side effects were prevented by changes to anaesthetic procedures like slow incremental dosing and the usage of test doses[5]. A significant effort was made to comprehend and circumvent the fundamental mechanism of bupivacaine toxicity as a result of an awareness of its clinical advantages with the development of its isomer levobupivacaine.

Enantiomers have fewer side effect while providing the desired pharmacological effect. Levobupivacaine, the s-enantiomer of bupivacaine, offers a more specific neuraxial blockade for obstetric spinal and epidural anesthesia.[7]

In clinical settings, levobupivacaine has not completely taken the role of bupivacaine. Levobupivacaine is equally as potent as bupivacaine. In contrast, levobupivacaine caused fewer CVS and CNS side effects in animal studies when compared with bupivacaine. Levobupivacaine produced less QTc interval prolongation than bupivacaine at i.v doses greater than 75 mg in healthy subjects and had a less

detrimental inotropic effect. With levobupivacaine, there were fewer EEG abnormalities that indicated CNS depression[6].

Another amide local anaesthetic which is similar to bupivacaine, Ropivacaine, has structural similarity to bupivacaine but is 30% lesser potency has been well-researched for spinal anesthesia (SA). It's available as pure S(-) enantiomer for clinical use. Its obvious advantages over Bupivacaine include lower cardiotoxicity and neurotoxicity, as well as a more targeted action on sensory rather than motor fibres. It is due to Ropivacaine's lower lipophilicity and enantiomer properties[8] Intrathecal ropivacaine was found to be safer in comparison to bupivacaine, with a shorter duration of action.

In this trial, the hyperbaric solutions of ropivacaine and levobupivacaine are compared for lower segment cesarean sections that are elective. The introduction of hyperbaric levobupivacaine in India and the lacunae in literature with respect to its comparison with hyperbaric ropivacaine, in terms of hemodynamic parameters, justifies the need for this study.

OBJECTIVE:

The Study Objectives are:

Primary Objective:

Hemodynamic parameter comparison, including heart rate, blood pressure, and mean arterial pressure of Hyperbaric Ropivacaine and Hyperbaric Levobupivacaine in elective LSCS cases.

Secondary Objective:

A comparison between the motor block and sensory block onset and duration of action of Hyperbaric Ropivacaine and Hyperbaric Levobupivacaine in elective LSCS cases.

The onset of action i,e time taken to achieve both motor and sensory block up to T-10 level from the time of injection of an spinal drug in minutes

Duration of action is the time from once the patient feels pain from the time of onset of action or regression of sensory block by two Dermatomal segments.

Review of Literature

The history of spinal anesthesia traces back to Carl Koller's[9] pioneering use of topical cocaine for eye analgesia in 1884. In 1885 James Leonard Corning described spinal anesthesia, and Halsted and Hall improved the procedure even further by injecting cocaine into tissues for surgical anesthetic. Corning's initial attempts, however, may have unintentionally led to epidural rather than spinal injections.

Notable developments over the years included Rudolph Matas's use of spinal cocaine and morphine and Augustus Karl Gustav Bier's experimentation with spinal cocaine, which resulted in postdural puncture headaches (PDPH). Dudley Tait and Guido Caglieri performed the first spinal anesthesia technique in the United States in 1899, while Theodore Tuffier emphasized the importance of recognizing cerebrospinal fluid (CSF) before injecting cocaine[10][11].

The goal of later advancements by Arthur Barker, Gaston Labat, and others was to improve sterility and safety, which made spinal anesthetic more widely utilized. But there were setbacks in the form of paraplegia post spinal anaesthesia in the mid 1900s which caused a temporary halt in its use as an anaesthetic modality. However, in 1954, Dripps and Vandam validated the safety of spinal anesthetics, which resulted in their comeback[11].

It was the main method used for both vaginal birth and cesarean sections in the US during the mid 1950s when over 500,000 obstetric treatments involving spinal anaesthesia were carried out . But by the late 1960s, spinal anesthesia was becoming less common for obstetrics due to developments in epidural anesthetic technology. According to estimates from the Third National Audit Project (NAP3), 133,525 obstetric spinal surgeries were carried out in the UK in 2006[12].

1. An article published by Kumar and Sharda et.al in 2021 conducted a randomized study between two groups with a total of 120 patients. First group received 0.5% levobupivacaine, while the other received 0.5% bupivacaine (both hyperbaric solutions and 3 ml each).They came to the inference that both drugs are equally efficacious for spinal anaesthesia in lower limb procedures. There was no major difference between the groups while comparing the sensory and motor parameters with respect to onset and duration. Although the levobupivacaine group needed fewer

doses of ephedrine to maintain blood pressure, hemodynamic stability was comparable. The side effect profiles, including incidence of intraoperative hypotension and bradycardia and postoperative nausea and vomiting were comparable amongst the groups. The research findings indicated that levobupivacaine is a viable alternative for spinal anesthesia. Furthermore, it showed faster bladder function recovery and reduced vasopressor needs.[13]

2. A comparison was made between ropivacaine and levobupivacaine for spinal anesthesia in elective lower limb procedures in the 2021 by Dikkala et al. The trial was randomized and carried out with 100 patients, and concluded that both anesthetic drugs effectively blocked sensory and motor functions. Grade 4 motor block and sensory block developed more quickly with levobupivacaine than with ropivacaine. The group which was administered ropivacaine experienced a longer period of sensory blockade, but levobupivacaine was shown to have relatively more hemodynamic stability and cardiac safety profile.The study concluded that both drugs are equally effective and the utility depends on the specific needs of the clinical scenario at hand[14].

3. In a 2019 research by Gorglas et al., “levobupivacaine and ropivacaine were used in equal dosages (5 mg/ml in an 80 mg/ml glucose solution) and administered intrathecally at the L3–4 interspace for 60 male patients categorized as ASA I–II who were listed for transurethral procedures”. The main parameters measured were the sensory and motor block characteristics. The outcomes showed that the maximal height of the block was comparable, indicating that both medications provided adequate anaesthesia for the procedures. Levobupivacaine had a longer duration of sensory(115.46 minutes vs. 73.42 minutes for ropivacaine) and motor block (189.47 minutes vs. 108.21 minutes for ropivacaine).The overall hemodynamic parameters

were comparable between the two groups. The study concluded that both anesthetic agents are effective, but ropivacaine provided quicker recovery of motor and sensory block compared to levobupivacaine, which indicated its effectivity in day care procedures. This quicker recovery period would entail shorter hospital stays, reducing medical expenses and patient discomfort.[15]

4. Ajay Singh and Anshu Gupta (2017) carried out a study comparing the "safety parameters and effectiveness of isobaric levobupivacaine and hyperbaric racemic bupivacaine in spinal anesthesia for inguinal hernia surgery", which was published in the 'Korean Journal of Anaesthesia'. The study looked at postoperative recovery patterns and the quality of intraoperative anesthesia in 100 patients, ages 18 to 60. The patients were randomized into two groups.The anesthetic quality produced by the two procedures was similar; there were no notable variations in the maximum block height or the commencement of sensory block.However, levobupivacaine demonstrated a shorter duration of anesthesia (206.2 ± 18.9 minutes vs. 224.1 ± 15.6 minutes) and motor block (185.9 ± 20.3 minutes vs. 196.4 ± 21.2 minutes). Patients receiving levobupivacaine also experienced faster mobilization (321.9 ± 19.2 minutes vs. 356.7 ± 26.6 minutes) and a lower incidence of hypotension (12% vs. 32%). Levobupivacaine is useful for daycare procedures because of its shorter duration of sensory and motor block, which allowed for early patient movement. Its safety profile was further emphasized by the lower incidence of hypotension as compared to bupivacaine. This research validates levobupivacaine as a viable and maybe less hazardous substitute for spinal anesthetic during inguinal hernia procedures.[16]

5. In order to determine whether ropivacaine is a suitable substitute for bupivacaine, "a comprehensive comparison of the clinical efficacy of hyperbaric ropivacaine and hyperbaric bupivacaine was carried out in a study by Kulkarni et al. in 2015 on 80

American Society of Anesthesiologists (ASA) grade I–II patients undergoing elective infraumbilical surgeries". Key findings included that ropivacaine produced a slower onset of sensory block (4.5 minutes) compared to bupivacaine (3.2 minutes) and had a significantly shorter duration of sensory block (155 minutes vs. 190.5 minutes). Both the time to initial micturition and the recovery from motor blockage were accelerated by ropivacaine. The demographic parameters of both groups were similar, and the incidence of adverse events, which included mild cases of hypotension and post-dural puncture headache, was also similar. According to the study's findings, hyperbaric ropivacaine is a feasible substitute for hyperbaric bupivacaine in spinal anesthetic procedures that call for a shorter duration of anesthesia.[17]

6. In the 2010 Turkiye Klinikleri Journal of Medical Sciences article "Spinal Anaesthesia with Hyperbaric Solutions of Ropivacaine, Levobupivacaine or Bupivacaine in Major Orthopedic Surgery," Kazak et al. examined the effectiveness, safety, and adverse effects of these three anesthetics in spinal blocks for patients having total hip or knee replacements.It was a randomized control trial which enrolled 90 individuals between the ages of 30 and 75 and assessed the effects of giving each anesthetic agent in 0.5% hyperbaric solutions. The increased duration of motor block and hemodynamic side effects were observed in hyperbaric bupivacaine group. At the T10 dermatome level, levobupivacaine (Group HL) exhibited the quickest onset of sensory block. Although the duration of motor and sensory blocks was the shortest with ropivacaine (Group HR), this also meant that more analgesics were needed sooner. Significantly, Group HR showed the least amount of hypotension, which made it a safer option in terms of cardiovascular stability. The study found that levobupivacaine and bupivacaine have comparable anesthetic potency and block properties at equivalent dosages. Roprivacaine, on the other hand, has less adverse

effects and a shorter duration of action, which highlights its potential benefits for shorter procedures or patients where reducing side effects was important. The results indicated that more study was necessary to improve anesthetic regimens in major orthopedic surgery by striking a balance between managing side effects and extending the duration of effective anesthesia.[18]

7. The article "Comparison of Plain Ropivacaine, Bupivacaine, and Levobupivacaine for Lower Abdominal Surgery" by Mantouvalou et al in 2008, examined the anesthetic efficacy and safety of three local anesthetics in spinal anesthesia for lower abdominal surgery. 120 patients were recruited in the trial and were assigned to one of three groups. Each group was administered 15 mg of isobaric bupivacaine, ropivacaine, or levobupivacaine intrathecally. The onset, duration and maximum height of sensory and motor block, and any negative consequences were assessed. While comparing ropivacaine to bupivacaine and levobupivacaine, the results showed that while ropivacaine had a slower onset of sensory and motor block than bupivacaine, it had a significantly shorter duration of both motor and sensory block. In comparison to levobupivacaine and ropivacaine, bupivacaine had a higher incidence of hypotension while required pharmacological intervention All three anesthetic agents produced comparable levels of effective anesthesia despite these variations. The study concluded that while ropivacaine had a shorter duration of anesthesia, it still provided effective and safe spinal anesthesia for lower abdominal surgeries, making it a suitable option when a shorter duration of action is desirable.[19]

8. In 2008 Luck, Fettes, and Wildsmith compared “the use of hyperbaric Bupivacaine, Levobupivacaine, and Ropivacaine solutions for spinal anesthesia during elective procedures”. It was a randomized control trial amongst 60 ASA 1 and 2 patient utilizing the drugs bupivacaine, ropivacaine and levobupivacaine . The main

outcomes measured were the onset and duration of sensory and motor block and time to first micturition. The results showed that ropivacaine produced shorter duration of sensory and motor block compared to levobupivacaine and bupivacaine. Roprivacaine was found to have a faster rate of recovery and mobilization in patients; hence indicating its utility in day care procedures. The study came to the conclusion that because of its good recovery profile, hyperbaric ropivacaine would be especially helpful in ambulatory settings.This could offer a significant clinical benefit by enabling quicker patient turnover and reducing hospital stay times[20].

9. For "lower abdominal surgery, three amide local anesthetics; ropivacaine, bupivacaine, and levobupivacaine were compared., with respect to efficacy and safety" and published by Cappelleri et al. in the Anaesthesia and Analgesia journal in 2005. The procedure involved spinal anesthesia. 120 patients were recruited in the trial and were assigned to one of three groups. Intrathecal injections of isobaric bupivacaine, ropivacaine, or levobupivacaine (15 mg) were administered to each group. Among the significant variables that were measured were the onset, duration, and maximum spread of sensory and motor block, the time it took for sensory block regression, and any adverse effects.

Comparing ropivacaine to bupivacaine and levobupivacaine, the results showed that while ropivacaine had a slower onset of motor block than bupivacaine, it had a much shorter duration of both motor and sensory block. Compared to ropivacaine and levobupivacaine, bupivacaine was higher incidence of hypotension requiring more administration of vasoactive and sympathomimetic medications. Despite these differences, all three anesthetic agents generated similarly effective anaesthesia. The study showed that ropivacaine was a good option when a shorter anesthetic duration is needed, despite producing analgesia for a shorter time. This study is significant

because it directly compared these three anesthetic agents under similar conditions and provided insight into its possible use in different clinical settings[21].

10. The article by P. Gautier and A. Hadzic (2011). explored “the efficacy of intrathecal Ropivacaine, Levobupivacaine, and Bupivacaine when used in Cesarean sections”.The study used a combination spinal-epidural approach on ninety parturients. Three groups containing 8 mg of bupivacaine, 8 mg of levobupivacaine, and 12 mg of ropivacaine, each with 2.5 mg of sufentanil, were randomly assigned to the subjects. The study showed that levobupivacaine (80%), ropivacaine (87%) and bupivacaine (97%), respectively, had the success rates in that order. In comparison with the other two drugs, bupivacaine produced anaesthesia for a significantly longer time. The success rate of bupivacaine was shown to be much higher than that of levobupivacaine, although it did not differ significantly from ropivacaine. The patient demographics were similar in each group, and secondary objectives including pain scores, prevalence of hypotension, and side effects like nausea and vomiting did not show any significant differences. Overall, the study findings suggested that bupivacaine is still a good option for spinal anesthesia during Cesarean sections because of its higher efficacy and longer duration of action, although ropivacaine and levobupivacaine seem promising in its utility[22].

11. To find out if ropivacaine, levobupivacaine, and bupivacaine when given intrathecally give comparable anesthetic and postoperative analgesia to bupivacaine, Chung et al. conducted a second study in 2001 comparing the effects of these three drugs during cesarean sections. Ninety parturients received one of three isobaric intrathecal solutions—eight milligrams of bupivacaine, eight milligrams of levobupivacaine, or twelve milligrams of ropivacaine—after undergoing a combination spinal-epidural procedure. They assessed the quality of anesthesia,

analgesia, and muscle relaxation. It showed that ropivacaine had a longer onset time but a shorter duration of both sensory and motor blockade. Levobupivacaine exhibited properties similar to bupivacaine with a minimal extended period of motor block. There were no appreciable differences in the good intraoperative conditions given by the three anesthetics.There were no appreciable variations in the newborn outcomes amongst the three anesthetics, and all three offered acceptable intraoperative circumstances. The study found that levobupivacaine and bupivacaine may be favored for longer surgeries because of their longer-lasting effects, even if ropivacaine delivers a shorter period of blocks, making it suited for shorter procedures[23].

BASIC SCIENCES

Applied Anatomy

For the safe and effective delivery of spinal anesthesia, an anesthesiologist needs a comprehensive and precise understanding of the vertebral column's structure and its contents. This knowledge is crucial not only for the procedure itself but also for understanding how the drug disperses in the sub arachnoid space and the extent of the block achieved.

Vertebral column

The primary role of the vertebral column is to protect the spinal cord. The vertebral column comprises 33 vertebrae[24].

- ●Cervical - 7
- ●Thoracic - 12
- ●Lumbar - 5
- ●Sacrum - 5 (fused)
- ●Coccyx - 4 (fused)

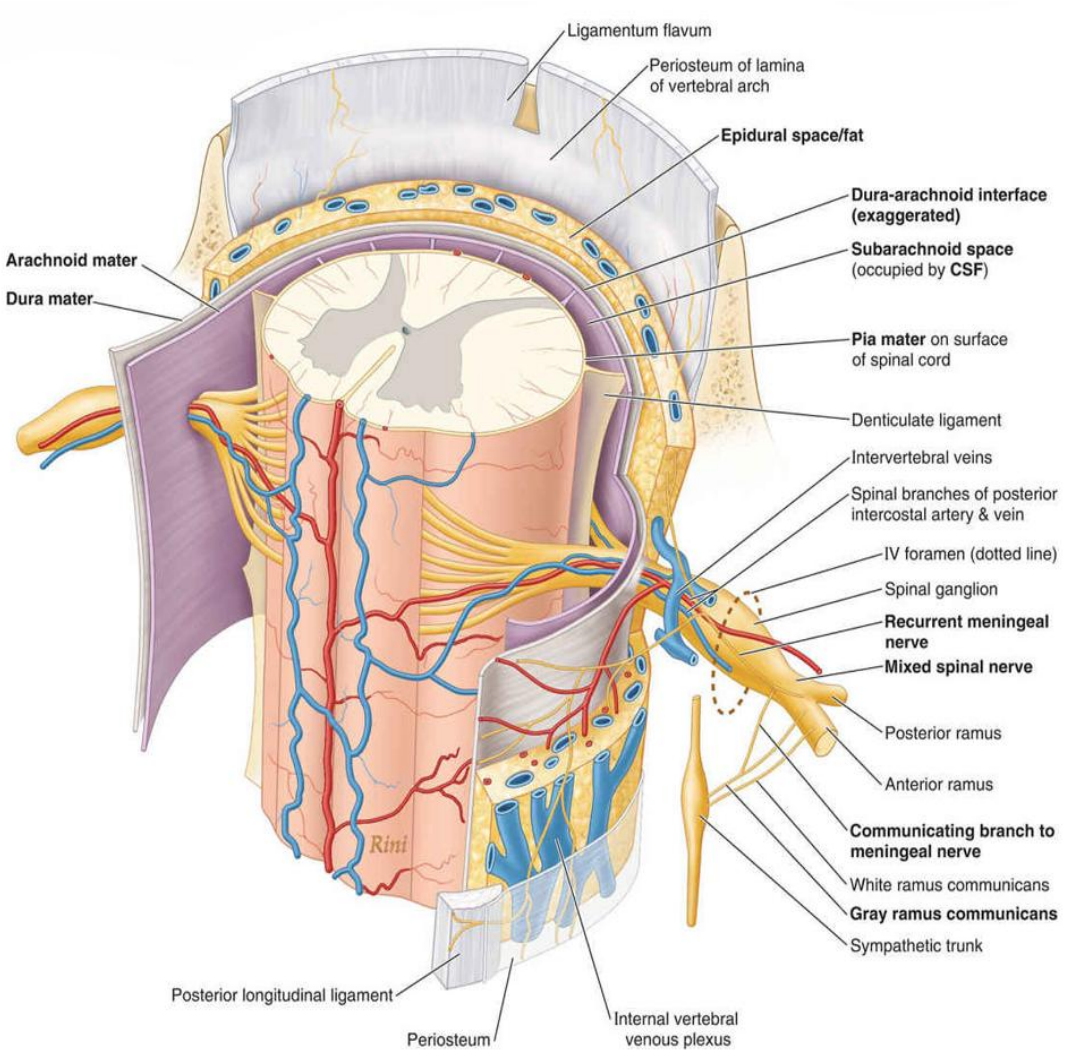
Curves of spine[25]

In adults, the curves of the vertebral column play a crucial role in the distribution of drugs in the subarachnoid space[25], and these curves include:

- ●Cervical curve - Convexity anterior
- ●Thoracic curve - Concave anterior
- ●Lumbar curve - Convexity anteriorly

Cervical (C) five and lumbar (L) five are the highest points of cervical and lumbar curves in supine position and the lowest points of thoracic and sacral are at thoracic (T) five and sacral (S) two respectively[24].

Figure 1: Vertebral Column [26]



Lumbar vertebrae

A typical lumbar vertebra consists of:

●A kidney shaped body.

●Two pedicles directed backwards from the upper part of the body.

●Two transverse processes

●Two laminae meeting posteriorly and enclosing the triangular vertebral foramen.

●Thick, broad and quadrilateral spinous processes.

●Two upper and lower articular processes which prevent rotation but allow limited flexion and extension between contiguous vertebrae.

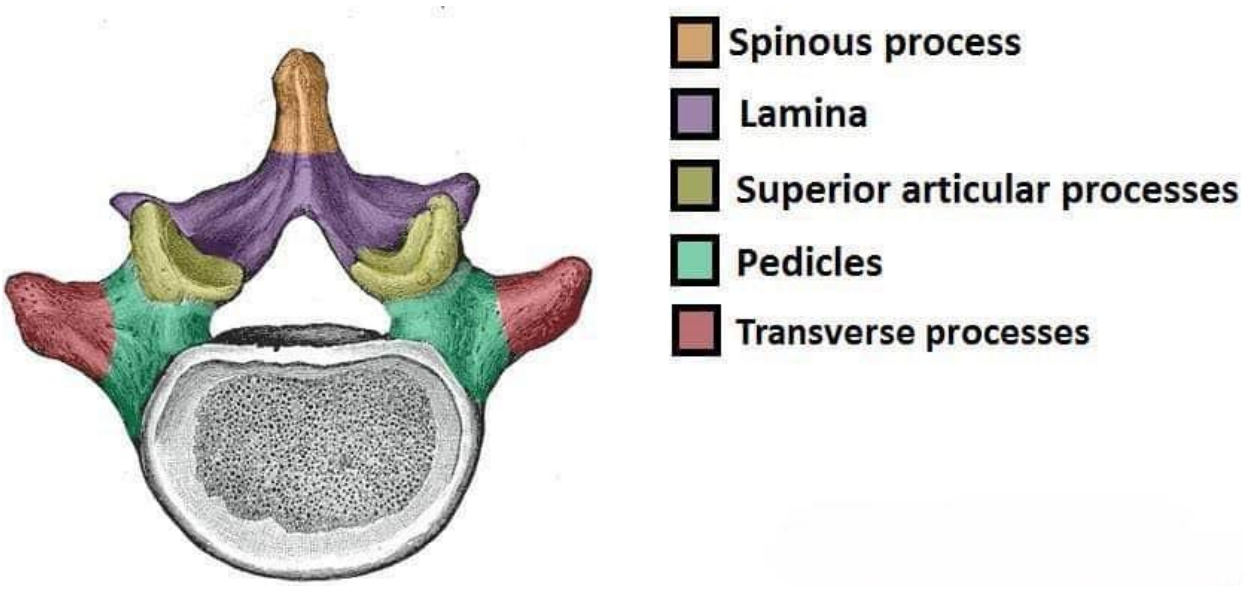


Figure 2: Typical lumbar vertebra[26]

Thoracic vertebrae :

·A heart shaped body

·A small costal demi facet on superior border of lateral side of body and a larger demi facet on the inferior surface

·Shallow superior vertebral notches and deeper inferior vertebral notches

·Transverse processes are directed backwards and laterally , carrying a costal facet for articulation with ribs.

Vertebral ligaments[27]

The following overlapping ligaments provide stability to the vertebral column and protect the spinal cord :

Supraspinous ligament: This is a strong fibrous cord which connects apices of spinous processes from sacrum to C5 where it is continued as the ligamentum nuchae . The width depends upon the width of the spinous process – in lumbar region it might be upto 1 cm wide. In elderly people and manual labourers this ligament calcifies thus making the midline approach difficult.

Interspinous ligament: This is a thin membranous ligament running obliquely and connecting spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament. In the lumbar region, this ligament is rectangular in shape leading to the characteristic and identifiable “loss of resistance” feel to air or saline.

Ligamentum flavum: This ligament comprises of yellow elastic fibres and connects adjacent laminae. Laterally, this ligament begins at the root of articular processes and extends posteriorly and medially to the point where laminae join to form spinous process. It provides the classic springy resistance in the lumbar region.

Longitudinal ligaments: There are two longitudinal ligaments (anterior and posterior) that bind vertebral bodies together.

In spinal anesthesia, the needle is advanced beyond the dura mater and into the subarachnoid space, which lies between the lumbar vertebrae. To access this space, the needle traverses several layers of tissue and ligaments, including the supraspinous ligament, interspinous ligament, and ligamentum flavum[27].

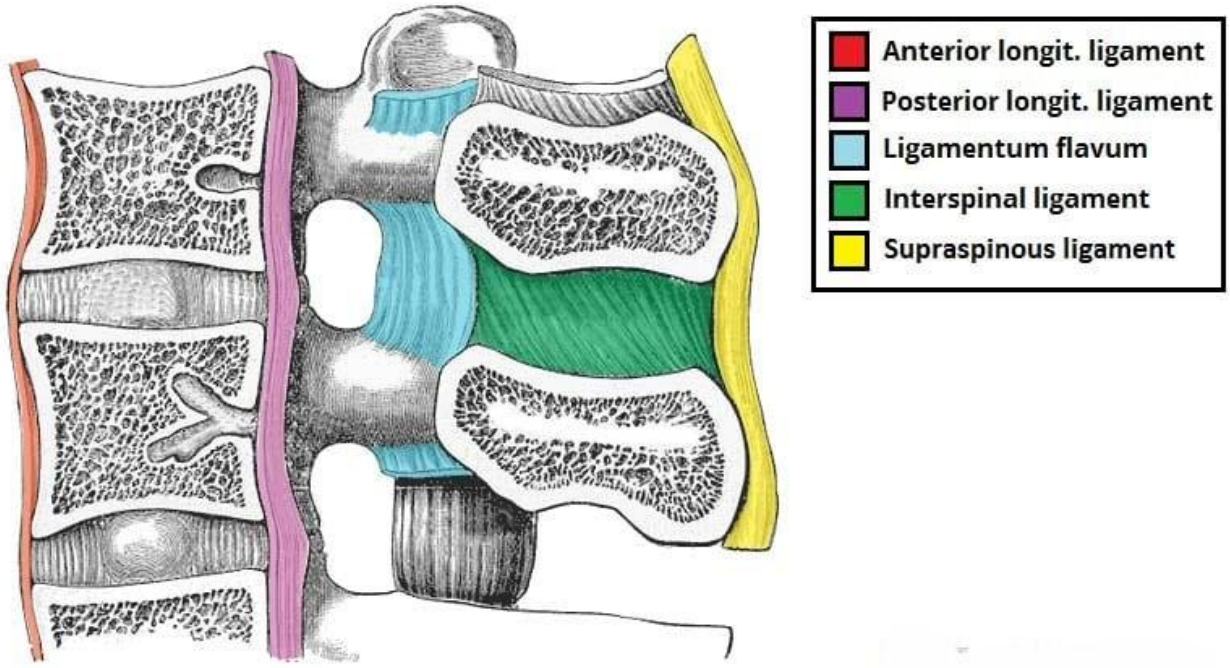


Figure 3 :Vertebral ligaments[27]

Intervertebral Discs

These are principle connecting link between vertebral bodies. They form about 25% of the length of the spine. They consist of two parts - The outer fibrous part called the annulus fibrosus (made up of fibrous tissue), while the nucleus pulposus is the softer core. The discs serve as shock absorbers and lend flexibility to the vertebral column[24].

Topographical Line of Tuffier

This is a horizontal line across the back between the crests of the iliac bone passing over the spine of the 4th lumbar vertebra in the upright position. In a patient lying in

the lateral position it may also pass through L4 and L5 interspaces. The superior iliac crest is used to identify the L4 and L5 interspace during epidural anesthesia[28].

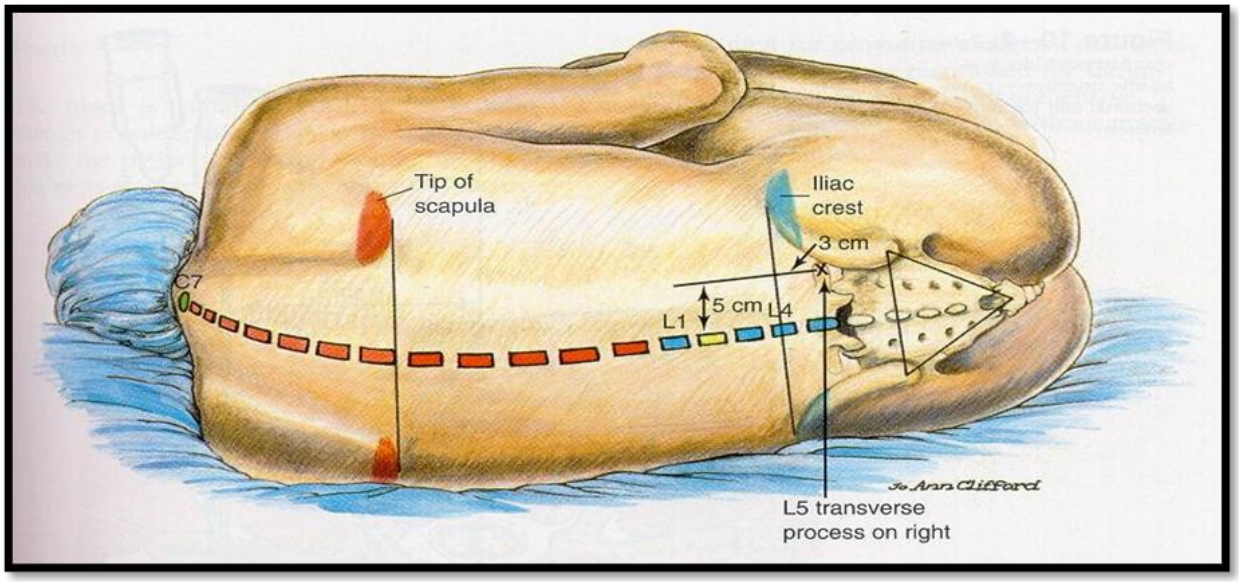


Figure 4: Topographical line of Tuffier

Vertebral canal:

The vertebral canal is bound by the vertebral bodies and intervertebral discs anteriorly , the laminae , ligamentum flavum and laterally by pedicles and laminae[29] .

The contents of vertebral canal are as follows :

- Spinal cord
- Spinal nerve roots
- Meninges
- Cerebrospinal fluid
- Vessels
- Fat
- Loose areolar tissue

Spinal cord[25]

The average length of the spinal cord in males is 45 centimetres (cms) and in females it is 42 cms. The average weight is approximately 30 gm.

The spinal cord is a continuation of the medulla oblongata below the level of foramen magnum and it tapers off into a conical extremity known as conus medullaris. Filum terminale descends to the back of first segment of coccyx from apex of conus medullaris.

At birth, Spinal cord ends at the level of lower border of lumbar (L) three vertebra and in adults, it is as follows;

- Lower border of L1 - 50%
- Upper border of L2 - 40%
- Upper border of L3 - 3%

From the spinal cord arise 31 pairs of spinal nerves, each made of a ventral and a dorsal root. These anterior and posterior roots after crossing the subarachnoid space, pass through the dura and extradural space independently and unite at the level of intervertebral foramen to form spinal nerve trunks, which further divide into anterior and posterior primary divisions.

The amount of white matter declines progressively from the cervical region down to the lumbar region. The gray matter is greatly increased in the both the lumbar and cervical enlargement[30].

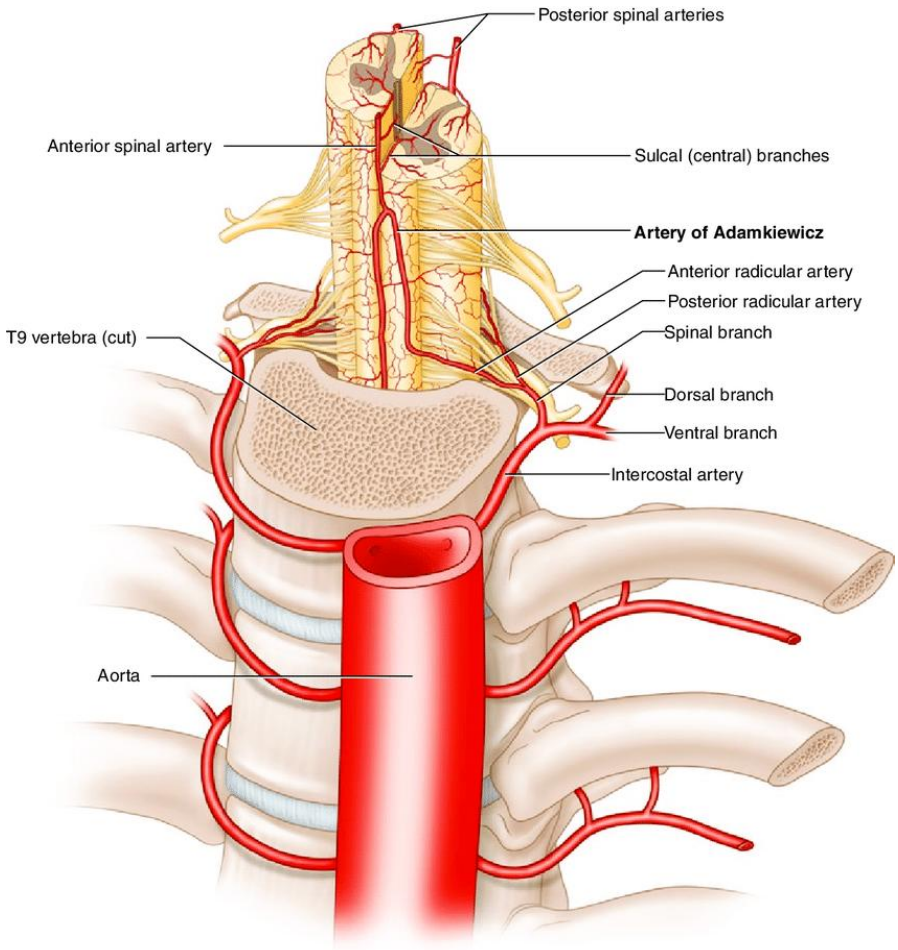


Figure 5: Blood supply of spinal cord[31]

Blood Supply of Spinal Cord:

The spinal cord receives its blood supply from anterior and posterior spinal arteries. The anterior spinal artery is a single vessel lying in front of the anterior median fissure. It is formed by two small arteries, one given off from each vertebral artery at the level of the foramen magnum. It receives small communications from the intercostal and lumbar arteries; to provide the extra blood supply needed in the cervical, thoracic and lumbar enlargements[31].

There are two posterior spinal arteries-one on each side. They are derived from the vertebral artery or more often from a primary branch of each vertebral artery. They supply the posterior one-third of the spinal cord. This supply is augmented by spinal

branches of vertebral, ascending cervical, posterior intercostals, lumbar and lateral sacral arteries, which pass through the intervertebral foramina.

Venous drainage is through a plexus of anterior and posterior veins in the neck, azygous veins in the thorax, lumbar veins in the abdomen, and lateral sacral veins in the pelvis. There is no anastomosis between the anterior and posterior spinal arteries.

The longest of the feeder arteries is the radicularis magna (artery of Adamkiewicz), which supplies the anterior spinal artery in the area of the lumbar enlargement of the cord. It enters by way of a single intervertebral foramen (78% of the time on the left) between the T8 and L3 foramina.[31]

Meninges

The spinal cord is covered by three membranes from inward to outward, they are the pia mater, the arachnoid mater and the dura mater. The dural sac is the continuation of meningeal layer of the cranial dura mater. It is a circular sac or sleeve surrounding the spinal cord. Above, it is attached firmly to the circumference of the foramen magnum[25].

Duramater

It is the outermost membrane, the fibres of which run longitudinally. Although continuous, it can be described in two parts: the cranial and the spinal. The cranial dura consists has two layers, outer endosteal layer, which lines the skull, and an inner meningeal layer, which invests the brain and folds inward to form the falx cerebri and tentorium cerebelli.

Arachnoid Mater

The arachnoid mater is a delicate non-vascular membrane applied closely to the dura mater. The lower extent of dural sac is as follows;

Below this the dura continues as the filum terminale. The subarachnoid space is the space between the arachnoid and pia mater. This space is occupied by the cranial and spinal nerves and by the cobweb trabeculae. The space is annular in the cranial and thoracic vertebrae and is about three mm deep. Below the first lumbar vertebrae it is circular in shape.

EPIDURAL SPACE[32]

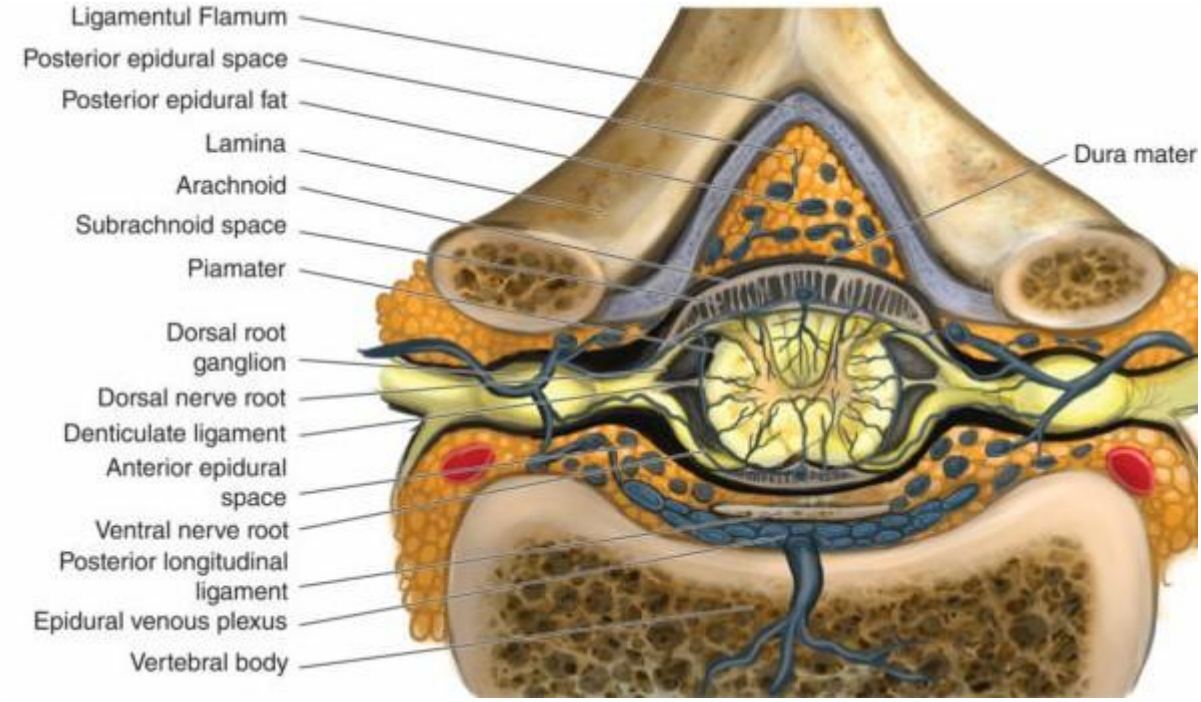


Figure 6 : Epidural Space[32]

Boundaries of the epidural space[33]

The epidural space is bounded

Superior: by foramen magnum , where periosteal and spinal layers of dura mater fuse.

Inferior: by sacrococcygeal membrane and sacral hiatus .

Anterior: by the posterior longitudinal ligament, vertebral bodies and discs

Posterior: by ligamentum flavum , periosteum of anterior surface of laminae and connecting ligaments.

Lateral: by periosteum of pedicles and intervertebral foramina.

Rarely, a fold of dura mater divides the space into ventral and dorso – medial compartments leading to patchy or unilateral analgesia or missed segments.

Shape and size: These are largely determined by the shape of the lumbar vertebral canal and the position and size of the dural sac within it.

- Cervical : 1.5 mm
- Upper thoracic : 2.5 – 3 mm
- Lower thoracic : 4-5 mm
- Lumbar : 5-6 mm

Types of epidural space

The epidural space can be categorized into cervical, thoracic, lumbar and sacral epidural spaces. These spaces can be defined according to their margins. At the cervical epidural space, there is a fusion of the spinal and periosteal layers of dura mater at the foramen magnum to lower margin of the 7th cervical vertebra. While the thoracic epidural space is formed by the lower margin of C7 to the upper margin of L1, the lumbar epidural space is formed by the lower margin of L1 vertebra to the

upper margin of S1 vertebra. The sacral epidural space is formed by the upper margin of S1 to sacrococcygeal membrane and sacral hiatus[32][33].

Contents of the epidural space :

Contains semi liquid fat , lymphatics , arteries , loose areolar tissue spinal nerve roots and a very rich plexus of veins[32][33].

PHARMACODYNAMICS OF SPINAL ANESTHESIA

The pharmacodynamics of spinal injection of local anesthesia vary widely. The following discussion covers the effects of spinal anesthesia on the cardiovascular, respiratory, gastrointestinal, hepatic, and renal systems.

Cardiovascular Effects of Spinal Anesthesia

It is well known that spinal anesthesia often leads to hypotension. In fact, some degree of hypotension can reassure the anesthesiologist that the nerve block is effective. However, this hypotension can also cause nausea and vomiting, ischemia of vital organs, cardiovascular collapse, and, in pregnant women, pose a risk to the fetus[34]. Over time, there have been changes in the definitions, proposed mechanisms, and management strategies for hypotension.

Many mechanisms have been proposed for spinal anesthesia-induced hypotension, including the direct circulatory effects of local anesthetics, relative adrenal insufficiency, skeletal muscle paralysis, ascending medullary vasomotor nerve block, and concurrent respiratory insufficiency. However, the primary cause is the preganglionic sympathetic nerve block produced by spinal anesthesia. Since the height of the nerve block determines the extent of the sympathetic block, it consequently affects the changes in cardiovascular parameters[34]. However, this relationship is unpredictable. The sympathetic nerve block can vary between two and six dermatomes above the sensory level and may be incomplete below this level. The sudden onset of the sympathetic nerve block with spinal anesthesia allows little time for cardiovascular compensation, which may explain why similar sympathetic nerve blocks with epidural anesthesia result in less hypotension.

Sympathetic nerve block induces hypotension by affecting preload, afterload, contractility, and heart rate essentially the determinants of cardiac output (CO)—as

well as by reducing systemic vascular resistance (SVR)[25]. Preload decreases due to venodilation caused by the sympathetic nerve block, leading to blood pooling in the peripheral areas and reduced venous return. During a sympathetic nerve block, the venous system is maximally vasodilated and depends heavily on gravity to return blood to the heart. Therefore, patient positioning and aortocaval compression, such as from a gravid uterus, significantly impact venous return during spinal anesthesia[34].

Sympathetic nerve block can also reduce arterial vasomotor tone, thereby lowering systemic vascular resistance (SVR) and afterload. Unlike venodilation, arterial vasodilation is not complete after a spinal block, as vascular smooth muscle retains some autonomic tone even after sympathetic denervation. This residual tone can be lost in the presence of hypoxia and acidosis, potentially leading to cardiovascular collapse following high spinal anesthesia without cardiorespiratory support. Despite vasodilation below the level of the spinal block, compensatory vasoconstriction occurs above it, mediated by carotid and aortic arch baroreceptors. This is crucial for two reasons: First, higher dermatomal blocks may result in reduced compensatory response. Second, using vasodilatory drugs such as glyceryl trinitrate (GTN), sodium nitroprusside, or volatile anesthetics can eliminate this compensatory mechanism, worsening hypotension or even causing cardiac arrest[35].

There may initially be an increase in cardiac output (CO) due to decreased afterload. Alternatively, CO might decrease because of reduced preload. Some studies have indicated that CO remains unchanged or is only slightly reduced during the onset of spinal anesthesia.

The impact of spinal anesthesia on contractility may be influenced by the blockade of upper thoracic sympathetic nerves. Intriguingly, a study exploring the common

occurrence of ST segment depression in healthy women undergoing cesarean section (25-60%) revealed that ST depression was linked to a hyperkinetic contractile state[36]. The effect of spinal anesthesia on heart rate (HR) is multifaceted. HR might rise (due to hypotension triggering the baroreceptor reflex) or fall (either from the blockade of sympathetic nerve fibers originating from T1–T4 spinal segments, or through the reverse Bainbridge reflex). The reverse Bainbridge reflex leads to a decrease in HR caused by reduced venous return, sensed by stretch receptors in the right atrium, albeit it is weaker than the baroreceptor reflex. Another reflex, the Bezold-Jarisch reflex (BJR), reduces HR and has been associated with bradycardia, hypotension, and cardiovascular collapse following central neuraxial anesthesia, especially spinal anesthesia[36].

While the BJR is a cardioinhibitory reflex, its association with spinal anesthesia is likely weak. The BJR has been implicated in bradycardia after spinal anesthesia, particularly following hemorrhage, where forceful contractions of an underfilled heart may initiate the reflex. This occurrence is more probable with ephedrine use rather than phenylephrine[37].

Young, healthy patients (American Society of Anesthesiologists class 1) and those using beta-blockers face a heightened risk of bradycardia. The incidence of bradycardia in the nonpregnant population is approximately 13%. Although bradycardia is generally well tolerated, it can lead to asystole and higher-degree heart nerve block, underscoring the importance of vigilant monitoring and prompt treatment post-spinal anesthesia[37].

Various risk factors contribute to hypotension, including hypovolemia, preoperative hypertension, high sensory nerve block height, age over 40, obesity, combined

general and spinal anesthesia, chronic alcohol consumption, elevated BMI, and the urgency of non-obstetric surgery. Hypotension is less common in women in labor compared to those undergoing elective cesarean section[37].

Management of Hypotension After Spinal Anesthesia

Evolving perspectives on the underlying mechanisms of spinal-induced hypotension have led to changes in its management strategies. For instance, if reduced preload is deemed the main issue, then positioning and fluid therapy are favored treatments; likewise, if vasodilation is identified as the cause, a vasoconstrictor is preferred. This has sparked intense debates. In the 1970s, there was a suggestion to avoid vasopressors until all other methods to address hypotension had been exhausted, highlighting the emphasis on preload. This notion was supported by extrapolated evidence from flawed studies on pregnant ewes undergoing general anesthesia, which indicated potential adverse effects of vasopressors on uteroplacental circulation. The choice of vasopressor has also been a contentious topic, with ephedrine traditionally favored due to its perceived preservation of uterine blood flow in animal studies. However, recent research, including studies by Ngan Kee and others, suggests that phenylephrine may be more suitable, particularly in elective obstetric cases[38].

Management of hypotension post-spinal anesthesia necessitates frequent blood pressure monitoring (initially every minute), along with electrocardiogram (ECG), oxygen saturation, and fetal monitoring in pregnant patients. Invasive blood pressure monitoring may be considered for patients with significant cardiac issues. Fluid therapy is crucial in dehydrated patients to restore volume before spinal anesthesia[38].

Non Pharmacological interventions such as positioning, leg compression, and uterine displacement are also effective in managing hypotension. While Trendelenburg positioning can enhance venous return, extreme angles should be avoided to prevent

reduced cerebral perfusion. To mitigate the risk of altering spinal anesthesia levels, maintaining a modest elevation of the upper body with a pillow under the shoulders is recommended. Lower limb compression has shown some benefit in pregnant women, although its efficacy varies depending on the method used. Additionally, aortocaval compression from a gravid uterus should be avoided[39].

There have been conflicting views on fluid management during spinal anesthesia, with early studies advocating for crystalloid "preloading" before the procedure, while recent research suggests minimal benefits from preloading. Colloid preloading appears to be effective but needs to be balanced against the risk of allergic reactions and increased costs. "Coloading" with crystalloid immediately after spinal anesthesia seems more effective than preloading in preventing hypotension[39].

Reducing the dose of spinal local anesthetic can help limit hypotension. However, lower doses may compromise anesthetic efficacy, necessitating early top-up doses via an epidural catheter. Regarding the choice of vasopressor, ephedrine and phenylephrine have been the main contenders, with phenylephrine gaining preference due to its superior efficacy in reducing hypotension and nausea. Although phenylephrine may decrease cardiac output and spinal nerve block height, concerns about its potential side effects, such as hypertensive crisis and drug concentration errors, persist[39]. Cardiovascular collapse following spinal anesthesia is rare but requires prompt treatment, typically involving intravenous atropine, ephedrine, and epinephrine.

Respiratory Effects of Spinal Anesthesia

In patients with normal lung function, spinal anesthesia typically has minimal impact on pulmonary physiology. Parameters such as lung volumes, resting minute ventilation, dead space, arterial blood gas levels, and shunt fraction tend to remain

relatively unchanged following spinal anesthesia. The primary respiratory effect occurs during a high spinal block when active exhalation is hindered due to the paralysis of abdominal and intercostal muscles. This can result in reductions in expiratory reserve volume, peak expiratory flow, and maximum minute ventilation, particularly in patients with obstructive pulmonary disease who rely on accessory muscles for adequate ventilation. However, patients with normal lung function experiencing a high spinal nerve block may experience dyspnea, which is typically due to the inability to sense chest wall movement during respiration. Simple reassurance is often sufficient to alleviate their distress[40].

Arterial blood gas measurements generally remain stable during a high spinal anesthesia in patients breathing room air spontaneously. The primary effect of a high spinal anesthesia is on expiration, as the muscles responsible for exhalation are impaired. Since a high spinal block typically spares the cervical area, the function of the phrenic nerve and the diaphragm remains normal, and inspiration is minimally affected. While some studies have shown no significant changes in vital capacity, maximal inspiratory pressure, or resting end-tidal PCO2 with spinal anesthesia, increased ventilatory responsiveness to CO2 has been observed with bupivacaine spinal anesthesia[40].

Gastrointestinal Effects of Spinal Anesthesia

Sympathetic innervation to the abdominal organs originates from T6 to L2. Following a spinal block, sympathetic blockade and the subsequent dominance of parasympathetic activity lead to increased secretions, sphincter relaxation, and bowel constriction.

Heightened vagal activity post-sympathetic nerve block triggers increased gastrointestinal peristalsis, often resulting in nausea. Additionally, nausea may stem

from gut ischemia induced by hypotension, which stimulates the production of serotonin and other emetogenic substances. The incidence of intraoperative and postoperative nausea and vomiting (IONV) in non-obstetric surgery can reach up to 42%, rising to as high as 80% in parturient women[40].

Hepatic and Renal Effects of Spinal Anesthesia

Hepatic blood flow is directly linked to arterial blood flow without autoregulation. Therefore, as arterial blood flow decreases following spinal anesthesia, so does hepatic blood flow. Maintaining the mean arterial pressure (MAP) post-spinal anesthesia ensures the preservation of hepatic blood flow. Patients with hepatic disease require careful monitoring and blood pressure control during anesthesia to safeguard hepatic perfusion. While no definitive studies have determined the superiority of regional versus general anesthesia in liver disease patients, either can be administered as long as MAP remains close to baseline.[40]

Renal blood flow, on the other hand, is autoregulated, with kidneys maintaining perfusion when MAP stays above 50 mm Hg. Temporary reductions in renal blood flow may occur if MAP drops below 50 mm Hg, but renal function typically returns to normal once blood pressure normalizes. Attention to blood pressure post-spinal anesthesia is crucial to maintaining MAP close to baseline. Importantly, spinal anesthesia does not disrupt the autoregulation of renal blood flow, as evidenced by minimal changes in renal perfusion observed in sheep following spinal anesthesia.

Factors affecting level of spinal block

Numerous factors have been proposed as potential determinants of spinal block level, broadly categorized into four main groups: (1) attributes of the local anesthetic solution, (2) patient-related variables, (3) aspects of the spinal block technique, and (4) diffusion dynamics. Attributes of the local anesthetic solution encompass factors such

as baricity, dosage, concentration, and volume administered[41]. Patient-related variables include age, weight, height, gender, intra-abdominal pressure, spinal column anatomy, cerebrospinal fluid characteristics, and patient positioning. Techniques of spinal block involve considerations like injection site, injection speed, needle bevel direction, injection force, and the inclusion of vasoconstrictors. While these factors have been theorized to influence the spread of anesthetic in the spinal region, only a few have demonstrated significant alteration in block distribution when other influencing factors remain constant.

Site of Injection

The injection site of local anesthetics for spinal anesthesia can influence the level of block achieved. For instance, in certain studies, the administration of isobaric spinal 0.5% bupivacaine at interspaces L2–L3, L3–L4, and L4–L5 has been associated with a sensory block reduction of two dermatomes per interspace. However, there is no discernible difference in nerve block height when hyperbaric bupivacaine or dibucaine is injected as a spinal anesthetic across different interspaces[41][42].

Age

Some studies have indicated varying alterations in nerve block height following spinal anesthesia in elderly patients compared to younger individuals, while others have found no significant difference. These investigations involved both isobaric and hyperbaric 0.5% bupivacaine[43].

Isobaric bupivacaine seems to elevate nerve block height, whereas hyperbaric bupivacaine shows no apparent change in nerve block height with advancing age. However, any potential correlation between age and spinal anesthesia height alone does not appear robust enough to serve as a reliable predictor in clinical practice. Similar to the role of injection site, it seems that baricity predominantly influences

nerve block height following spinal anesthesia in older populations, with age not acting as an independent determinant[44].

Position

The positioning of the patient is crucial in determining the level of block following hyperbaric and hypobaric spinal anesthesia, but not for isobaric solutions. Variations in positioning such as sitting, Trendelenburg, and prone jackknife positions can significantly influence the distribution of the local anesthetic, primarily due to the gravitational effects[45].

The level of spinal nerve block is determined by the combination of the baricity of the local anesthetic solution and patient positioning. For instance, sitting posture combined with a hyperbaric solution can induce analgesia in the perineum. Trendelenburg positioning also impacts the spread of hyperbaric and hypobaric local anesthetics due to gravitational effects. Prone jackknife positioning, typically utilized for rectal, perineal, and lumbar procedures with a hypobaric local anesthetic, prevents upward spread of the spinal block post-injection[45].

Flexing the hips and knees of a supine patient flattens lumbar lordosis and reduces pooling of local anesthetic in the sacral area. When combined with Trendelenburg positioning, this may facilitate upward spread. This position may inadvertently occur during urinary catheterization following spinal insertion[45].

Speed of Injection

The impact of injection speed on spinal nerve block height has been investigated, but findings in the literature are inconsistent. Studies using isobaric bupivacaine have shown no variation in spinal nerve block height with different injection speeds[46]. Despite the lack of effect on nerve block height, it is recommended to administer a smooth, slow injection when delivering a spinal anesthetic. Forceful injection,

especially if the syringe is not tightly connected to the spinal needle, may result in needle disconnection from the syringe and subsequent loss of local anesthetic[46].

Volume, Concentration, and Dose of Local Anesthetic

Maintaining consistency in the volume, concentration, or dose of local anesthetic while altering other variables poses a challenge, making it difficult to conduct high-quality studies investigating these factors individually. Axelsson et al. demonstrated that the volume of local anesthetic can impact both the height and duration of spinal nerve block when equivalent doses are administered[47].

Similarly, Peng et al. found a direct correlation between the concentration of local anesthetic and the effective anesthesia dose. However, when it comes to determining the duration of spinal nerve block, the dose of local anesthetic emerges as the primary determinant, with neither volume nor concentration of isobaric bupivacaine or tetracaine affecting block duration when the dose remains constant. Numerous studies have consistently shown that higher doses of local anesthetic lead to longer durations of spinal nerve block. It is crucial to consider not only the dose of local anesthetic but also its volume and concentration during spinal anesthesia to avoid over- or under-dosing the patient[47].

The utilization of hyperbaric solutions diminishes the significance of dose and volume, except in instances where doses of hyperbaric bupivacaine equal to or less than 10 mg are employed, resulting in reduced cephalad spread and shorter durations of action. However, doses ranging between 10 and 20 mg of hyperbaric bupivacaine yield comparable nerve block heights. When employing hyperbaric solutions, it's essential to recognize that patient positioning and baricity exert the most influence on nerve block height, except in cases of low-dose hyperbaric bupivacaine usage[48][49].

ROPIVACAINE

INTRODUCTION

Ropivacaine, a newer and longer-lasting local anesthetic belonging to the amino amide group, was synthesized by Ekenstam in 1957 but wasn't introduced for clinical use until 1996. Chemically akin to bupivacaine and mepivacaine, ropivacaine is a pipecoloxylidide local anesthetic[50].

Research revealed that butyl derivatives of pipecoloxylidides, such as bupivacaine, posed greater cardiotoxicity risks, leading to numerous cardiac arrests. In response, ropivacaine was developed as a pure S-enantiomeric form of pipecoloxylidides. While ropivacaine has been available internationally for over three decades, its introduction to the Indian market is relatively recent[50].

Ropivacaine is gaining popularity among anesthesiologists and is extensively utilized in various regional anesthesia techniques, including infiltration, peripheral nerve blocks, spinal anesthesia, epidural anesthesia, and caudal epidural blocks in pediatric patients[49].

CHEMICAL STRUCTURE

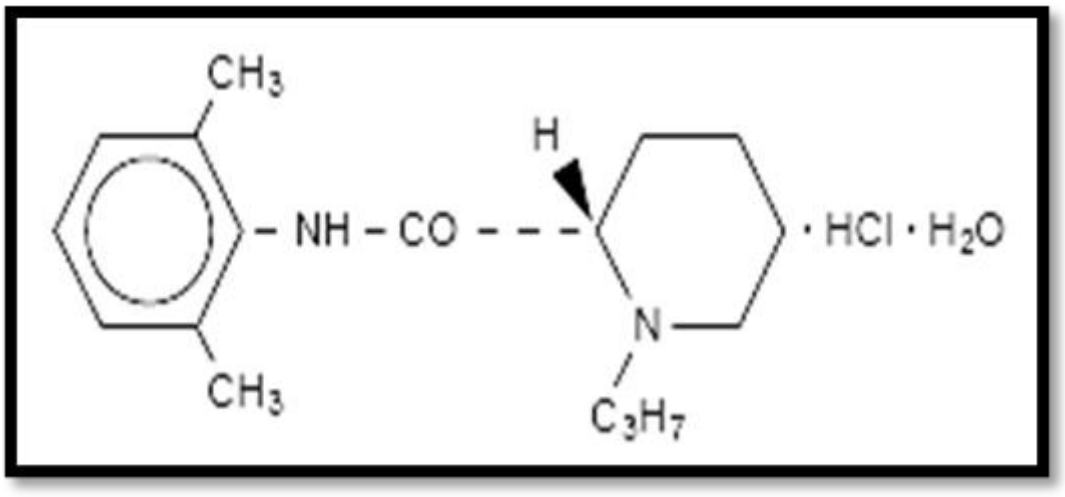


Figure 7: Chemical structure of ropivacaine[50]

Ropivacaine is an amino amide local anaesthetic agent, chemically described as S-(-)-1-propyl-2',6'-pipecoloxylidide hydrochloride monohydrate. The International Union of Pure and Applied Chemistry name is (S)-N-(2,6-dimethylphenyl) -1-propylpiperidine-2-carboxamide. It's molecular formula is C17H26N2O•HCl•H2O and it has a molecular weight of 328.89[51].

Ropivacaine is a white crystalline powder. At 25°C ropivacaine hydrochloride has a solubility of 53.8 mg/mL in water and a distribution ratio between n-octanol and phosphate buffer at pH 7.4 of 14:1. The pKa of ropivacaine is 8.07 which is very similar to that of bupivacaine (8.1)[52] .

However, ropivacaine has a much lesser lipid solubility as compared to bupivacaine and mepivacaine. This can be explained on the basis of presence of a propyl (3 Carbon) side chain in ropivacaine as compared to a butyl (4 Carbon) side chain in the other two local anaesthetics. This lower lipid solubility of ropivacaine has a significant effect on the block characteristics of ropivacaine as discussed ahead[51]

Mechanism Of Action And Correlation With Structure

Ropivacaine reversibly inhibits the voltage gated sodium channels present on the nerve cell membranes thus preventing the influx of sodium ions into the cells. This:

I) Block generation and conductance of nerve impulses.

II) Slows propagation of nerve impulses

III) Reduces the rate of rise of action potential

Almost all local anaesthetic agents block the unmyelinated C and myelinated Aδfibres, which transmit pain impulses, at the same rate.

The rate of blockade of motor fibres (Aα and Aβ), however depends upon the physio chemical properties like pKa and lipid solubility of the individual drug. As ropivacaine is less lipid soluble than bupivacaine, the Aα and Aβ blockade is slower and hence motor blockade is less potent. Studies of lumbar epidural block in humans have confirmed that equal volumes and concentrations of bupivacaine and ropivacaine produce similar degree of sensory block but the motor block produced by ropivacaine is slower in onset, lesser in intensity and shorter in duration[51].

Clinically the order of blockade of nerve fibres is autonomic, sensory and motor, while the regression of the block occurs in reverse order[50].

The nerve impulse transmission is lost in the following order:

The order of the loss of nerve function is

1. Pain
2. Temperature
3. Touch
4. Proprioception
5. Skeletal muscle tone.

Pharmacokinetics

Absorption :

The systemic concentration of ropivacaine depends on the total dose and concentration of drug given, the route of administration, the patient's haemodynamic state and the vascularity of the site of administration. When administered in the epidural space, ropivacaine has a biphasic absorption. The half-lives of the two phases (mean+ SD) are 14+7 minutes and 4.2 +0.9 hours respectively[51].

Distribution :

After intravascular infusion, ropivacaine has a steady state of distribution of 41 ± 7 litres. It is 94% protein bound, mainly to α1-acid glycoprotein. In case of continuous epidural infusion of ropivacaine the plasma concentration can rise due to increased protein binding and reduced clearance. Ropivacaine can easily cross the placenta[51].

Metabolism and excretion :

Ropivacaine is extensively metabolized by the liver, predominantly by the cytochrome P4501A mediated aromatic hydroxylation to produce 3 – hydroxyl ropivacaine. After a single IV dose, approximately 37% of the total dose is excreted in the urine as both free and conjugated 3-hydroxy ropivacaine. An additional unquantified amount of 2 – hydroxyl – methyl ropivacaine has also been identified as metabolite[51].

Ropivacaine metabolites are mainly excreted via kidney. After i.v. administration 86% of the dose is excreted in urine of which only 1% is in unchanged form. Following IV administration, ropivacaine has a mean ± SD total plasma clearance of 387 ± 107 mL/min, an unbound plasma clearance of 7.2 ± 1.6 L/min and a renal clearance of 1 mL/min. The mean ± SD terminal half life is 1.8 ± 0.7 h and 4.2 ±1.0 h after i.v. and epidural administration respectively[51].

Pharmacodynamics

Central Nervous System &Cardio-VascularSystem :

Ropivacaine exhibits a higher threshold for both cardiac and neurotoxicity compared to bupivacaine, attributed to its lower lipid solubility and stereo-selective properties. This characteristic applies to both isomers of ropivacaine, which have demonstrated less cardiodepressant effects than their respective bupivacaine counterparts in animal

studies. In healthy volunteers, CNS toxicity manifests earlier than cardiac toxicity during intravenous infusion[52].

Potency :

Lipid solubility of a local anaesthetic correlates well with its potency and toxicity. Compounds which are more lipophilic penetrate the nerve cell membrane more readily. Thus, fewer molecules are required to produce the desired conduction blockade.

Others :

Continuous epidural infusion of 0.375 % and 0.188% ropivacaine has been shown to inhibit platelet aggregation in plasma.

Adverse Effects

Excessive plasma levels are due to over dosage, unintentional intravascular injection or slow metabolic degradation. The mean doses at which CNS symptoms of toxicity begin to occur in human beings are 4.3 and 0.6 mcg/mL of total and free plasma concentrations respectively. When prolonged blocks are used the risks of reaching a toxic plasma concentration or inducing local neural injury are increased. Various possible side effects include

a. Injection site pain

b. Cardiovascular system toxicity: Vasovagal reaction, syncope, postural hypotension, non-specific ECG abnormalities which include wide QRS complexes, increased conduction time and reduced contractility.

c. Gastrointestinal system toxicity: Faecal incontinence, tenesmus, nausea, vomiting.

d.Central nervous system toxicity: Tremor, Horner's syndrome, dyskinesia, neuropathy, vertigo, convulsion and coma. Because of depressant effect of ropivacaine on medulla, excitatory stage of CNS might not occur.

e.Liver and Biliary system toxicity: Jaundice

f.Metabolic disorders: Hypomagnesemia[52]

Local anesthetic	Plain		With epinephrine	
	Maximum dose	Maximum dose	Maximum dose	Maximum dose
Bupivacaine	2 $mg \cdot kg^{-1}$	175 mg	3 $mg \cdot kg^{-1}$	225 mg
Levobupivacaine	2 $mg \cdot kg^{-1}$	200 mg	3 $mg \cdot kg^{-1}$	225 mg
Lidocaine	5 $mg \cdot kg^{-1}$	350 mg	7 $mg \cdot kg^{-1}$	500 mg
Mepivacaine	5 $mg \cdot kg^{-1}$	350 mg	7 $mg \cdot kg^{-1}$	500 mg
Ropivacaine	3 $mg \cdot kg^{-1}$	200 mg	3 $mg \cdot kg^{-1}$	250 mg
Prilocaine	6 $mg \cdot kg^{-1}$	400 mg	8 $mg \cdot kg^{-1}$	600 mg

Figure 8: 'Toxic Doses of Local Anaesthetic agents'[53]

Advantages Over Other Local Anaesthetics

Ropivacaine offers a more distinct blockade, providing improved differentiation between sensory and motor functions. Consequently, it is favored for labor analgesia and postoperative pain relief. In comparison to bupivacaine, ropivacaine induces a less intense motor blockade of shorter duration, facilitating earlier patient mobilization and discharge. This leads to reduced morbidity and treatment costs. Additionally, ropivacaine exhibits lower systemic toxicity and a more favorable cardiovascular profile than bupivacaine. Developed as a safer alternative to bupivacaine, ropivacaine maintains the desirable blocking properties of racemic bupivacaine[50].

LEVOBUPIVACAINE

Introduction

Levobupivacaine is the S(–)-enantiomer of the local anaesthetic bupivacaine. Racemic bupivacaine (herein called bupivacaine) has traditionally been the longest acting local anaesthetic commercially available and is widely used.Its prolonged duration of action reduces the need for repeated administration or top-up doses.Its clinical profile closely resembling that of bupivacaine. However, current preclinical safety and toxicity data show an advantage for levobupivacaine over bupivacaine[54][55]

Chemical Structure

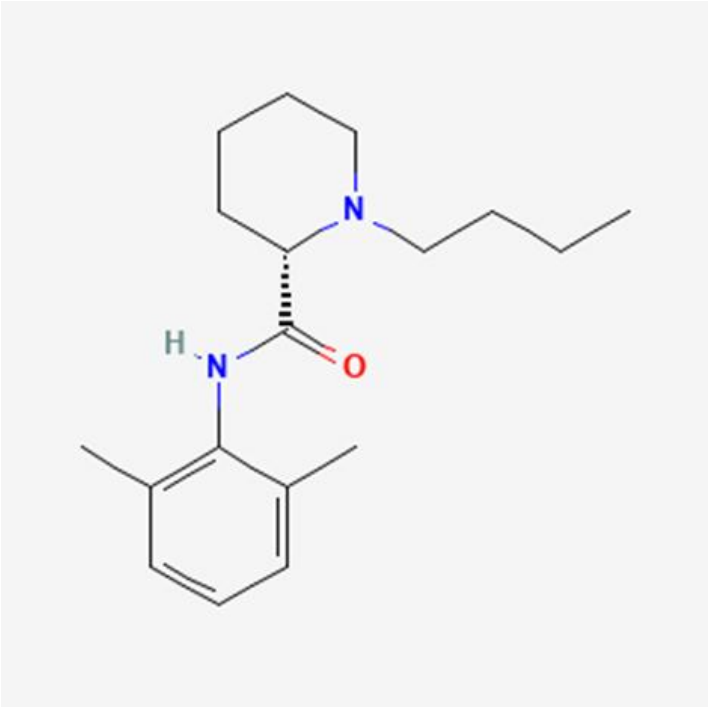


Figure 9: Chemical structure of levobupicaine[54]

Physical Properties

Levobupivacaine is a white solid. Levobupivacaine hydrochloride has a solubility of 0.0267 mg/mL in water. The pKa of Levobupivacaine is 8.0 which is very similar to that of bupivacaine (8.1).

Mechanism Of Action And Correlation With Structure

Levobupivacaine block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibers. Specifically, the drug binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization[55]

Pharmacokinetics

Absorption :

The plasma concentration of levobupivacaine following therapeutic administration depends on dose and also on route of administration, because absorption from the site of administration is affected by the vascularity of the tissue. Peak levels in blood were reached approximately 30 minutes after epidural administration, and doses up to 150 mg resulted in mean Cmax levels of up to 1.2 μg/mL[54].

Distribution :

After intravenous administration of 40 mg in healthy volunteers, levobupivacaine has a steady state of distribution of 66.91 ±18.23 L. It is 97% protein bound. Its classified as category B drug in pregnancy[54].

Metabolism and excretion :

Levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine or feces. In vitro studies using [14 C] levobupivacaine showed that CYP3A4 isoform and CYP1A2 isoform mediate the metabolism of levobupivacaine to desbutyl levobupivacaine and 3-hydroxy levobupivacaine, respectively. In vivo, the 3-hydroxy levobupivacaine appears to undergo further transformation to glucuronide

and sulfate conjugates. Metabolic inversion of levobupivacaine to R(+)-bupivacaine was not evident both in vitro and in vivo[55].

Following intravenous administration, recovery of the radiolabelled dose of levobupivacaine was essentially quantitative with a mean total of about 95% being recovered in urine and feces in 48 hours. Of this 95%, about 71% was in urine while 24% was in feces. After intravenous administration of 40 mg in healthy volunteers clearance 39.06 ±13.29 L/h.The mean half life is 3.3 hours[55].

Pharmacodynamics

Central Nervous System &Cardio-VascularSystem :

Levobupivacaine demonstrates a reduced risk of CNS toxicity compared to bupivacaine in human volunteers. In a study where volunteers received intravenous doses of levobupivacaine (mean 67.7mg), central or peripheral nervous system disorders were observed in 36% of recipients. Additionally, intravenous levobupivacaine induces CNS depression, including tinnitus, as observed on EEG. However, the magnitude and area of effect are diminished with levobupivacaine compared to bupivacaine. For example, levobupivacaine leads to a lesser decrease in high alpha power and does not cause the increase in theta power in specific brain regions seen with bupivacaine[54][55].

Moreover, levobupivacaine exhibits a milder effect on atrioventricular conduction and QRS complex duration, along with less impairment of contractile function in isolated animal hearts. It also demonstrates lower potency in blocking cloned human heart sodium and potassium channels[55].

Potency :

The nerve blocking potency of levobupivacaine is similar to that of bupivacaine and the R(+)-enantiomer of bupivacaine (dexbupivacaine) in vitro.In vivo, the

comparative effects of levobupivacaine and dexbupivacaine or bupivacaine were affected by the route of administration and concentration[55].

Adverse Effects

- Cardiovascular system toxicity: bradycardia, hypotension, sudden cardiovascular collapse
- Gastrointestinal system toxicity: nausea (12%), vomiting (14%), constipation (7%),
- Central nervous system toxicity: Headache (7%) disorientation, drowsiness, slurred speech, which may culminate with tonic-clonic seizures
- Hematological: Anemia (12%), increased serum albumin level, leukocytosis and purpura

Advantages Over Other Local Anaesthetics

Levobupivacaine is designed to be a safer substitute for bupivacaine, maintaining the beneficial blocking characteristics of racemic bupivacaine. It exhibits a superior cardiac stability and has less systemic toxicity compared to bupivacaine[55]

MATERIALS AND METHODS

Type of Study: A One Year Double blind Randomized controlled trial

Study duration and population:

Patients aged 20-40 years referring to “American Society of Anaesthesiologists”(ASA) II Undergoing lower segment cesarean section under spinal anaesthesia at “KLE’s Dr Prabhakar Kore Charitable Hospital And Medical Research Centre, Nehru Nagar, Belagavi” during the period from “March 2023 to April 2024”.

(Data Collection-12 Months)

Inclusion criteria:	**Exclusion criteria** *:*
● ASA status II.	● Patient undergoing emergency surgery.
● Between the ages of 20 to 40 years	● Patient who are unable to give consent.
● Weight ranging from 60-90kg	● Patient with obstetric complications
● Height ranging from 155-185cm (5ft to 6ft)	● Patient with suspected fetal compromise
● Patients for elective LSCS under spinal anesthesia	● Coagulopathy “HELLP, DIC, Eclampsia”
● Provides Consent	● Patients who do not fulfill inclusion criteria.

Sample Size Calculation

The mean and standard deviation was used to calculate minimum sample size.

$$n = \frac{(z_\alpha + z_\beta)^2(s_1^2 + s_2^2)}{(\bar{X}_1 - \bar{X}_2)^2}$$

where "zα is linked with the level of significance and zβ is with the power of the test". For 5% level of the significance zα =1.96 and for 80% power of the test zβ =0.84. Using this data the Sample Size obtained was 38. The sample size was increased to 75 cases in two groups for a cumulative sample size of 150.

Sampling procedure:

A one-year randomized clinical trial.

Methodology:

Using randomization software, 75 patients who satisfied the inclusion criteria were assigned to each study group before being put under anesthesia, following approval from the ethics committee and informed permission.

Group R: Patients will be administered with 2.2ml of Hyperbaric ropivacaine in the L3-L4 sub arachnoid space under strict aseptic precaution using a 25G spinal-needle after confirming adequate flow of clear CSF.

Group L: Patients will be administered with 2.2ml of Hyperbaric levobupivacaine in the L3-L4 sub arachnoid space under strict aseptic precaution using a 25G spinal-needle after confirming adequate flow of clear CSF.

At the preoperative holding area, an 18G IV cannula was used to secure intravenous access.

All standard monitors, such as an Electrocardiogram, Non-invasive blood pressure, and pulse oximeter were attached after bringing the patients into the operating theater.

SpO2, mean arterial pressures along with systolic and diastolic pressure and heart rate were all recorded preoperatively along with Preloading the patient with lactated Ringer's intravenous fluid (10-15 ml per kg body weight).

The patient in a sitting position and following aseptic precautions, a subcutaneous wheal was raised at the L3-L4 (lumbar) interspace using 2 ml of 2 % lidocaine. a 25G spinal needle was introduced into the Subarachnoid space of the patient at relevant level. Spinal anesthesia was performed with the patient in seated position at the corresponding space by using a midline approach. After confirmation of adequate flow of clear CSF the study drug was injected at 0.2ml per second all with the spinal needle bevel facing cephalad.

Group R was administered with 2.2ml of Hyperbaric ropivacaine in the L3-L4 sub arachnoid space under strict aseptic precaution using a 25G spinal needle after confirming adequate flow of clear CSF. While Group L was administered 2.2ml of hyperbaric levobupivacaine.

The patient was then made to lie supine upon administration of spinal medication. Maternal hemodynamic parameters were measured and baseline values were defined as blood pressure and heart rate values.

An anesthetist prepared the study drug solutions following written instructions and without being aware of the study's design.

Prior to induction, the patient's Heart rate and blood pressure along with mean arterial pressure were recorded after which it was measured every 2,4,6,8,10,15,30,45,60,90 minutes. The level and onset of sensory block after spinal anaesthesia was assessed using pin prick method.

Assessment of motor block was done using Bromage scale,

Grade 0	no paralysis, able to flex hips/knees/ankles;
Grade 1	able to flex knees and ankles, unable to raise extended legs;
Grade 2	able to flex ankles, unable to flex knees and hips
Grade 3	Unable to flex ankles, only able to move toes
Grade 4	Total paralysis

Following surgery, the patient was monitored every five minutes in the postoperative care unit for two points of sensory block regression and motor movement recovery. Heart rate, blood pressure, SpO2, and respiratory rate were measured every two minutes for the first ten minutes; after that, they were measured every fifteen minutes until the 90-minute mark.

During surgery, every patient received oxygen at a rate of 5L/min via an oxygen mask. The patients were observed for hypotension, nausea, vomiting and shivering. Ephedrine 6mg before the delivery of the baby and Mephentermine 6 mg after, was used to treat hypotension, along with fluids. A 4 mg injection of ondansetron was administered to relieve nausea and vomiting.

Statistical Analysis:

Microsoft-Excel and the statistical program R-4.4.0 were used for data analysis.. Categorical variables given in the form of frequency tables. Continuous variables given in Mean ± SD / Median (Min, Max) form. The ‘chi square test’ was employed to examine the relationship between groups and categorical variables..The ‘QQ plot and Shapiro-Wilk test’ were used to determine whether the variable was normal. Otherwise, non- parametric tests were used.The variables over groups were compared using ‘two sample t test and mann whitney U’ was the test utilized to compare the distribution of variables over groups. Comparison of variables over time was done using ‘Friedman Test’. P-value less than or equal to 0.05 indicating statistical significance.

RESULTS

Data contains measurements on 150 subjects which are divided into 2 groups of 75 subjects each. The following table gives the Comparison of Demographic Details over Groups.

TABLE 1: Comparison of Demographic details over groups.

Variables	Sub Category	Group L	Group R	Total	P-value
Age (in years)	Mean ±SD Median(Min, Max)	26.16 ± 4.29 26 (20, 36)	25.07 ± 3.39 24 (19, 33)	25.61 ± 3.89 25 (19, 36)	0.1970^{MW}
Sex	Female	75 (100%)	75 (100%)	150 (100%)	1^{C}
Weight (in Kg)	Mean ± SD Median (Min, Max)	68.63 ± 7.35 68 (58, 95)	66.04 ± 6.3 65 (55, 82)	67.33 ± 6.95 66 (55, 95)	**0.0254^{MW*}**

" indicates statistical significance".*

For age, Group L has a mean age of 26.16 ± 4.29years with a median of 26 years (range 20-36), while Group R exhibits a mean age of 25.07 ± 3.39 years with a median of 24 years (range 19-33). The Mann Whitney U test reveals no difference in age across the groups despite these minor variations.(p-value=0.1970).

In terms of sex distribution, both Group L and Group R consist entirely of female participants, with each group having 100% female representation (p-value = 1).

Regarding weight, Group L displays a mean weight of 68.63 ± 7.35 kg with a median of 68 kg (range 58-95), while Group R shows a mean weight of 66.04 ± 6.3 kg with a median of 65 kg (range 55-82). The two groups have observably significant difference in weight (p-value = 0.0254) from Mann Whitney U test, indicating that Group L has a higher average weight compared to Group R.

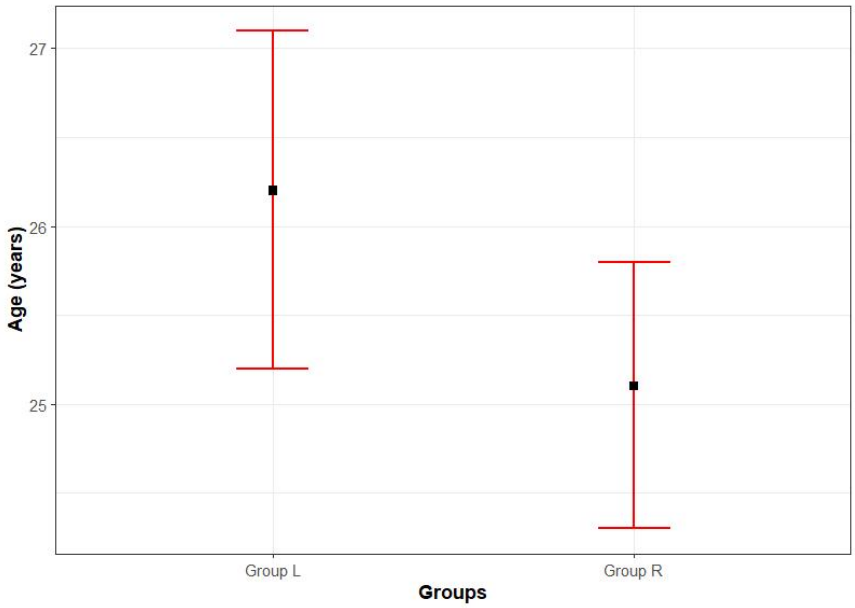


Figure 1:Mean Plot of Age over groups.

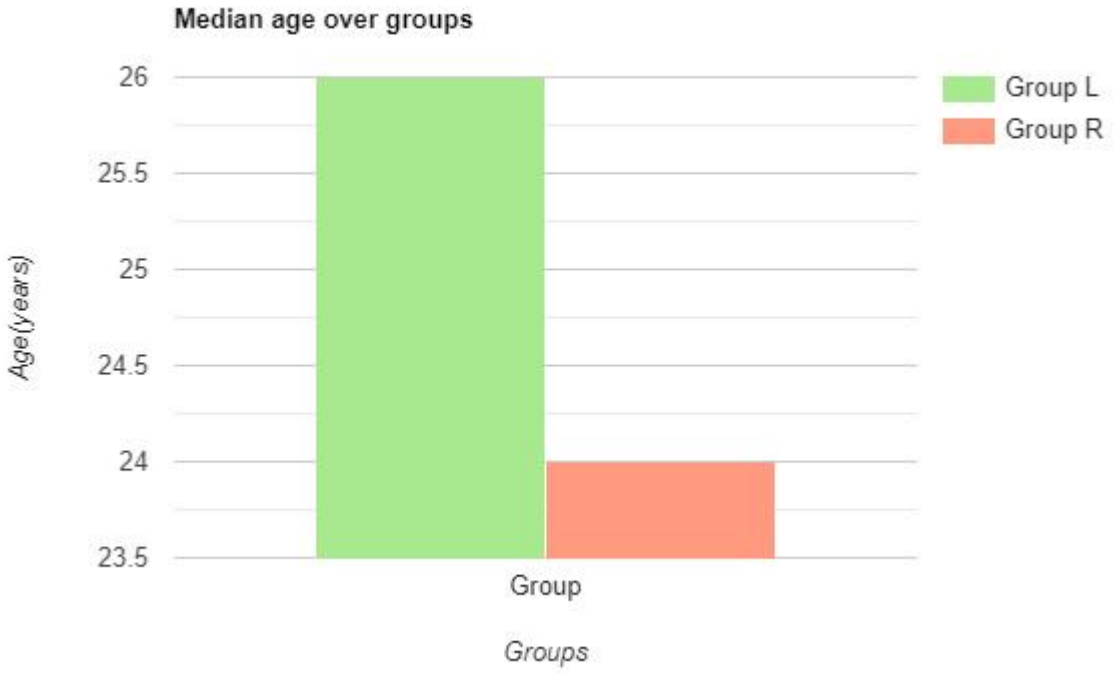


Figure 2:Median Graph of Weight over groups.

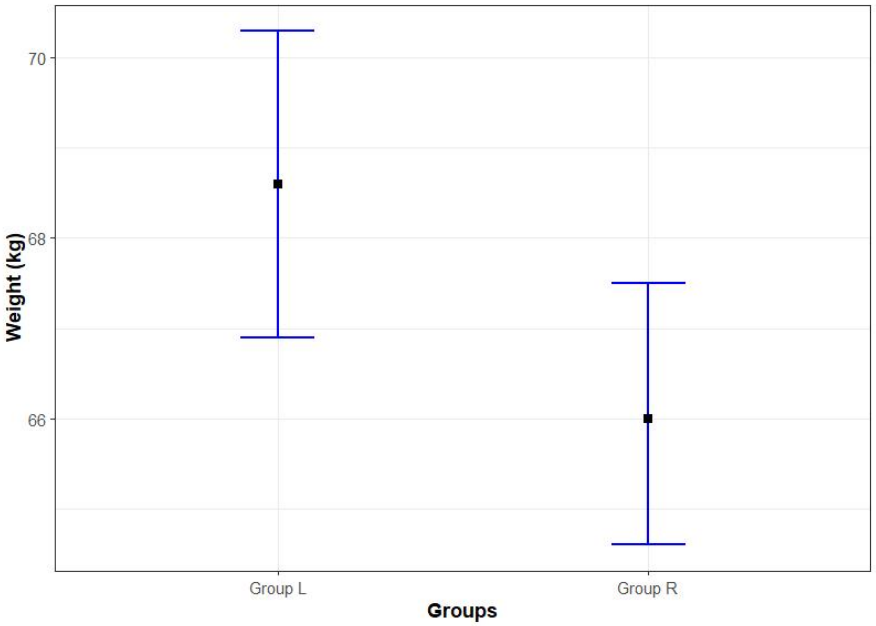


Figure 3:Mean Plot of Weight over groups.

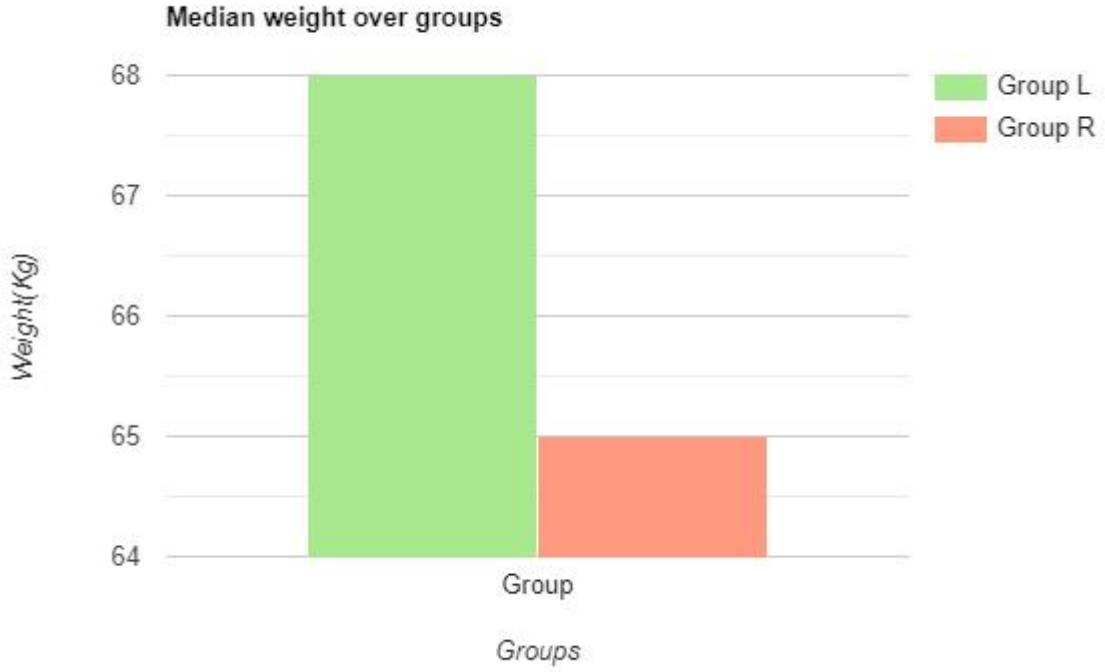


Figure 4:Median graph of Weight over groups.

Table 3: Comparison of sensory block details over groups.

Sensory block	Sub Category	Group L	Group R	Total	p-value
Onset at T10 (min)	Mean ±SD Median(Min, Max)	1.11 ±0.54 1 (0.5,2.5)	1.56 ±0.67 1.5 (0.5,3.5)	1.34 ± 0.65 1.45 (0.5, 3.5)	**< 0.001**^{MW*}
Duration of sensory block (min)	Mean ± SD Median (Min, Max)	165.59 ± 8.46 165 (150, 180)	145.17 ± 8.09 145 (130, 166)	155.38 ± 13.15 155.5 (130, 180)	**< 0.001**^{MW*}
Highest level of sensory block	T6	54 (72%)	57 (76%)	111 (74%)	0.7061^{MC}
	T7	20 (26.67%)	18 (24%)	38 (25.33%)	
	T8	1 (1.33%)	0 (0%)	1 (0.67%)	

With a mean Onset time of 1.11 ± 0.54 minutes, Group L has a quicker onset than Group Rs, which has a mean Onset time of 1.56 ± 0.67 minutes. The Mann-Whitney U test results show a significant distribution difference within the groups, with respect to onset of sensory block at T10 (p-value < 0.001), suggesting that Group L experiences a Sensory block with a faster onset.

Group L displays a longer duration, with a mean duration of 165.59 ± 8.46 minutes, while Group R's mean duration is shorter at 145.17 ± 8.09 minutes. Regarding the distribution of sensory block time between the groups, the Mann-Whitney U test indicates a significant distribution difference. (p-value < 0.001),suggesting that, in comparison to Group R, Group L experiences sensory block for a longer period of time.

In terms of the sensory block and the highest level achieved, the majority of patients in both groups reach the T6 level, with 72% and 76% in Group L and Group R respectively. The highest level of Sensory block does not differ across the groups, according to the results of the Chi square test.s. (p-value = 0.7061).

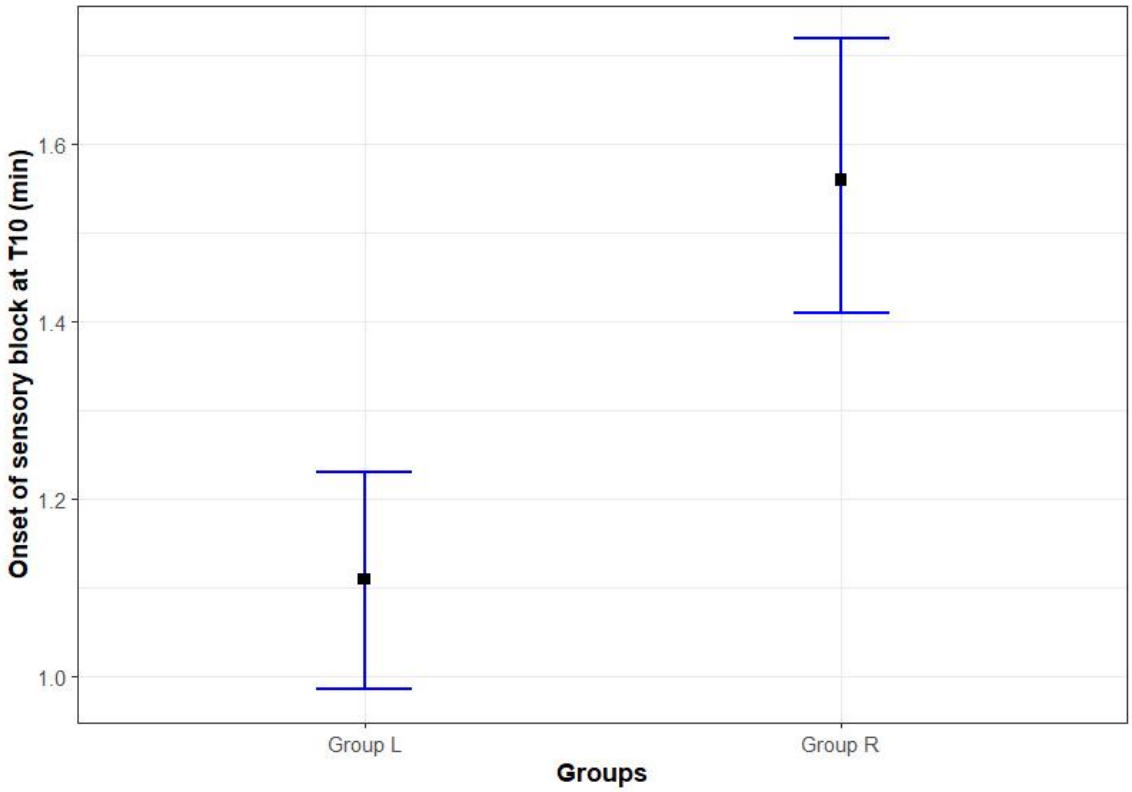


Figure 5: Mean plot of onset at T10 over groups.

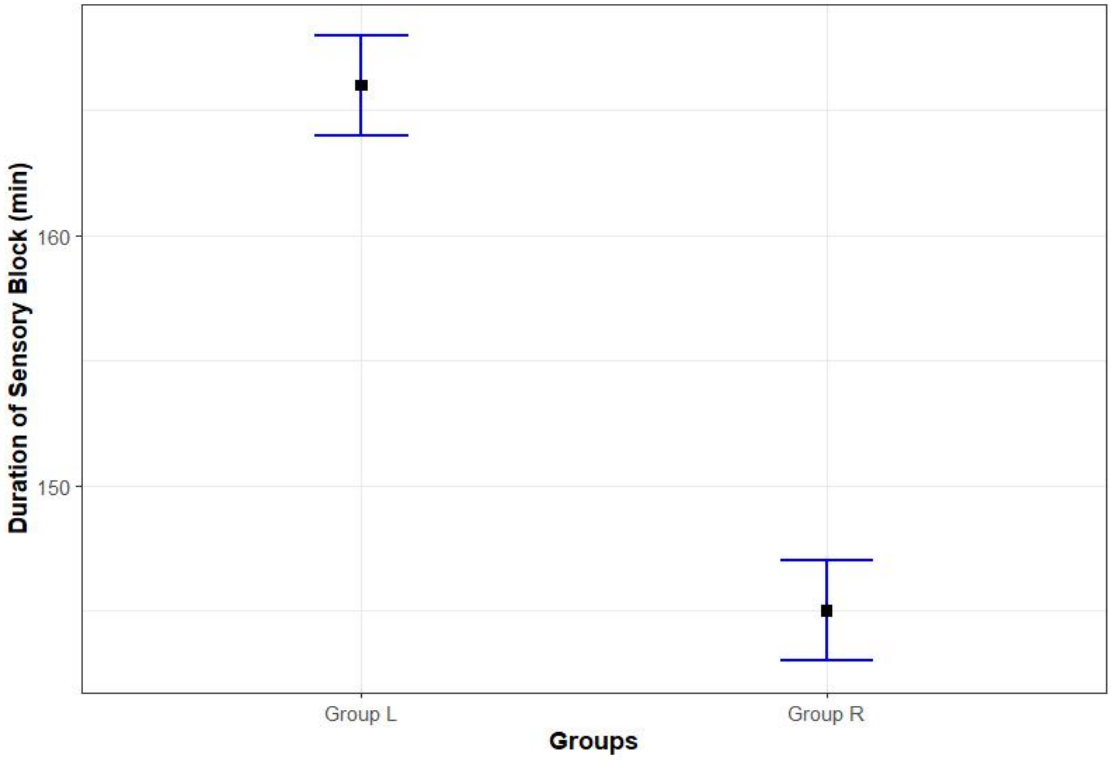


Figure 6: Mean plot of duration of sensory block over groups.

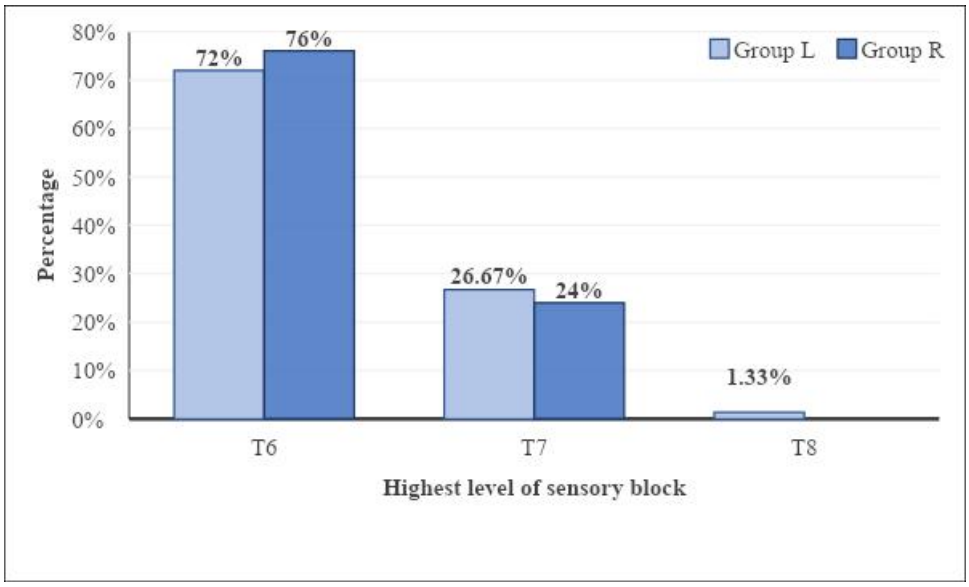


Figure 7: Distribution of the Highest level of Sensory block over groups.

The following table gives the comparison of motor block details over groups.

TABLE 4: Comparison of Motor Block details over groups.

Motor blockade	Sub Category	L	R	Total	p-value
Onset grade 3 motor blockade (min)	Mean ±SD Median(Min, Max)	1.16 ±0.53 1(0.5, 3)	2.01 ±0.85 2(0.5, 3.8)	1.58 ± 0.83 1.5 (0.5, 3.8)	**< 0.001^{MW*}**
Total duration (Movement of toes)	Mean ± SD Median (Min, Max)	161.33 ± 8.07 160 (140, 180)	140.32 ± 8.35 140 (120, 160)	150.83 ± 13.34 150 (120, 180)	**< 0.001^{MW*}**

With a mean onset time of 1.16 ± 0.53 minutes, Group L has a quicker onset than Group R, which shows a mean onset time of 2.01 ± 0.85 minutes. The distribution of grade 3 motor block and its onset varies significantly between the groups when the

Mann-Whitney U test is used to analyze the data(p-value < 0.001),suggesting that compared to Group R, Group L exhibits a faster start of grade 3 motor block.

Additionally, there are noticeable variations between the groups in the overall amount of time the motor block lasts (until movement of toes). Group L displays a longer duration, with a mean duration of 161.33 ± 8.07 minutes, while Group R's mean duration is shorter at 140.32 ± 8.35 minutes.Following examination using the Mann-Whitney U test, there is a significant difference in the distribution of the total motor block time (p-value < 0.001),demonstrating that Group L experiences from motor block for a longer period of time than Group R.

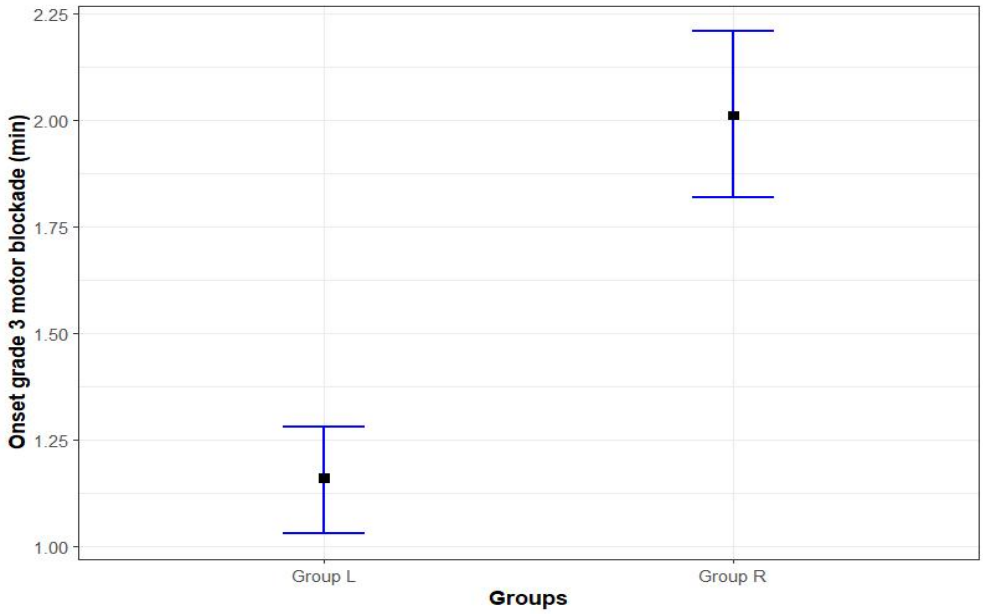


Figure 8:Mean plot of onset grade 3 motor blockade over groups.

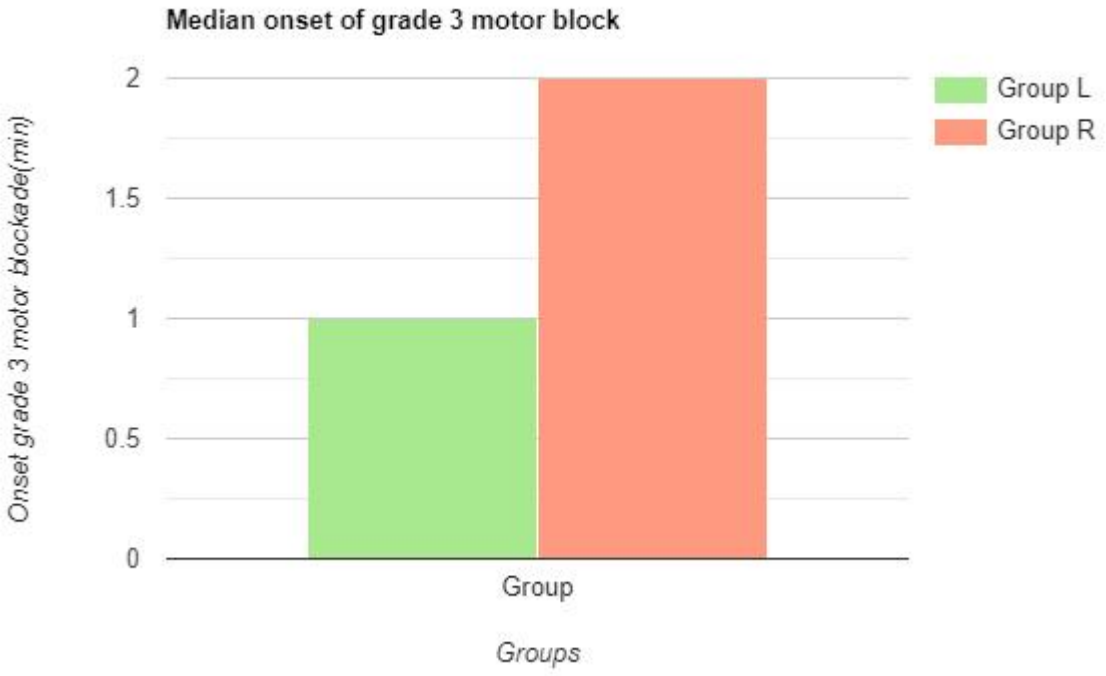


Figure 9:Median graph of onset grade 3 motor blockade over groups.

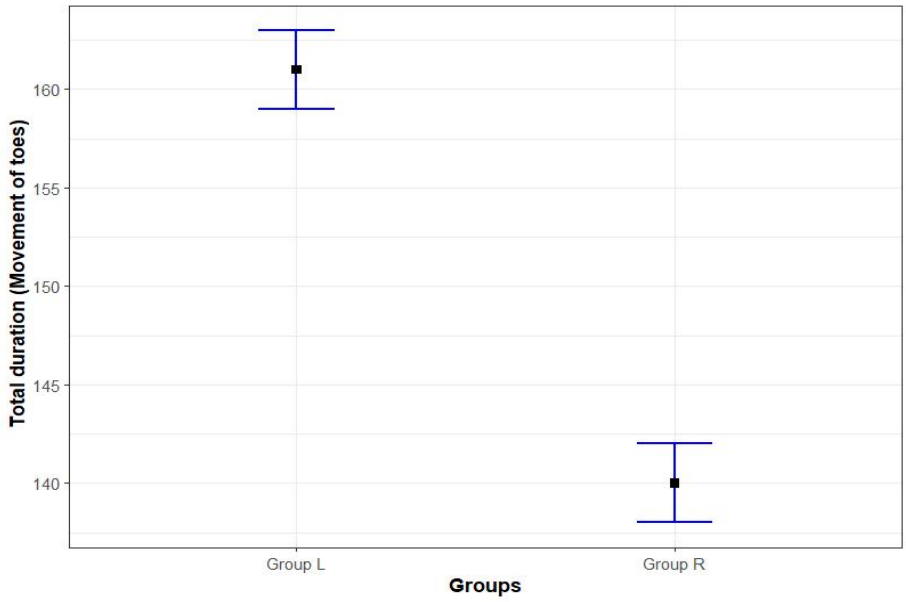


Figure 10: Mean plot of total duration (movement of toes) over groups.

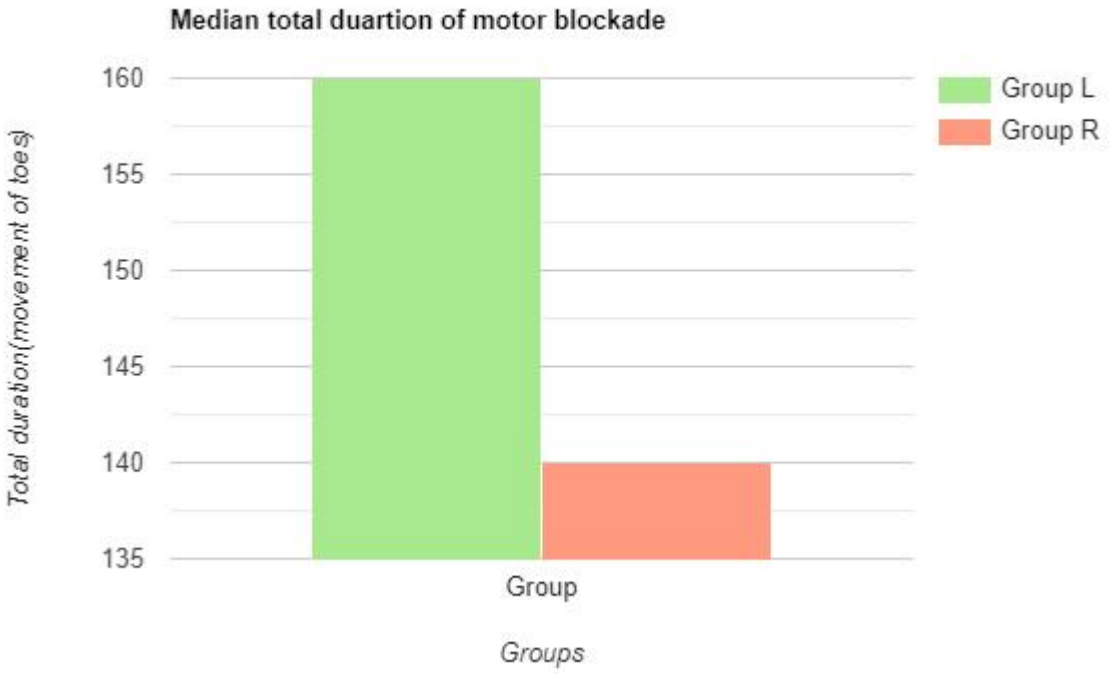


Figure 11: Median graph of total duration (movement of toes) over groups.

The following table gives the comparison of HR over time and group.

TABLE 5:Comparison of HR over Time and group.

Heart Rate	L	R	Total	P-value
0 min	91.21 ± 13.31 90 (57, 132)	88.17 ± 13.31 87 (60, 116)	89.69 ± 13.35 89 (57, 132)	0.1640^{t}
2 mins	92.87 ± 13.88 90 (60, 122)	86.57 ± 14.01 84 (58, 118)	89.72 ± 14.25 88 (58, 122)	**0.0065^{t}***
4 mins	90.85 ± 18.5 92 (16, 133)	86.55 ± 14.55 85 (58, 127)	88.7 ± 16.73 87 (16, 133)	**0.0445^{MW}***
6 mins	89.4 ± 15.2 89 (53, 150)	83.92 ± 17.28 83 (53, 128)	86.66 ± 16.45 86 (53, 150)	**0.0169^{MW}***
8 mins	89.48 ± 15.53 89 (59, 135)	83.24 ± 14.85 81 (53, 113)	86.36 ± 15.46 86.5 (53, 135)	**0.0189^{MW}***
10 mins	90.6 ± 16.35 88 (59, 136)	84.47 ± 15.94 85 (52, 119)	87.53 ± 16.38 87 (52, 136)	**0.0214^{t}***
15 mins	93.55 ± 15.27 91 (58, 129)	85.87 ± 15.65 86 (56, 121)	89.71 ± 15.88 88.5 (56, 129)	**0.0028^{t}***
30 mins	94.77 ± 14.15 93 (62, 140)	87.24 ± 17.22 86 (55, 137)	91.01 ± 16.15 89 (55, 140)	**0.0040^{t}***
45 mins	92.16 ± 15.33 90 (60, 130)	84.39 ± 16.05 85 (52, 130)	88.27 ± 16.12 88 (52, 130)	**0.0029^{t}***
60 mins	86.41 ± 15.93 85 (52, 123)	81.08 ± 13.69 81 (50, 112)	83.75 ± 15.04 82 (50, 123)	**0.0294^{t}***
90 mins	85.4 ± 15.61 85 (53, 120)	81.91 ± 12.11 81 (60, 118)	83.65 ± 14.03 82.5 (53, 120)	0.1885^{MW}
p-value	**< 0.001^{F}***	**< 0.001^{F}***	-	-

*Abbreviation:" MW – Mann-Whitney U test, t – Two sample t test, F – Friedman's test, * indicates statistical significance."*

At 0 min, Group L exhibits a slightly higher mean HR of 91.21 ± 13.31 bpm compared to Group R's mean HR of 88.17 ± 13.31 bpm. However, there is no statistical significance in this difference(p-value = 0.1640). Subsequent time intervals reveal noteworthy variations in HR between the two groups. At 2, 4, 6, 8, 10, 15, 30, 45, and 60 minutes, there are significant differences in heart rate (HR) amongst the two groups (p-value < 0.05) with Group L consistently exhibits a higher HR compared to Group R during these time points.

At 90 minutes, although Group L still exhibits a slightly higher mean HR than Group R (85.4 ± 15.61 bpm vs. 81.91 ± 12.11 bpm), the difference is analyzed to be statistically insignificant (p-value = 0.1885).

Using Friedman's test, it is observed that heart rate across time points showed statistically significant difference for both Group L and R (p-value < 0.001).

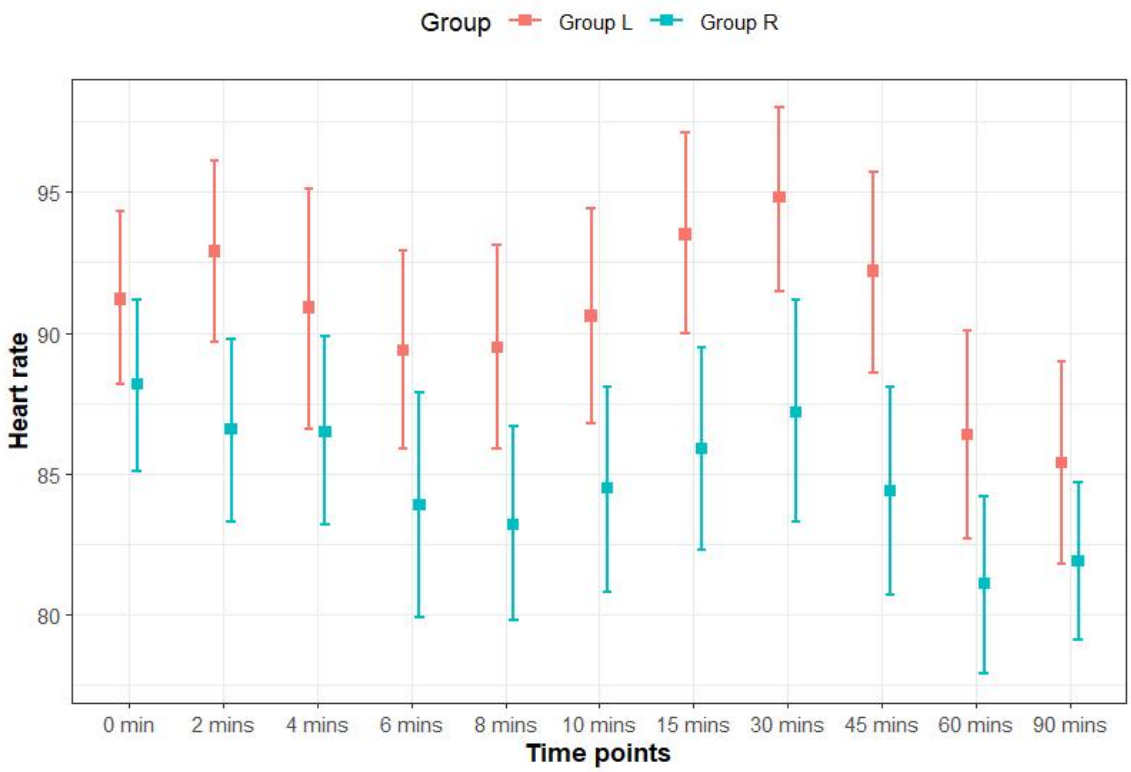


Figure 12: Mean plot of HR over time and groups.

The following table gives the comparison of SBP over time and group.

Table 8: Comparison of SBP over time and group.

SBP	Group L	Group R	Total	p-value
0 min	126.68 ± 14.2 126 (100, 166)	119.21 ± 12 118 (97, 145)	122.95 ± 13.63 122 (97, 166)	**< 0.001^{t*}**
2 mins	114.61 ± 15.05 114 (86, 145)	111.61 ± 13.37 112 (77, 139)	113.11 ± 14.26 113 (77, 145)	0.1988^{t}
4 mins	106.28 ± 17.73 105 (64, 152)	108.37 ± 13.91 109 (66, 140)	107.33 ± 15.91 107.5 (64, 152)	0.2722^{MW}
6 mins	103.67 ± 18.86 100 (66, 160)	106.83 ± 13.74 108 (62, 135)	105.25 ± 16.52 105 (62, 160)	0.0950^{MW}
8 mins	103.48 ± 17.09 100 (71, 159)	106.39 ± 13.57 108 (68, 137)	104.93 ± 15.45 105 (68, 159)	0.2505^{t}
10 mins	107 ± 17.58 105 (58, 162)	106.77 ± 12.74 107 (80, 139)	106.89 ± 15.3 106 (58, 162)	0.9281^{t}
15 mins	107.31 ± 16.12 104 (77, 154)	106.4 ± 11.78 105 (78, 142)	106.85 ± 14.08 105 (77, 154)	0.6947^{t}
30 mins	108.11 ± 15.27 107 (76, 158)	106.61 ± 11.76 106 (81, 137)	107.36 ± 13.61 106.5 (76, 158)	0.6627^{MW}
45 mins	111.37 ± 12.35 110 (86, 143)	108.49 ± 11.44 109 (64, 139)	109.93 ± 11.95 110 (64, 143)	0.2812^{MW}
60 mins	116.11 ± 13.15 117 (88, 147)	112.6 ± 10.94 114 (91, 138)	114.35 ± 12.18 115 (88, 147)	0.0779^{t}
90 mins	119.97 ± 11.99 120 (96, 160)	115.68 ± 9.53 116 (99, 142)	117.83 ± 11.01 120 (96, 160)	**0.0284^{MW*}**
p-value	**< 0.001^{F*}**	**< 0.001^{F*}**	-	-

Subsequent time points from 2 minutes showed no discernible variation in SBP across the groups (p-values > 0.05).At 90 minutes, Group L exhibits a higher mean SBP (119.97 ± 11.99 mmHg) compared to Group R (115.68 ± 9.53 mmHg), inferring that this difference is statistically significant (p-value = 0.0284).

There is no statistically significant difference in SBP across time points for both Group L and Group R using Friedman's test (p-value < 0.001).

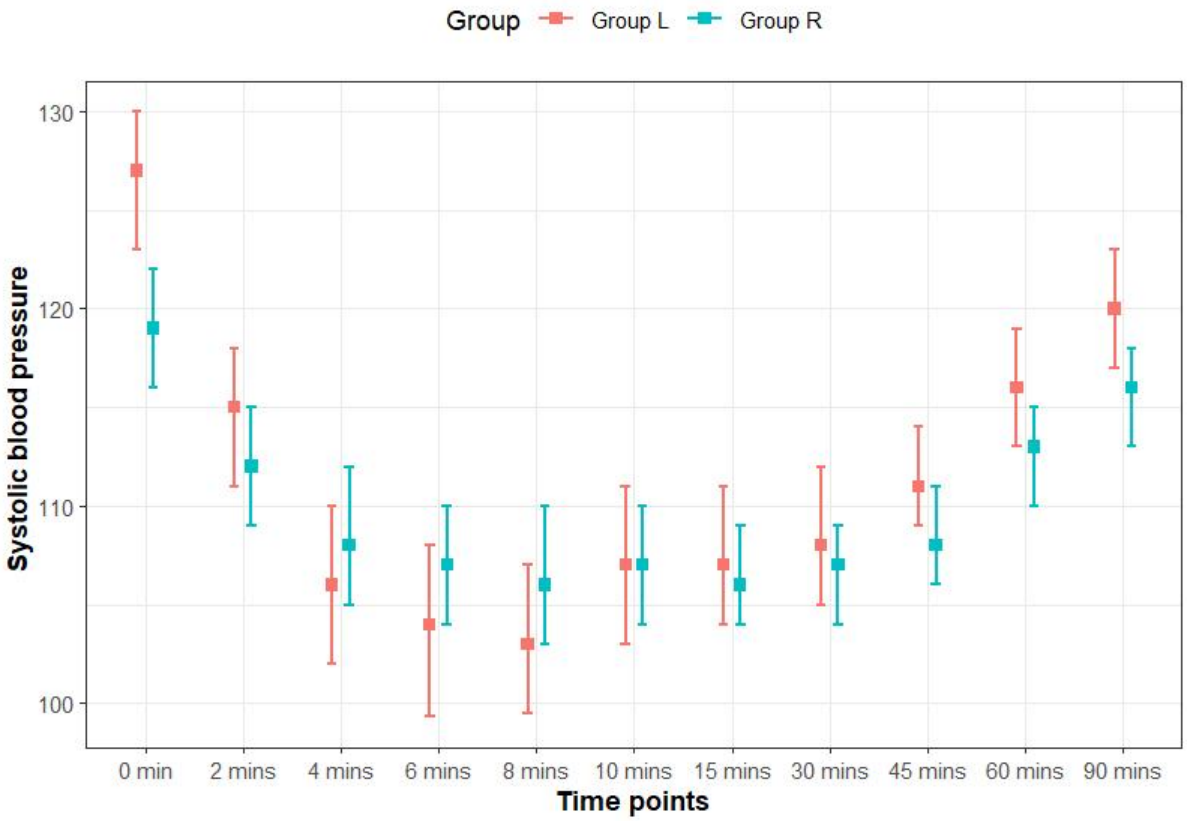


Figure 13: Mean plot of SBP over time and groups.

The following table gives the comparison of DBP over time and group.

Table 9: Comparison of DBP over time and group.

DBP	Group L	Group R	Total	p-value
0 min	81.05 ± 10.69 79 (61, 109)	75.24 ± 9.57 75 (50, 99)	78.15 ± 10.52 78 (50, 109)	**< 0.001^{t*}**
2 mins	71.69 ± 13.3 71 (40, 103)	69.53 ± 10.46 70 (48, 96)	70.61 ± 11.97 70 (40, 103)	0.2707^{t}
4 mins	65.29 ± 14.6 65 (34, 103)	66.71 ± 11.07 65 (40, 96)	66 ± 12.93 65 (34, 103)	0.5052^{t}
6 mins	62.81 ± 14.14 63 (35, 102)	64.88 ± 12.26 65 (34, 97)	63.85 ± 13.23 64 (34, 102)	0.3404^{t}
8 mins	63.13 ± 14.59 61 (35, 99)	64.65 ± 11.86 66 (33, 94)	63.89 ± 13.28 64 (33, 99)	0.4851^{t}
10 mins	63.45 ± 13.52 62 (34, 103)	64.95 ± 9.74 65 (43, 88)	64.2 ± 11.76 64 (34, 103)	0.4388^{t}
15 mins	63.31 ± 12.55 61 (40, 106)	63.55 ± 10.8 62 (40, 92)	63.43 ± 11.67 62 (40, 106)	0.7110^{MW}
30 mins	63.39 ± 13.04 61 (42, 103)	63.53 ± 10.95 63 (40, 90)	63.46 ± 12 61.5 (40, 103)	0.5080^{MW}
45 mins	66.83 ± 11.09 64 (41, 100)	66.05 ± 10.96 65 (46, 96)	66.44 ± 11 64.5 (41, 100)	0.7265^{MW}
60 mins	72.08 ± 11.5 70 (51, 107)	69.72 ± 8.48 70 (51, 90)	70.9 ± 10.14 70 (51, 107)	0.4273^{MW}
90 mins	76.2 ± 10.37 74 (56, 104)	73.25 ± 9.64 72 (55, 95)	74.73 ± 10.09 73 (55, 104)	0.1064^{MW}
p-value	**< 0.001^{F*}**	**< 0.001^{F*}**	-	-

*Abbreviation: "F – Friedman's test, * indicates statistical significance".*

At the initial time point of 0 minutes, Group L presents a slightly higher mean DBP of 81.05 ± 10.69 mmHg compared to Group R's mean DBP of 75.24 ± 9.57 mmHg. At 0

minute, there was a substantial difference in DBP between the two groups, as indicated by the significant difference (p-value < 0.001).

There was no discernible change in DBP between the groups at the subsequent time points (p-values >0.05).

Using Friedman's test, it is found that both Group L and R have significantly different DBP with time(p-value < 0.001).

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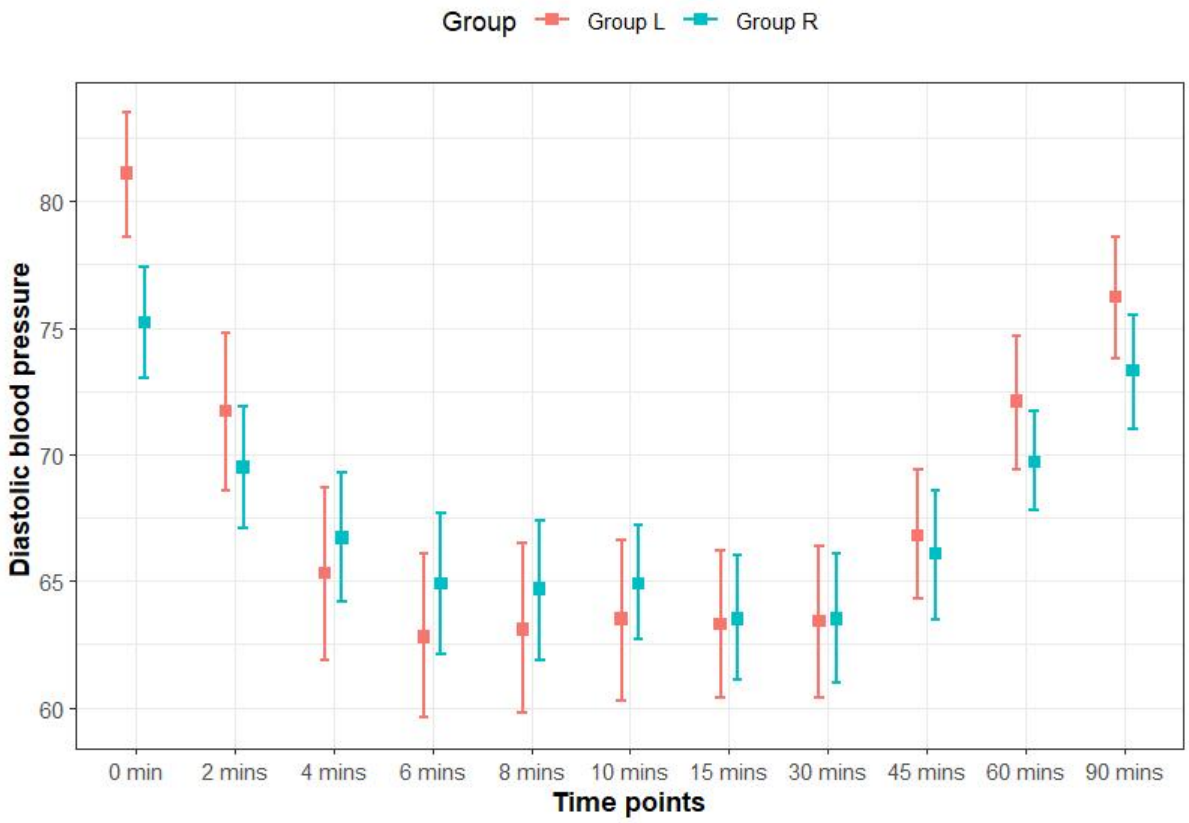

Figure 14: Mean plot of DBP over time and groups.

The following table gives the comparison of MAP over time and group.

Table 8: Comparison of MAP over time and group.

MAP	Group L	Group R	Total	p-value
0 min	96.29 ± 10.73 95 (74, 127)	89.92 ± 9.32 91 (67, 112)	93.11 ± 10.51 92 (67, 127)	**< 0.001^{MW*}**
2 mins	86.11 ± 13.53 86 (56, 117)	83.15 ± 10.42 82 (61, 108)	84.63 ± 12.13 85 (56, 117)	0.1355^{t}
4 mins	79.32 ± 16.22 78 (46, 119)	79.93 ± 11.29 79 (49, 111)	79.63 ± 13.93 78.5 (46, 119)	0.5499^{MW}
6 mins	76.45 ± 15.22 75 (49, 120)	77.96 ± 11.21 77 (51, 105)	77.21 ± 13.34 77 (49, 120)	0.3922^{MW}
8 mins	77.44 ± 16.38 75 (49, 132)	77.99 ± 11.47 79 (45, 101)	77.71 ± 14.1 77.5 (45, 132)	0.3027^{MW}
10 mins	77.93 ± 14.37 76 (43, 122)	78.71 ± 10.17 78 (56, 104)	78.32 ± 12.41 78 (43, 122)	0.4656^{MW}
15 mins	78.09 ± 13.09 77 (55, 118)	78.15 ± 10.45 78 (55, 108)	78.12 ± 11.8 77.5 (55, 118)	0.7996^{MW}
30 mins	78.21 ± 13.4 74 (56, 121)	77.56 ± 10.59 77 (54, 107)	77.89 ± 12.04 75.5 (54, 121)	0.7040^{MW}
45 mins	81.25 ± 10.99 79 (62, 114)	79.77 ± 10.24 80 (60, 110)	80.51 ± 10.61 79.5 (60, 114)	0.4713^{MW}
60 mins	86.64 ± 11.25 87 (67, 119)	83.43 ± 8.54 84 (67, 102)	85.03 ± 10.08 84.5 (67, 119)	0.0960^{MW}
90 mins	90.48 ± 10.43 90 (67, 121)	85.59 ± 9.42 84 (57, 106)	88.03 ± 10.2 87 (57, 121)	**0.0047^{MW*}**
p-value	**< 0.001^{F*}**	**< 0.001^{F*}**	-	-

*Abbreviation: "F – Friedman's test, * indicates statistical significance".*

At the initial time point of 0 minutes, Group L demonstrates a slightly higher mean MAP of 96.29 ± 10.73 mmHg compared to Group R's mean MAP of 89.92 ± 9.32

mmHg (p-value < 0.001). This indicates a notable variation in Mean arterial pressure between the two groups at 0 minute.

There was no discernible difference in MAP between the research groups at later time points. (p-values > 0.05). At 90 minutes, Group L exhibits a higher mean MAP (90.48 ± 10.43 mmHg) compared to Group R (85.59 ± 9.42 mmHg), with this being statistically significant (p-value = 0.0047).

MAP for both Group L and Group R shows statistically significant fluctuation over time, according to the Friedman's test(p-value < 0.001).

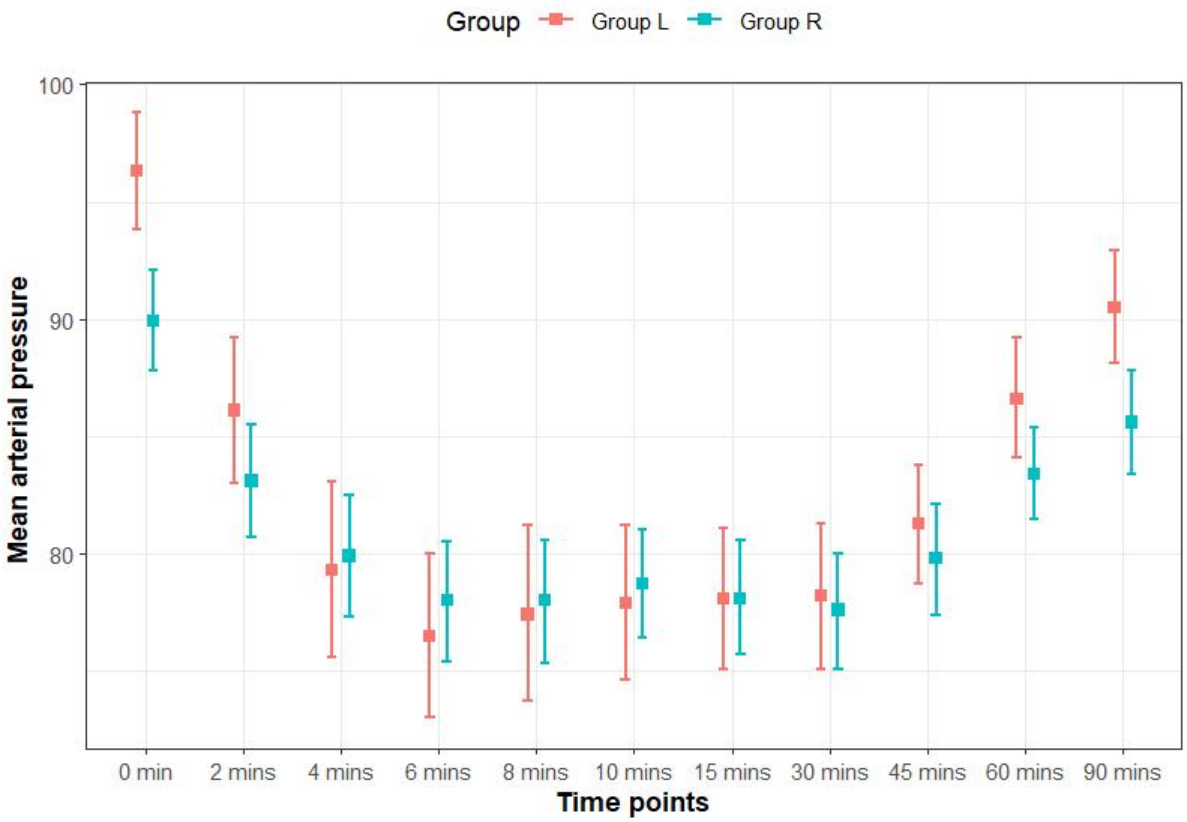

Figure 15: Mean Plot of MAP over time and groups.

The following table gives the comparison of SPO2 over time and group.

TABLE 9: Comparison of SPO_2 in time and group.

SPO2	Group L	Group R	Total
0 min	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
2 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
4 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
6 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
8 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
10 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
15 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
30 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
45 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
60 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)
90 mins	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)	100 ± 0 100 (100, 100)

At each time point from 0 to 90 minutes, both Group L and Group R consistently exhibit a mean SPO2 of 100 ± 0%, with no observed variations within each group over time.

Note: When there is no variation in the data (in this case, SPO2 values are consistently 100% for all measurements), statistical tests are not applicable because they rely on

variability to determine differences or changes. Since the SPO2 values are identical across all time points and groups, no statistical test can be conducted to show differences or changes.

DISCUSSION

This study compares and assesses the effectiveness and hemodynamic characteristics of spinal anesthetics for elective lower segment cesarean sections using 0.5% hyperbaric levobupivacaine versus 0.75% hyperbaric ropivacaine. We compared it using a volume of 2.2ml of both drugs which was decided upon using pilot studies, i.e; 16.5 mg or 2.2ml of 0.75% Hyperbaric Ropivacaine and 11 mg or 2.2ml of 0.5% Hyperbaric Levobupivacaine.

Historically, the preferred medication for spinal anaesthesia in lower segment cesarean section has been bupivacaine. The potential cardiac toxicity of bupivacaine was exposed as its negative aspect. Mild symptoms, seizures, cardiovascular instability, and sudden cardiac death were long thought to be all indicators of local anaesthetic overdose[7].

In clinical settings, levobupivacaine has not completely taken the role of bupivacaine. Levobupivacaine is equally as potent as bupivacaine. In contrast, levobupivacaine caused less CVS and Central nervous system harm in animal studies than bupivacaine. Levobupivacaine produced less QTc interval prolongation than bupivacaine at i.v doses greater than 75mg in healthy subjects and had a less detrimental inotropic effect. With levobupivacaine, there were less EEG abnormalities that indicated CNS depression[54].

Ropivacaine is a recently developed local anaesthetic that is promoted as the ‘pure S(-) enantiomer’ of the parent compound ropivacaine. Its obvious advantages over Bupivacaine include lower cardiotoxicity and neurotoxicity, as well as a more targeted action on sensory rather than motor fibres. It is due to Ropivacaine's lower lipophilicity and enantiomer properties[51].

Using the software method of randomization, 150 patients undergoing spinal anesthesia for a lower segment cesarean delivery were split into two groups at random.

Group L:- Patients received 2.2 ml of 0.5% Hyperbaric levobupivacaine "11mg"

Group R:- Patients received 2.2 ml of 0.75% Hyperbaric ropivacaine "16.5mg"

The mean age of Group L was 26.16±4.29 years, with a median age of 26 years (range 20–36), whereas the mean age of Group R was 25.07±3.39 years, with a median age of 24 years (range 19–33). Notwithstanding these minor variations, the study showed that there was no statistically significant difference between the ages of the two groups.(p-value = 0.1970).

Regarding weight, Group L displayed a mean weight of 68.63 ± 7.35 kg with a median of 68 kg (range 58-95), while Group R shows a mean weight of 66.04 ± 6.3 kg with a median of 65 kg (range 55-82).According to study analysis, there is a significant weight difference between the two groups (p-value = 0.0254), suggesting that Group L weighs more on average than Group R.

With a mean onset time of 1.11 ± 0.54 minutes for sensory block, Group L showed a speedier onset than Group R, which had a mean onset time of 1.56 ± 0.67 minutes.Based on statistical analysis, it was shown that the groups' distributions of sensory block onset at T10 differed significantly (p-value < 0.001), indicating that Group L experienced a quicker start of sensory block than Group R.

Levobupivacaine had a faster start time at T10 than ropivacaine, according to a research by Gorgias et.al[15]. comparing the two drugs for spinal anesthesia during transurethral operations.

In the study performed by Kulkarni et.al[17], “the onset of sensory block for ropivacaine was delayed (4.5 minutes) compared to bupivacaine (3.2 minutes)”.This study was comparable with our findings. Supporting this another study by Kalbande et al[56] indicated that “ropivacaine had a slower onset for sensory (153.90 vs. 92.46 seconds) block compared to bupivacaine”. Nonetheless, the research conducted by Singh and colleagues[18] demonstrated that there was no difference in the onset of the sensory block.

Important results comparing levobupivacaine with bupivacaine for spinal anesthetic during lower limb procedures were published by Kumar et al. in 2021[13]. The results showed that the onset of sensory block was corresponding to our study, with 4.4 ±2.1min vs 4.2 ±1.7min.

Group L displays a longer duration, with a mean duration of sensory block 165.59 ± 8.46 minutes, while Group R's mean duration is shorter at 145.17 ± 8.09 minutes. From data collected and analyzed,a significant variance in the groups' distribution of sensory block duration is noted. (p-value < 0.001), suggesting that, in contrast to Group R, Group L endures a longer duration of sensory block.

Majority of patients in both groups, 72% in Group L and 76% in Group R, reached the T6 level, which is the highest level of sensory block achieved. It is noted that the groups' greatest level of sensory block does not significantly differ from one another. (p-value = 0.7061).

Gorgias et al.'s[15] findings demonstrated that “the duration of anesthesia varied noticeably. At the T10 level, levobupivacaine produced a greater duration (115.46 minutes vs to 73.42 minutes for ropivacaine)”.

Findings by Kumar et al[12] did not suggest major differences between levobupivacaine and bupivacaine, which corresponds with the structural similarity

between the two local anesthetic drugs, in the duration of sensory blocks, but ropivacaine exhibited a shorter duration of sensory block in comparison to bupivacaine, according to a study by Kulkarni et al[17]. This is further supported by feroz et al[57] which showed “The ropivacaine group experienced a substantially shorter total period of sensory block (160 ± 12.9 min) compared to the bupivacaine group. (260 ± 16.1 min; $P < 0.05$)”. The greatest level of block in the medications under study in the aforementioned trial was comparable and similar, displaying no statistically significant difference.

The duration needed to attain bromage grade 3 functioned as a marker for the onset of motor block in our investigation. Compared to Group Rs, which had a mean onset time of 2.01 ± 0.85 minutes for motor block, Group L had a speedier onset, with a mean onset time of 1.16 ± 0.53 minutes. The grade 3 motor block onset time distribution showed a significant difference (p-value<0.001) between the groups, indicating that Group L developed the disease more quickly than Group R.

According to Kulkarni et.als[17] research, “ropivacaine causes motor block more slowly than bupivacaine” which is further bolstered by Gogias et al.'s findings, which indicated a quicker onset time for motor block in the group receiving levobupivacaine. According to the study by Feroz et al[57] “the mean time of motor block onset 13±1.6 min vs. 9±1.3 min;($P < 0.05$) was much slower in ropivacaine group than compared to bupivacaine group”..

In our study, the period of time required till movement of toes served as a gauge for duration of motor block. Group L displays a longer duration, with a mean duration of 161.33 ± 8.07 minutes, while Group R's mean duration is shorter at 140.32 ± 8.35 minutes. From statistical analysisIt is observed that there are notable differences in the

groups' distribution of the overall movement time. (p-value < 0.001), indicating that Group L experiences motor block for a longer duration than Group R.

Levobupivacaine demonstrated a “longer total motor block duration than ropivacaine, according to Gorgias et al”.,[15] while kulkarni et al[17] derived similar inferences.This is also implied by the studies conducted by Singh et al[16]. (levobupivacaine vs. bupivacaine) and Feroz et al[57]. (ropivacaine and bupivacaine comparison).

At 0 min, Group L exhibits a slightly higher mean HR of 91.21 ± 13.31 bpm compared to Group R's mean HR of 88.17 ± 13.31 bpm. That being said, this difference is hardly significant. (p-value = 0.1640). Subsequent time intervals reveal noteworthy variations in HR between the groups. At 2, 4, 6, 8, 10, 15, 30, 45, and 60 minutes, heart rate (HR) varies significantly (p-value<0.05) between the two groups, with Group L consistently displaying a greater HR than Group R at these time periods. At 90 minutes, although Group L still exhibits a slightly higher mean HR than Group R (85.4 ± 15.61 bpm vs. 81.91 ± 12.11 bpm), the difference is not significant (p-value = 0.1885)

At the initial time point of 0 minutes, Group L demonstrates a slightly higher mean SBP of 126.68 ± 14.2 mmHg compared to Group R's mean SBP of 119.21 ± 12 mmHg. This difference is significant statistically(p-value < 0.001), indicating a notable disparity between the two groups in SBP at 0 minute.

Subsequent time points showed no discernible variation in SBP across the groups. (p-values > 0.05). At 90 minutes, Group L exhibits a higher mean SBP (119.97 ± 11.99 mmHg) compared to Group R (115.68 ± 9.53 mmHg), with this difference being significant statistically (p-value = 0.0284).

At the initial time point of 0 minutes, Group L presents a slightly higher mean DBP of 81.05 ± 10.69 mmHg compared to Group R's mean DBP of 75.24 ± 9.57 mmHg.

With a p-value of less than 0.001, this difference was deemed significant, suggesting a discernible difference in DBP between the two groups at zero minutes.

Subsequent time points revealed no discernible variation in DBP across the groups. (p-values > 0.05).

At the initial time point of 0 minutes, Group L demonstrates a slightly higher mean MAP of 96.29 ± 10.73 mmHg compared to Group R's mean MAP of 89.92 ± 9.32 mmHg (p-value < 0.001). This indicates a notable disparity in Mean arterial pressures between the two groups at 0 minutes.

Subsequent time points showed no discernible variation in MAP between the groups(p-values > 0.05). At 90 minutes, Group L exhibits a higher mean MAP (90.48 ± 10.43 mmHg) compared to Group R (85.59 ± 9.42 mmHg), with this difference being significant (p-value = 0.0047).

Systolic and diastolic blood pressure readings, as well as mean arterial pressure, were similar between groups L and R during the surgery.There were no notable differences between the groups.

SpO2 levels of groups L and R were similar during the process. To manage the decline in vital parameters, neither patient in either group needed any intervention.

There was “no discernible change in hemodynamic measures between the levobupivacaine and ropivacaine groups, according to the Gorgias et al. study”[15]. The studies by Kumar et al[13] between levobupivacaine and ropivacaine showed “no considerable variation”and so did the trial by Singh et al[16].

SUMMARY

This “one-year randomized controlled trial was conducted in KLES Dr Prabhakar Kore Charitable Hospital Belagavi, from March 2023 to April 2024 in 150 participants undergoing elective lower segment cesarean section under spinal anaesthesia”.

Group L:Received 2.2 ml of 0.5% Hyperbaric Levobupivacaine “11mg”

Group R:Received 2.2 ml of 0.75% Hyperbaric Ropivacaine “16.5mg”

Vital factors and the onset and duration of sensory and motor block were investigated. The parameters related to hemodynamics were continuously observed.

Both groups had comparable patient demographics. In this study, the sensory block saw a faster onset in group L (1.11±0.54minutes) than in group R (1.56±0.67minutes) while the duration was longer in group L (165.59 ±8.46 minutes) than in group R (145.17 ± 8.09 minutes). The motor block saw a faster onset time group L (1.16±0.53minutes) when compared to group R (2.01±0.85minutes) while the duration was longer in group L (161.33±8.07minutes) when compared to group R (140.32±8.35 minutes). In the preoperative and postoperative period the SBP, DBP and MAP had statistical significance but this could most likely be attributed to patient characteristics. During the procedure the Group L consistently exhibited a higher HR compared to Group R. Nonetheless, both groups' intraoperative drops in mean arterial pressure and systolic and diastolic blood pressure were similar. The time of onset of sensory and motor blockade was earlier in 0.5% Hyperbaric levobupivacaine compared to 0.75% Hyperbaric ropivacaine group. Overall, based on this study it may be concluded that “0.5% Hyperbaric Levobupivacaine is more potent than 0.75%

Hyperbaric Ropivacaine in patients undergoing lower segment cesarean sections when comparing motor and sensory block".

CONCLUSION

In patients undergoing elective lower segment cesarean sections under spinal anesthesia, our study demonstrated that 0.5% hyperbaric Levobupivacaine is more effective than 0.75% hyperbaric Ropivacaine, with an earlier onset of motor and sensory block and a longer duration of action.

Haemodynamic parameters including HR, SBP and DBP are comparable and have no statistical significance in 0.75% Ropivacaine group and 0.5% Levobupivacaine group during the course of the procedure.

SCOPE AND LIMITATIONS

Sample size: Although sample size of 150 is adequate for the study, larger sample size will provide more comprehensive data and potentially reveal smaller effect sizes the study would have missed.

Single-center study: A multi center trial would have given a more diverse demographic to validate the study findings across different setting and populations

Demographic homogeneity : Study was performed in ASA 2 participants for elective cesarean sections, but including patients with higher ASA status can provide added validity to the study findings.

Blinding and bias : Despite the study being blinded and randomized a certain amount of bias could have existed while carrying out the study.

Inter individual variability: Difference in patient anxiety varying hemodynamic parameters especially during the preoperative or postoperative period could have

contributed to varying results. This is especially true while comparing primigravid patients to multigravid.

External validity: The study was conducted in elective cesarean section cases, hence results may vary in emergency and acute settings where patient and anaesthesiologist factors may vary widely.

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ANNEXURE I

INFORMED CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr. /Mrs. /Miss. _____ we are requesting you to enroll you in the study titled ““A COMPARATIVE EVALUATION BETWEEN HYPERBARIC ROPIVACAINE AND HYPERBARIC LEVOBUPIVACAINE IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA; A RANDOMIZED CONTROLLED TRIAL.’ conducted by Department of Anesthesiology, J.N. Medical College, Belagavi under KAHER, Belagavi.-10

Respected Sir/Madam, we request you to participate in our study as you are eligible for it. During the study you will be asked some questions regarding your medical history and you are supposed to answer to the best of your knowledge.

Your participation in this research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N.Medical College. If you decide to participate you are free to withdraw at any time.

Purpose of the study: To compare onset and duration and hemodynamic effects of study drug.

Procedure Involved: If you agree to enroll in my study, I will ask you present and past history medical history and family history, then u will be clinically examined in details. Epidural anaesthesia will be given by senior anaesthesiologist. Each is randomly assigned in to two groups . Group R will be given Hyperbaric Ropivacaine and Group L will be given Hyperbaric Levobupivacaine for spinal anaesthesia and will be monitored throughout the procedure and in post-operative period.

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change any health care services offered to you or your ward at K.L.E. S Hospital & MRC.

Benefits: Efficacy ,hemodynamic effects can be studied and in anaesthesiology practice

Risks: There are no risks associated with this study

Privacy and Confidentiality:

The only people to know that you are as research subject are you and members of the research team. No information provided by you during the research will be disclosed to other without your written permission except:

1.In emergency to protect your rights and welfare.

2.If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with your identity remaining confidential.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation:

In the event of injury related to the study, treatment will be made available through KLES Hospital and MRC, Belagavi. There is no compensation or payment for such medical treatment by law. If you get injured you may contact Department of Anesthesiology, J.N. Medical College.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Department of Anesthesiology, J.N. Medical College, Belagavi. If you have any queries about your rights as a study subject, you may call Dr. HARSHA HEGDE M.D Chairperson , J.N. Medical college, IEC & scientist department, ICMR , national institute of traditional medicine, belagavi - 9480422500.

INFORMED CONSENT FOR PARTICIPATION IN RESEARCH TRIAL

"A COMPARATIVE EVALUATION OF HEMODYNAMIC EFFECTS BETWEEN HYPERBARIC ROPIVACAINE AND HYPERBARIC LEVOBUPIVACAINE IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA; A ONE YEAR RANDOMIZED CONTROLLED TRIAL'

Mr./Ms./Mrs. _____ voluntarily agree for the participation of as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject/Guardian: _____

Date:

Witness Name: _____ Signature: _____

Investigators Name: _____ Signature: _____

Date:

Place : _____.

ANNEXURE II

PROFORMA

"A COMPARATIVE EVALUATION OF HEMODYNAMIC EFFECTS BETWEEN HYPERBARIC ROPIVACAINE AND HYPERBARIC LEVOBUPIVACAINE IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA; A ONE YEAR RANDOMIZED CONTROLLED TRIAL"

Group allotted :

Name	:	Age	:
Gender	:	Weight	:
Height	:	Date of Examination	:
Address	:	Occupation	:

Pre examination evaluation

Past History

●HTN DM IHD Arrhythmia Valvular heart diseases .

●H/o previous surgery/(s) where airway difficulty will be encountered. Yes No

General physical examination

Weight (Kg)	:	Temperature (0F)	:	Pallor :
Cyanosis	:	Pedal edema	:	Clubbing :

PR : BP : RR :

Musculoskeletal disorders:

Jaw movements : Teeth:

Airway assessment : Spine:

Investigations

Hb%: TLC: Platelet Count : INR: FBS:

Systemic examination:

RS: CNS:

CVS: GIT:

Proposed surgery

Post-operative baseline values

HR : BP: SpO2:

Monitors attached:

Pulse oxymetry: NIBP:

ECG:

Group: A B

Sensory Block:

a)	Onset at T10(min)	
b)	Duration at T10(min)	
c)	Highest level of sensory block	

Motor Block:

a)	Onset (min)Grade 3 motor blockade	
b)	Total duration of Motor blockade (Able to move bilateral toes)	

Vital Parameters

Time	**HR**	**SBP**	**DBP**	**MAP**	**SpO2**
0min					
2 min					
4 min					
6 min					
8 min					
10 min					
15 min					

30 min					
45 min					
60 min					
90 min					

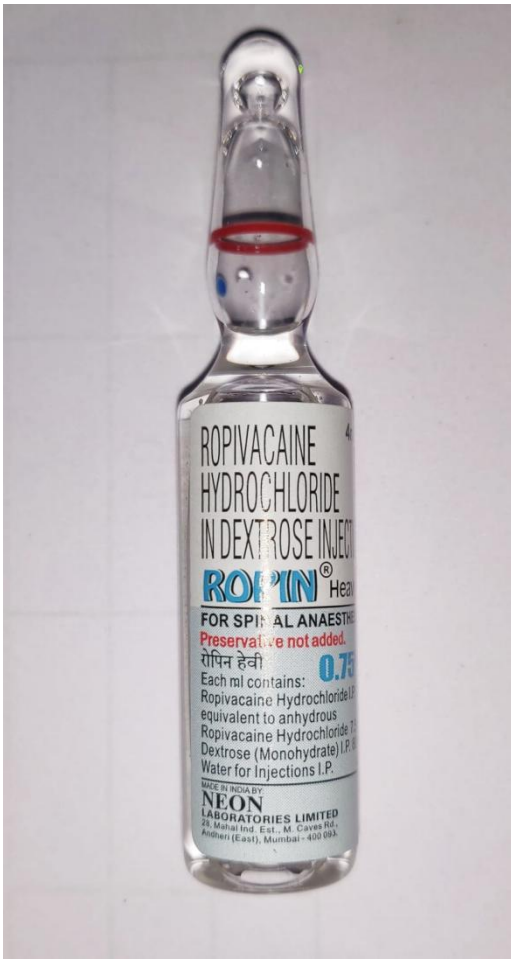
SIGNATURE OF THE ANAESTHESIOLOGIST: _____

SIGNATURE OF THE WITTNESS - _____

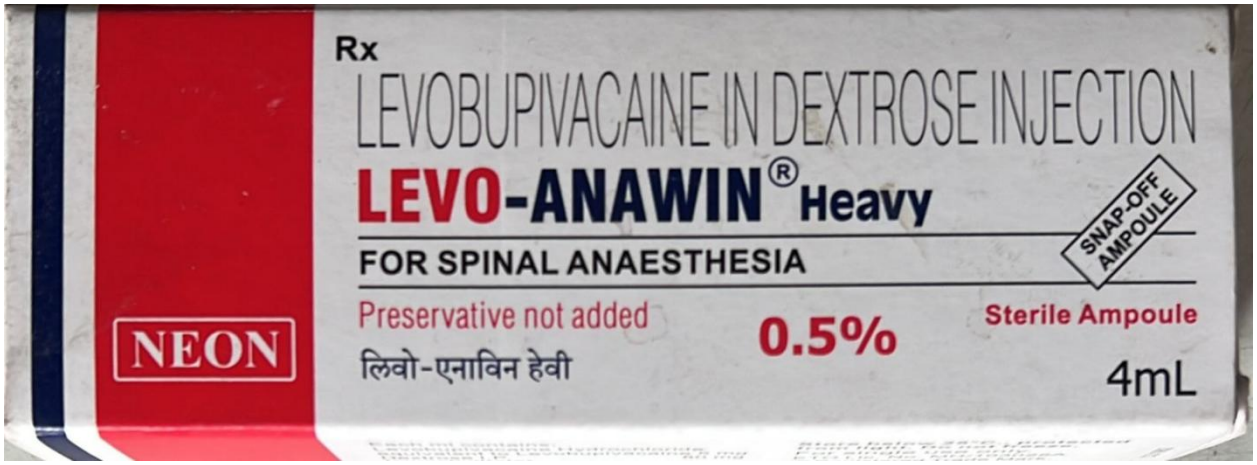
SIGNATURE OF THE PRINCIPAL INVESTIGATOR - _____

ANNEXURE III: PHOTOGRAPHS

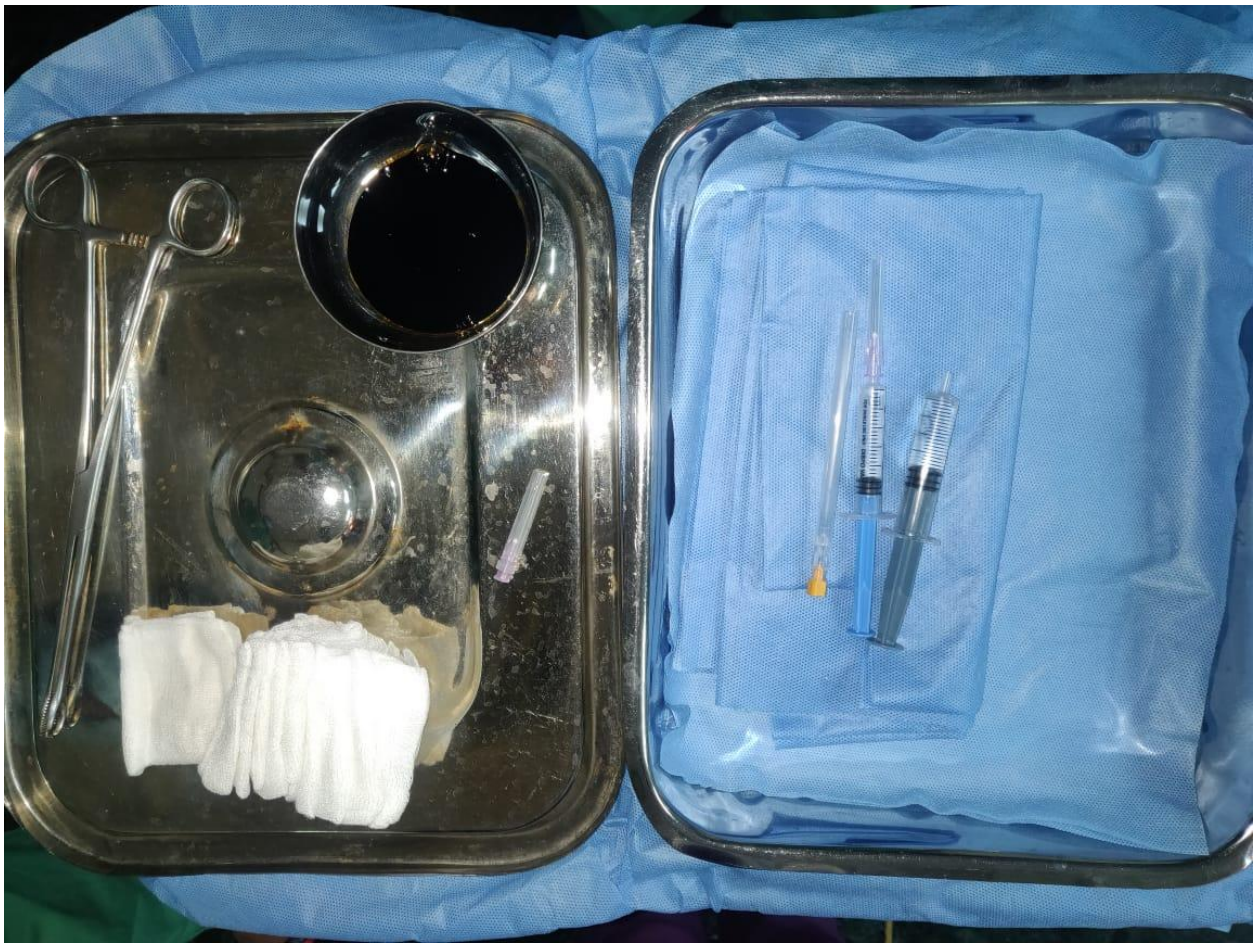
Photograph 1: 0.75% Hyperbaric Ropivacaine ampoule



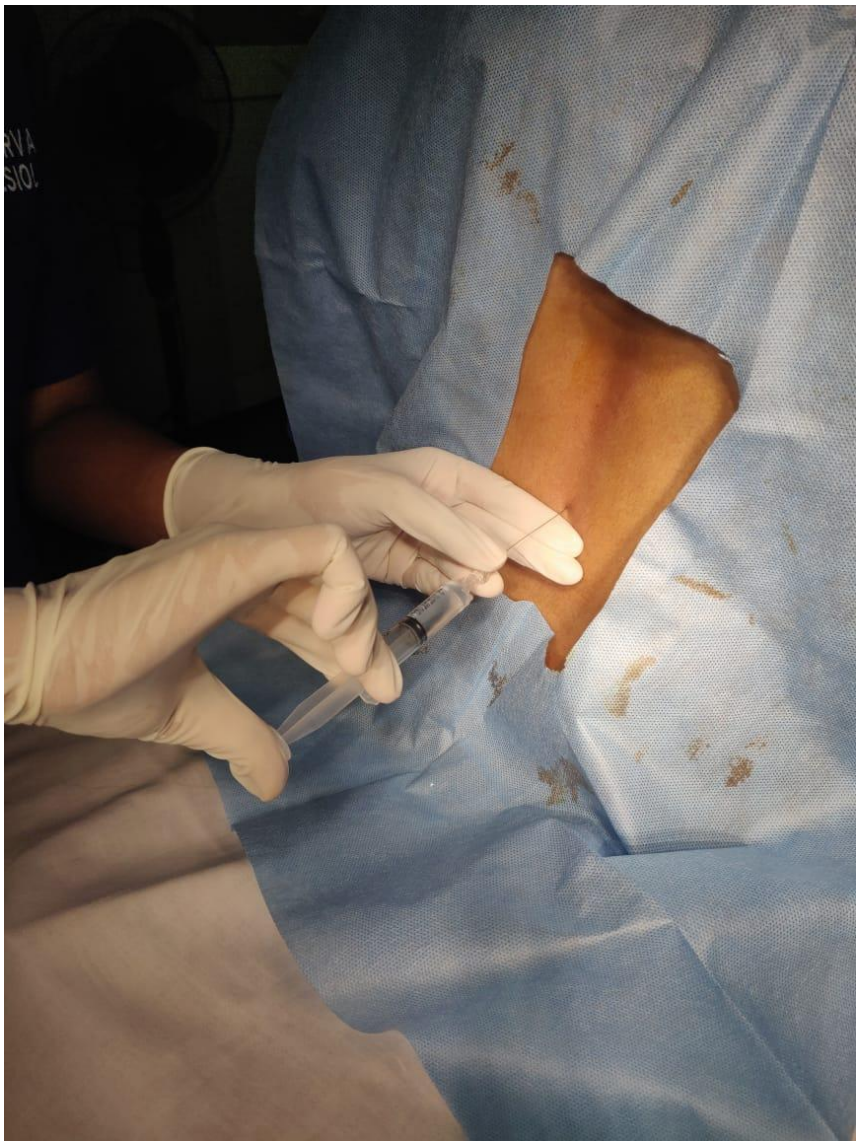
Photograph 2: 0.5% Hyperbaric Levobupivacaine ampoule



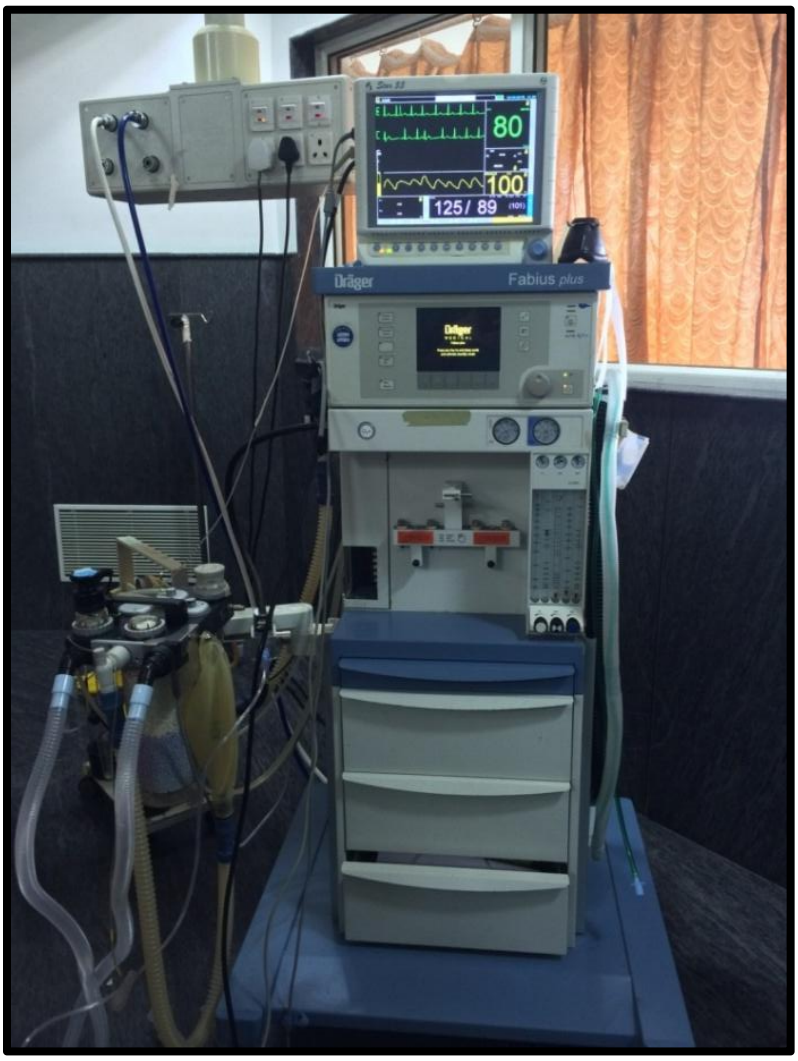
Photograph 3 : Spinal tray



Photograph 4 : Procedure of spinal



Photograph 5 : Monitoring during surgery



ANNEXURE IV