"A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES".

By

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Dissertation submitted to

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In partial fulfilment of the requirements for the degree of

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IN

ANAESTHESIOLOGY

Under the guidance of

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Dr. MASARADDI. DEEPAK. K

LIST OF ABBREVIATIONS

µ	Micro
^{o}C	Degree centigrade
AR	Adrenergic receptor
ASA	American Society of Anaesthesiologists
SBP	Systolic blood Pressure
CNS	Central Nervous System
CO	Cardiac output
CSF	Cerebrospinal fluid
CVS	Cardiovascular system
DBP	Diastolic blood pressure
dl	Decilitre
ECG	Electrocardiogram
G	Gauge
gm	Gram
HR	Heart rate
hr	hour
Inj.	Injection
IV	Intravenous
kg	Kilograms
L	Litres
MAP	Mean Arterial Pressure
mEq/L	Milliequivalents / Litre
mcg	Micrograms
mg	Milligrams
Min	Minute

ml	Millilitres
mm Hg	Millimetres of mercury
O2	Oxygen
PR	Pulse rate
SAB	Subarachnoid block
SBP	Systolic blood pressure
SD	Standard deviation
sec	Second
VAS	Visual analogue scale
RSS	Ramsay sedation score
bpm	beats per minute
S	significant
NS	Not significant
LA	Local Anaesthetic
OT	Operation Theatre
Yr	Year
LA	Lower Abdominal
LL	Lower Limb

ABSTRACT

INTRODUCTION:

Spinal and epidural anaesthesia are regional anaesthesia methods that are widely used, especially in lower abdominal and lower extremity operations.

Bupivacaine, is the widely used local anaesthetic in regional anaesthesia. Stereoisomers of the agent are being developed for use instead of the isomers, in order to avoid the toxic effects of local anaesthetic agents as much as possible. Bupivacaine is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, Levo-Bupivacaine, S (-) isomer and Dextro-Bupivacaine, R (+) isomer. Several central nervous system and cardiovascular adverse reactions reported in the literature have been linked to the R (+) isomer of Bupivacaine.

This study aims to compare the clinical efficacy of 0.5% Levo-Bupivacaine and 0.5% Bupivacaine without adjuvant medication in patients undergoing elective lower abdominal and lower limb surgeries under epidural anaesthesia.

AIM : To evaluate the clinical efficacy of 0.5% Levobupivacaine with 0.5% Bupivacaine in epidural anaesthesia for lower abdominal and lower limb surgeries with respect to onset of action of sensory block, duration of analgesia, onset of action and duration of motor block, hemodynamic changes and side effects.

METHODS:

Study Design: Prospective Randomised clinical trial

Study Period: One and half years from December 2015 to August 2017.

Sample Size: 100 patients with 50 in each group.

PROCEDURE: All patients who belonged in the inclusion criteria , after giving a written informed valid consent were randomly allocated into the following groups.

Group B(n=50)-- patients receiving 0.5% isobaric Bupivacaine 17 ml.

Group L(n=50) -- patients receiving 0.5% isobaric levo-Bupivacaine 17ml.

In the operation theatre, a good peripheral intravenous access was secured using 18 gauge canula and preloaded with 500ml Ringer Lactate solution. Multiparameter monitor was connected which records heart rate, non-invasive measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), continuous electrocardiogram (ECG) monitoring and arterial oxygen saturation (SpO2) .Baseline non invasive blood pressure, pulse rate, electrocardiograph, SpO2 were recorded.Premedication with Inj. Ondensetrone 4mg i.v and Inj. Ranitidine 150mg i.v was be given.Under all aseptic precautions using a sterile epidural kit and autoclaved epidural tray the 18g epidural catheter was secured in L3-L4 intervertebral space. Patients in group B received 0.5% isobaric Bupivacaine (17 ml) and group L received 0.5% isobaric levo-Bupivacaine (17 ml) epidurally.

PARAMETERS OBSERVED :

1) Onset time of sensory block :
2) Highest level of sensory block.
3) Duration of sensory block / Time to two-segment regression.
4) Duration of sensory analgesia.
5) Onset time of motor block.
6) Degree of motor block.
7) Duration of motor block.
8) Haemodynamic changes: HR, SBP, DBP at 0, 2, 5, 15, 30, 60, 90, 120 and 180 minutes.
9) Side effects if any. (hypotension,bradycardia,nausea,vomiting)

RESULTS: Both groups are comparable with respect to age, sex, weight and duration of surgery.

Group-L has similar onset of sensory block as compared to Group-B. Mean onset time to sensory block at T-10 in Group-L is 11.6 mins and In Group-B is 11.62 mins. P-value= 0.820.

Group L has similar highest level of sensory block reached as compared with Group B p value 0.1.

Group-L has a longer duration of sensory block as compared to Group-B, which is in contrast to our hypothesis that duration of sensory block is similar with both drugs. Mean Time to two segment regression / Duration of sensory block in Group-L being 132.46 minutes and Group-B being 89.28 minutes. P-value=0.000.

Group-L has longer duration of sensory analgesia as compared to Group-B . Mean Time of sensory analgesia in block in Group-L is 326.5 mins and in Group-B is 284.42 mins. P-value= 0.000.

Group-L has a slower onset of motor block as compared to Group-B, which is in accordance to our hypothesis that onset of motor block is delayed with Levobupivacaine as compared to Bupivacaine. Mean Time to onset of motor block in Group-L is 19.6 mins and in Group-B is 17.74 mins. P-value= 0.000.

Group-L has shorter duration of motor block as compared to Group-B .Mean Duration of motor block in Group-L is 197.4 mins and in Group-B is 203.3 mins. P-value= 0.017.

Group L has similar degree of motor blockade as compared to Group B. P-value = 0.633

No difference was found between Group-L and Group-B with respect to variability in systolic blood pressure, diastolic blood pressure, men heart rate and oxygen saturation at various time intervals. P-value >0.05 at various time intervals.

Group L has similar complications as compared to Group B. P-value=1.000. Most common complications were Hypotension and bradycardia were not significant.. Other complications like nausea or shivering were not observed in any patients of Group-L or Group-B.

CONCLUSION: From this study, we infer that epidurally administered isobaric 0.5% Levobupivacaine has a Similar onset and longer duration of sensory blockade and slower onset and similar duration of motor blockade, with comparable quality of analgesia and hemodynamic parameters as with epidurally administered isobaric 0.5% Bupivacaine. Owing to its better safety profile, Levobupivacaine is a good alternative to Bupivacaine. Also, levobupivacaine is a good alternative to bupivacaine, for surgeries requiring early mobilisation or shorter duration of motor block.

KEYWORDS: Epidural anaesthesia, Levobupivacaine, Bupivacaine.

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INTRODUCTION

Regional anaesthesia with Spinal and Epidural anaesthesia are the most widely used anaesthesia techniques for lower abdominal and lower limb surgeries. [1,2]
Their advantages over general anaesthesia are [3] avoidance of Polypharmacy, avoidance of airway manipulation and protection of airway reflexes, good motor and sensory blockade, better hemodynamic stability, lesser incidence of post operative nausea and vomiting and prolonged postoperative analgesia.

The advantages of epidural anaesthesia[4] over spinal anaesthesia are extension of anaesthesia for prolonged duration of surgeries, prolonged post operative analgesia, better hemodynamic stability and the incidence of post dural puncture headache is not there as the dura is not pierced.

Bupivacaine is the widely used local anaesthetic in regional anaesthesia. Stereoisomers of the agent are being developed for use instead of the isomers, in order to avoid the toxic effects of local anaesthetic agents as much as possible. Bupivacaine is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, Levo-Bupivacaine, S (-) isomer and Dextro-Bupivacaine, R (+) isomer. Several central nervous system and cardiovascular adverse reactions reported in the literature have been linked to the R (+) isomer of Bupivacaine.

The levorotatory isomers were shown to have a safer pharmacological profile with less cardiotoxic and neurotoxic effects and it is attributed to its faster protein binding rate. S forms of the isomers are less toxic and provide longer lasting analgesia

x[5,6,7,8] . The pure S (-) enantiomers of Bupivacaine, i.e., Dextro-Bupivacaine and Levo-Bupivacaine were thus introduced into clinical anaesthesia practice.

This study aims to compare the clinical efficacy of 0.5% Levo-Bupivacaine and 0.5% Bupivacaine without adjuvant medication in patients undergoing elective lower abdominal and lower limb surgeries under epidural anaesthesia with respect to the onset & highest level of sensory block, duration of sensory analgesia, onset, degree & duration of motor blockade, hemodynamic changes like heart rate, blood pressure at various time intervals. Intra-operative and post-operative complications such as nausea, vomiting, hypotension, bradycardia, respiratory depression.

AIMS AND OBJECTIVES OF THE STUDY

AIM :- To compare the sensory blockade, motor blockade, hemodynamic effects and side effects produced by isobaric Bupivacaine and isobaric Levobupivacaine when used for epidural anaesthesia in lower abdominal and lower limb surgeries and thus determine a more effective regional anesthetic drug among the two.

OBJECTIVE :- To evaluate the clinical efficacy of 0.5% Levobupivacaine with 0.5% Bupivacaine in epidural anaesthesia for lower abdominal and lower limb surgeries with respect to

1. Onset of action of sensory block.
2. Duration of analgesia.
3. Onset of action and duration of motor block
4. Hemodynamic changes.
5. Side effects.

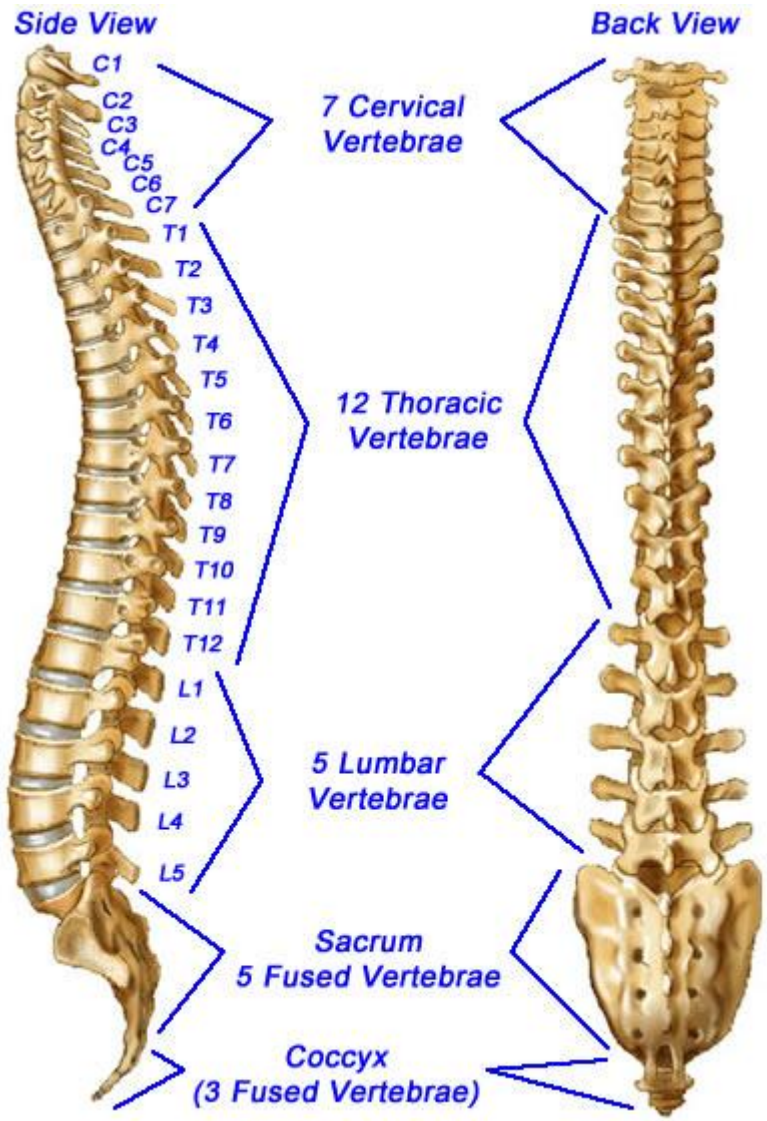
REVIEW OF LITERATURE

APPLIED ANATOMY

Epidural blockade is one of the most commonly used and useful procedure in anaesthesiology. It is unique in that, it can be placed at virtually any level of the spinal spine, allowing more flexibility in its application to clinical practice.[9]

Anatomy

The key to safe and effective administration of an epidural anaesthesia begins with a thorough understanding of the anatomy of the vertebral column, ligaments and blood supply, the epidural space, spinal canal and associated structures.[9]

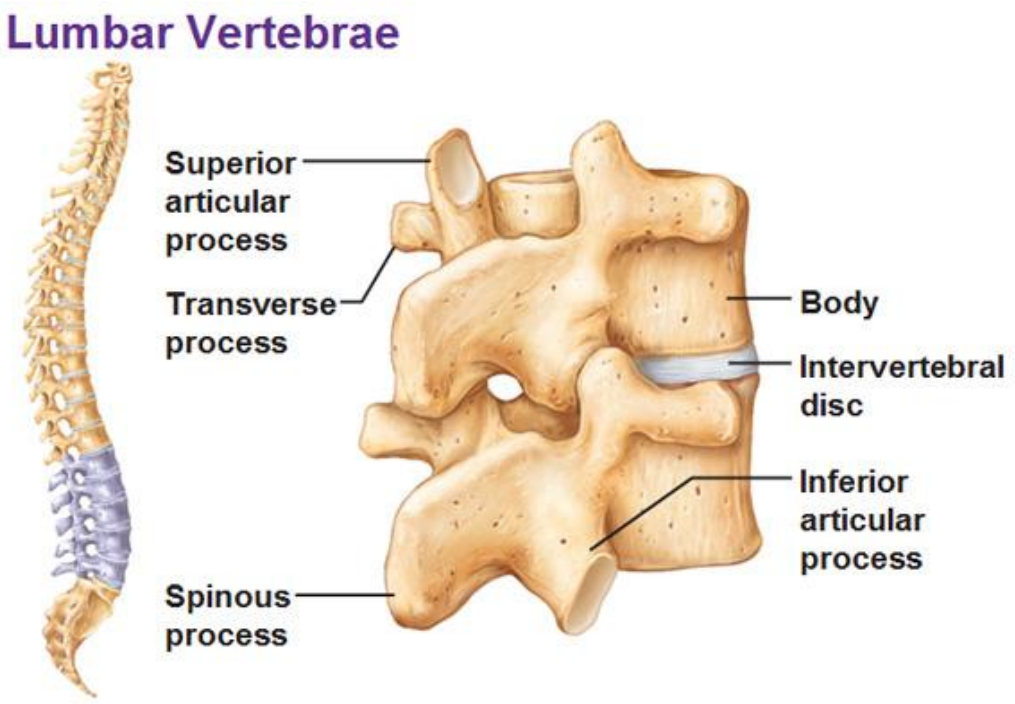


Vertebral column (side view and back view)

The vertebral column consists of 7 cervical, 12 thoracic and 5 lumbar vertebrae. At the caudal end, the 5 sacral vertebrae are fused to form the sacrum, and the 4 coccygeal vertebrae are fused to form the coccyx.[9]

The normal spinal column is straight when viewed dorsally or ventrally. When viewed from the side, there are two ventrally convex curvatures in the cervical and lumbar regions, giving the spinal column the appearance of double C.[9]

Structure of the vertebrae.[10]



Lumbar vertebrae.

Each vertebra is composed of a vertical body and a bony arch.

Body: The mass of the bone through which the weight of the subject is transmitted.

Vertebral arch: Surrounds and protects the spinal cord lying in the vertebral foramen. The arch comprises of pedicles, lamina and spinous process.

Pedicles: Are notched. The notches of the adjacent vertebrae pair together to form an intervertebral foramen through which the spinal nerves emerge on each side. Lamina carries a transverse process, superior and inferior articular processes which bear the articular facets on each side.

Spinous process: Projects backwards from the centre of the vertebral arch and forms an important palpable land mark for the anaesthesiologist.

Spinous process of the cervical vertebrae [10]

The spinous process of the cervical vertebrae is short and bifid [with exception of C1 and C7] and is directed almost horizontally to the body of the vertebra.

Spinous process of the thoracic vertebra[10]

The spinous process of the [T5-T8] thoracic vertebra is long and is inclined at an angle of 45 to 60 degree to the body of the vertebra and the skin. So the needle should be directed at an angle of 45-60° cranially, to follow the upper border of the spine to enter the ligamentum flavum.

Spinous process of lumbar vertebra[10]

The spinous process of the lumbar vertebra is directed horizontally backwards virtually 90 degree to the body of the vertebra and the skin. So the needle is to be directed perpendicular to the skin.

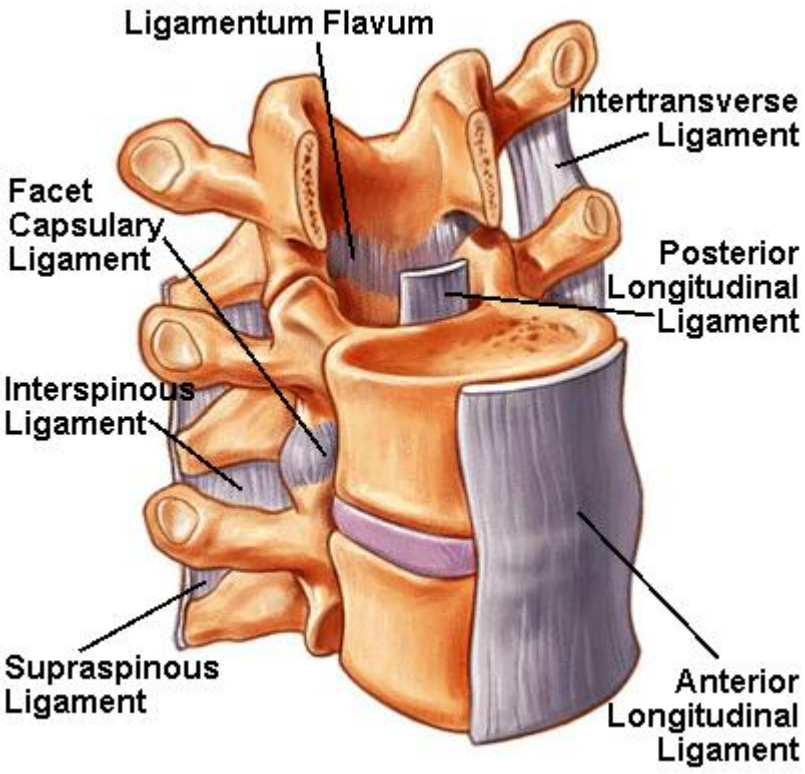
Intervertebral disc

These are the connecting links between the vertebral bodies and they account for 25% of the length of spine. Each disc adheres above and below to the hyaline cartilage which covers the facet of adjacent vertebral body in front and behind and also attached to the anterior and posterior longitudinal ligaments.

Joints of the vertebral column.[9]

The vertebrae articulate at the intervertebral and facet joints. The intervertebral joints are located between adjacent vertebral bodies. They maintain the strength of attachment between vertebrae. The facet joints form between superior and inferior articular processes.

Ligaments.[3]



Ligaments of Lumbar vertebrae.

The vertebrae are joined together by a series of ligaments and discs. Slight movement, flexion, extension and rotation are possible between the adjacent vertebrae but the individual joint movements summate and produce the marked flexibility of

vertebral column. The vertebral column is bound together by several ligaments which give it stability and elasticity.

Supraspinous ligament

It is a strong fibrous cord that connects the apices of the spinous processes from the sacrum to C7, where it is continued as ligamentum nuche. It is thickest and broadest in the lumbar region and varies with patient age, sex and body built.

Interspinous ligament

It is a thin membranous ligament that connects the spinous processes blending anteriorly with the ligamentum flavum and posteriorly with the supraspinous ligaments. Like supraspinous ligaments, the interspinous ligaments are thickest and broadest in the lumbar region.

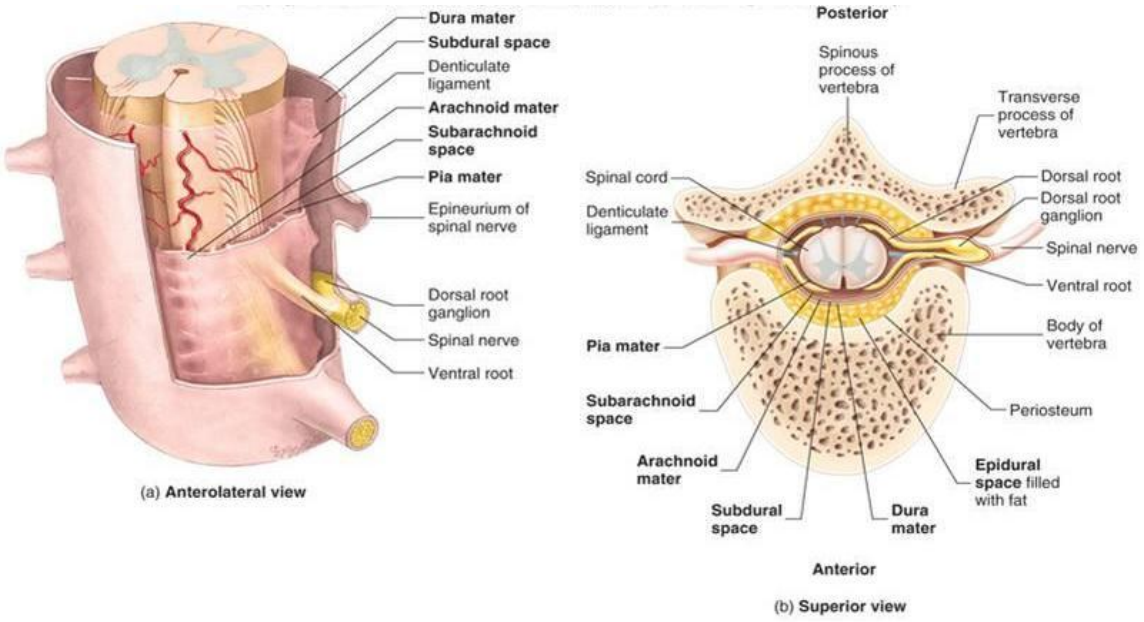
Ligamentum flavum.[3]

It comprises of yellow elastic fibers and connects adjacent laminae that run from the caudal edge of vertebra above to the cephalad edge of the lamina below. Laterally, this ligament begins at the roots of the articular processes and extends posteriorly and medially to the point where the laminae join to form the spinous process. Hence the two components of the ligament are limited, thus covering the interlaminar space. Because of its elasticity and its thickness of several millimeters in the lumbar region, the ligaments impart a characteristic 'springy' resistance, particularly to large bore needle with an up turned end [Tuohy needle].

Longitudinal Ligament

Anterior and posterior longitudinal ligaments bind vertebral bodies together.

Epidural Space.[3]



Boundaries of Epidural Space.

It is the space that lies between the spinal meninges and the sides of the vertebral canal. It extends from the foramen magnum where the dura is fused to the base of the skull, to the sacral hiatus, which is covered by sacrococcegeal ligament. It is bounded anteriorly by the posterior longitudinal ligament, laterally the pedicles and the intervertebral foramina and posteriorly by the ligamentum flavum and anterior surface of lamina. The anterior epidural space is very narrow because of the proximity of the dura and the anterior surface of the vertebral canal. The epidural space is widest posteriorly and varies with the vertebral level ranging from 1 to 1.5 mm at Cervical, 2.5 to 3 mm at

Upper thotacic, 4-5mm at Lower thoracic and to its widest point 5 to 6 mm at Lumbar vertebrae.

It is a space filled with fat, areolar tissue, lymphatics, veins and nerve roots that traverse it but no free fluid. The epidural space is rich in blood vessels, including Batson's venous plexus. Batson's plexus is continuous with the iliac vessels in the pelvis and the azygous system in the abdominal and thoracic body walls. Because this plexus has no valves, blood from any of the connected system can flow into the epidural vessels and connect with intracranial veins. This is a potential direct route to brain for drugs, air or other material inadvertently injected into an epidural vein. Within the cranium, there is no epidural space as the meningeal dura and the endosteal dura are closely adherent, except where they separate to form the venous sinuses.

Epidural Fat.[3]

Is semifluid lobulated areolar tissue extends throughout the spinal and caudal epidural space. It is most abundant posteriorly, diminishes adjacent to the articular processes, and increase laterally around spinal nerve roots, where it is continuous with the fat surrounding the spinal nerves in the intervertebral foramina and hence with the fat in the paravertebral space. Overall the amount of fat in the epidural space tends to vary in direct relation to that present elsewhere in the body, so that obese patients may have epidural spaces that are occupied by generous amount of fat. The fat itself has a great affinity for drugs with high lipid solubility, which may remain in epidural fat for longer periods. Uptake of local anaesthetics into epidural fat competes with vascular and neural uptake.

Epidural Veins.[3]

The large valveless epidural veins are part of the internal vertebral venous plexus, which drains the neural tissue of the cord, the CSF and the bony spinal canal. The major portion of this plexus lies in the anterolateral part of the epidural space, out of reach of a correctly placed epidural needle. The plexus has rich segmental connections at all levels within the intervertebral foramina and the epidural space and within the body of the vertebrae. Superiorly, the plexus communicates with the occipital, sigmoid and basilar venous sinuses within the cranium. Inferiorly, anastomosis by way of the sacral venous plexus links the vertebral plexus to uterine and iliac veins. By way of intervertebral foramina at each level, the vertebral plexus communicates with the thoracic and abdominal veins, so that pressure changes in these cavities are transmitted to epidural veins but not to the supporting bony elements of the neural arch and vertebral bodies.

Spinal Arteries.[3]

It is of significance to epidural block that the spinal branches of the subclavian, aortic and iliac arteries cross the epidural space and enters the epidural space in the region of the dural cuffs. The anterior spinal artery territory supplying the anterior horn or motor area of the spinal cord is most vulnerable as it is a single artery and does not anastomose with the two posterior spinal arteries.

Epidural Lymphatics.[3]

The dural cuff region is supplied with rich lymphatic network that rapidly conveys debris from arachnoid villi out through intervertebral foramina to reach lymph channels in front of the vertebral bodies.

Dural Sac

Containing dura, arachnoid, spinal fluid, pia, spinal nerves and spinal cord is contained within the annular epidural space.

Dura.[11]

Dura mater is the outermost and the thickest meningeal tissue. The spinal dura mater begins at the foramen magnum where it fuses with the periosteum of the skull forming the cephalad border of the epidural space. Caudally dura mater ends at approximately S2, where it fuses with the filum terminale. The dura mater extends laterally along the spinal nerve roots and becomes, continuous with the connective tissue of the epineurium at approximately the level of the intervertebral foramina. The dura mater is largerly acellular except for a layer of cells that form the border between the dura and arachnoid mater. The inner edge of the dura mater is highly vascular which likely results in the dura mater being an important route of drug clearance from

both the epidural space and the sub arachnoid space.

Arachnoid Mater.[11]

The arachnoid mater is a delicate, avascular membrane. In the region where the spinal nerve roots traverse the dura and arachnoid membranes, the arachnoid mater herniates through the dura mater into the epidural space to form arachnoid granulations. The granulations serve as sites for material in the subarachnoid space to exit the central nervous system.

Epidural Pressure

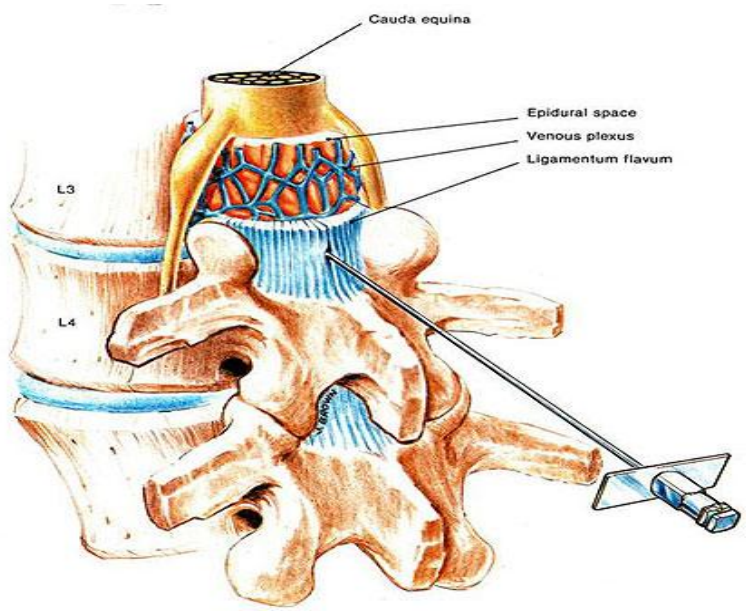
In the lumbar region, the major cause of generation of a negative pressure lies in coning of the dura by the advancing needle point. Negative pressure increases as the needle advances across the epidural space towards the dura. Blunt needles with side openings produce the greatest negative pressure; they produce a good coning effect on the dura without puncturing it and transmit the negative pressure well because of their side opening.

Slow introduction of the needle produces the greatest negative pressure.

Greatest negative pressure can be obtained if the dura is not distended [eg. By gravity in sitting position or by high abdominal or thoracic pressure]. In pregnancy, the epidural space may well have a positive pressure. Hence hanging drop technique may not be reliable in pregnant women to identify the epidural space.

Detection of epidural space.[4]

The methods for identification of the epidural space take the advantage of either the potential negative pressure or the sudden loss of resistance when the needle tip penetrates the tough ligamentum flavum.



Epidural Block technique.

Negative pressure techniques

1. Hanging drop technique of Gutierrez

2. Odom's capillary tube method

3. Manometer method

Loss of resistance technique [described by Sicard, Forester and Dogliotti]

1. Syringe technique [using either normal saline or air]

2. Spring loaded syringe

3. Macintosh balloon technique

4. Brookes device

5. Vertical tube of Bawkins

Factors affecting epidural blockade.[3]

Many factors may affect the efficacy, spread of blockade, fiber types blocked and other aspects of epidural blockade.

Site of injection and nerve root size

Blockade tends to be most intense and has the most rapid onset close to the site of injection. After lumbar epidural injection, there is a somewhat greater cranial than caudal spread and there may be a delay in the L5 and S1 segments. The delay in onset at these segments appears to be due to the large size of these nerve roots. Hence keeping the patient in sitting posture for a few minutes after injecting local anaesthetic agent will help in blocking these large nerves due to gravity.

Age

With advancing age, anatomic changes occur in the epidural space. In young individual, the areolar tissue around the intervertebral foramina is soft and loose. In elderly areolar tissue becomes dense and firm, partially sealing the intervertebral foramina. With aging, the dura becomes more permeable to local anaesthetics because of significant increase in the size of the arachnoid villi.

The onset time to maximal caudad spread decrease with advancing age following epidural administration of Bupivacaine. Bromage demonstrated that with age the epidural segmental dose requirement decreases in a linear way and also the technique is technically difficult and hence there is always a chance of failure.

Height and weight

The correlation between patient height or weight and spread of epidural block is weak and of little clinical significance.

Position

Comparison of sitting and lateral positions for epidural block reveals no significant difference in cephalad spread. Caudal spread of block in seated patients is slightly favoured by the sitting position.

Speed of injection

Increasing the speed of injection has no effect on bulk flow of solutions in the epidural space. Also, spread of analgesia is only minimally influenced. However, rapid injection of large volumes of solution may increase CSF pressure, decrease spinal cord blood flow, increase intracranial pressure and pose a risk of spinal or cerebral complications. Local anaesthetics should be injected into the epidural space slowly and preferably in incremental doses.

Volume, concentration and doses of local anaesthetics.[11]

Within the range typically used for surgical anaesthesia, drug concentration is relatively unimportant in determining block spread. However, drug dose and volume are important variables determining both spread and quality of epidural block.

Increasing the volume of local anaesthetics will result in significantly greater average spread and greater block density, with regard to motor blockade, dosage becomes less important when dilute solutions are used. Increasing the dosages results in a linear

increase in degree of sensory block and duration of epidural block, where as increasing concentration results in a reduction in onset time and intensity of motor blockade.

Local anaesthetics.[11]

Choice of local anaesthetics is the most important determinant of the duration of epidural block. Chloroprocaine is the shortest duration drug, Lidocaine and Mepivacaine provides intermediate duration, and Bupivacaine, Levobupivacaine, Ropivacaine and Etidocaine provide the longest lasting epidural block. The differential capabilities of local anaesthetics to block sensory and motor fibers have been referred to as 'sensory motor dissociation'.

Epinephrine.[11]

Epinephrine in a concentration of 5µg/ml [1:200000] is the most common adrenergic agonist added to epidural local anaestheticsto prolong the duration of Lidocaine and Mepivacaine epidural block.

Vasoconstrictors have been assumed to prolong block by producing local vasoconstriction and thus decreased local anesthetic clearance from the epidural space. Prolongation of motor and sensory block may be due in part to direct inhibitory effects of epinephrine on sensory and motor neurons. Epinephrine does not significantly prolong the duration of anaesthesia when added to concentrated solutions of Bupivacaine or Levobupivacaine.

PHYSIOLOGICAL EFFECTS OF EPIDURAL BLOCKADE.[3]

Epidural neural blockade implies sympathetic blockade accompanied by somatic blockade, which involves sensory and motor blockade.

Zone of differential blockade.[11]

Sensory

In spinal block sympathetic fibers are blocked two or three segments higher than sensory fibers. In epidural block, the relationship is complex. Level of sympathetic block is the same as (or lower than) sensory with epidural blockade. Sympathetic block will be greater when more concentrated solutions are used or when adrenaline added, as this has similar effect.

Motor

In spinal block, the difference between sensory and motor block is slight (two segments). In epidural block, the difference in levels is greater, depending very much on nature of local analgesic solution. All types of nerve fibers are affected by local anaesthetics, but with in any one fiber type, there is tendency for small, slower conducting fibers to be more readily blocked than large, fast conducting fibers. Between fiber types however, these rules do not hold good. Myelinated preganglionic B fibers which have a faster conduction time are about three times more sensitive to local anaesthetics than the slower nonmyelinated post ganglionic C fibers.

Sensory Aβ fibers appear to be more sensitive to blockade than motor Aα fibers, although of the same conduction velocity, this may be because sensory fibers conduct at a

higher frequency. It has been suggested that this selectivity for sensory fibers exhibited by Bupivacaine and Ropivacaine is a function of frequency dependent block.

Cardiovascular System.[11]

These are different ways in which epidural block can influence the cardiovascular system.

1. Vasodilatation of resistance and capacitance vessels. Block of cardiac efferent sympathetic fibers from T1 to T4 resulting in loss of chronotropic and Inotropic drive and fall in cardiac output.

2. The arterial or Bainbridge reflex causing-bradycardia.

3. The operation of Marey's law causing tachycardia.

4. Depression of vascular smooth muscle and β adrenergic blockade of myocardium with fall in cardiac output.

5. Adrenaline effect (if used) following absorption, resulting in β stimulation and associated rise in cardiac output and reduction in peripheral resistance.

Cause of fall in blood pressure

1. Diminished cardiac output consequent on reduction of venous return to heart, and lack of muscular propulsive force on veins.

2. Dilatation of post arteriolar capillaries and small venules due to paralysis of vasoconstrictors, compensatory vasoconstriction takes place in areas not anaesthetized via carotid sinus reflexes. In high spinal blocks, majority of vasoconstrictor fibers

including those to arm [T2-T10], are paralyzed, hence low blood pressure. Total peripheral resistance decreases by only 18% following complete sympathetic block in healthy young adults.

3. Paralysis of sympathetic nerve supply to heart T1-T4. Bradycardia may give rise to fall in cardiac output.

4. Paralysis of sympathetic nerve supply to adrenal glands splanchnic nerves, with consequent catecholamine depletion

Respiratory system.[11]

Alterations in pulmonary physiology are minimal with neuraxial blocks as diaphragm is innervated by phrenic nerve originating from C3 – 5. Tidal volume remains unchanged. There is small decrease in vital capacity due to loss of abdominal muscle contribution to forced expiration. Intercostals muscle paralysis is compensated for by descent of diaphragm, which is made easier the by the lax abdominal walls. This is not accompanied by hypoxia and hypercapnia although the ability to cough forcibly to expel secretion is impaired. The ventilation perfusion during epidural block is not greatly altered with as FRC or V/Q ratio changes are minimal. The pulmonary gas exchange is preserved.

Gastrointestinal system.[11]

Preganglionic sympathetic fibers from T5 to L1 are inhibitory to gut, there is no effect on oesophagus, the innervations of which is Vagus. The small gut is contracted as the sympathetic inhibitory impulses are removed, the Vagus being all powerful,

sphincters are relaxed and peristalsis is active although not more frequent. Pressure within the bowel lumen is increased.

Nausea and vomiting due to the hypotension may occur. Colonic blood supply and oxygen availability are increased, perhaps an important factor in the prevention of anastomotic breakdown following gut resection.

Liver.[11]

There are no specific effects of significance. Hepatic blood flow will decrease due to reduction in mean arterial pressure. Liver disease may interfere with the metabolism of local anaesthetic drugs.

Endocrine system.[11]

The usual increase in neuroendocrine stress response to surgery is suppressed but there is no difference in the postoperative period once the effects of the block wears off.

Genito urinary system.[11]

Sympathetic supply of kidney is from T11 to L1 via the lowest splanchnic nerves. Any effects on renal function are due to hypotension. Auto regulation of renal blood flow is impaired if mean arterial pressure falls below 50 mmHg. These changes are transient and disappear when blood pressure rises again. Sphincters of bladder are not relaxed, so soiling of table by urine is not seen and tone of ureters is not greatly altered. The penis is often engorged and flaccid due to paralysis of the Nervi Erigentes [S2 and S3]. This is a useful positive sign of successful block. Post operative retention of urine may be

moderately prolonged as L2 and L3 contain small autonomic fibers and their paralysis lasts longer than of the larger sensory and motor fibers.

Body temperature.[11]

Vasodilatation favors heat loss. Absence of sweating favors hyperpyrexia in hot environments. Catecholamine secretion is depressed, hence less heat is produced by metabolism.

PHARMACOLOGY

Local anaesthetics are chemical compounds which are capable of reversibly inhibiting the propagation of impulses in nerve cells. The amino ester group have an ester link and include Procaine, Chloroprocaine and Amethocaine. The amino amides have an amide link between the aromatic head and the intermediate chain and include Lignocaine, Bupivacaine, Mepivacaine, Prilocaine, Etidocaine and Ropivacaine.

PHARMACOLOGY OF LEVOBUPIVACAINE

Introduction

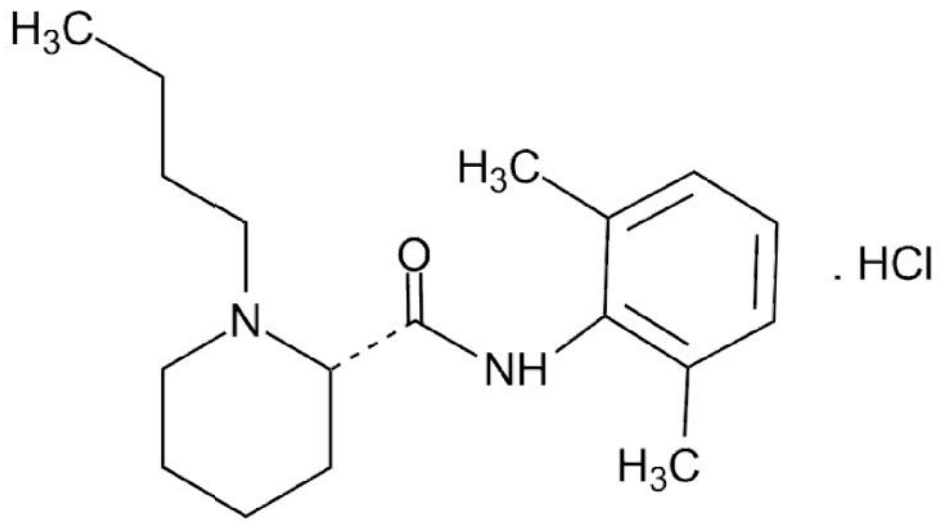
Bupivacaine, the widely used local anesthetic in regional anesthesia is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, Levobupivacaine, S (−) isomer and DextroBupivacaine, R (+) isomer. Severe central nervous system (CNS) and cardiovascular adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anesthesia have been linked to the R (+) isomer of Bupivacaine. The levorotatory isomers were shown to have a safer pharmacological profile [12],[13] with less cardiac and neurotoxic adverse effects. [14],[15] The decreased toxicity of Levobupivacaine is attributed to its faster protein binding rate. [16] .

Stereoisomerism

Bupivacaine exhibits the phenomenon of stereoisomerism because of the presence of an asymmetric carbon, which acts as a chiral center.

Chemical structure

Levobupivacaine ([2S]-1-butyl-N- [2, 6-dimethylphenyl] piperidine-2-carboxamide) is an amino-amide local anesthetic drug belonging to the family of n-alkyl substitute pipecoloxylidide. Its chemical formula is $C_{18} H_{28} N_2 O$



Chemical structure of Levobupivacaine

Mechanism of action

Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at the nodes of Ranvier more readily than unmyelinated nerves; and small nerves are blocked more easily than larger ones. In general, the progression of anesthesia is related to the diameter, myelination and conduction velocity of the affected nerve fibers. Specifically, the drug binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization. It blocks nerve conduction in sensory and motor nerves mainly by interacting with voltage sensitive sodium channels on the cell

membrane. It also interferes with impulse transmission and conduction in other tissues. [17],[18]

Pharmacokinetics

The dose as well as the route of administration of Levobupivacaine determines the plasma concentration following therapeutic administration as the absorption is dependent upon the vascularity of the tissue. After epidural administration of Levobupivacaine, the absorption is biphasic, with rapid absorption of a small quantity of drug into the circulation and slower absorption of the remainder of the drug. It has been observed that peak levels of Levobupivacaine in the blood reaches approximately 30 min after epidural administration and doses up to 150 mg had resulted in mean C_{max} levels up to 1.2 g/mL. The epidural absorption gets affected by age as the fraction absorbed decreases and the fast absorption phase is shorter in older (aged > 70 years) compared with the younger (aged 18-44 years) patients. The older patients also have a higher spread of analgesia by ~ 3 dermatomes. Therefore, in the elderly patients a lower dose of Levobupivacaine, according to their physical status is recommended. The volume of distribution is estimated at 66.91 ± 18.23 L (after intravenous administration of 40 mg in healthy volunteers). The pKa of Levobupivacaine is 8.1, similar to the pKa of the racemic Bupivacaine. The half-life is 3.3h. The rate of clearance is 39.06 ± 13.29 L/h (after intravenous administration of 40 mg in healthy volunteers). [38],[6]

Alpha1-glycoprotein is the main binding site for Levobupivacaine. Protein binding of Levobupivacaine is more (97%) than that of racemic Bupivacaine (95%). Less than 3% of the drug circulates free in plasma. The free proportion of the drug can have an action on the other tissues, causing unwanted side-effects and toxic manifestations. In

newborns and in protein-deficient states like under nutrition and nephrotic syndrome, lesser amount of protein is available for binding, causing higher levels of free drug, resulting in toxic effects at lower doses. [17],[18]

Levobupivacaine is extensively metabolized by liver and excreted in urine or feces.

Clinical utility

The incidence of adverse cardiac and neurological events was significantly higher with Bupivacaine as compared to Levobupivacaine when used in regional anesthesia. Similarly, the potential for CNS toxicity is lower with Levobupivacaine as compared to Bupivacaine. [14],[16],[18] . The low cardiovascular and neurological toxicity of Levobupivacaine has led to its application as a local anesthetic in a wide variety of specialist applications including sub-arachnoid block, epidural anesthesia and analgesia, brachial plexus blocks, peripheral nerve blocks, ocular blocks as well as local infiltration. It is also being used for labor analgesia, post-operative pain as well as management of acute and chronic pain.

Adverse effects

Levobupivacaine produces the same adverse effects as seen with racemic Bupivacaine and other local anesthetics. The most common adverse drug reaction reported is hypotension (31%) followed by nausea (21%), vomiting (14%), headache (9%), procedural pain (8%) and dizziness (6%). The cardiac toxicity, neurological injury after peripheral nerve block and unwanted CNS effects, may be lower than Bupivacaine. Allergic type reactions are rare and range in severity from urticaria to anaphylactoid-like

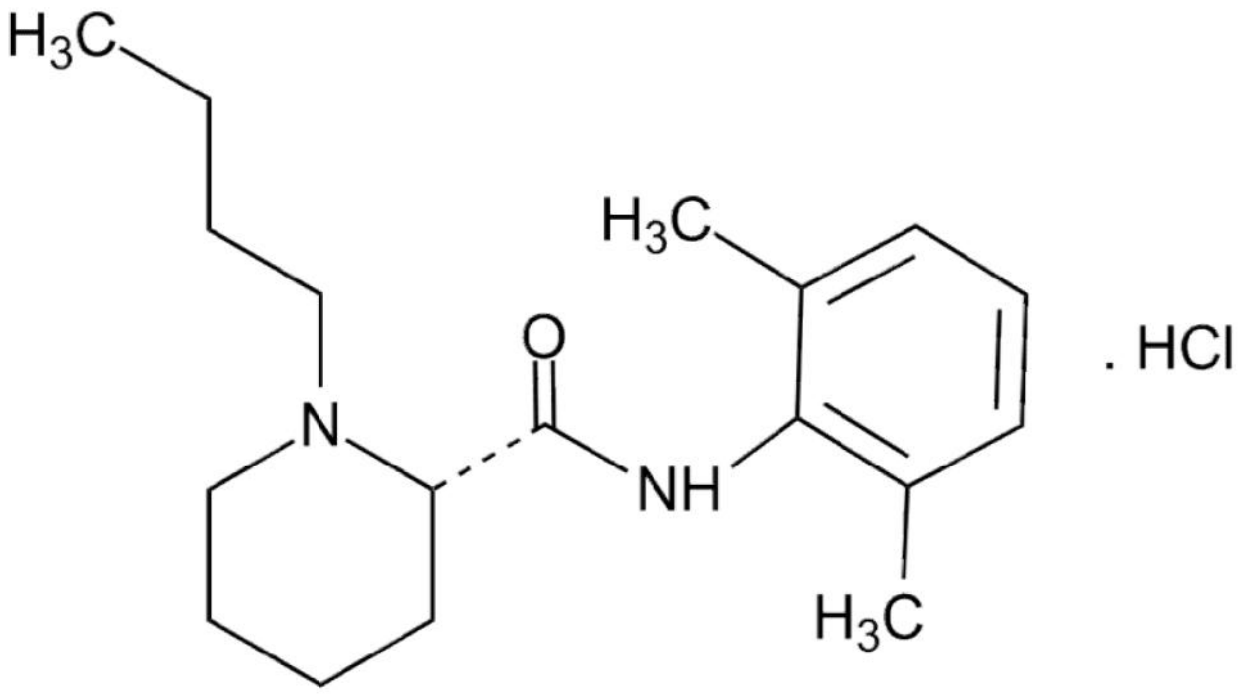
reaction. During the administration of epidural anesthesia, it is recommended that a test dose is administered initially and the effects monitored before the full dose is given. A test dose of a short-acting amide anesthetic, such as three milliliters (3 mL) of Lignocaine, is recommended to detect unintentional intrathecal administration. Accidental intrathecal injection during epidural blockade can produce high spinal anesthesia with severe hypotension and loss of consciousness.Safety issues in case of inadvertent intravenous administration.

Levobupivacaine has a safety margin of 1.3, which means toxic effects are not seen until the concentration rises by 30%. The concentration necessary to produce cardiac and neurotoxicity is higher for Levobupivacaine than for racemic Bupivacaine. There are three case reports of successful resuscitation after inadvertent intravenous injection. The presentations were severe hypotension and bradycardia after a drug error; loss of consciousness, convulsions, hypotension and changes in QRS pattern of ECG after presumed intravenous injection during lumbar plexus block and loss of consciousness and convulsions after (a) spinal (b) sciatic nerve and (c) continuous lumbar plexus blocks. In all cases, resuscitation was successful with supportive measures, with or without pressor drugs and intravenous lipid emulsion. [17] [18]Recently studies have been carried out comparing the beneficial effects of vasopressor drugs and lipid therapy in local anesthetic systemic toxicity (LAST). Epinephrine should be used in small doses (1-10 mg) in adults. The use of vasopressin is not recommended. Lipid emulsion therapy should be considered at the first signs of LAST, after airway management. [19] Successful resuscitation has been reported with intralipid emulsions in a peri-arrest condition following use of Levobupivacaine in lumbar plexus block. [20]

Conclusion

Levobupivacaine is a long-acting local anesthetic with a clinical profile similar to that of Bupivacaine. In an individual patient, the clinical anesthetic effect from the drug is indistinguishable from that of Bupivacaine. The better safety profile of Levobupivacaine confers an advantage over its racemic parent, Bupivacaine.

PHARMACOLOGY OF BUPIVACAINE[4],[21].



Chemical structure of Bupivacaine

Chemical name: l-n-butyl-DL-piperidine-2-carboxylic acid-2, 6 dimethylanilide hydrochloride.

Bupivacaine hydrochloride is an amide type of local anaesthetic drug, which was synthesized by A. F. Ekenstam in 1957 and used clinically in 1963.

Physicochemical properties

Molecular weight	288 (base), 325 (chloride salt)
pKa	8.1
Plasma protein binding	95%

Solubility: Base is sparingly soluble, but hydrochloride is readily soluble in water.

Stability and sterilization: Bupivacaine is highly stable and can withstand repeated autoclaving.

Melting point: 258°C.

Potency: Bupivacaine is approximately three to four times more potent than Lidocaine.

Mechanism of action

Local anaesthetics prevent transmission of nerve impulses (conduction blockade) by inhibiting passage of sodium ions through ion selective sodium channels in nerve membranes. The sodium channel itself is a specific receptor for local anaesthetic molecules. Occlusion of open sodium channels by local anesthetic molecules contributes little to overall inhibition of sodium permeability. Failure of sodium ion channel permeability to increase slows the rate of depolarization such that threshold potential is not reached and thus an action potential is not propagated.

Because the concentration of local anaesthetics in cerebrospinal fluid decreases as a function of distance from the site of injection, and because different types of nerve

fibers differ in their sensitivity to the effects of local anaesthetics, zones of differential anaesthesia develop.

The minimum concentration of local anaesthetic necessary to produce conduction blockade of nerve impulses is termed the Cm. Nerve fiber diameter influences Cm with larger nerve fibers requiring higher concentration of local anaesthetic for production of conduction blockade. An increased tissue pH or high frequency of nerve stimulation decreases Cm.

The Cm of motor fibers is approximately twice that of sensory fibers; thus, sensory anaesthesia may not always be accompanied by skeletal muscle paralysis. For conduction blockade to occur in an A fiber, it is necessary to expose at least two and preferably three successive Nodes of Ranvier (approximately 1 cm) to an adequate concentration of local anesthetic. Both types of pain conducting fibers (myelinated A-delta and non myelinated C fibers) are blocked by similar concentration of local anaesthetics, despite the differences in the diameters of these fibers. Preganglionic B fibers are more readily blocked by local anesthetics than any fiber, even though these fibers are myelinated.

Pharmacodynamics:

The onset of action of Bupivacaine is between 5 and 7 minutes, and maximum anaesthesia is obtained between 15 and 25 minutes. The duration of anesthesia varies according to the type of block, the average duration for peridural block is about 3.5 to 5 hours. For nerve blocks, it is about 5 to 6 hours.

Pharmacokinetics:

Absorption and distribution

Absorption of local anaesthetic from site of injection into the systemic circulation is influenced by the site of injection and dosage, use of epinephrine, and pharmacologic characteristics of the drug. The ultimate plasma concentration of a local anaesthetic is determined by the rate of tissue distribution and the rate of clearance of the drug.

Lipid solubility is important in redistribution as well as being a primary determinant of intrinsic local anaesthetic potency. Ultimately the local anaesthetic is eliminated from the plasma by metabolism and excretion.

The alpha half life in plasma of Bupivacaine, after attaining levels of 1.0 to 2.0 μg/ml, is approximately 2.5 hours. The beta half life is about 4 to 5 hours.

Plasma binding

In plasma, the drug binds avidly with protein to the extent of 95%. Protein binding of local anaesthetic will influence their distribution and excretion. In this regard protein binding parallels lipid solubility of the local anaesthetic and is inversely related to the plasma concentration of drug. For Bupivacaine, the first pass pulmonary extraction is dose dependent, suggesting that the uptake process becomes saturated rapidly. There may be clinically significant transplacental transfer of local anaesthetic between the mother and fetus. Plasma protein binding influences the rate and degree of diffusion of local anesthetics across the placenta. Bupivacaine, which is highly protein bound

(approximately 95%) has an umbilical vein-maternal arterial concentration ratio of about 0.32.

Metabolism

They undergo varying rates of metabolism by microsomal enzymes located primarily in the liver. Bupivacaine undergo the slowest metabolism among the amide local anaesthetics. Pathways for metabolism of Bupivacaine include aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation.

Systemic toxicity

Systemic toxicity of a local anaesthetic is due to an excess plasma concentration of the drug. Plasma concentrations determined by the rate of drug entrance into the systemic circulation relative to their redistribution to inactive tissue sites and clearance by metabolism.

Central Nervous System toxicity

It causes curcumoral numbness, restlessness, vertigo, tinnitus and difficulty in focusing occurs initially. Further increase in concentration results in slurred speech and skeletal muscle twitching. Skeletal muscle twitching is often first evident in the face and extremities and signals the imminence of tonic-clonic seizures.

Drowsiness before the onset of seizures. Seizures are classically followed by CNS depression which may be accompanied by hypotension and apnea.

The typical plasma concentration associated with seizures is 4.5 to 5.5 μg/ml.

Cardiac toxicity: After accidental IV injection of Bupivacaine the protein binding sites (alpha1 acid glycoprotein and albumin) are quickly saturated, leaving a significant mass of unbound drug available for diffusion into the conducting tissue of the heart. This may result in precipitous hypotension, cardiac dysrhythmias and atrioventricular heart block. Cardiotoxic plasma concentration of Bupivacaine is 8 to 10 μg/ml. The threshold for cardiac toxicity produced by Bupivacaine may be decreased in patients being treated with drugs that inhibit myocardial impulse propagation (beta adrenergic blockers, digitalis preparations, calcium channel blockers).

It depresses the maximal depolarization rate of cardiac action potential (Vmax) by virtue of their ability to inhibit sodium ion influx via sodium channels.

Bupivacaine depresses Vmax considerably more than Lidocaine. The resulting slowed conduction of the cardiac action potential manifest on the electrocardiogram as prolongation of the P-R and QRS intervals and reentry ventricular cardiac dysrhythmias. The R enantiomer of Bupivacaine is more toxic than the S enantiomer.

Hepatotoxicity

Continuous or intermittent epidural administration of Bupivacaine has been associated with increased plasma concentration of liver transaminase enzymes that normalized when Bupivacaine infusion was discontinued.

Review of historical perspective of epidural anaesthesia:

J Leonard Corning, a neurologist in New York, injected Cocaine intervertebrally in dogs and in patients to relieve chronic pain and not to provide operative anaesthesia[22]. Spinal anaesthesia with Cocaine was initially produced inadvertently by J Leonard Corning, in 1885 and first used deliberately by August Bier in 1898. On August 15 1898, August Bier and his assistant August Hildebrandt used the Quinckes method of entering the Intrathecal space and injected between 5 and 15 mg of Cocaine to produce spinal anaesthesia in six cases for operations on the lower part of the body. They also reported the result of spinal anaesthesia given to each other.[22]

Jean Enthuse Sicard and Fernand Cathelin independently introduced Cocaine through the sacral hiatus in 1901, becoming the first practitioners of caudal epidural anaesthesia. 19 years later, a Spanish military surgeon Archile Mario Dogliotti performed abdominal surgery using single shot lumbar epidural anaesthesia. He correctly identified the epidural space describing the sudden loss of resistance noted after the needle had crossed the ligamentum flavum. Aburel, Higson and Edwards all devised methods for continuous but cumbersome epidural blockade. However Cuba anaesthesiologist, Manual Martinez Curbelo, is credited with making the technique more practical. On his visit to Mayo Clinic in 1947, he watched Tuohy perform continuous spinal block. Curbelo used the Tuohy needle with a silk ureteral catheter to provide continuous segmental lumbar peridural anaesthesia. Several modifications of the Tuohy-Huber epidural needle have been developed in the more recent past and are being utilized in modern anaesthesia practice.[3] Crawford used epidural anaesthesia for thoracic surgery

History of local anaesthetics

The toxicity of Cocaine, coupled with its vast potential for usefulness in surgery, led to an intensive search for less toxic substitutes. Procaine was synthesized by Einhorn in 1904, but the limitation was its short duration of action. Mcisches synthesized Dibucaine in 1925, Uhlmann introduced it clinically. In 1928, Eisleb synthesized Tetracaine and introduced into clinical practice.[22]

Most of these amino ester agents were relatively unstable and could not be subjected to repeated autoclaving for sterilization. In addition, the hydrolysis of aminoesters by enzyme psuedocholinesterase resulted in the formation of para amino benzoic acid which was responsible for reported allergic reactions.

Lidocaine, synthesized in 1943 by Lofgren and Lundquist was a stable compound that was not influenced by repeated exposures to high temperature and thus could be resterilised often. In addition, the metabolites of Lidocaine did not include p-amino benzoic acid. Thus allergic reactions were avoided.[22]

Subsequent to Lidocaine release, a number of amino amide compounds were synthesized and four eventually found their way into clinical practice. In 1956, Ekenstam in Sweden synthesized Mepivacaine, whose anesthetic properties were similar to Lidocaine. In 1959, Lofgren and co-workers synthesized Prilocaine.

Lidocaine and Mepivacaine were tertiary amide compounds while Prilocaine was secondary amide.[22]

Bupivacaine was synthesized by Ekenstam in 1956 and introduced into clinical practice in 1963 by Telivuo. In 1971 Takman synthesized Etidocaine and it was found that etidocaine produced more intense and prolonged motor blockade than sensory blockade, hence not producing ideal perioperative anaesthesia.[22]

Since then Bupivacaine is extensively used and became very popular for epidural anaesthesia , because of its long duration of action and preferential sensory block in lower concentrations. Only drawback of Bupivacaine was cardiotoxicity, which when accidentally injected intravascularly. Hence there was a need for introduction of drugs with all the advantages of Bupivacaine without the cardiotoxicity.

Ropivacaine and Levobupivacaine are the newer long acting amide local anaesthetics which have wide margin of safety compared to Bupivacaine, with all its advantages[6].

Cox CR et al in 1998[23] compared epidural Levobupivacaine and Bupivacaine for lower limb surgeries. 88 patients were randomly selected to receive 0.75% Levobupivacaine, 0.5% Levobupivacaine or 0.5% Bupivacaine epidurally. The following observations were made- Mean onset times for loss of sensation to pinprick were 8 min for 0.5% S(-)-Bupivacaine, 6 min for 0.75% S(-)- Bupivacaine and 7 min for 0.5% RS-Bupivacaine. Median maximum sensory block height was T8 in the 0.5% and 0.75% S(-)-Bupivacaine groups and T7 in the 0.5% RS-Bupivacaine group and median time to reach this level was 25 min in all groups. Duration of sensory block was significantly longer in the 0.75% S(-)-Bupivacaine group (*P*- 0.001 on the right, *P* - 0.016 on the left), with a mean duration of 460 min compared with 377 min for 0.5% S(-)-Bupivacaine and 345 min for 0.5% RS-Bupivacaine. There was no significant difference in onset time or grade of motor block between the three groups. However, in the 0.5% S(-)-Bupivacaine group, 14 of 29 patients did not develop motor block and 9 out of 29 patients did not develop motor block in 0.5%RSBupivacaine group; there was a trend in the 0.75% S(-)-Bupivacaine group to have a longer duration of block. There were no significant differences between the three groups in arterial pressure (systolic, mean and diastolic) or heart rate. There was a reduction in both heart rate and arterial pressure during the first hour, with a subsequent return to baseline values. Hypotension was observed in 18 patients, evenly distributed between the three groups. All episodes responded to treatment. It was concluded that there was no significant difference in onset time, maximum spread of sensory block or intensity of motor block between three groups. However duration of sensory block in 0.75% Levobupivacaine group was significantly longer than other two groups.

Burke D et al in 1999[24] compared 0.25% Levobupivacaine and 0.25% Bupivacaine for epidural analgesia in labour. 137 patients in labour were selected randomly to receive either 0.25% Levobupivacaine or 0.25% Bupivacaine. Median onset of pain relief was 12 min for both drugs and median duration was 49 (range 3-129) min and 51 (7-157) min for S(-)-Bupivacaine and RS Bupivacaine, respectively. The estimated difference for duration of pain relief was -4 (90% CI -13, 6) min. Thirty patients failed to achieve pain relief after the first injection (20 patients after S(-)-Bupivacaine and 10 after RS-Bupivacaine; P = 0.039). However, median duration of pain relief from the first top-up was 82 (range 3-164) min for S(-)- Bupivacaine and 76 (22-221) min for RS-Bupivacaine. It was concluded that there was no significant difference in extent of sensory block, motor block or incidence of adverse outcomes.

Bader et al in 1999[9] compared the efficacy of 0.5% Levobupivacaine with 0.5% Bupivacaine for epidural anesthesia in parturients undergoing elective cesarean delivery.Sixty healthy obstetric patients undergoing elective cesarean delivery with epidural anesthesia completed the study. Patients were randomized to receive 30 ml of either 0.5% Levobupivacaine or 0.5% Bupivacaine in a double-blind fashion. The efficacy endpoint measures included onset, offset, and quality of anesthesia. Neonatal blood gas analyses, Apgar score determinations, and neurobehavioral examinations were performed. Venous samples for pharmacokinetic studies and serial electrocardiograms were obtained in 10 patients in each group. Levels of sensory block, motor block, muscle relaxation, and overall quality of anesthesia did not differ between groups. The frequency of hypotension was 84.4% in the Levobupivacaine group and 100% for the Bupivacaine group (P <or= 0.053). It was concluded that the use of epidural 0.5% Levobupivacaine

for cesarean delivery results in equally efficacious anesthesia compared with 0.5% Bupivacaine. Pharmacokinetic parameters were similar in the two groups.

Kopacz et al in 2000[26] by prospective, randomized, double-blinded study of epidural anesthesia compared the onset, extent, and duration of sensory and motor block produced by 0.75% Levobupivacaine (20 mL, 150 mg) with that of 0.75% racemic Bupivacaine in 56 patients undergoing elective lower abdominal surgery. The time to onset of adequate sensory block (T10 dermatome) was similar in both treatment groups (13.6 ± 5.6 min for Levobupivacaine and 14.0 ± 9.9 min for Bupivacaine), with an average peak block height of T5 reached at 24.3 ± 9.4 and 26.5 ± 13.2 min, respectively. Time to complete regression of sensory block was significantly longer with Levobupivacaine (550.6 ± 87.6 min) than Bupivacaine (505.9 ± 71.1 min) (P = 0.016). Patients administered Levobupivacaine showed a significantly slower onset of lower extremity motor block, with only 4 of 28 patients (14%) having detectable lower extremity motor block after 30 min compared with 20 of 28 patients (71%) administered Bupivacaine (P < 0.001) The duration of lower extremity motor block was similar for patients administered Levobupivacaine and Bupivacaine (355.4 ± 83.4 vs 375.7 ± 99.2 min, respectively;P = 0.311). Abdominal muscle relaxation was adequate for the scheduled procedure in all patients, and there were no significant differences between the groups in rectus abdominis muscle scores (P = 0.386) and quality of muscle relaxation as determined by the surgeon and anesthesiologist (P = 0.505 and 0.074, respectively). In conclusion, both 0.75% Levobupivacaine and 0.75% Bupivacaine produced effective epidural anesthesia and their effects were clinically indistinguishable. The results of this study indicated that the sensory and motor block produced by 0.75% Levobupivacaine is equivalent to that of

0.75% racemic Bupivacaine. Both local anesthetics are well tolerated and effective in producing epidural anesthesia for patients undergoing lower abdominal surgery.

Kopacz et al in 2001[27] compared epidural 0.5% Levobupivacaine with or without epinephrine for lumbar spine surgery. 117 patients received 15 ml of 0.5% Levobupivacaine(plain) or with epinephrine(1;200,000 or 1;400,000). The time to onset of adequate sensory block (T10 dermatome) was similar in all groups (12.4 +/- 6.6 min for plain Levobupivacaine, 13.9 +/- 7.9 min for Levobupivacaine with 1:400,000 epinephrine, and 12.7 +/- 4.9 min for Levobupivacaine with 1:200,000 epinephrine), with an average peak block height of T5. Time to complete regression of sensory blockade was also similar between groups (357 +/- 119 min for plain Levobupivacaine, 378+/- 98 min for Levobupivacaine with 1:400,000 epinephrine, and 348 +/- 80 min for Levobupivacaine with 1:200,000 epinephrine). Peak serum Levobupivacaine levels were reduced in each of the epinephrine-containing groups. It was concluded that, both, plain Levobupivacaine and adrenalized Levobupivacaine produced effective anesthesia. Patients receiving adrenalized Levobupivacaine had lower serum Levobupivacaine levels after epidural anesthesia.

Garcia JBS et al in 2001[28] compared the efficacy of 0.5% racemic Bupivacaine and 0.5% Levobupivacaine, both associated to sufentanil, for epidural anesthesia in parturients undergoing cesarean delivery.52 obstetric patients posted for elective cesarean delivery under epidural anesthesia were randomized to receive 27 ml of 0.5% Levobupivacaine and 30 mcg sufentanil (Group I n=26) or 27 ml of 0.5% Bupivacaine and 30 mcg sufentanil (Group II n=26). Characteristics of sensory and motor block, time for analgesics request in the postoperative period and the incidence of side effects were

investigated. Mean heart rate variation along time showed a significant decrease as from 60 minutes for GI and 90 minutes for GII, without significant differences between groups. A significant systolic blood pressure decrease as from 15 minutes for GI and 20 minutes for GII, without significance when comparing both groups was observed. Diastolic blood pressure significantly decreased in both groups as from 20 minutes, also without significance when comparing both groups. Paresthesia was observed at (min) 4.15 ± 1.56 in GI and at 4.46 ± 1.30 in GII. Sensory block onset was observed at (min) 6.88 ± 2.81 in GI and 7.85 ± 2.92 in GII. Maximum sensory block was observed at (min) 18.27 ± 5..82 in GI and 17.88 ± 4.72 in GII. Maximum relaxation was observed at (min) 16.92 ± 4.91 in GI and 17.12 ± 5.50 in GII. T6 level reached at (min) 15. 00 ± 9.68 in GI and 16.92 ± 13.71 in GII. Duration of Surgical anesthesia observed was (min) 200.77 ± 41.36 in GI and 201.54 ± 43.05 in GII. Duration of Muscular relaxation observed was (min) 303.85 ± 48.66 in GI and 272.31 ± 41.98 in GII. Time to Two segment regression was (min) 147.69 ± 41.50 in GI and 148.46 ± 37.06 in GII. Sensory and motor block, time for analgesics request and adverse effects did not differ between groups. However, motor block was significantly longer with Levobupivacaine as compared to racemic Bupivacaine ($p < 0.05$). It was concluded that, although a longer motor block duration with 0.5% epidural Levobupivacaine associated to sufentanil, the efficacy of both local anesthetics associated to sufentanil for cesarean delivery was similar.

Cheng CR et al in 2002[29] compared the safety and efficacy between Levobupivacaine and Bupivacaine in epidural anesthesia for Cesarean delivery. A prospective, controlled, double-blinded study was conducted in 45 ASA class I-II Taiwanese obstetric patients undergoing elective Caesarean Section under extradural anesthesia. Patients were

randomized to receive either 25 ml of 0.5% Bupivacaine or 0.5% Levobupivacaine in a double-blinded fashion. The end points of measurements relevant to efficacy included onset, fade-out, and quality of anesthesia. The safety end-point measurements included Apgar scores, maternal ECG, maternal and neonatal blood pH, and adverse events. There was no significant difference between groups in the profile of sensory and motor blockade produced. Comparison of visual analogue pain scores did not show significant differences between groups at the corresponding times. There were no significant differences between groups in muscle relaxation scores assessed by obstetricians as well as the overall assessment of block quality rated by anesthesiologists. Apgar scores, maternal and neonatal blood pH, maternal ECG, and adverse events did not differ between groups. The drug-related adverse events were hypotension and shivering which were equally seen in Levobupivacaine and Bupivacaine groups. There was no other serious adverse event that happened in both groups. The onset and fade-out of sensory and motor blockade, quality of anesthesia, muscle relaxation and overall quality of anesthesia as assessed were comparable between two groups. No significant maternal or neonatal adverse events were found between the treatment groups. In comparison, Levobupivacaine had the efficacy and safety profile equivalent to Bupivacaine in epidural anesthesia for Caesarean section.

Casati A et al in 2003[30] compared Bupivacaine, Levobupivacaine and Ropivacaine when used for epidural anesthesia for major orthopedic surgeries (intra-operatively & post-operatively). 45 patients undergoing elective total hip replacement surgery were randomly selected to receive either 0.5% Levobupivacaine, 0.5% Bupivacaine or 0.5% Ropivacaine intra-operatively and 0.125% Levobupivacaine, 0.125% Bupivacaine or

0.2% Ropivacaine post-operatively. The onset time of sensory block was 31 +/- 16 minutes with Levobupivacaine, 25 +/- 19 minutes with Bupivacaine, and 30 +/- 24 minutes with Ropivacaine (p = 0.98), after a median (range) volume of 15 (10-18) mL in Group Levobupivacaine, 14 (10-18) mL in Group Bupivacaine, and 15 (10-18) mL in Group Ropivacaine (p = 0.85). Six patients in the Ropivacaine group (40%) showed an intraoperative Bromage score <2 as compared with only three patients of Group Levobupivacaine (20%) and no patient of Group Bupivacaine (p = 0.02). Recovery of pinprick sensation at T(t) occurred after 214 +/- 61 minutes with Levobupivacaine, 213 +/- 53 minutes with Bupivacaine, and 233 +/- 34 minutes with Ropivacaine (p = 0.26). It was concluded that a similar onset, quality and duration of sensory block was produced by same volume of 0.5% Levobupivacaine, 0.5% Bupivacaine & 0.5% Ropivacaine with a lesser degree of motor block with Ropivacaine. Post-operatively all three drugs produced similar and adequate pain relief with similar recovery of motor action.

Peduto VA et al in 2003[31] compared onset time and duration of epidural anaesthesia produced by Levobupivacaine and Ropivacaine for lower limb surgery. ASA I-III adult patients undergoing elective lower limb procedures were randomized to receive epidural Levobupivacaine 0.5% 15 mL (n = 30) or epidural Ropivacaine 0.75% 15 mL (n = 35). With Levobupivacaine, onset time was 29 +/- 24 min, with Ropivacaine it was 25 +/- 22 min (P = 0.41). Complete resolution of motor block required 105 +/- 63 min with Levobupivacaine and 95 +/- 48 min with Ropivacaine (P = 0.86). The time for regression of sensory block to T12 was 185 +/- 77 min with Levobupivacaine and 201 +/- 75 min with Ropivacaine (P = 0.46). Analgesic supplementation was required in one patient receiving Levobupivacaine (3.5%) and in two patients receiving Ropivacaine (5.7%) (P =

0.99).It was concluded, that in adults undergoing lower limb surgery, Levobupivacaine 0.5% 15 mL produces an epidural block with the same clinical profile as Ropivacaine 0.75% 15mL.

M. Kountoudi in 2004[32] compared 0.5% solution of Levobupivacaine and Ropivacaine as far as blood pressure and heart rate alterations during surgery are concerned.30 patients ASA I–III, scheduled for elective inguinal hernia repair, undergoing epidural anaesthesia, were randomized into two groups: group L received Levobupivacaine 0.5% while group R received Ropivacaine 0.5%. After the intravenous infusion of 500 ml of crystalloid solution, an epidural block was performed using either a midline or a paramedian aproach at L 4–5 interspace. The volume of the local anesthetic given, was estimated so as to provide anesthesia up to T 7 dermotome according to patient's age and height. Mean arterial pressure (MAP), heart rate (HR) and oxygen saturation (SpO2) were recorded before (baseline) and every five minutes after epidural block performance, until the end of the surgery. Statistical analysis was performed using Mann Whitney U test. In all cases the tests were double sided and p value of 0.05 was considered to indicate statistical significance.There were no statistical differences in demographic characteristics between the two groups. There was also no statistical difference between the two groups regarding other measured parameters: (MAP, HR , height of the sensory block and duration of surgery). However MAP was statistically significantly lower ($p < 0.05$) in group L compared to group R in all measurements following 15 min after epidural block performance. HR and SpO2 did not differ significantly between the two groups. There were also no differences in the total fluids given [1620 $\pm$120 ml (group L) vs 1510 $\pm$ 50 ml (group R)]. 2 patients in group L and 1

patient in group R received atropine (HR< 45 beats per minute), while vasoconstrictor was not used**.** There was no difference as far as the level of the sensory block is concerned. Levobupivacaine seems to reduce MAP more than Ropivacaine indicating an extended sympathetic block.

Bergamaschi F et al in 2005[33] compared Levobupivacaine and Bupivacaine in epidural anesthesia for elective cesarean section. 47 patients were selected randomly to receive either 20 ml of 0.5% Levobupivacaine or 0.5% Bupivacaine with 10mcg of sufentanyl and epinephrine(1;200,000). Both groups were comparable regarding maternal-fetal characteristics. Fifteen minutes after epidural anesthesia, 62.5% of Levobupivacaine group patients experienced Bromage 2 or 3 motor block, whereas the same event was documented in 72.7% of Bupivacaine group patients ($p = 0.83$). After 20 minutes, 66.7% of Levobupivacaine group patients experienced Bromage 2 or 3 motor block versus 86.3% of Bupivacaine group patients ($p = 0.21$). There was no statistically significant difference between groups in sensory block level in all studied moments. Sensory block level of T-10 was reached at 10 minutes in both groups, and T-6 level was achieved at 15 minutes in both groups. Most common complication was hypotension, detected in 16 (66.7%) Levobupivacaine group patients and in 10 (43.5%) Bupivacaine group patients ($p = 0.11$). It was concluded that Levobupivacaine and Bupivacaine were equally effective for epidural block in patients undergoing cesarean section.

Ngamprasertwong P et al in 2005[34] investigated the clinical efficacy and safety of Levobupivacaine compared with racemic Bupivacaine for extradural anesthesia.The authors studied 61 patients undergoing elective cesarean delivery who received either 0.5% Levobupivacaine ($n = 31$) or 0.5% Bupivacaine ($n = 30$) extradurally, in a

randomized, double blind study. It was observed that,The 2 groups were similar in terms of time to block suitable for surgery, duration of sensory block, time to T10 regression, time to onset and offset of motor block, verbal numeric pain scores at abdominal opening and at child birth. Time to onset of sensory block (T6) was 16.7± 5.7 minutes for Levobupivacaine and 15.0±5.5 minutes for Bupivacaine. Time to regression of sensory block to T10 was 244.4±65.9 for Levobupivacaine and 281.4±85.8 minutes for Bupivacaine. Time to onset of motor block was 12.3±1.5 minutes for Levobupivacaine and 12.0±1.1 minutes for Bupivacaine.Time to starting of regression of motor block was 126.2 ± 58.6 minutes for Levobupivacaine and 129.9±89.3 minutes for Bupivacaine. Mean (SD) dose of 0.5% Levobupivacaine and 0.5% Bupivacaine were 19.3 (4.6) ml and 17.3 (3.8) ml respectively (p = 0.069). It was concluded that Levobupivacaine produces an extradural block that is similar to Bupivacaine, and is an alternative to Bupivacaine for cesarean delivery patients.

Tanaka et al in 2006[35] studied in 87 patients regarding sensory and motor block produced by 0.5% Levobupivacaine and 0.5% Bupivacaine when used for epidural anesthesia for lower abdominal surgeries. Both groups received 27ml of anesthetic drug along with epinephrine(1;200,000) and fentanyl(100mcg). Results suggested that, Hemodynamic parameters were similar between groups. Sensory block was similar with both Levobupivacaine and Bupivacaine. However Levobupivacaine produced a lesser degree of motor block as compared to Bupivacaine. It was concluded that, both Levobupivacaine and 50% enantiomeric excess Bupivacaine are local anesthetic solutions suitable for lower abdominal surgeries and clinically comparable to racemic

Bupivacaine. Levobupivacaine has promoted less motor block as compared to the two solutions**.**

Koch et al in 2008[36] studied in 88 patients regarding efficacy of Levobupivacaine, Bupivacaine and Ropivacaine when used for epidural anesthesia in hip surgery. Intra-operative and post-operative degree of sensory blockade was compared. Epidurally 0.5% of Levobupivacaine, 0.5% of Bupivacaine and 0.75% of Ropivacaine was used in 3 respective groups for intraoperative period. For post-operative analgesia 0.125% of Levobupivacaine, 0.125% Bupivacaine and 0.2% of Ropivacaine was used. With respect to onset and offset of sensory and motor blockade, 0.5% Levobupivacaine, 0.5% Bupivacaine and 0.75% Ropivacaine showed clinically significant equivalent profiles for all primary study endpoints. However, the Levobupivacaine group showed a higher demand for intraoperative anesthesia. Postoperative analgesia request and pain scales did not differ significantly between groups, but comparatively lower total drug volumes were required in the Bupivacaine group. No relevant differences between the trial groups concerning safety parameters were observed. It was concluded that, the efficacy of epidural Levobupivacaine for hip surgery and postoperative analgesia is equivalent and shows a comparable clinical profile to Bupivacaine and 50-60% higher concentrated Ropivacaine**.**

Casimiro et al in 2008[37] compared the anaesthetic epidural effects of Levobupivacaine plus fentanyl versus Bupivacaine plus fentanyl in patients undergoing lower limb surgery. A total of 96 patients who were ASA I or II, who required at least a 24-hourstay in the hospital and who were subjected to surgery of lower limbs with epidural anaesthesia were enrolled in this study. Treatments were administered at a dosage of 1.2 ml per metamera,

including a test dose (3 mL) and the dose of fentanyl (100 μg). Patients were then randomly allocated to receive either Levobupivacaine (n = 49) or Bupivacaine (N.= 47). The primary endpoint was sensory blockade (SB) duration. Secondary evaluations included motor blockade (MB), post-surgery analgesic medication usage, safety and the investigator global evaluation. SB duration was similar for both interventions: 195 min (165-205) in the Bupivacaine group versus 170 min (140-185) in the levobupivicaine group (log-rank test, P=0.884). However, the lack of MB as evaluated by the modified Bromage scale was significantly higher in the Levobupivacaine group than in the Bupivacaine group (39% *vs* 13%, P=0.017). Although no significant differences in MB duration were observed between the groups, a trend was observed in the Levobupivacaine group, which had a lesser MB (P=0.093). Investigator satisfaction was high and was assessed to a similar extent for both interventions. Forty-one adverse events were detected in 28 patients, with no differences between groups: 15 (33%) with Bupivacaine and 13 (27%) with Levobupivacaine, P=0.516.It was concluded that, Although both interventions showed similar anaesthetic effects, a higher proportion of patients receiving Levobupivacaine lacked MB.

Surav DB et al in 2011[38] studied to determine the clinical efficacy and hemodynamic effects of different concentrations and equivalent volumes of Levobupivacaine in epidural anesthesia. Forty adult patients with an American Society of Anesthesiology (ASA) I-III physical status undergoing transurethral endoscopic surgery were randomly divided into 2 groups to receive either 10 mL of isobaric Levobupivacaine (0.5% + 5 mL 0.9% saline [group 1; n = 20]) or 10 mL of isobaric Levobupivacaine (0.75% + 5 mL saline 0.9% saline [group 2; n = 20]) for epidural anesthesia. An observer blinded to

group division evaluated the time of onset, maximum level, and time to 2-segment regression of sensory block.There were no differences between the 2 groups in terms of hemodynamic parameters and time of onset of the sensory block. There were significant differences, however, between the 2 groups in the maximum level of the sensory block (group 1, T9; group 2, T8; P = 0.010) and the time to 2-segment regression of sensory block (group 1, 46.35 minutes; group 2, 62.94 minutes; P = 0.013).This study indicated that 10 mL of 0.5% Levobupivacaine plus 5 mL of 0.9% saline is a suitable solution for use in epidural anesthesia because it produces a block clinically comparable to that of 10 mL of 0.75% Levobupivacaine plus 5 mL of 0.9% saline for transurethral resection of prostate surgery.

Fesih Kara et al in 2013[39] compared the anesthetic effectiveness of epidural 0.5% Levobupivacaine and 0.5% Bupivacaine without adjuvant medication in patients who were to have elective operations on the lower extremities and hips.This study was conducted on a total of 70 ASA I-II patients aged between 30 and 70 years, who underwent elective hip and lower extremity operations. The patients that received 15ml of 0.5% Bupivacaine were assigned to Group B (n = 35) and those that received 15ml of 0.5%Levobupivacaine to Group L (n = 35). No statistically significant difference was found between the groups in terms of the onset and regression times of the sensory and motor blockade, time to reach dermatomes, initial analgesic requirement time, resolution time of the motor block, patient and surgeon satisfaction, heart rate, noninvasive systolic artery pressure, diastolic artery pressure, mean artery pressure, and peripheral oxygen saturation values (P > 0.05). Sensory block onset time in groupL and GroupB is 6.82$\pm$1.94 min and 6.80$\pm$1.812 min. Time of sensory block to reach T6 in groupL and

GroupB is 24.54±2.27 min and 23.97±1.485 min. Motor block onset time groupL and GroupB is 15.37±1.46 min and 15.60±1.288 min. Sensory block regression time groupL and GroupB is 180.54±9.34 min and 183.17±7.48 min. Motor block regression time groupL and GroupB is 191.60±9.34 min and 195.60±6.40 min. Time of motor block to reach maximum level groupL and GroupB is 26.80±1.96 min and 26.54±1.88 min .Thus it was concluded that,Levobupivacaine could be a good alternative to Bupivacaine in patients administered epidural anesthesia in elective hip and lower extremity.

S. A. Aasim in 2014[40] compared the effect of 0.5% Levobupivacaine and 0.5% racemic Bupivacaine in epidural anaesthesia for lower limb surgeries. The study was conducted with fifty ASA (American society of Anaesthesiologists) grade I and II patients undergoing elective lower-limb surgery under epidural anaesthesia. Exclusion criteria were patients with contraindication for epidural block or history of sensitivity to any studied drug. All patients gave their informed consent. Patients were randomly allocated to the following groups Group LB (n=25) received 20 ml of 0.5% Levobupivacaine and Group B (n=25) received 20 ml of 0.5% Bupivacaine. The onset, duration of sensory and motor block and side-effects were observed. The onset of sensory blockade were similar with Bupivacaine (11.32 ± 1.64 mins) and Levobupivacaine (12.16 ± 1.376 mins) with no statistically significant difference . The time to reach peak block height was similar with Bupivacaine(24.60± 2.545 mins) and Levobupivacaine (26.04 ± 2.78 mins) with no statistically significant difference. The duration of sensory blockade were similar with Bupivacaine (326.4 ± 23.64 mins) and Levobupivacaine (335.2 ± 18.57 mins) with no statistically significant difference (p=0.1498). The duration of motor blockade were also similar with both Bupivacaine (229.6 ± 24.41) and Levobupivacaine (218.4 ± 18.04) with

no statistically significant differences (p=0.071). However patients allocated to receive Levobupivacaine showed a higher proportion of lack of motor blockade as determined by the modified Bromage scale and was statistically different. Bradycardia was seen in 2 patients in Bupivacaine group and 1 patient in Levobupivacaine group. Hypotension was observed in 5 patients of Bupivacaine group and 3 patients of Levobupivacaine group. Thus it was concluded that both drugs showed similar anaesthetic effects but a higher proportion of patients receiving Levobupivacaine lacked motor blockade.

MATERIALS AND METHODS

MATERIALS REQUIRED:

1. Sterile trolley with towels
2. Antiseptic solutions - Betadine & Spirit
3. Sponge Holder
4. Gauze pieces
5. Stainless Steel Bowl
6. Syringes (2 cc, 10 cc x 2)
7. Epidural needle 16G, epidural catheter 18 G.
8. Drug for injection :-

i. 0.5% Bupivacaine isobaric (Bupivacaine 0.5% preservative free -ANAWIN 0.5% 20 ml vials – Neon laboratories India limited).

8ANAWIN 0.5% 20 ml vial

ii. 0.5% Levobupivacaine isobaric(Levobupivacaine 0.5% preservative free – LEVOANAWIN 0.5% 10 ml ampules – Neon laboratories India limited).

LEVOANAWIN 0.5% 10 ml ampule.

iii. Lignocaine 2% plus 1: 200000 Adrenaline Vial.

9. Normal Saline

SOURCE OF DATA :

This clinical study entitled "**A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES**" was carried out at Shri B.M Patil Medical College, Vijayapur during the period from December 2015 to August 2017.

This study was only undertaken on consenting patients after obtaining the ethical clearance from institutional ethical committee.

METHODS OF COLLECTION OF DATA:

Design of Study :A Prospective Randomized Controlled Trial.

Study period : 18 months

Sample size : 100 patients aged 18-60 years ; scheduled for an elective lower abdominal or lower limb surgery belonging to ASA grade I and II were included in this study.

With anticipated mean difference of onset of motor blockade x[6,7] between the study groups as 4.1min and anticipated SD as 5.7min, the minimum sample size is 50/group with 90% power and 5% level of significance.

n = 50/ group.

Total size = $50 \times 2 = 100$.

Formula: $$n = \frac{(Z\alpha + Z\beta)^2 2SD^2}{MD^2}$$

Method of randomization

The study population of 100 age and sex matched patients were randomly selected by and divided by computer into two groups with 50 patients in each group.

Study group L (n = 50) - received 0.5% Levo-Bupivacaine.

Study group B (n = 50) - received 0.5% Bupivacaine.

Result values were recorded using a preset Performa.

INCLUSION CRITERIA:

- Age group of 18-60 years of both sexes.
- ASA grade I and II.
- Patients coming for elective surgeries.

EXCLUSION CRITERIA:

- Patient refusal.
- ASA grade III and IV.
- Patients with infection at site of injection.
- Patient with coagulopathy.
- Patients on anti coagulation treatment (INR >1.5).
- Patients with congenital abnormalities of lower spine and meninges.
- Patients with history of allergy to local anaesthetics.
- Patients with uncorrected hypovolemia.
- Obstetric patients.

METHOD OF STUDY:

1) All pre-anaesthetic evaluation of the patients was performed by an anaesthesiologist a day before the surgery, assessing
   a) History and general condition of the patient
   b) Airway assessment by Mallampati grading.
   c) Nutritional status, height and weight of the patient
   d) Vital signs – heart rate, blood pressure, respiratory rate were recorded.
   e) A detailed examination of the Cardiovascular system, Respiratory system and Central nervous system.
   f) Examination of the spine
2) The following investigations were done in all patients
   - Urine : albumin, sugar, microscopy
   - Blood : Hemoglobin,
     Total Count, Differential Count, Platelet count,
     Bleeding Time , Clotting Time
   - HBsAg, HIV
   - Blood urea, Serum Creatinine.
   - ECG
   - Chest x-ray (if required).
3) All patients who belonged in the inclusion criteria , after giving a written informed valid consent were randomly allocated into the following groups.

Group B(n=50)-- patients receiving 0.5% isobaric Bupivacaine 17 ml.

Group L(n=50) -- patients receiving 0.5% isobaric levo-Bupivacaine 17ml.

In the operation theatre, a good peripheral intravenous access was secured using 18 gauge canula and preloaded with 500ml Ringer Lactate solution.

4) Multiparameter monitor was connected which records heart rate, non-invasive measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), continuous electrocardiogram (ECG) monitoring and arterial oxygen saturation (SpO2) .
5) Baseline non invasive blood pressure, pulse rate, electrocardiograph, SpO2 were recorded.
6) Premedication with Inj. Ondensetrone 4mg i.v and Inj. Ranitidine 150mg i.v was be given.
7) Under all aseptic precautions using a sterile epidural kit and autoclaved epidural tray the 18g epidural catheter was secured in L3-L4 intervertebral space
8) After exclusion of blood/CSF in the epidural catheter with negative aspiration ,3ml of lignocaine with adrenaline 1:200,000 test dose was administered to exclude intrathecal or intravascular placement of the catheter.
9) After 5 minutes of administering test dose, patients in group B received 0.5% isobaric Bupivacaine (17 ml) and group L received 0.5% isobaric levo-Bupivacaine (17 ml) epidurally.

PARAMETERS OBSERVED WERE:

1) Baseline pulse rate, noninvasive blood pressure, arterial oxygen saturation (SpO2).
2) **"0" time** is time of injection of epidural study anaesthetic drug (Levobupivacaine/Bupivacaine).
3) **Onset time of sensory block :** The time interval between administration of drug into the epidural space and the absence of pain from pin prick at the T10 level was recorded as the onset time for sensory block.
4) **Highest level of sensory block** : highest dermatome of sensory block reached.
5) **Duration of sensory block - Time to two-segment regression** : time for regression of sensory block by two dermatomes from highest level of sensory block.
6) **Duration of sensory analgesia:** The time interval between the administration of epidural block and the first requirement of supplementary analgesia will be noted.
7) **Onset time of motor block:** The time interval between the administration of drug into epidural space and the patient's inability to lift the straight extended leg (Modified Bromage scale) was recorded as onset time for motor block.
8) **Degree of motor block:** The degree of motor block was assessed by Modified Bromage scale.

Modified Bromage Scale2:

0- Able to raise leg straight, full flexion of knees and feet.

1- Inability to raise leg, just able to flex knees, full flexion of feet.

2- Unable to flex knees, but some flexion of feet possible.

3- Unable to move legs or feet.

9) **Duration of motor block** is taken as time between "0" time & time to complete regression of motor block.

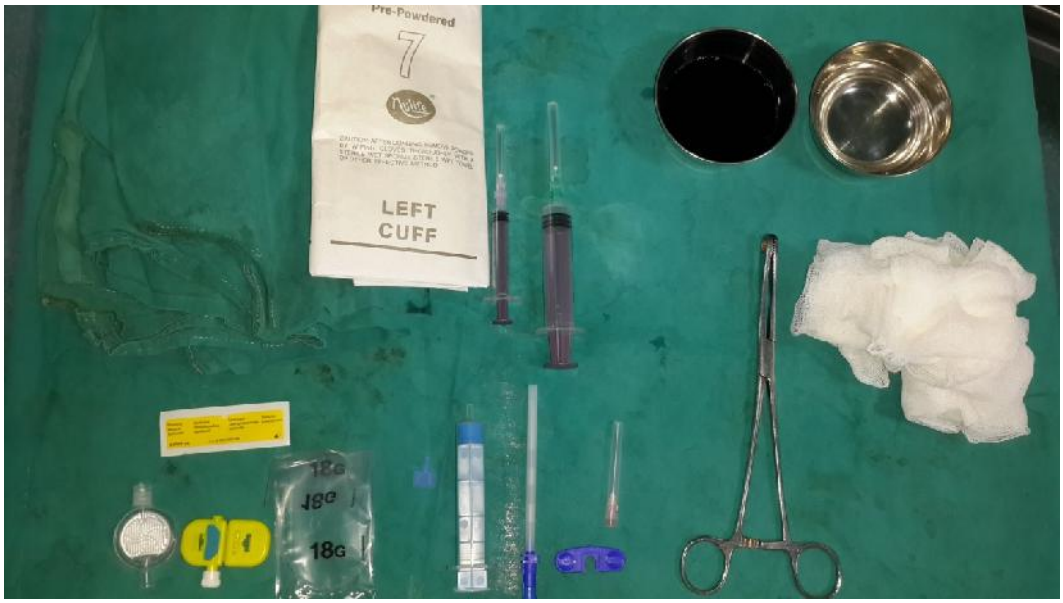
10) **Haemodynamic changes:** Patients were monitored for heart rate, blood pressure at 0, 2, 5, 15, 30, 60, 90, 120 and 180 minutes after administration of epidural block.

11) **Intra operative and post operative complications if any:** such as nausea, vomiting, hypotension, bradycardia, respiratory depression, shivering will be looked for, recorded and treated accordingly.

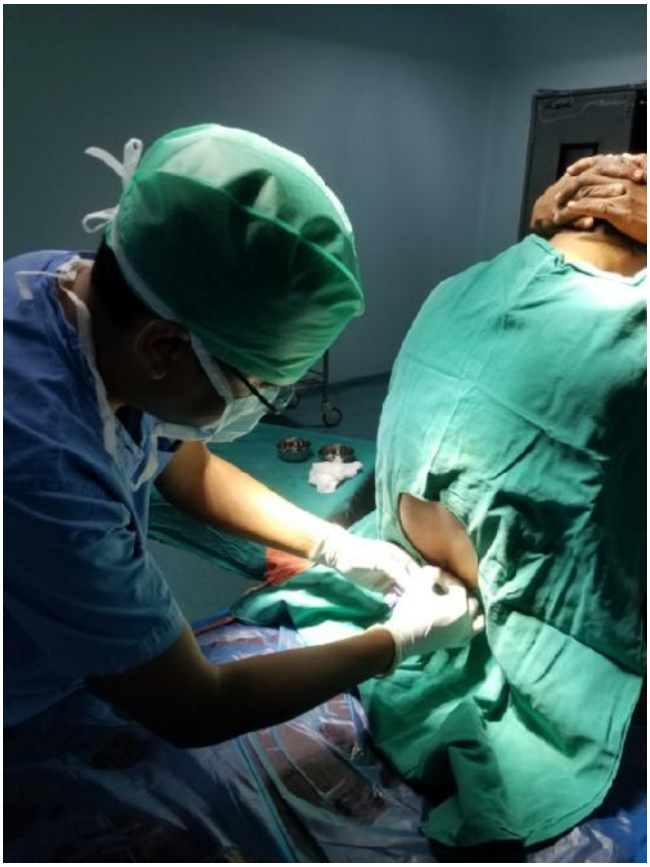
STATISTICAL ANALYSIS:

After data collection, data entry was done in Excel.div. Data analysis was done with the help of SPSS Software ver 15 and Sigmaplot Ver 11.div. Quantitative data is presented with the help of Mean, SD and Median, and comparison between study groups is done by Unpaired or Mann-Whitney test as per results of normality test. Qualitative data is presented with the help of Frequency and Percentage table, association among study group is assessed with the help of Chi-Square test and Fisher's Exact Test. P value less than 0.05 is taken as significant level.

P-value: It is the probability rate at 0.05 level of significance for corresponding degree of freedom.



Sterile Epidural trolley



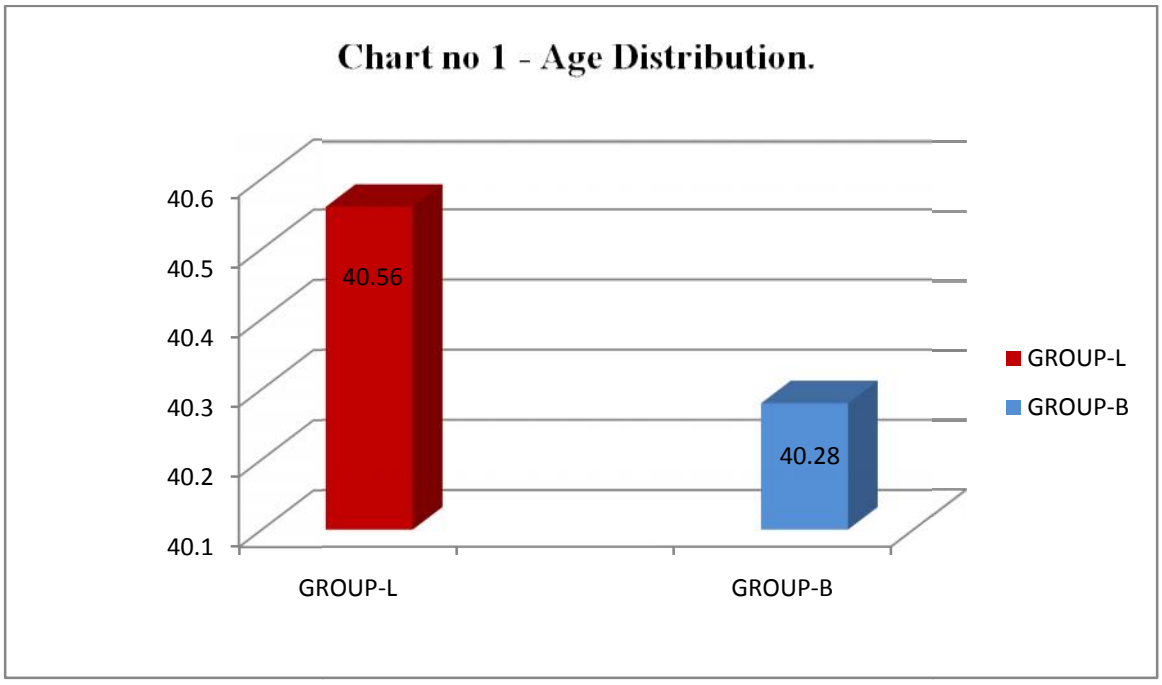
Epidural Anaesthesia Procedure

OBSERVATIONS AND RESULTS

1. **Age distribution**

	Group –L	Group-B	
Mean age in years.	40.56	40.28	P value= 0.899
SD	11.22	10.73	
Total Patients	50	50	

Table no.1- Age distribution



Both groups are **comparable** with respect to age distribution.

Mean age in Group-L: 40.56 yrs and in Group-B : 40.28 yrs.

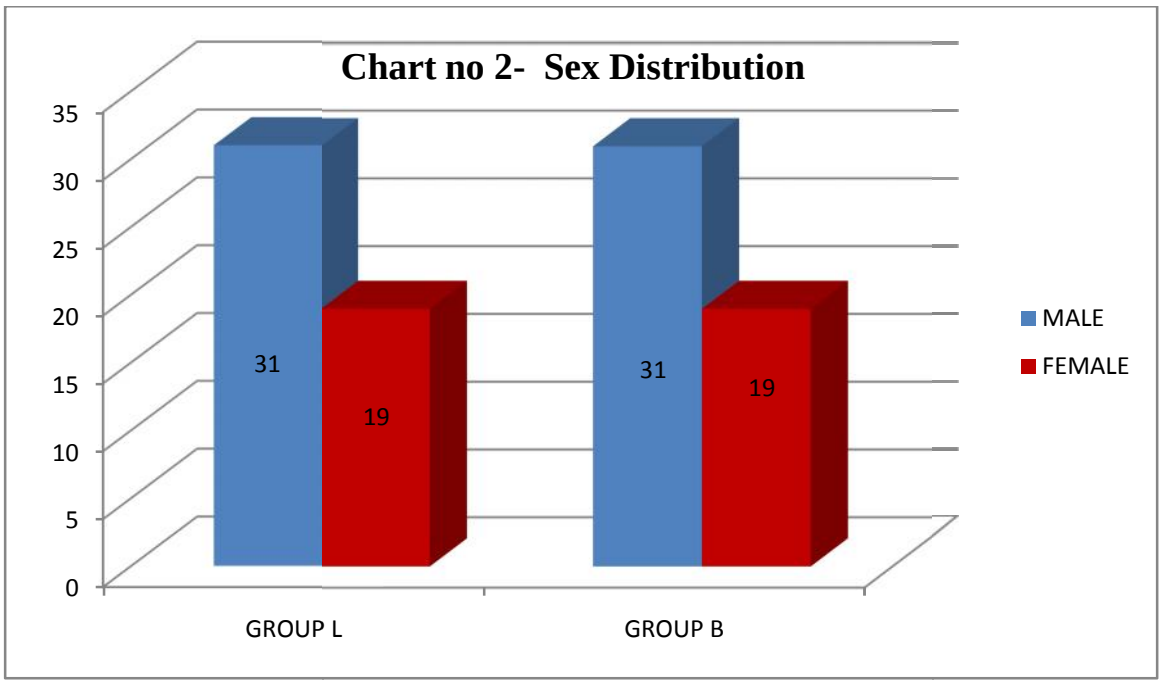
P -value is **not significant**. P-value= 0.899 i.e. P-value>0.05.

Result calculated using Students Unpaired ‘t’ Test.

2. **Sex Distribution**

	Group –L		Group-B		
	No of Patients	Percent	No of Patients	Percent	
Male	31	62	31	62	P value=1.000
Female	19	38	19	38	
Total	50	100%	50	100%	

Table no.2 - Sex Distribution



Both groups are **comparable** with respect to sex distribution.

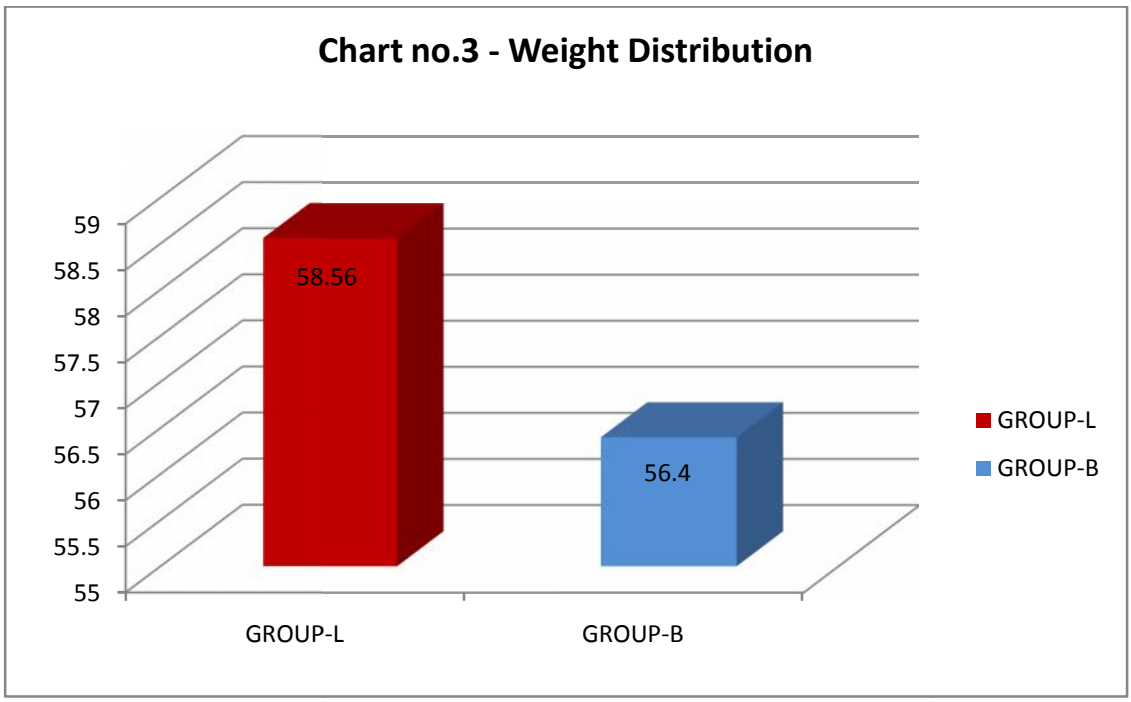
P -value is **not significant**. P-value= 1.000 i.e. P-value>0.05.

Result calculated using Pearsons Chi Square Test.

3. **Weight Distribution**

	Group -L	Group-B	
Mean weight in kg	58.56	56.40	P value= 0.052
SD	6.05	4.87	
Total Patients	50	50	

Table no.3- Weight Distribution



Both groups are **comparable** with respect to weight distribution.

Mean weight in Group-L: 58.56 kgs and Group-B: 56.40 kgs.

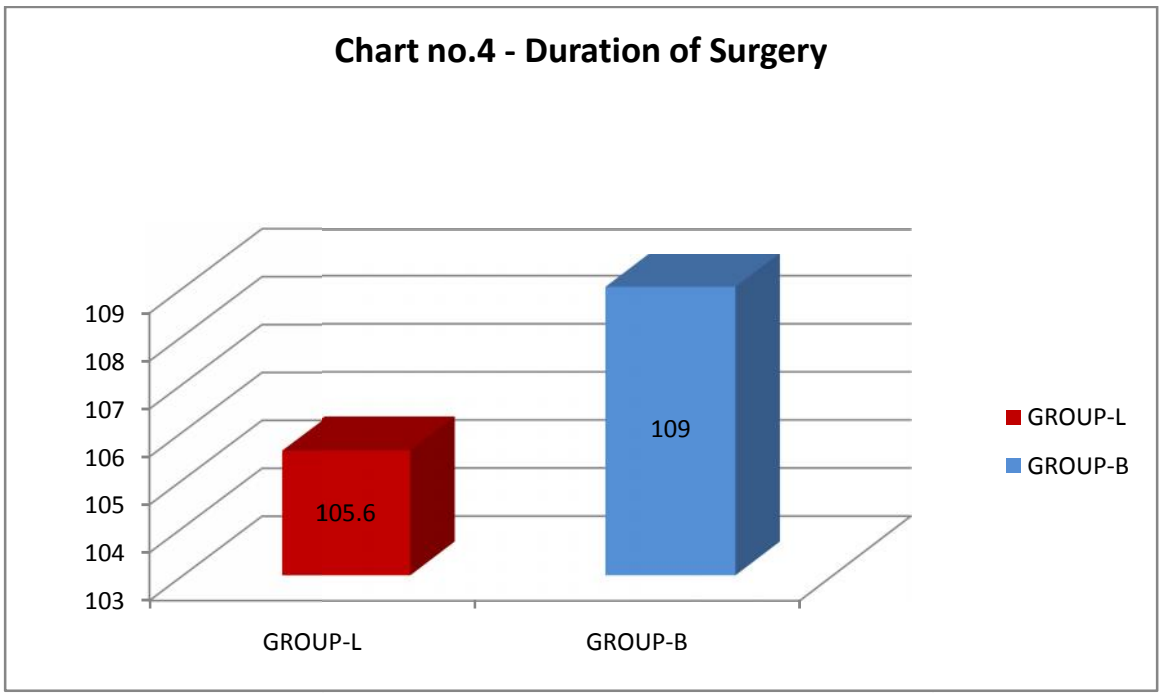
P -value **is not significant**. P-value= 0.052 i.e. P-value>0.05

Result calculated using Students Unpaired‘t’ Test.

4. **Duration of surgery**

	Group -L	Group-B	
Mean time in minutes.	105.6	109	P value= 0.129
SD	10.529	11.650	
Total Patients	50	50	

Table no.4- Duration of surgery



Both groups are **comparable** with respect to duration of surgery.

Mean duration of surgery in Group-L: 105.6 mins and Group-B: 109 mins.

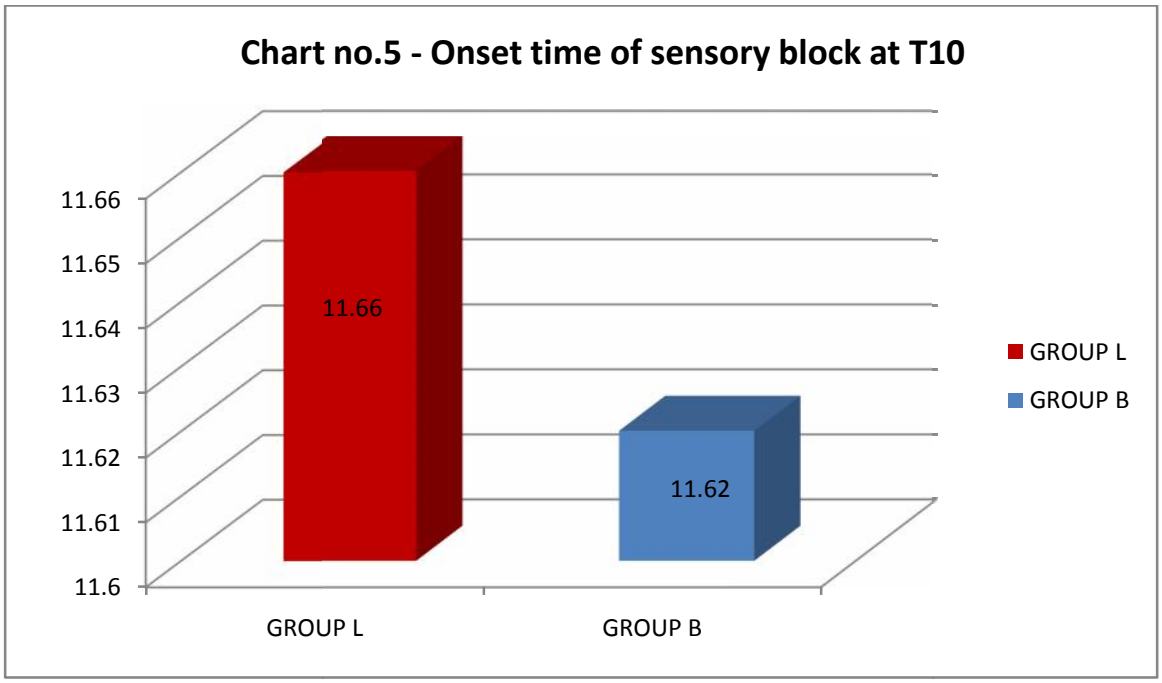
P -value is **not significant**. P-value= 0.129 i.e. P-value>0.05

Result calculated using Students Unpaired‘t’ Test.

5. **Onset time of sensory block at T10 (in minutes)** - .time interval between the end of administration of anaesthetic("0" time) and loss of pin prick sensation at T10.

	Group –L	Group-B	
Mean time in minutes.	11.66	11.62	P value= 0.820
SD	0.917	0.830	

Table no.5- Onset time to sensory block at T-10(minutes)



Group-L has **similar** onset of sensory block as compared to Group-B.

Mean onset time to sensory block at T-10 in Group-L is 11.6 mins and

In Group-B is 11.62 mins.

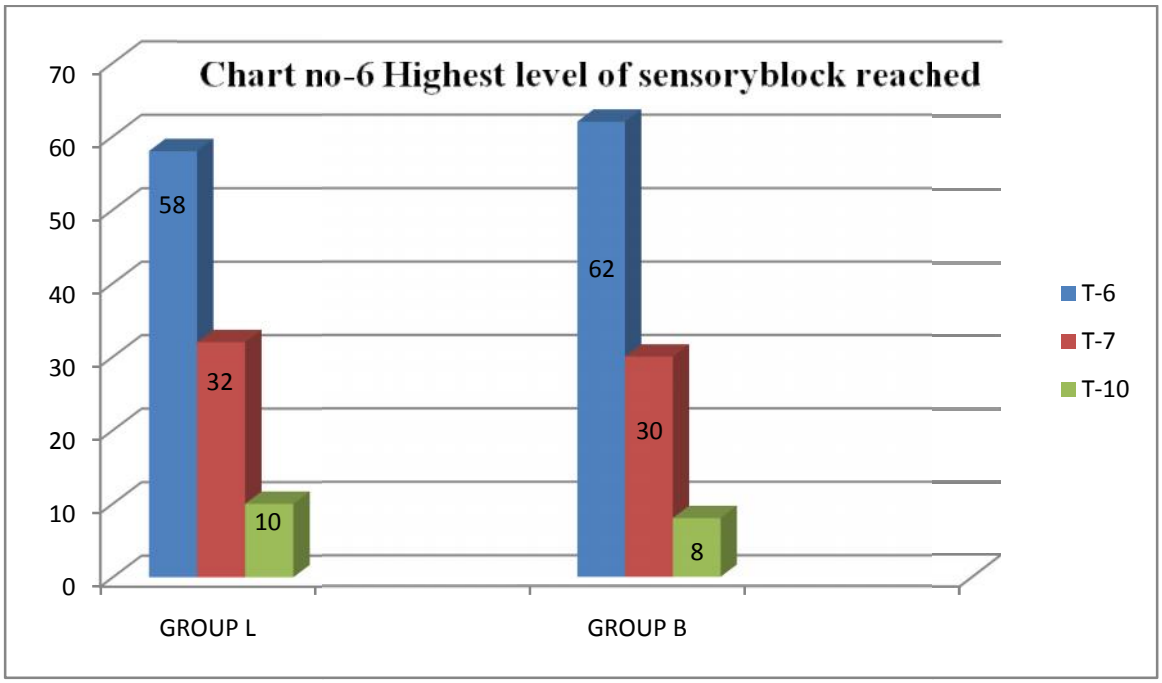
P -value being **not significant**. P-value= 0.820 i.e. P-value<0.05

Result calculated using Students Unpaired 't' Test.

6. **Highest level of Sensory block reached** i.e. highest dermatome of sensory block achieved.

	Group –L	% Group-L	Group-B	% Group-B
T-6	29	58	31	62
T-7	16	32	15	30
T-10	5	10	4	8

Table no:-6:- Highest level of Sensory block reached.



In Group L T-6 level was reached in 29 patients(58%) , T-7 level was reached in 16 patients (32%) and T-10 level was reached in 5 patients (10%).

In Group B T-6 level was reached in 31 patients(62%) , T-7 level was reached in 15 patients (30%) and T-10 level was reached in 4 patients (8%).

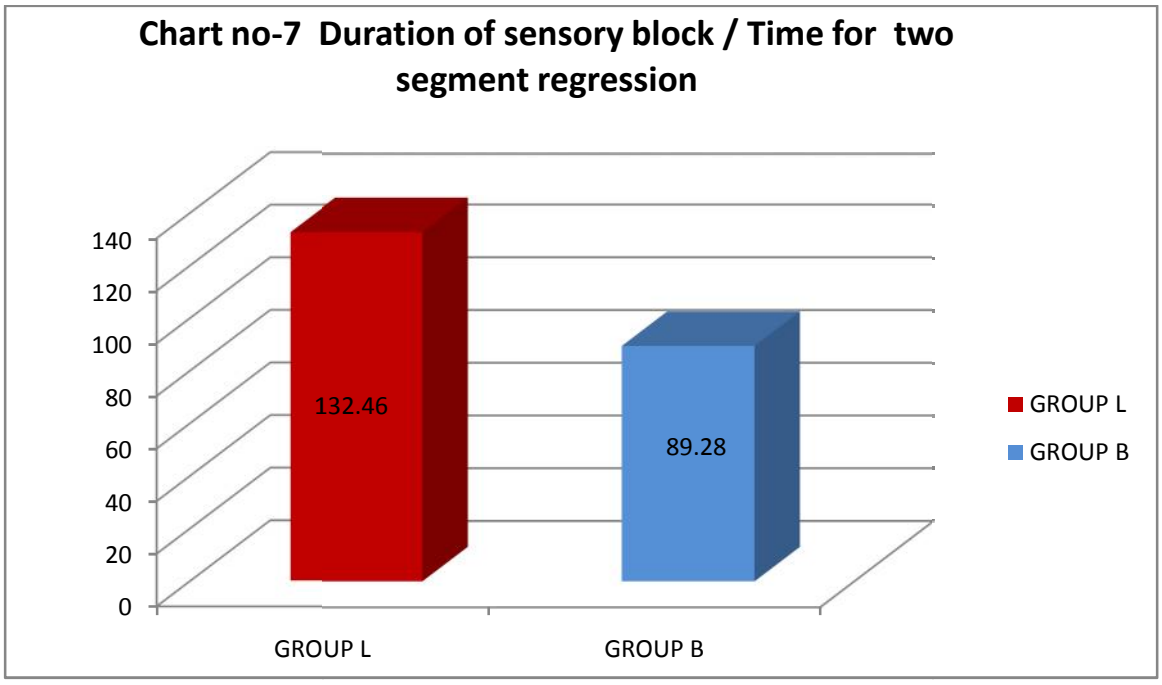
This is statistically not **significant**. P-value is 0.1 i.e. P-value>0.05.

Result calculated using Students Unpaired‘t’ Test.

7. **Duration of sensory block / Time for two segment regression** - time for regression of sensory block by two dermatomes from peak block height.

	Group –L	Group-B	
Mean time in minutes.	132.46	89.28	P value= 0.000
SD	10.74	4.75	

Table no.7 - Time to two segment regression



Group-L has **slower** regression of sensory block as compared to Group-B.

Mean Time for two segment regression in Group-L is 132.46 mins and in Group-B is 89.28 mins.

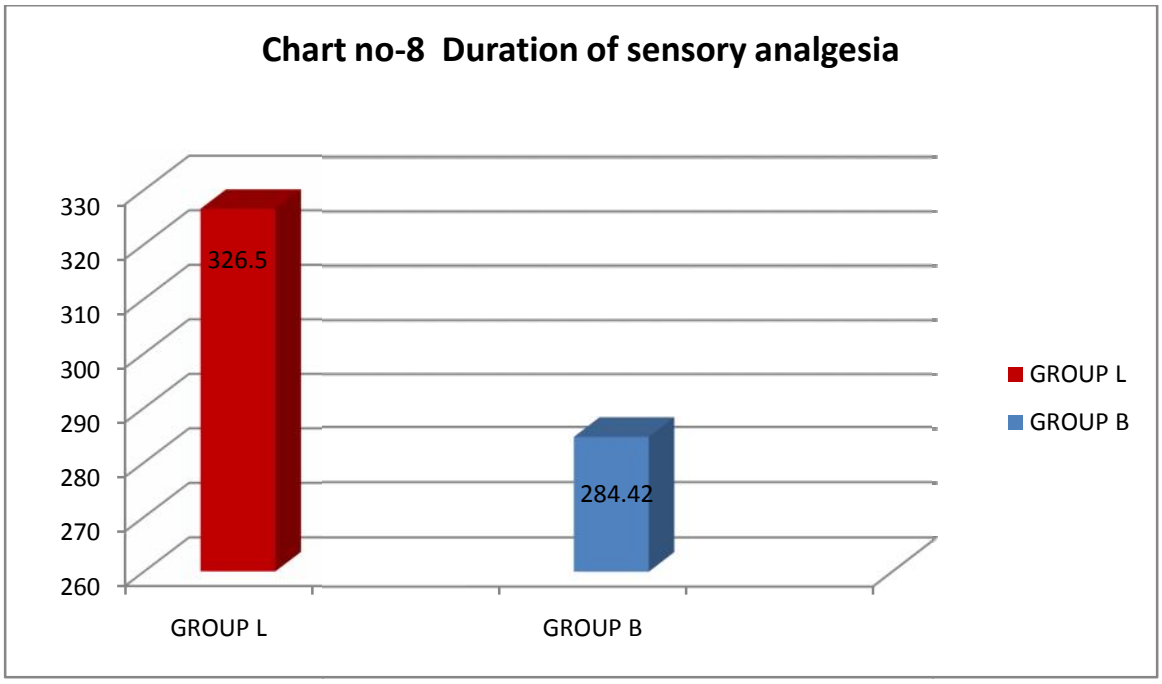
P -value is **significant**. P-value= 0.000 i.e. P-value<0.05

Result calculated using Students Unpaired 't' Test.

8. **Duration of sensory analgesia:** The time interval between the administration of epidural block and the first requirement of supplementary analgesia.

	Group –L	Group-B	
Mean time in minutes.	326.5	284.42	P value= 0.000
SD	6.64	7.18	

Table no8:- duration of sensory analgesia



Group-L has **longer** duration of sensory analgesia as compared to Group-B .

Mean Time of sensory analgesia in block in Group-L is 326.5 mins and in Group-B is 284.42 mins.

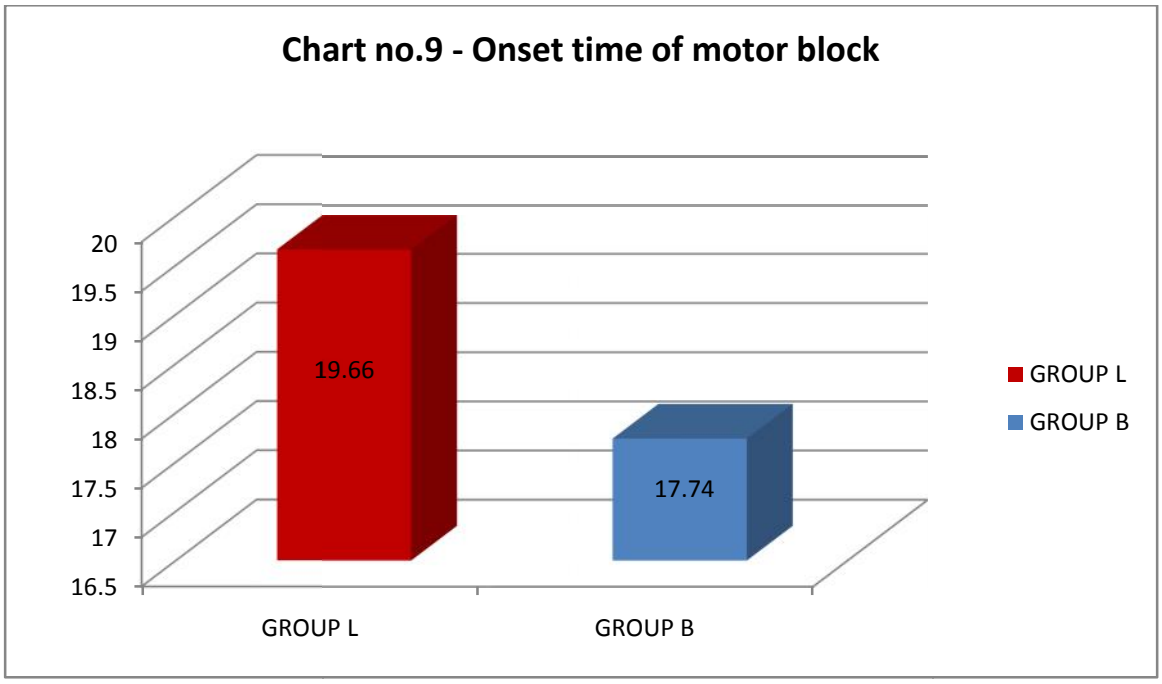
P -value is **significant**. P-value= 0.000 i.e. P-value<0.05

Result calculated using Students Unpaired 't' Test.

9. **Onset time of motor block** :The time interval between the administration of drug into epidural space and the patient's inability to lift the straight extended leg (Modified Bromage scale) was recorded as onset time for motor block.

	Group –L	Group-B	
Mean time in minutes.	19.66	17.74	P value= 0.000
SD	1.67	1.19	

Table no.9 :- onset time of motor block



Group-L has a **slower** onset time of motor block as compared to Group-B.

Mean Time to onset of motor block in Group-L is 19.6 mins and in Group-B is 17.74 mins.

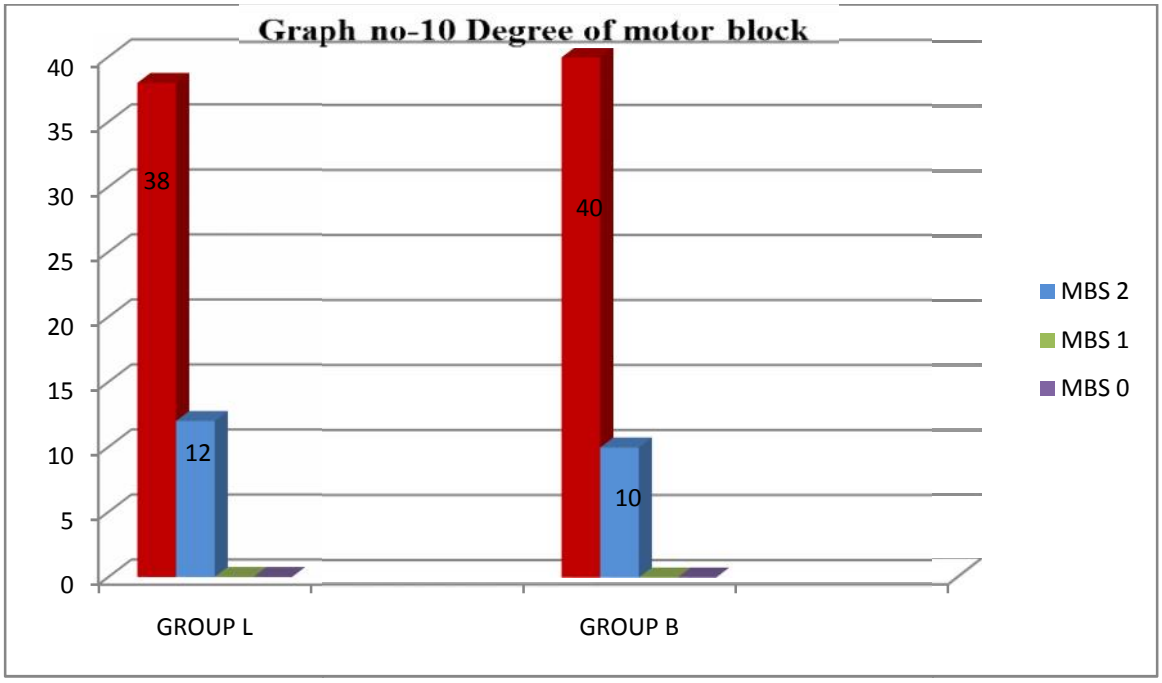
P -value is **significant**. P-value= 0.000 i.e. P-value<0.05

Result calculated using Students Unpaired't' Test.

10) **Degree of motor block** - The degree of motor block was assessed by Modified Bromage scale..

MBS	Group –L	% Group-L	Group-B	% Group-B
3	38	76	40	80
2	12	24	10	20
1	0		0	
0	0		0	

Table no10:- degree of motor block.



In Group L MBS 3 was reached in 38 patients (76%) , MBS 2 was reached in 12 patients (24%)

In Group B MBS 3 was reached in 40 patients (80%) , MBS 2 was reached in 10 patients (20%)

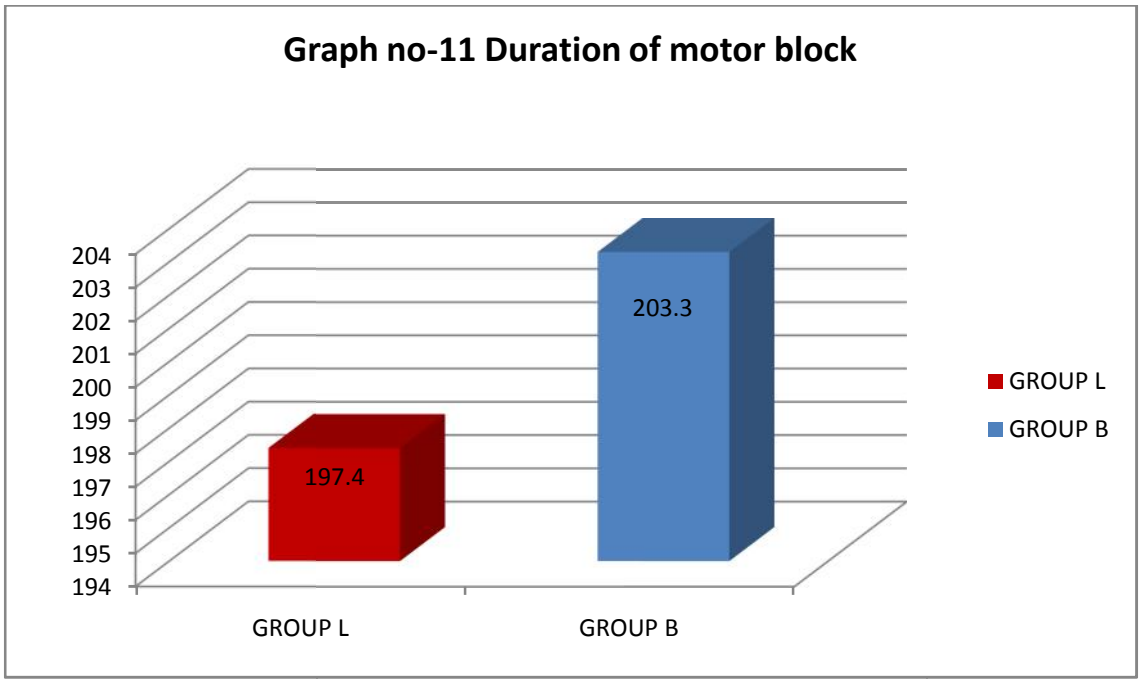
This is statistically is **not significant**. P-value = 0.633 i.e. P-value>0.05.

Result calculated using Students Unpaired‘t’ Test.

11) **Duration of motor block**.: time between “0” time & time to regression of motor block.

	Group –L	Group-B	
Mean time in minutes.	197.4	203.3	P value= 0.017
SD	14.22	9.50	

Table no. 11 - Duration of motor block



Group-L has **shorter** duration of motor block as compared to Group-B .

Mean Duration of motor block in Group-L is 197.4 mins and in Group-B is 203.3 mins

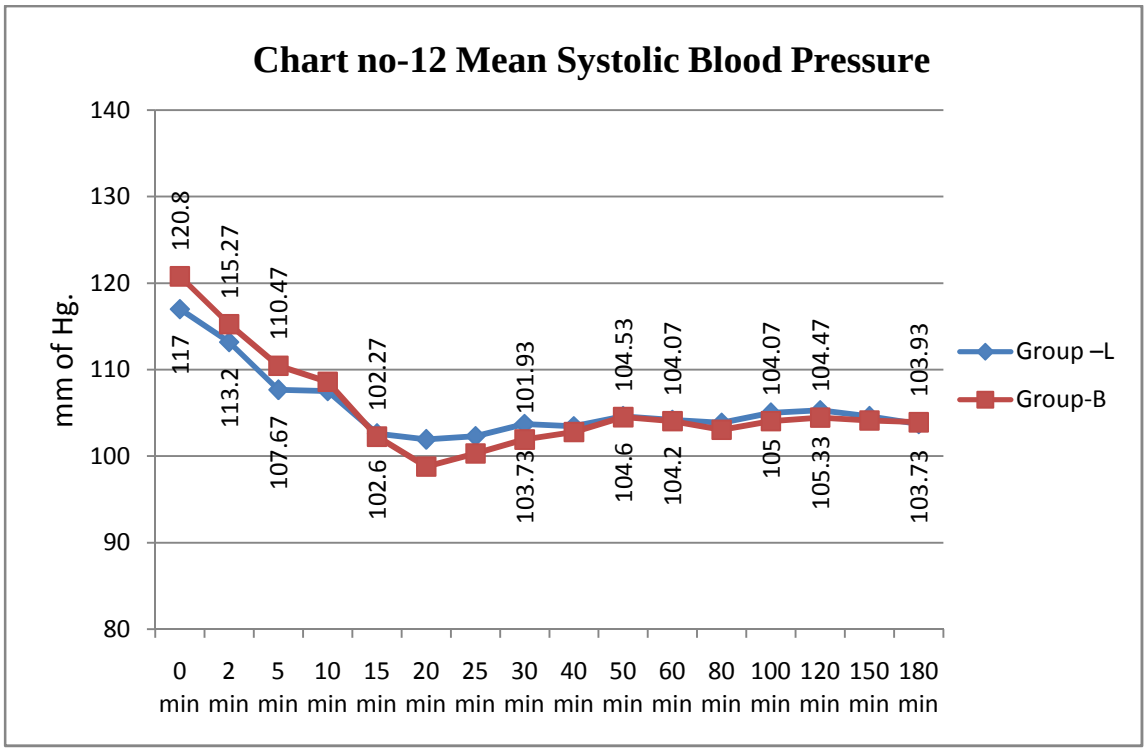
P -value is **significant**. P-value= 0.017 i.e. P-value < 0.05

Result calculated using Students Unpaired‘t’ Test.

12) **Mean systolic blood pressure at various intervals.**

Time	Group –L		Group-B		P-value
	Mean	SD	Mean	SD	
0 min	117	10.409	120.80	7.494	0.110
2 min	113.20	8.062	115.27	6.313	0.274
5 min	107.67	7.029	110.47	6.447	0.113
15 min	102.60	9.220	102.27	7.839	0.881
30 min	103.73	4.450	101.93	4.563	0.131
45 min	104.60	4.461	104.53	4.066	0.952
60 min	104.20	4.310	104.07	4.118	0.903
90 min	105.00	4.661	104.07	5.051	0.460
120 min	105.33	5.182	104.47	5.374	0.527
180 min	103.73	4.127	103.93	4.085	0.851

Table no.12 - Mean systolic blood pressure at various intervals.



Graph no 12- Mean systolic blood pressure at various intervals.

There is **no difference** between Group-L and Group-B with respect to variability in systolic blood pressure at various time intervals.

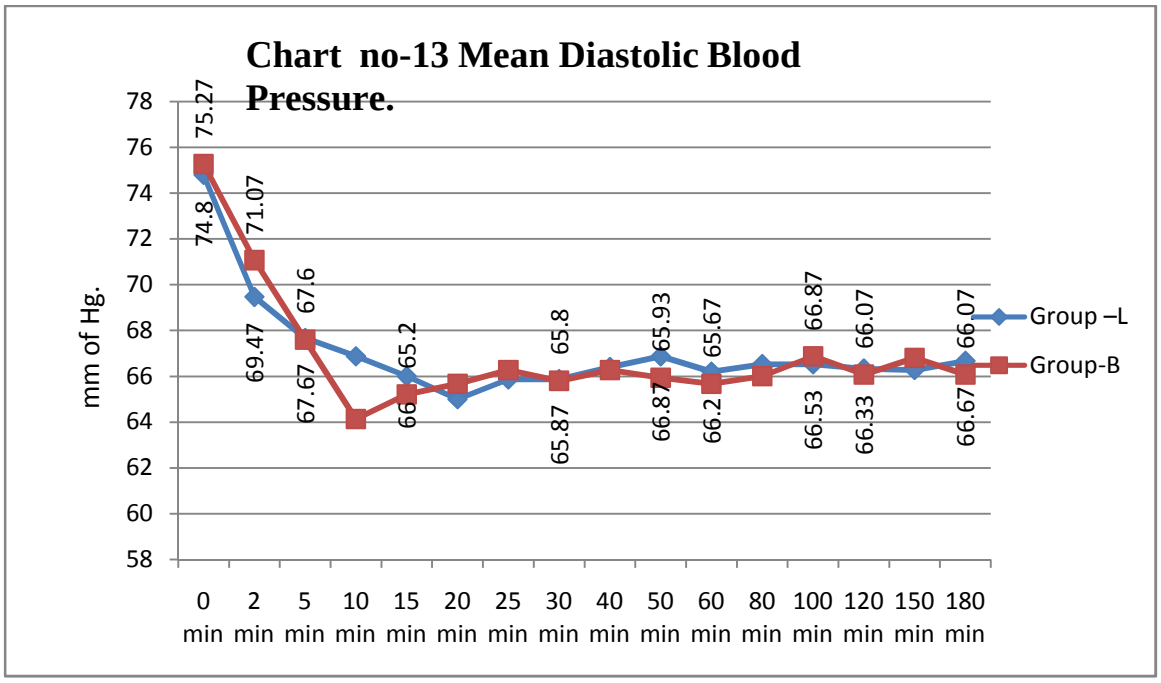
P-value is **not significant** i.e. P-value>0.05 at all time intervals.

Result calculated using Students Unpaired 't' Test.

13) **Mean diastolic blood pressure at various intervals.**

Table no13 - Mean diastolic blood pressure at various intervals.

	Group –L		Group-B		P-value
	Mean	SD	Mean	SD	
0 min	74.80	3.347	75.27	2.852	0.563
2 min	69.47	3.148	71.07	3.183	0.055
5 min	67.67	3.241	67.60	3.297	0.937
15 min	66.00	4.136	65.20	4.859	0.495
30 min	65.87	2.968	65.80	1.424	0.912
45 min	66.87	2.270	65.93	1.856	0.087
60 min	66.20	2.250	65.67	2.294	0.367
90 min	66.53	2.345	66.87	1.252	0.495
120 min	66.33	2.106	66.07	1.780	0.598
180 min	66.67	2.482	66.07	1.617	0.272



Graph no13- Mean diastolic blood pressure at various intervals.

There is **no difference** between Group-L and Group-B with respect to variability in diastolic blood pressure at various time intervals;

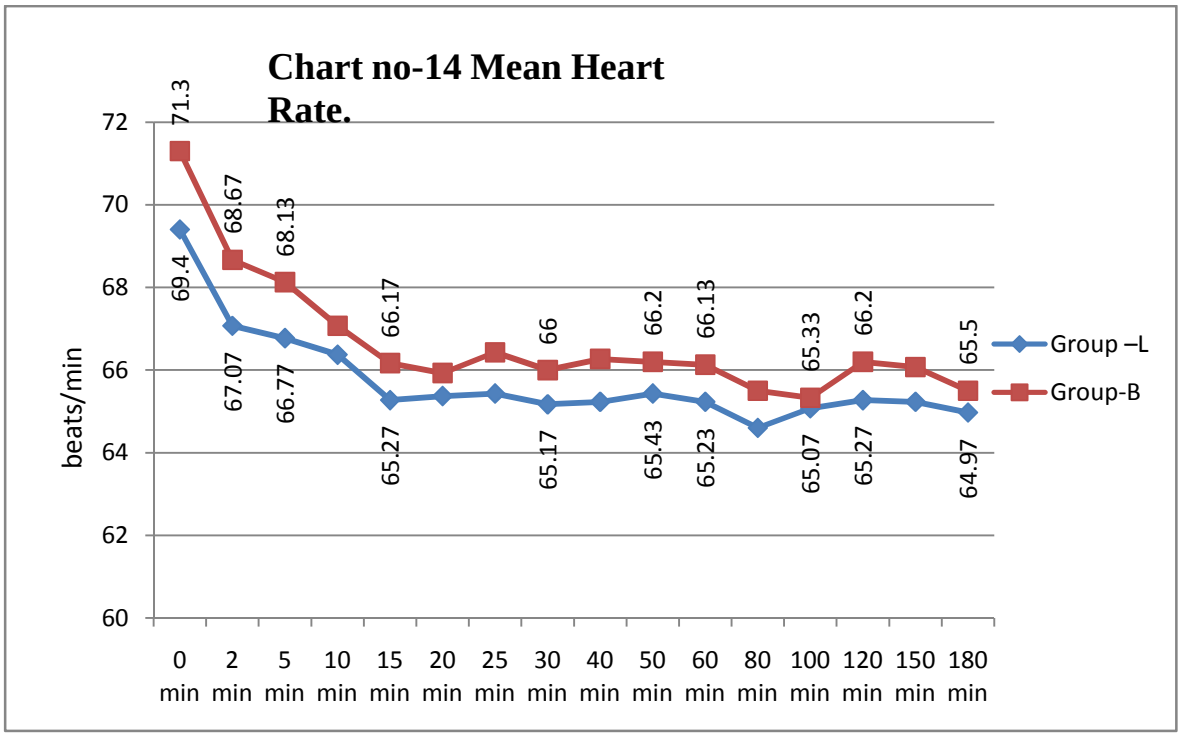
P-value is **not significant**. P-value >0.05 at all time intervals.

Result calculated using Students Unpaired 't' Test.

14) **Mean Heart rate at various intervals.**

Table no14- Mean Heart rate at various intervals.

	Group –L		Group-B		P-value
	Mean	SD	Mean	SD	
0 min	69.40	5.612	71.30	4.692	0.160
2 min	67.07	5.239	68.67	4.663	0.213
5 min	66.77	4.897	68.13	3.946	0.239
15 min	65.27	4.785	66.17	3.824	0.424
30 min	65.17	4.878	66.00	3.096	0.433
45 min	65.43	4.659	66.20	2.784	0.442
60 min	65.23	4.224	66.13	3.115	0.352
90 min	65.07	4.578	65.33	2.869	0.788
120 min	65.27	4.409	66.20	2.870	0.335
180 min	64.97	4.709	65.50	2.713	0.593



Group-L and Group-B are comparable with respect to changes in heart rate at various time intervals.

P-value is statistically **not significant** at all time intervals. P-value=0.023 i.e. P-value>0.05.

Result calculated using Students Unpaired ‘t’ Test.

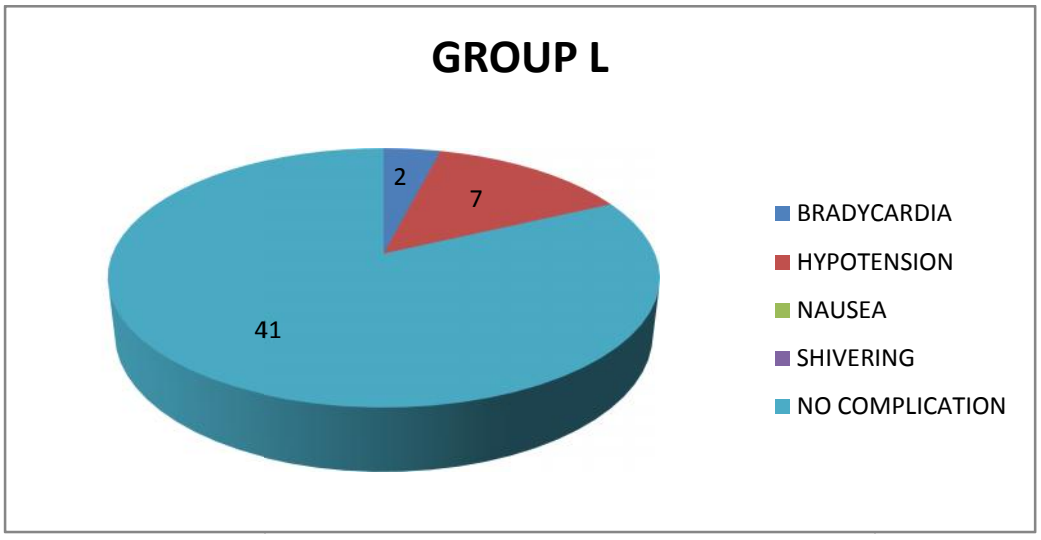
15) **Spo2 at various time intervals:**

Spo2 < 95% is defined as hypoxia & treated with supplemental O2 via face mask . In our study 02 saturation was found > 95% in both the groups at all intervals , so none of the patient required 02 mask.

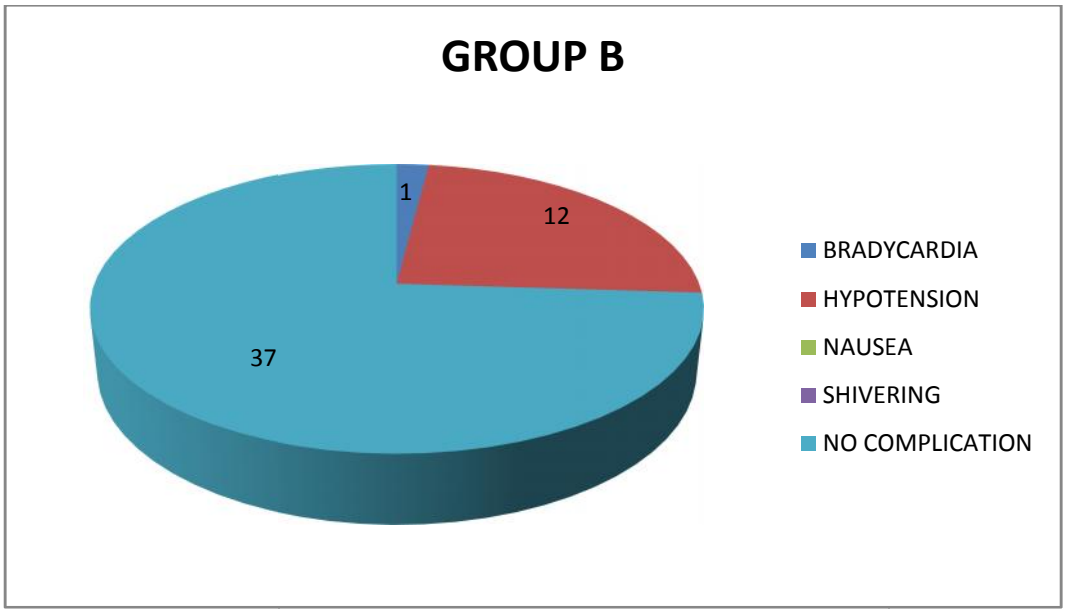
16) **Complications:**

	Group L		Group B	
Complication	Frequency	Percent	Frequency	Percent
Bradycardia	2	4	1	2
Hypotension	7	14	12	24
Nausea	-	-	-	-
Shivering	-	-	-	-
No Complication	41	82	37	74
Total	50	100.0	50	100

Table no:-15:- Distribution of complications in Group L and Group B.



Graph no 15- Complications in Group L



Graph no 16- Complications in Group B

Hypotension was seen in 7 cases(14%) and Bradycardia in 2 cases (4%) of Group-L. Hypotension was seen in 12 cases(24%) and Bradycardia in 1 case (2%) of group-B. Thus indicating higher chances of hypotension with Group-B patients. Hypotension and bradycardia were not significant. P-value=1.000 i.e P-value>0.0 Other complications like nausea or shivering were not observed in any patients of Group-L or Group-B.

DISCUSSION

Regional anaesthesia has many advantages like consciousness of the patient, early awareness of complications owing to the ongoing cooperation of the patient, protection of the airway reflexes, better hemodynamic stability compared to general anesthesia, while it has the disadvantages of late onset of its effects and possible development of motor block.[41] This method is preferred by anaesthesiologists, especially in patients who suffer from respiratory system problems.[42] Epidural anesthesia followed by epidural postoperative analgesia is also preferred for high-risk cardiac patients.[43]

Bupivacaine is a long-acting local anesthetic from the amino-amide subgroup, which is frequently used in local infiltration and epidural and spinal anesthesia. Although it has been safely used in all types of regional applications for many years, fatal cardiotoxic effects may be seen following accidental intravascular injection.[44,45] An important cause of cardiovascular side effects is Bupivacaine leaving sodium channels slowly. Therefore, local anesthetics with similar actions to Bupivacaine, but with fewer effects on the cardiovascular system, have been needed.

Levobupivacaine is an S (-) enantiomer of racemic Bupivacaine. The affinity of the S (-) isomer to the cardiac sodium channel in the inactive state is lower than that of the R (+) isomer.[46,47,48] In the studies conducted, Levobupivacaine has been demonstrated to present similar pharmacokinetic characteristics to Bupivacaine and to be less cardiotoxicity. Levobupivacaine is considered a good alternative to Bupivacaine, because of its lower side effects on the cardiovascular and central nervous system.[49,50,51,52]

Equal doses of Levobupivacaine and Bupivacaine (17 mL of 0.5%) provide similar onset of sensory block (8-30 min), maximum cephalic spread (T6-T7) and duration of analgesia (4-6 hours). [23,30] Though, the onset of motor block is delayed with Levobupivacaine [26] it is less dense as compared to Bupivacaine but with a similar duration. [23,26,30,31] Higher concentration of Levobupivacaine (i.e., 0.75% vs. 0.5%) provides a longer duration of sensory and motor block without any increase in the incidence of adverse side effects[39] An increase in both volume and concentration of Levobupivacaine is however associated with a higher incidence of hypotension (82%) and delayed block regression. [53] The incidence of hypotension is similar when either Levobupivacaine or Bupivacaine is used for epidural anesthesia for cesarean section. [33]
So a study was conducted by us , to compare the clinical profile of Levobupivacaine and Bupivacaine when administered epidurally.

Hypothesis postulated:-

Based on previous studies, we postulated a hypothesis that Levobupivacaine has similar onset of sensory blockade when compared with Bupivacaine, and Levobupivacaine has similar duration of sensory and motor blockade when compared with Bupivacaine , whereas incidence of successful motor block is lower and delayed with Levobupivacaine as compared to Bupivacaine. Variation in Hemodynamic parameters with both drugs is similar with increased chances of hypotension in patients receiving Bupivacaine as compared to Levobupivacaine.

Dose of the drugs selected.

As seen by previous studies, Equal doses of Levobupivacaine and Bupivacaine (17 mL of 0.5%) provide similar onset of sensory block (11-12 min), maximum cephalic spread (T6-T7) and duration of analgesia (4-6 h).[7,14] . A sensory block level of T-6 is enough for below umbilical surgeries.

DEMOGRAPHIC DATA (Table no-1,2 & 3)

Demographic data comparing Age (P value= 0.899), Sex (P value= 1.000), Weight (P-value=0.052) shows **no statistically significant difference** among both the groups and are comparable.

DURATION OF SURGERY (Table no-4)

Both groups are comparable with respect to duration of surgery. Mean duration of surgery in Group-L being 105.6 minutes and Group-B being 109 minutes. P-value is **not significant**. (P-value= 0.129)

SENSORY BLOCKADE:-

Time to sensory block at T-10 (minutes) (Table no-5) i.e .time interval between the end of administration of anaesthetic ("0" time) and the onset of cutaneous analgesia at T10.

In our study, we found that, Group-L has **similar** onset of sensory block as compared to Group-B. Mean onset time to sensory block at T-10 in Group-L is 11.6 mins and

In Group-B is 11.62 mins. P -value being not **significant**. P-value= 0.820 i.e. P-value<0.05

In a study done by **Kopacz et al in 2000**[10], The time to onset of adequate sensory block (T10 dermatome) was similar in both treatment groups (13.6 ± 5.6 min for Levobupivacaine and 14.0 ± 9.9 min for Bupivacaine), with an average peak block height of T5 reached at 24.3 ± 9.4 and 26.5 ± 13.2 min, respectively. Whereas, in our study, Mean Time to sensory block at T-10 in Group-L was found as 11.10±0.237 minutes and Group-B was 9.83±0.791 minutes ,with an average peak block height of T-6 reached at 14.97±1.497 minutes in Group-L and 13.07±0.828 minutes in Group-B.

In a study done by**Fesih Kara et al in 2013**[39], Time of sensory block to reach T6 in GroupL and GroupB is 24.54±2.27 min and 23.97±1.485 min respectively. Onset was similar with Levobupivacaine and Bupivacaine.

Kopacz et al(2000)[26]**,Garcia JBS et al(2001)**[28]**, Fesih Kara et al(2013)**[39]; found that Mean time to onset of sensory block was similar in both Levobupivacaine and Bupivacaine groups.

Highest level of Sensory block reached

In Group L T-6 level was reached in 29 patients(58%) , T-7 level was reached in 16 patients (32%) and T-10 level was reached in 5 patients (10%).

In Group B T-6 level was reached in 31 patients(62%) , T-7 level was reached in 15 patients (30%) and T-10 level was reached in 4 patients (8%).

This is statistically not **significant**. P-value is 0.1 i.e. P-value>0.05.

Cox et al.(1998)[23], Bader et al. (1999) [25], Kopacz and Allen (2000) [26], and Fesih Kara et al(2013) [23] also found no significant difference between the two groups with respect to peak block height attained, which is similar to our study.

Regression and duration of sensory block:

Time to two segment regression (Table no-7) i.e. time for regression of sensory block by two dermatomes from peak block height.

Duration of sensory block (Table no-7) i.e. Duration between "0" time & time at which two-segment regression takes place.

In our study, we found that , **Group-L has a longer duration of sensory block** as compared to Group-B, which is in contrast to our hypothesis that duration of sensory block is similar with both drugs.Mean Time to two segment regression / Duration of sensory block in Group-L being 132.46 minutes and Group-B being 89.28 minutes. **P-value is significant**(P-value=0.000).

Duration of sensory analgesia: The time interval between the administration of epidural block and the first requirement of supplementary analgesia.Group-L has **longer** duration of sensory analgesia as compared to Group-B . Mean Time of sensory analgesia in block in Group-L is 326.5 mins and in Group-B is 284.42 mins.P -value is **significant**. P-value= 0.000 i.e. P-value<0.05

In a study done by **Cox CR et al in 1998[23]**, Duration of sensory block was longer in the 0.5% Levobupivacaine group, with a mean duration of 377 min for 0.5% Levobupivacaine and 345 min for 0.5% Bupivacaine. This is in contrast to our study as

we found Duration of sensory block by Levobupivacaine to be significantly shorter than Bupivacaine.

In a study done by **Kopacz et al in 2000**[26], Time to complete regression (Duration) of sensory block was significantly longer with Levobupivacaine (550.6 ± 87.6 min) than Bupivacaine (505.9 ± 71.1 min) (*P* = 0.016). It is in contrast to our study.

In a study done by, **Cox CR et al(1998)** [23]**, Kopacz et al(2000)** [26]; Duration of sensory block was longer with Levobupivacaine as compared to Bupivacaine.

MOTOR BLOCKADE :

Time to onset of motor block. (Table no-9) i.e. time interval between the end of administration of anaesthetic("0" time) and the onset of motor

In our study, we found that , Group-L has a **slower** onset of motor block as compared to Group-B, which is in accordance to our hypothesis that onset of motor block is delayed with Levobupivacaine as compared to Bupivacaine. Mean Time to onset of motor block in Group-L is 19.6 mins and in Group-B is 17.74 mins. P -value is **significant**. P-value= 0.000 i.e. P-value<0.05

In a study done by **Cox CR et al in 1998**[23], There was no significant difference in onset time or grade of motor block between the groups. However, in the 0.5% Levobupivacaine group, 14 of 29 patients did not develop motor block and 9 out of 29 patients did not develop motor block in 0.5% Bupivacaine group. In our study all patients in both the groups developed MBS Score-2 0r 3.

In a study done by **Kopacz et al in 2000**[26], Levobupivacaine showed a significantly slower onset of lower extremity motor block. At 30 mins , 4 of 28 patients (14%) had detectable lower extremity motor block with Levobupivacaine as compared to 20 of 28 patients (71%) with Bupivacaine ($P < 0.001$) . Some motor block of the lower extremities was eventually achieved in 25 of 28 patients (89%) administered Levobupivacaine and 27 of 28 patients (96%) who received Bupivacaine. In our study, Mean Time to onset of motor block in Group-L was 19.67$\pm$1.649 minutes and Group-B was 17.70$\pm$1.149 minutes and all patients acheieved MBS score-3 in both the groups.

In a study done by **Fesih Kara et al in 2013**[39], Time of motor block to reach maximum level observed in GroupL and GroupB was 26.80 ± 1.96 min and 26.54 ± 1.88 min respectively, which was statistically not significant(P-value=0.574).In our study, Mean Time to onset of motor block(MBS Score-3) in Group-L was 19.67$\pm$1.649 minutes and Group-B was 17.70$\pm$1.149 minutes, which was statistically significant(P-value=0.000).

Cox CR et al(1998) [23], Garcia JBS et al(2001) [28], Ngamprasertwong P et al(2005) [34] ,Fesih Kara et al(2013) [39]; found in their study that Onset of motor block was similar with Levobupivacaine and Bupivacaine. In a study by, **Kopacz et al(2000) [26]**, slower onset of motor block was found with Levobupivacaine as compared to Bupivacaine, as seen in our study, but in our study we found this difference to be statistically significant.

Duration of motor block (Table no-11) .i.e .time between “0” time & time to regression of motor block.

In our study, we found that , Group-L has **shorter** duration of motor block as compared to Group-B .Mean Duration of motor block in Group-L is 197.4 mins and in Group-B is 203.3 mins. P -value is **significant**. P-value= 0.017 i.e. P-value < 0.05.

In a study done by **Ngamprasertwong P et al in 2005**[34] , Time to starting of regression of motor block was 126.2 ± 58.6 minutes for Levobupivacaine and 129.9±89.3 minutes for Bupivacaine(P-value=0.886) which is similar to our study.

In a study done by **Garcia JBS et al in 2001**[28], Duration of Muscular relaxation observed was 303.85 ± 48.66 minutes with Levobupivacaine and 272.31 ± 41.98 with Bupivacaine.i.e. Duration of motor block was longer with Levobupivacaine as compared to bupivacine, which is similar to our study.

In a study done by **S. A. Aasim in 2014**[40], The duration of motor blockade observed were similar with both Bupivacaine (229.6 ± 24.41) and Levobupivacaine (218.4 ± 18.04) with no statistically significant differences (p=0.071), which is similar to our study. to our study.

In a study by,**Kopacz et al(2000)** [26] **, Ngamprasertwong P et al(2005)** [34]**, Fesih Kara et al(2013)** [39]**,S A Aasim et al(2014)** [40]; Duration of of motor block was similar in both Levobupivacaine and Bupivacaine groups. **Garcia JBS et al(2001)** [28] found that Duration of motor block was longer with Levobupivacaine as compared to Bupivacaine. In our study, we found that , Group-L has similar duration of motor block as compared to Group-B.

In a study done by **Kopacz et al in 2000**[26], The duration of lower extremity motor block was shorter for patients administered Levobupivacaine (355.4 ± 83.4min) as

compared to Bupivacaine(375.7 ± 99.2 min) which was statistically not significant. In our study we found this difference to be significant

Degree of motor block - The degree of motor block was assessed by Modified Bromage scale (Table no.10)

In Group L MBS 3 was reached in 38 patients (76%) , MBS 2 was reached in 12 patients (24%)

In Group B MBS 3 was reached in 40 patients (80%) , MBS 2 was reached in 10 patients (20%) This is statistically is **not significant**. P-value = 0.633 i.e. P-value>0.05.

HEMODYNAMIC CHANGES

Mean systolic blood pressure at various intervals.(Table no-14)

In our study we observed that, There is no difference between Group-L and Group-B with respect to variability in systolic blood pressure at various time intervals, which is in accordance with our hypothesis. P-value is not significant. P value = P-value>0.05 at various time intervals.

Mean diastolic blood pressure at various intervals.(Table no-15)

In our study we observed that, There is no difference between Group-L and Group-B with respect to variability in diastolic blood pressure at various time intervals; except at 10 minutes (P-value=0.023). P-value is not significant (P-value>0.05) at all other time intervals except at 10 minute.

Mean Heart rate at various intervals.(Table no-16)

In our study we observed that, Group-L and Group-B are comparable with respect to changes in heart rate at various time intervals; which is in accordance with our hypothesis. P-value is not significant (P-value>0.05) at various time intervals.

In a study done by **Cox CR et al in 1998**[23], There were no significant difference between the two groups receiving 0.5% Levobupivacaine and 0.5% Bupivacaine in arterial pressure (systolic, mean and diastolic) or heart rate. There was a reduction in both heart rate and arterial pressure during the first hour, with a subsequent return to baseline values.

In a study done by **Garcia JBS et al in 2001**[28] , Mean heart rate variation along time showed a significant decrease as from 60 minutes for Levobupivacaine and 90 minutes for Bupivacaine, without significant differences between groups. A significant systolic blood pressure decrease as from 15 minutes for Levobupivacaine and 20 minutes for Bupivacaine, without significance when comparing both groups was observed. Diastolic blood pressure significantly decreased in both groups as from 20 minutes, also without significance when comparing both groups.

In a study done by **Fesih Kara et al in 2013**[39], No statistically significant difference was found between the Levobupivacaine and Bupivacaine groups in terms of heart rate, noninvasive systolic artery pressure, diastolic artery pressure($P > 0.05$).

Thus we inferred from our study, that Levobupivacaine and Bupivacaine have comparable variations in hemodynamic parameters when used for epidural anesthesia. There was no rise in Systolic blood pressure, Diastolic blood pressure or Heart rate

among any patient in both the groups intra-operatively, indicating a good quality of analgesia throughout the surgery; by epidural Levobupivacaine and Bupivacaine.

Spo2 at various time intervals.

Spo2 < 95% is defined as hypoxia & treated with supplemental O2 via face mask . In our study 02 saturation was found > 95% in both the groups at all time intervals.

COMPLICATIONS : (Table no- 15)

Hypotension was seen in 7 cases(14%) and Bradycardia in 2 cases (4%) of Group-L. Hypotension was seen in 12 cases(24%) and Bradycardia in 1 case (2%) of group-B. Thus indicating higher chances of hypotension with Group-B patients. Other complications like nausea or shivering were not observed in any patients of Group-L or Group-B. Hypotension and bradycardia were not significant. P-value=1.000 i.e P-value>0.05

In a study done by **Cox CR et al in 1998**[23], Hypotension was observed in 18 out of 96 patients, evenly distributed between the three groups receiving 0.75% Levobupivacaine , 0.5% Levobupivacaine and 0.5% Bupivacaine. All episodes responded to treatment.

In a study done by **Bader et al in 1999**[25], The frequency of hypotension was observed as 84.4% in the Levobupivacaine group and 100% for the Bupivacaine group without any significant difference (P <= 0.053).

In a study done by **S. A. Aasim in 2014**[40], Bradycardia was seen in 2 patients in Bupivacaine group and 1 patient in Levobupivacaine group. Hypotension was observed

in 12% patients of Levobupivacaine group and 20% patients of Bupivacaine group. No significant difference between the two groups.

Thus from this study, we infer that epidurally administered isobaric 0.5% Levobupivacaine has a Similar onset and longer duration of sensory blockade and slower onset of motor blockade with comparable quality of analgesia and hemodynamic parameters as with epidurally administered isobaric 0.5% Bupivacaine. Owing to its better safety profile, Levobupivacaine is a good alternative to Bupivacaine.

CONCLUSION

We conclude from our study that epidurally administered isobaric 0.5% Levobupivacaine has a similar onset and longer duration of sensory blockade and slower onset and similar duration of motor blockade with comparable hemodynamic parameters as with epidurally administered isobaric 0.5% Bupivacaine. Owing to its better safety profile, Levobupivacaine is a good alternative to Bupivacaine. Also, levobupivacaine is a good alternative to bupivacaine, for surgeries requiring early mobilisation or shorter duration of motor block.

SUMMARY

This Prospective Randomized Study entitled "A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES" was carried out at Shri B.M Patil Medical College, Hospital & Research centre, Vijayapur from December 2015 through August 2017 after institutional and ethical committee approval. 100 patients of ASA I & II physical status aged between 18-60 yrs scheduled to undergo elective lower abdominal and lower limb surgery and satisfying all the inclusion criteria were enrolled in the study after written informed consent and were randomly allocated into two groups(n=50) to receive 17 ml epidural dose of 0.5% isobaric Bupivacaine(Group B) / 0.5%isobaric Levobupivacaine(Group L) . Both groups are comparable with respect to age, sex, weight and duration of surgery.

Group-L has **similar** onset of sensory block as compared to Group-B. Mean onset time to sensory block at T-10 in Group-L is 11.6 mins andIn Group-B is 11.62 mins.P-value= 0.820

Group L has similar highest level of sensory block reached as compared with Group B p value 0.1

Group-L has a longer duration of sensory block as compared to Group-B, which is in contrast to our hypothesis that duration of sensory block is similar with both drugs. Mean Time to two segment regression / Duration of sensory block in Group-L being 132.46 minutes and Group-B being 89.28 minutes. P-value=0.000

Group-L has **longer** duration of sensory analgesia as compared to Group-B . Mean Time of sensory analgesia in block in Group-L is 326.5 mins and in Group-B is 284.42 mins P-value= 0.000

Group-L has a **slower** onset of motor block as compared to Group-B, which is in accordance to our hypothesis that onset of motor block is delayed with Levobupivacaine as compared to Bupivacaine. Mean Time to onset of motor block in Group-L is 19.6 mins and in Group-B is 17.74 mins. P-value= 0.000

Group-L has **shorter** duration of motor block as compared to Group-B .Mean Duration of motor block in Group-L is 197.4 mins and in Group-B is 203.3 mins. P-value= 0.017

Group L has similar degree of motor blockade as compared to Group B. . P-value = 0.633

No difference was found between Group-L and Group-B with respect to variability in systolic blood pressure, diastolic blood pressure, men heart rate and oxygen saturation at various time intervals. P-value>0.05 at various time intervals.

Group L has similar complications as compared to Group B. P-value=1.000. Most common complications were Hypotension and bradycardia were not significant.. Other complications like nausea or shivering were not observed in any patients of Group-L or Group-B.

Thus from this study, we infer that epidurally administered isobaric 0.5% Levobupivacaine has a similar onset and longer duration of sensory block and slower onset and similar duration of motor blockade with comparable hemodynamic parameters as with epidurally administered isobaric 0.5% Bupivacaine. Owing to its better safety profile, Levobupivacaine is a good alternative to Bupivacaine. Also, levobupivacaine is a good alternative to bupivacaine, for surgeries requiring early mobilisation or shorter duration of motor block.

LIMITATIONS

a) For Epidural anesthesia, requirement of epidurally administered drug varies with the height of the patient. We administered a fixed dose of drug in our study. So further studies need to done with variation in dose of drug administerd according to the height of the patient.

b) Our study included only ASA-I and ASA-II physical status patients. As evident from previous studies, Levobupivacaine has a better cardiac and neurological safety profile. So it could be of benefit in high risk patients. Thus further studies should be done in high risk patients.

RECOMMENDATIONS

a) Owing to its better safety profile, Levobupivacaine is a good alternative to Bupivacaine.

b) Epidural Levobupivacaine is a good alternative to bupivacaine in surgeries requiring early mobilisation or shorter duration of motor block

c) The addition of adjunctive agents (epinephrine, opioids or clonidine) to Levobupivacaine in epidural anesthesia and analgesia may increase the duration and quality of analgesia, and further decrease the risk of toxicity. It is recommended that, further studies to be done by addition of adjunctive agents to Levobupivacaine and to study the difference in duration and quality of analgesia and toxicity.

d) As evident from previous studies, Levobupivacaine has a better cardiac and neurological safety profile. So it could be of benefit in high risk patients. Thus further studies should be done in high risk patients.

BIBLIOGRAPHY

1. Kleinman W. Regional anesthesia and pain management: spinal, epidural and caudal blocks. In: Morgan GE, Mikhail MS, Murray MJ, editors. Clinical Anesthesiology. 3rd ed. Los Angeles: Appleton & Lange; 2002. p.253–82.
2. Longo S. Postdural puncture: implications and complications. Curr Opin Anaesth 1999; 12: 271–5.
3. Michael J Cousins. Neural blockade in clinical anesthesia and pain medicine.4th ed. Philadelphia: Lippincott Williams and Wilkins; 2009.
4. Collin VJ. Principles of anesthesiology. 3rd ed. Philadelphia: Lea and Febiger;1993.
5. Casati A, Putzu M. Bupivacaine, Levobupivacaine and Ropivacaine: are they clinically different? Best Practice and Research Clinical Anaesthesiology2005; 19:247-68.
6. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. Drugs. 2000 Mar, 59 (3) ; 551-579.
7. Apan A, Sarı F, Ekmekçi AB. Single shot “3-in-1” femoral nerve blockade with 0.25% or 0.375% levobupivacaine provides similar postoperative analgesia for total knee replacement. Turk J Med Sci 2010; 40: 77–82.
8. Yurtlu BS, Hancı V, Ege A, Bostankolu SE, Ayoğlu H, Özkoçak Turan I. Tramadol as an adjunct for levobupivacaine in axillary plexus blockade: a prospective, randomized, double-blind study. Turk J Med Sci 2012; 42: 55–62.
9. Nysora – The new York school of regional anesthesia – epidural blockade.NYSORA.com 2017

10. Ellis H. Anatomy for anaesthetists. 8th ed. Massachusetts: BlackwellPublishing; 2004.
11. Paul G Barash. Clinical anesthesia. 6th ed. Philadelphia: Lippincott Williamsand Wilkins; 2009.
12. McLeod GA, Burke D. Levobupivacaine. Anaesthesia 2001;56:331-41.
13. Casati A, Baciarello M. Enantiomeric local anesthetics: Can Ropivacaine and Levobupivacaine improve our practice? Curr Drug Ther 2006;1:85-9.
14. Huang YF, Pryor ME, Mather LE, Veering BT. Cardiovascular and central nervous system effects of intravenous Levobupivacaine and Bupivacaine in sheep. Anesth Analg 1998;86:797-804
15. Morrison SG, Dominguez JJ, Frascarolo P, Reiz S. A comparison of the electrocardiographic cardiotoxic effects of racemic Bupivacaine, Levobupivacaine, and Ropivacaine in anesthetized swine. Anesth Analg 2000;90:1308-14.
16. Burm AG, van der Meer AD, van Kleef JW, Zeijlmans PW, Groen K. Pharmacokinetics of the enantiomers of Bupivacaine following intravenous administration of the racemate. Br J Clin Pharmacol 1994;38:125-9.
17. Leone S, Di Cianni S, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting local anesthetics, Ropivacaine and Levobupivacaine. Acta Biomed 2008;79:92-105.
18. Burlacu CL, Buggy DJ. Update on local anesthetics: focus on Levobupivacaine. Ther Clin Risk Manag. 2008;4 (2):381–392.

19. Weinberg GL. Treatment of local anesthetic systemic toxicity (LAST). Reg Anesth Pain Med 2010;35:188-93.
20. Foxall G, McCahon R, Lamb J, Hardman JG, Bedforth NM. Levobupivacaine-induced seizures and cardiovascular collapse treated with intralipid. Anaesthesia 2007;62:516-8.
21. Stoelting RK. Pharmacology and Physiology in anesthetic practice. 4th ed.2006. Philadelphia: Lippincott Williams & Wilkins.
22. Ronald D. Miller, Lars I. Eriksson, Lee A. Fleisher. Miller's Anesthesia 7th ed. Churchill Livingstone Elsevier ;2010. Chapter 51, Spinal, Epidural, and Caudal Anaesthesia, 1611-1638.
23. Cox CR, Faccenda KA, Gilhooly C, Bannister J, Scott NB, Morrison LM.Extradural S(-)-Bupivacaine: comparison with racemic RS-Bupivacaine.Br J Anaesth. 1998 Mar;80(3):289-93.
24. Burke D, Henderson DJ, Simpson AM, Faccenda KA, Morrison LM, McGrady EM, McLeod GA, Bannister J. Ninewells Hospital and Medical School, Dundee, UK. Comparison of 0.25% S(-)-Bupivacaine with 0.25% RS-Bupivacaine for epidural analgesia in labour.Br J Anaesth. 1999 Nov;83(5):750-5.
25. Bader AM, Tsen LC, Camann WR. Clinical effects and maternal and fetal plasma concentrations of 0.5% epidural Levobupivacaine versus Bupivacaine for Cesarean delivery.Anesthesiology 1999 Jun; 90 (6): 1596-601
26. Kopacz, Dan J. MD; Allen, Hugh W. MD; Thompson, Gale E. MD. A Comparison of Epidural Levobupivacaine 0.75% with Racemic Bupivacaine for Lower Abdominal Surgery. Anesthesia & Analgesia . 90(3):642-648, March

2000.

27. Kopacz DJ, Helman JD, Nussbaum CE, et al. A Comparison of Epidural Levobupivacaine 0.5% With or Without Epinephrine for Lumbar Spine Surgery. Anesth Analg 2001;93:755–60.
28. GARCIA, João Batista Santos et al . Comparative study of 0.5% Levobupivacaine and 0.5% racemic Bupivacaine associated to sufentanil in epidural anesthesia for cesarean delivery. Rev. Bras. Anestesiol., Campinas , v. 51, n. 5, Oct. 2001
29. Cheng CR, Su TH, Hung YC, Wang PT.A comparative study of the safety and efficacy of 0.5% Levobupivacaine and 0.5% Bupivacaine for epidural anesthesia in subjects undergoing elective caesarean section. Acta Anaesthesiol Sin. 2002 Mar;40(1):13-20.
30. Casati A, Santorsola R, Aldegheri G, Ravasi F, Fanelli G, Berti M, Fraschini G,Torri G.Vita-Salute University of Milano-Department of Anesthesiology, IRCCS H SanRaffaele, Milan, Italy.Intraoperative epidural anesthesia and postoperative analgesia with Levobupivacaine for major orthopedic surgery: a double-blind, randomizedcomparison of racemic Bupivacaine, Levobupivacaine and Ropivacaine.J Clin Anesth. 2003 Mar;15(2):126-31.
31. Peduto VA, Baroncini S, Montanini S, et al. 2003. A prospective, randomized, double-blind comparison of epidural Levobupivacaine 0.5% with epidural Ropivacaine 0.75% for lower limb procedures. Eur J Anaesthesiol, 20:979–83.
32. M. Kountoudi, E. Papadaki, A. Pandazi, E. Theohari, I. Kouroukli, L. Georgiou. Department of Anesthesiology, Ippokrateio, Agia Paraskevi, Greece A comparison of epidural Levobupivacaine 0.5% with Ropivacaine 0.5% for

inguinal hernia repair procedure:blood pressure and heart rate alterations. European Journal of Anaesthesiology - EUR J ANAESTH 01/2004; 21.

33. Bergamaschi F, Balle V R , Gomes ME , et al. Levobupivacaine Versus Bupivacaine in Epidural Anesthesia for Cesarean Section.Comparative Study. Rev Bras Anestesiol 2005; 55: 6: 606 -613
34. Ngamprasertwong P, Udomtecha D, Charuluxananan S, et al. Levobupivacaine versus racemic Bupivacaine for extradural anesthesia for Cesarean delivery. J Med Assoc Thai 2005 Nov; 88 (11): 1563-8
35. Tanaka PP, Ogleari M, Valmorbida P, et al. Levobupivacaine 0.5%, 50% enantiomeric excess Bupivacaine and racemic Bupivacaine in epidural anesthesia for lower abdominal procedures. Comparative study. Revista brasileira de anestesiologia 01/2006; 55(6):597-605
36. Koch T, Fichtner A, Schwemmer U, et al. Levobupivacaine for epidural anaesthesia and postoperative analgesia in hip surgery: a multi-center efficacy and safety equivalence study with Bupivacaine and Ropivacaine. Anaesthesist. 2008 May;57(5):475-82.
37. Casimiro C, Rodrigo J, Mendiola MA, Rey F, Barrios A, Glisanz F. Levobupivacaine plus fentanyl versus racemic Bupivacaine plus fentanyl in epidural anesthesia for lower limb surgery. Minerva Anestesiologica 2008;74:381-91.
38. Surav DB, Hanci A, Sivrikaya GU, Bektas M, Kilinc LT. The effects of Different Concentrations and Equivalent Volumes of Levobupivacaine in Epidural Anesthesia. Current Therapeutic Research, Clinical and Experimental

2011;72(2):71-78.

39. Fesih Kara, Husnu Kursad, Mine Celik, Aysenur Dostbil, Ilker Ince, Ahmet Faruk Giren et al. Comparison of the effects of epidural 0.5% Bupivacaine and 0.5% Levobupivacaine administration on anesthesia quality, side effect incidence, and analgesia requirement times in hip and lower extremity surgery .Turkey Turk J Med Sci 2013;43:580-585.
40. S. A. Aasim, B. Syamasundara Rao, Nagaraj Gajagouni. “A Comparative study of 0.5% Levobupivacaine and 0.5% Racemic Bupivacaine in Epidural Anaesthesia for Lower Limb Surgeries”. Journal of Evidence based Medicine and Healthcare; Volume 1, Issue 15, December 15, 2014; Page: 1874-1881.
41. Ouellette SM, Ouelette R. Regional anesthesia: is it safer? CRNA 1995; 6: 70–8.
42. Burke D, Kennedy S, Bannister J. Spinal anaesthesia with 0.5% S(-)-Bupivacaine for elective lower limb surgery. Region Anaesth Pain Med 1999; 24: 519–23.
43. Atalay C, Dağlı C, Bayram E, Alıcı HA, Erdem AF, Keleş MS et al. Effects of three different methods of anesthesia on the release of brain natriuretic peptid in patients with cardiac riskundergoing lower extremity surgery. Turk J Med Sci 2010; 40: 405–14.
44. Reiz S, Nath S. Cardiotoxicity of local anaesthetic agents. Br J Anaesth 1986; 58: 736–46.
45. Marx GF. Cardiotoxicity of local anesthetics - the plot thickens. Anesthesiology 1984; 60: 3–5.

46. Huang YF, Pryor ME, Mather LE Veering BT. Cardiovascular and central nervous system effects of intravenous Levobupivacaine in sheep. Anesth Analg 1998; 86: 797–804.
47. Aberg G. Toxicological and local anaesthetic effects of optically active isomers of two local anaesthetic compounds. Acta Pharmacol Toxicol 1972; 31: 273–86.
48. Luduena FP, Bogado EF, Tullar BF. Optical isomers of Mepivacaine and Bupivacaine. Arch Int Pharmacodyn Ther 1972; 200: 359–69.
49. McClellan KJ, Spencer CM. Levobupivacaine. Drugs 1998; 56: 355–62.
50. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. Drugs 2000; 59: 531–79.
51. Van F, Rolan PE, Brennan N, Gennery B. Differential effects of levo- and racemic Bupivacaine on the EEG in volunteers. Regional Anesth Pain Med Suppl 1998; 23: 48.
52. Valenzuela C, Snyders DJ, Bennett PB, Tamargo J, Hondeghem LM. Stereoselective block of cardiac sodium channels by Bupivacaine in guinea pig ventricular myocytes. Circulation1995; 92: 3014–24.
53. Senard M, Kaba A, Jacquemin MJ, Maquoi LM, Geortay MP, Honoré PD, et al. Epidural Levobupivacaine 0.1% or Ropivacaine 0.1% combined with morphine provides comparable analgesia after abdominal surgery. Anesth Analg 2004;98:389-94.

ANNEXURES

ETHICAL CLERANCE CERTIFICATE

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE No/568/2015 20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17/11/2015 *at* 03 pm *scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.*

Title "A Comparative Study of 0.5% Levobupivacaine with 0.5% Bupivacaine in epidural Anaesthesia for lower abdominal and lower limb Surgeries"

Name of P.G. Student : Dr. Masaraddi Deepak. K.
Dept of Anaesthesiology

Name of Guide/Co-investigator : Dr. D.G. Talikoti
Prof & HOD. Anaesthesiology.

DR.TEJASWINI VALLABHA
CHAIRMAN

Following documents were placed before E.C. for Scrutinization:
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

INFORMED CONSENT FORM

TITLE OF THE PROJECT: **"A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES"**

PRINCIPAL INVESTIGATOR : Dr. Masaraddi Deepak K
Department of Anaesthesiology
Email: dr.masaraddi@gmail.com

PG GUIDE : Dr.D.G.Talikoti
Professor and HOD,
Dept of Anaesthesiology
B.L.D.E. University's Shri B.M. Patil
Medical College Hospital & Research
Centre, Sholapur Road,
BIJAPUR-586103
Karnataka.

I have been informed that this study is **:" A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES".**

I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

PROCEDURE:

I understand that I will be participating in the study**: "A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES".**

RISKS AND DISCOMFORTS:

I understand that I/my ward may experience some pain while intubating and I understand that necessary measures will be taken to reduce these complications as and when they arise.

BENEFITS:

I understand that my/my wards participation in this study will help in finding out: "A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES".

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr. Masaraddi Deepak K is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

And that a copy of this consent form will be given to me for keep for careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr Masaraddi Deepak K will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Patient's Signature :	Witness Signature:
Name :	Name :
Date :	Date :
Dr. D. G. TALIKOTI	Dr. MASARADDI DEEPAK K
(GUIDE)	(INVESTIGATOR)

PERFORMA

STUDY: "A COMPARATIVE STUDY OF 0.5% LEVOBUPIVACAINE WITH 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL SURGERIES**"**

Patient Name : I.P. No :

Age : Weight:

Height : Gender:

Date of Operation : Occupation :

Address : Anaesthesiologist:

Preanaesthetic evaluation

Chief Complaints

Past History

a. HTN / DM / Asthma / Epilepsy / Drug allergy
b. Previous exposure to anaesthesia

General Physical Examination

Pallor / Icterus / Clubbing / Lymphadenopathy / Odema

B.P.: PR:

R.R.: Spine:

Airway assessment:

Systemic examination

R.S. CNS CVS

Investigations

- Urine : albumin, sugar, microscopy
- Blood : Hemoglobin,

  Total Count, Differential Count, Platelet count,

  Bleeding Time , Clotting Time
- HBsAg, HIV
- Blood urea, Serum Creatinine.
- ECG
- Chest x-ray (if required).

Preoperative physical status: ASA Grade I II

Diagnosis:

Proposed surgery:

Monitors attached:

Pulse oximeter Non invasive blood pressure:

ECG

Premedication: Inj. Ondensetron 4mg iv Inj. Ranitidine 150mg iv

Epidural Anesthesia:

Group L ( ) **Group B** ( )

Observations:

- Onset time of sensory block (in mins) :
- Highest level of sensory block :
- Time for two segment regression of sensory block (in mins) :
- Duration of sensory analgesia (in mins) :
- Onset time of motor block (in mins) :
- Degree of motor blockade (0-3) :

  using Modified Bromage scale

  - **Modified Bromage Scale2:**
  - 0-Able to raise leg straight, full flexion of knees and feet.
  - 1-Inability to raise leg, just able to flex knees, full flexion of feet.
  - 2-Unable to flex knees, but some flexion of feet possible.
  - 3-Unable to move legs or feet.
- Duration of motor block (in mins) :

õ Haemodynamic changes- heart rate, blood pressure, mean arterial pressure and respiratory rate

TIME (in mins)	PULSE RATE (bpm)	SBP / DBP (mmHg)	MAP (mmHg)
Baseline			
2			
5			
15			
30			
45			
60			
90			
120			
180			

õ Intra operative and post operative complications if any –

Nausea	( )
Vomiting	( )
Hypotension	( )
Bradycardia	( )
Respiratory Depression	( )

GROUP-B

Sl No.	IP No	Age (years)	SEX	Weight in kg	height in cm	Duration of surgery (min)	type of surgery	onset of sensory block (min)	highest level of sensory block (min)	time to two-segment regression of sensory block (min)	duration of sensory analgesia (min)	onset time of motor block (min)	degree of motor block (min)	duration of motor block (min)	BP Systolic										BP Diastolic										Heart Rate										SPO2 (%)										Complications if any.
															0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min	0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min	0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min	0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	
1	16984	45	F	52	160	120	LA	11	T-6	95	280	17	3	200	122	116	110	108	102	102	100	100	104	102	74	70	64	66	66	64	62	68	68	68	70	68	66	65	68	65	66	66	65	65	100	100	100	100	100	100	100	100	100	100	
2	17809	50	F	48	163	120	LA	12	T-7	88	285	19	3	210	110	106	102	98	102	104	106	104	106	102	72	68	66	64	64	64	68	66	64	66	68	66	65	64	66	65	66	65	66	66	100	100	100	100	100	100	100	100	100	100	
3	18131	45	F	54	159	120	LA	12	T-10	95	290	18	3	210	122	120	116	112	110	112	106	108	104	104	78	78	76	66	66	68	68	66	68	68	72	70	70	69	67	68	68	66	65	66	100	100	100	100	100	100	100	100	100	100	
4	18081	40	F	58	162	120	LA	12	T-7	98	270	17	3	200	116	102	98	90	98	102	100	98	100	100	80	78	74	52	66	64	66	66	64	66	77	74	72	62	64	66	64	63	66	65	100	100	100	100	100	100	100	100	100	100	hypotension
5	18659	49	F	50	166	120	LA	10	T-6	87	280	19	3	190	124	118	110	108	102	108	106	110	112	108	80	74	70	68	68	66	68	68	66	68	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	
6	10363	45	F	50	163	120	LA	13	T-7	86	280	19	3	190	126	116	112	102	102	104	106	100	104	112	76	72	70	68	64	66	64	68	68	64	77	75	72	71	71	70	70	70	70	69	100	100	100	100	100	100	100	100	100	100	
7	11196	40	F	54	165	120	LA	10	T-6	90	290	19	2	195	124	120	110	108	104	110	110	110	104	104	76	72	70	68	64	68	68	68	68	66	65	64	62	66	62	60	61	62	62	64	100	100	100	100	100	100	100	100	100	100	
8	10667	29	F	56	167	120	LA	11	T-6	98	295	20	3	190	110	110	108	104	102	98	100	100	96	102	74	70	64	66	66	64	62	68	68	68	70	68	66	65	68	65	66	66	65	64	100	100	100	100	100	100	100	100	100	100	
9	12879	45	F	51	168	120	LA	13	T-7	85	288	19	3	210	108	106	104	98	102	104	106	104	106	104	70	68	66	64	64	64	66	66	64	66	68	66	65	64	66	65	66	65	66	65	100	100	100	100	100	100	100	100	100	100	
10	13296	55	F	48	164	120	LA	12	T-6	85	290	18	3	210	128	110	108	104	102	98	100	100	96	104	74	70	64	66	66	64	62	68	68	66	70	68	66	65	68	65	66	66	65	67	100	100	100	100	100	100	100	100	100	100	
11	10927	35	M	60	170	120	LL	12	T-6	87	280	18	2	205	128	122	116	112	112	112	106	108	104	102	72	66	64	66	66	68	68	66	68	64	72	70	70	69	67	68	68	66	65	66	100	100	100	100	100	100	100	100	100	100	
12	8072	57	M	58	173	100	LL	11	T-7	89	275	17	3	220	120	118	116	100	94	104	104	98	102	104	76	74	64	50	64	66	66	66	64	66	74	70	66	62	64	62	64	63	66	65	100	100	100	100	100	100	100	100	100	100	hypotension
13	9123	51	M	56	167	120	LL	12	T-6	88	290	18	3	190	128	118	120	90	98	102	100	96	100	102	78	74	66	54	66	64	64	64	64	66	72	63	64	60	62	66	62	63	64	64	100	100	100	100	100	100	100	100	100	100	hypotension
14	9741	35	M	67	164	100	LL	11	T-6	99	285	17	2	210	126	120	118	92	96	100	102	98	104	102	76	76	70	66	64	66	64	68	64	64	66	64	66	64	65	64	64	61	66	63	100	100	100	100	100	100	100	100	100	100	hypotension
15	9427	58	F	54	169	90	LL	12	T-6	87	290	20	3	220	128	124	120	106	100	106	104	106	110	106	70	66	64	66	64	66	66	66	64	66	65	63	66	62	64	66	64	63	66	65	100	100	100	100	100	100	100	100	100	100	hypotension
16	11975	50	F	55	166	90	LL	11	T-6	85	290	17	3	210	126	122	116	112	112	112	106	108	104	102	72	66	64	66	66	68	68	66	68	64	72	70	70	69	67	68	68	66	65	64	100	100	100	100	100	100	100	100	100	100	
17	10113	19	M	55	159	120	LL	13	T-7	80	275	16	3	200	122	110	108	104	102	98	100	100	96	102	74	70	64	66	66	64	62	68	68	66	70	68	66	65	68	65	66	66	65	65	100	100	100	100	100	100	100	100	100	100	
18	10337	40	M	57	165	100	LL	11	T-7	90	290	18	3	210	110	110	102	100	100	104	104	104	100	98	78	70	68	72	66	66	64	68	66	64	80	77	75	73	70	71	72	71	72	70	100	100	100	100	100	100	100	100	100	100	
19	11506	28	M	58	163	100	LL	12	T-6	89	270	17	2	190	124	118	110	108	102	108	106	110	112	100	78	72	70	66	68	68	68	68	66	66	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	
20	11507	35	M	59	166	110	LL	13	T-6	84	275	16	2	200	136	126	120	116	112	110	120	116	118	116	78	72	72	68	66	70	70	68	68	68	72	70	71	69	70	68	67	67	69	68	100	100	100	100	100	100	100	100	100	100	
21	10620	50	M	60	170	100	LL	11	T-7	82	290	18	3	205	122	118	110	82	102	108	106	110	112	110	78	72	70	66	68	68	68	68	66	66	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	
22	15645	47	F	65	166	120	LL	12	T-6	87	270	18	3	210	118	110	106	98	102	104	106	100	104	102	76	72	70	68	64	66	64	68	68	66	77	75	72	71	71	70	70	70	70	69	100	100	100	100	100	100	100	100	100	100	
23	13335	25	M	62	168	110	LL	11	T-6	88	295	18	3	205	124	108	108	106	106	102	104	110	112	110	72	68	66	66	66	62	64	66	64	64	71	69	68	66	65	68	66	66	67	64	100	100	100	100	100	100	100	100	100	100	
24	12902	60	F	50	163	90	LL	12	T-10	92	290	16	3	190	126	110	102	100	100	104	104	104	100	98	78	70	68	72	66	66	64	68	66	64	80	77	75	73	70	71	72	71	72	70	100	100	100	100	100	100	100	100	100	100	
25	40887	41	M	58	164	110	LL	11	T-6	93	280	17	3	210	120	120	112	102	100	102	102	104	104	106	76	70	68	66	66	68	68	66	68	70	68	67	69	68	65	64	62	66	64	65	100	100	100	100	100	100	100	100	100	100	
26	18896	45	M	60	166	100	LL	11	T-6	89	290	16	3	210	110	110	102	100	98	102	100	106	102	104	72	68	66	68	66	66	64	64	66	68	69	67	69	68	65	68	68	68	69	68	100	100	100	100	100	100	100	100	100	100	
27	24903	36	M	64	169	100	LL	12	T-7	95	275	16	3	190	106	118	110	108	102	108	106	110	112	108	78	72	70	66	68	68	68	66	66	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	100	
28	12752	41	M	59	158	90	LL	11	T-6	90	290	18	2	190	124	122	120	90	96	104	102	100	102	102	74	72	70	66	64	66	66	66	64	68	65	63	66	62	64	66	64	63	66	65	100	100	100	100	100	100	100	100	100	100	hypotension
29	16480	34	M	60	163	110	LL	12	T-6	89	280	17	3	210	126	122	118	110	98	102	100	98	100	100	76	74	64	66	68	64	66	66	64	66	69	63	67	65	63	65	64	63	65	64	100	100	100	100	100	100	100	100	100	100	hypotension
30	15538	59	M	60	164	90	LL	11	T-6	94	290	18	3	210	110	108	102	100	100	102	100	102	104	102	72	68	66	64	68	66	64	66	64	64	60	57	56	56	56	59	58	58	57	55	100	100	100	100	100	100	100	100	100	100	bradycardia
31	16960	26	F	52	160	120	LA	11	T-6	95	280	17	3	200	122	116	110	108	102	102	100	100	104	102	74	70	64	66	66	64	62	68	68	68	70	68	66	65	68	65	66	66	65	65	100	100	100	100	100	100	100	100	100	100	
32	29471	30	M	54	159	120	LA	12	T-10	95	290	18	3	210	122	120	116	112	110	112	106	108	104	104	78	78	76	66	66	68	68	66	68	68	72	70	70	69	67	68	68	66	65	66	100	100	100	100	100	100	100	100	100	100	
33	29728	56	F	50	163	120	LA	13	T-7	86	280	19	3	190	126	116	112	102	102	104	106	100	104	112	76	72	70	68	64	66	64	68	68	64	77	75	72	71	71	70	70	70	70	69	100	100	100	100	100	100	100	100	100	100	
34	16794	18	F	51	168	120	LA	13	T-7	85	288	19	3	210	108	106	104	98	102	104	106	104	106	104	70	68	66	64	64	64	66	66	66	64	68	66	65	64	66	65	66	65	66	65	100	100	100	100	100	100	100	100	100	100	
35	16817	50	M	58	173	100	LL	11	T-7	89	275	17	3	220	120	118	116	100	94	104	104	98	102	104	76	74	64	50	64	66	66	66	64	66	74	70	66	62	64	62	64	63	66	65	100	100	100	100	100	100	100	100	100	100	hypotension
36	29702	35	M	54	169	90	LL	12	T-6	87	290	20	3	220	128	124	120	106	100	106	104	106	110	106	70	66	64	66	64	66	66	66	64	66	65	63	66	62	64	66	64	63	66	65	100	100	100	100	100	100	100	100	100	100	hypotension
37	27531	35	F	57	165	100	LL	11	T-6	90	290	18	3	210	110	110	102	100	100	104	104	104	100	98	78	70	68	72	66	66	64	68	66	64	80	77	75	73	70	71	72	71	72	70	100	100	100	100	100	100	100	100	100	100	
38	29119	43	M	60	170	100	LL	11	T-7	82	290	18	3	205	122	118	110	82	102	108	106	110	112	110	78	72	70	66	68	68	68	68	66	66	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	
39	31869	35	M	50	163	90	LL	12	T-10	92	290	16	3	190	126	110	102	100	100	104	104	104	100	98	78	70	68	72	66	66	64	68	66	64	80	77	75	73	70	71	72	71	72	70	100	100	100	100	100	100	100	100	100	100	
40	36137	28	M	59	158	90	LL	11	T-6	90	290	18	2	190	124	122	120	90	96	104	102	100	102	102	74	72	70	66	64	66	66	66	64	68	65	63	66	62	64	66	64	63	66	65	100	100	100	100	100	100	100	100	100	100	hypotension
41	36229	38	F	48	163	120	LA	12	T-7	88	285	19	3	210	110	106	102	98	102	104	106	104	106	102	72	68	66	64	64	64	68	66	64	66	68	66	65	64	66	65	66	65	66	66	100	100	100	100	100	100	100	100	100	100	
42	34667	55	M	50	166	120	LA	10	T-6	87	280	19	3	190	124	118	110	108	102	108	106	110	112	108	80	74	70	68	68	66	68	68	66	68	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	
43	35427	35	M	56	167	120	LA	11	T-6	98	295	20	3	190	110	110	108	104	102	98	100	100	96	102	74	70	64	66	66	64	62	68	68	68	70	68	66	65	68	65	66	66	65	64	100	100	100	100	100	100	100	100	100	100	
44	34245	40	M	60	170	120	LL	12	T-6	87	280	18	2	205	128	122	116	112	112	112	106	108	104	102	72	66	64	66	66	68	68	66	68	64	72	70	70	69	67	68	68	66	65	66	100	100	100	100	100	100	100	100	100	100	
45	38536	42	M	67	164	100	LL	11	T-6	99	285	17	2	210	126	120	118	92	96	100	102	98	104	102	76	76	70	66	64	66	64	68	64	64	66	64	66	64	65	64	64	61	66	63	100	100	100	100	100	100	100	100	100	100	hypotension
46	18094	45	M	55	159	120	LL	13	T-7	80	275	16	3	200	122	110	108	104	102	98	100	100	96	102	74	70	64	66	66	64	62	68	68	66	70	68	66	65	68	65	66	66	65	65	100	100	100	100	100	100	100	100	100	100	
47	37077	29	M	59	166	110	LL	13	T-6	84	275	16	2	200	136	126	120	116	112	110	120	116	118	116	78	72	72	68	66	70	70	68	68	68	72	70	71	69	70	68	67	67	69	68	100	100	100	100	100	100	100	100	100	100	
48	32799	24	M	62	168	110	LL	11	T-6	88	295	18	3	205	124	108	108	106	106	102	104	110	112	110	72	68	66	66	66	62	64	66	64	64	71	69	68	66	65	68	66	66	67	64	100	100	100	100	100	100	100	100	100	100	
49	18260	38	M	60	166	100	LL	11	T-6	89	290	16	3	210	110	110	102	100	98	102	100	106	102	104	72	68	66	68	66	66	64	64	66	68	69	67	69	68	65	68	68	68	69	68	100	100	100	100	100	100	100	100	100	100	
50	39415	23	M	60	163	110	LL	12	T-6	89	280	17	3	210	126	122	118	110	98	102	100	98	100	100	76	74	64	66	68	64	66	66	64	66	69	63	67	65	63	65	64	63	65	64	100	100	100	100	100	100	100	100	100	100	hypotension

MASTER CHART

GROUP-L

Serial No.	IP No	Age (years)	SEX	Weight in kg	height in cm	Duration of surgery (min)	type of surgery	onset of sensory block (min)	highest level of sensory block (min)	time to two-segment regression of sensory block (min)	duration of sensory analgesia (min)	onset time of motor block (min)	degree of motor block (min)	duration of motor block (min)	BP Systolic										BP Diastolic										Heart Rate										SPO2 (%)										Complications if any.
															0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min	0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min	0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min	0 min	2 min	5 min	15 min	30 min	45 min	60 min	90 min	120 min	
1	17293	45	F	50	158	120	LA	11	T-6	125	330	20	3	180	110	110	108	104	102	98	100	100	96	104	74	70	64	66	66	64	62	68	68	66	70	68	66	65	68	65	66	66	65	66	100	100	100	100	100	100	100	100	100	100	
2	17743	52	F	52	164	120	LA	12	T-7	115	335	19	3	185	108	106	104	98	102	104	106	104	106	104	70	68	66	64	64	64	66	66	64	66	68	66	65	64	66	65	66	65	66	64	100	100	100	100	100	100	100	100	100	100	
3	18012	40	F	56	160	120	LA	11	T-6	135	320	18	2	185	128	122	116	112	112	112	106	108	104	102	72	66	64	66	66	68	68	66	68	64	72	70	70	69	67	68	68	66	65	68	100	100	100	100	100	100	100	100	100	100	
4	18271	40	F	54	167	120	LA	13	T-7	138	325	20	3	170	134	126	120	116	112	110	110	116	118	110	78	72	72	68	66	70	70	68	68	68	72	70	71	69	70	68	67	67	69	68	100	100	100	100	100	100	100	100	100	100	
5	18428	50	F	48	168	120	LA	12	T-6	110	320	21	3	180	126	118	110	108	102	108	106	110	112	100	78	72	70	66	68	68	68	68	66	66	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	
6	10083	45	F	46	163	120	LA	11	T-7	116	320	19	3	175	122	110	106	98	102	104	106	100	104	102	76	72	70	68	64	66	64	68	68	66	77	75	72	71	71	70	70	70	70	69	100	100	100	100	100	100	100	100	100	100	
7	10209	42	F	51	161	120	LA	10	T-6	122	330	19	2	210	124	120	110	108	104	110	110	110	104	112	78	72	70	68	64	68	68	68	68	68	65	64	62	66	62	60	61	62	62	64	100	100	100	100	100	100	100	100	100	100	
8	10632	30	F	46	170	120	LA	13	T-6	125	320	20	2	210	130	126	120	118	114	116	112	108	110	104	78	72	70	68	66	66	68	66	66	66	68	67	66	65	65	63	65	64	62	66	100	100	100	100	100	100	100	100	100	100	
9	12066	45	F	56	160	120	LA	12	T-6	130	325	20	3	215	110	110	106	102	110	102	104	100	106	106	72	68	66	64	64	66	64	68	68	64	69	66	67	65	65	67	66	64	66	64	100	100	100	100	100	100	100	100	100	100	
10	13153	55	F	50	168	120	LA	11	T-6	135	340	18	3	220	108	108	106	100	100	104	100	106	110	100	74	70	66	64	60	66	64	62	64	64	77	74	75	72	75	76	72	71	70	73	100	100	100	100	100	100	100	100	100	100	hypotension
11	7656	32	M	65	162	100	LL	11	T-10	140	335	18	3	190	110	108	108	106	106	102	104	110	112	112	72	68	66	66	66	62	64	66	64	64	71	69	68	66	65	68	66	66	67	64	100	100	100	100	100	100	100	100	100	100	
12	8043	58	M	59	164	90	LL	12	T-6	142	320	18	3	205	128	126	118	106	108	102	106	112	118	110	78	72	68	66	66	66	64	68	68	68	70	68	69	66	68	67	66	67	65	68	100	100	100	100	100	100	100	100	100	100	
13	9047	54	M	55	158	100	LL	13	T-6	145	335	21	3	205	134	126	120	118	106	108	110	110	110	112	80	76	74	72	70	70	68	70	70	66	68	66	67	68	66	67	68	67	65	64	100	100	100	100	100	100	100	100	100	100	
14	19807	38	M	63	161	110	LL	13	T-7	145	320	22	3	210	110	108	106	102	102	104	104	106	102	102	72	68	66	64	64	66	68	66	64	70	66	63	66	62	64	62	64	63	66	65	100	100	100	100	100	100	100	100	100	100	
15	8312	60	F	64	165	90	LL	12	T-7	148	340	19	2	195	108	108	106	100	102	104	106	104	104	104	72	66	64	64	66	68	66	66	66	66	60	59	58	58	57	57	58	56	55	56	100	100	100	100	100	100	100	100	100	100	
16	9649	55	F	65	159	100	LL	11	T-10	137	330	18	3	220	102	100	98	90	102	98	96	100	102	100	70	64	62	58	62	66	64	62	64	64	62	60	59	57	56	58	59	57	58	57	100	100	100	100	100	100	100	100	100	100	hypotension
17	10084	18	M	65	172	110	LL	10	T-6	126	335	17	2	210	118	110	106	100	102	104	106	102	102	102	78	72	70	68	68	66	68	64	64	70	72	68	67	67	69	68	67	65	67	69	100	100	100	100	100	100	100	100	100	100	
18	11009	45	M	60	167	100	LL	10	T-6	127	320	17	3	185	100	100	96	78	100	104	98	100	102	98	74	66	68	52	62	66	64	64	64	64	78	73	71	70	70	69	70	72	70	69	100	100	100	100	100	100	100	100	100	100	hypotension
19	11076	28	M	70	156	110	LL	11	T-7	129	320	20	3	190	124	110	102	100	100	104	104	104	100	98	78	70	68	72	66	66	64	68	66	64	80	77	75	73	70	71	72	71	72	70	100	100	100	100	100	100	100	100	100	100	
20	11502	40	M	65	164	100	LL	12	T-6	128	320	22	3	210	136	124	118	114	110	110	108	112	110	108	82	78	76	74	74	72	70	70	70	72	75	72	70	68	69	69	67	68	68	66	100	100	100	100	100	100	100	100	100	100	
21	11880	46	M	57	164	90	LL	13	T-7	122	325	23	3	190	112	112	110	106	102	104	108	106	104	102	74	68	66	68	66	64	66	66	68	68	65	63	66	62	64	63	66	63	62	65	100	100	100	100	100	100	100	100	100	100	
22	12933	40	F	67	170	100	LL	12	T-6	135	320	23	2	185	118	110	106	100	104	104	106	102	102	102	78	72	70	68	72	70	70	72	70	72	74	69	68	66	65	65	65	68	66	67	100	100	100	100	100	100	100	100	100	100	
23	11466	30	M	70	165	100	LL	11	T-6	134	330	18	3	190	124	120	110	112	110	112	110	106	104	102	74	68	66	68	66	68	66	64	66	66	62	60	58	56	57	56	56	58	60	57	100	100	100	100	100	100	100	100	100	100	bradycardia
24	12197	60	F	55	162	90	LL	12	T-10	126	320	19	2	190	126	122	110	108	104	106	102	104	106	104	78	70	72	68	70	72	68	70	68	70	66	66	64	63	63	66	64	63	66	62	100	100	100	100	100	100	100	100	100	100	
25	13961	47	M	60	169	110	LL	11	T-6	136	335	19	3	210	120	120	112	102	100	102	102	104	104	106	76	70	68	66	66	68	68	66	68	70	68	67	69	68	65	64	62	66	64	65	100	100	100	100	100	100	100	100	100	100	
26	18094	45	M	58	172	110	LL	12	T-7	140	330	22	3	210	110	110	102	100	98	102	100	106	102	100	72	68	66	68	66	66	64	64	66	68	69	67	69	68	65	68	68	68	69	68	100	100	100	100	100	100	100	100	100	100	
27	25080	35	M	66	165	110	LL	11	T-7	142	325	20	3	220	106	106	100	98	98	98	100	104	104	104	70	66	64	66	64	66	64	64	64	66	61	58	60	57	56	59	58	58	59	58	100	100	100	100	100	100	100	100	100	100	
28	14277	43	M	52	168	100	LL	13	T-10	148	330	21	3	215	102	102	98	90	98	102	100	98	100	102	70	66	64	66	64	66	66	66	64	64	65	63	66	62	64	66	64	63	66	62	100	100	100	100	100	100	100	100	100	100	hypotension
29	7053	38	M	54	161	100	LL	12	T-7	145	325	20	3	190	112	110	96	84	100	98	96	96	98	102	74	66	68	60	62	66	68	64	64	66	77	75	72	71	71	72	70	75	74	74	100	100	100	100	100	100	100	100	100	100	hypotension
30	15123	60	M	52	167	90	LL	11	T-6	150	320	19	3	210	110	108	102	100	100	102	100	102	104	98	72	68	66	64	68	66	64	66	64	64	60	57	56	56	56	59	58	58	57	55	100	100	100	100	100	100	100	100	100	100	bradycardia
31	14423	26	F	55	158	110	LL	11	T-6	125	330	20	3	180	110	110	108	104	102	98	100	100	96	104	74	70	64	66	66	64	62	68	68	66	70	68	66	65	68	65	66	66	65	66	100	100	100	100	100	100	100	100	100	100	
32	15697	28	M	60	166	110	LL	11	T-6	135	330	20	3	180	110	110	108	104	102	98	100	100	96	104	74	70	64	66	66	64	62	68	68	66	70	68	66	65	68	65	66	66	65	66	100	100	100	100	100	100	100	100	100	100	
33	16659	55	F	58	168	90	LL	11	T-6	116	320	18	2	185	128	122	116	112	112	112	106	108	104	102	72	66	64	66	66	68	68	66	68	64	72	70	70	69	67	68	68	66	65	68	100	100	100	100	100	100	100	100	100	100	
34	8735	18	F	53	164	120	LL	11	T-7	130	320	19	3	175	122	110	106	98	102	104	106	100	104	102	76	72	70	68	64	66	64	68	68	66	77	75	72	71	71	70	70	70	70	69	100	100	100	100	100	100	100	100	100	100	
35	16618	50	M	57	165	90	LL	12	T-6	142	325	20	3	215	110	110	106	102	110	102	104	100	106	106	72	68	66	64	64	66	64	68	68	64	69	66	67	65	65	67	66	64	66	64	100	100	100	100	100	100	100	100	100	100	
36	17641	32	M	64	162	110	LL	12	T-6	148	320	18	3	205	128	126	118	106	108	102	106	112	118	110	78	72	68	66	66	66	64	68	68	68	70	68	69	66	68	67	66	67	65	68	100	100	100	100	100	100	100	100	100	100	
37	17750	34	F	57	158	100	LL	12	T-7	127	340	19	2	195	108	108	106	100	102	104	106	104	104	104	72	66	64	64	66	68	66	66	66	66	60	59	58	58	57	57	58	56	55	56	100	100	100	100	100	100	100	100	100	100	
38	17664	42	M	60	164	110	LL	10	T-6	122	320	17	3	185	100	100	96	78	100	104	98	100	102	98	74	66	68	52	62	66	64	64	64	64	78	73	71	70	70	69	70	72	70	69	100	100	100	100	100	100	100	100	100	100	hypotension
39	30155	39	M	67	166	100	LL	13	T-7	126	325	23	3	190	112	112	110	106	102	104	108	106	104	102	74	68	66	68	66	64	66	66	68	68	65	63	66	62	64	63	66	63	62	65	100	100	100	100	100	100	100	100	100	100	
40	28631	27	M	63	165	90	LL	12	T-6	148	320	19	2	190	126	122	110	108	104	106	102	104	106	104	78	70	72	68	70	72	68	70	68	70	66	66	64	63	63	66	64	63	66	62	100	100	100	100	100	100	100	100	100	100	
41	31115	36	F	52	162	90	LL	13	T-6	115	330	21	3	215	102	102	98	90	98	102	100	98	100	102	70	66	64	66	64	66	66	66	64	64	65	63	66	62	64	66	64	63	66	62	100	100	100	100	100	100	100	100	100	100	hypotension
42	31060	55	M	59	166	90	LL	12	T-7	110	335	19	3	185	108	106	104	98	102	104	106	104	106	104	70	68	66	64	64	64	66	66	64	66	68	66	65	64	66	65	66	65	66	64	100	100	100	100	100	100	100	100	100	100	
43	32732	31	M	60	168	110	LL	12	T-6	125	320	21	3	180	126	118	110	108	102	108	106	110	112	100	78	72	70	66	68	68	68	68	66	66	75	72	71	68	66	67	68	65	67	66	100	100	100	100	100	100	100	100	100	100	
44	34259	38	M	62	161	100	LL	13	T-6	140	320	20	2	210	130	126	120	118	114	116	112	108	110	104	78	72	70	68	66	66	68	66	66	66	68	67	66	65	65	63	65	64	62	66	100	100	100	100	100	100	100	100	100	100	
45	34399	45	M	59	162	110	LL	11	T-10	145	335	18	3	190	110	108	108	106	106	102	104	110	112	112	72	68	66	66	66	62	64	66	64	64	71	69	68	66	65	68	66	66	67	64	100	100	100	100	100	100	100	100	100	100	
46	38451	40	M	60	164	110	LL	13	T-7	126	320	22	3	210	110	108	106	102	102	104	104	106	102	102	72	68	66	64	64	66	68	66	64	70	66	63	66	62	64	62	64	63	66	65	100	100	100	100	100	100	100	100	100	100	
47	36137	28	M	59	165	110	LL	10	T-6	128	335	17	2	210	118	110	106	100	102	104	106	102	102	102	78	72	70	68	68	66	68	64	64	70	72	68	67	67	69	68	67	65	67	69	100	100	100	100	100	100	100	100	100	100	
48	38544	20	M	60	166	100	LL	12	T-6	134	320	22	3	210	136	124	118	114	110	110	108	112	110	108	82	78	76	74	74	72	70	70	70	72	75	72	70	68	69	69	67	68	68	66	100	100	100	100	100	100	100	100	100	100	
49	18896	45	M	65	167	110	LL	11	T-6	140	330	18	3	190	124	120	110	112	110	112	110	106	104	102	74	68	66	68	66	68	66	64	66	66	62	60	58	56	57	56	56	58	60	57	100	100	100	100	100	100	100	100	100	100	bradycardia
50	39797	23	M	67	165	110	LL	12	T-7	145	330	22	3	210	110	110	102	100	98	102	100	106	102	100	72	68	66	68	66	66	64	64	66	68	69	67	69	68	65	68	68	68	69	68	100	100	100	100	100	100	100	100	100	100	