"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE WITH INTRATHECAL ISOBARIC BUPIVACAINE VERSUS ISOBARIC LEVOBUPIVACAINE FOR INFRAUMBILICAL SURGERIES- A ONE YEAR HOSPITAL BASED DOUBLE- BLIND RANDOMISED CONTROLLED TRIAL"

By

(REG. NO. BA0112004)

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY,

JAWAHARLAL NEHRU MEDICAL COLLEGE,

BELGAUM, KARNATAKA

APRIL – 2015

KLE UNIVERSITY, BELGAUM, KARNATAKA

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This is to certify that the dissertation entitled **"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE WITH INTRATHECAL ISOBARIC BUPIVACAINE VERSUS ISOBARIC LEVOBUPIVACAINE FOR INFRAUMBILICAL SURGERIES- A ONE YEAR HOSPITAL BASED DOUBLE- BLIND RANDOMISED CONTROLLED TRIAL"** is a bonafide research work done by **REG. NO. BA011.**

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LIST OF ABBREVIATIONS USED

ASA	-	American Society of Anaesthesiologists
Bpm	-	Beats per minute
C	-	Cervical
cc	-	Cubic centimeter
CNS	-	Central nervous system
CSF	-	Cerebrospinal fluid
CVS	-	Cardiovascular system
DBP	-	Diastolic blood pressure
ED	-	Effective dose
GA	-	General anaesthesia
HCL	-	Hydrochloric Acid
HCO_3	-	Bicarbonate
HR	-	Heart rate
I.V	-	Intravenous
KCl	-	Potassium chloride
kg	-	Kilogram
L	-	Lumbar
m	-	Meters
MAP	-	Mean arterial pressure
Mcg	-	Microgram
mg	-	Milligram
Mins	-	Minutes
ml	-	Millilitre

NIBP	-	Non invasive blood pressure
O_2	-	Oxygen
$PaCO_2$	-	Partial pressure of carbon dioxide
S	-	Sacral
SAB	-	Subarachnoid block
SBP	-	Systolic blood pressure
SD	-	Standard deviation
Sec	-	Second
SpO_2	-	Peripheral saturation of oxygen
T	-	Thoracic
TNS	-	Transient neurological symptoms
v/s	-	Versus
α	-	Alpha
β	-	Beta
δ	-	Delta
μ	-	Micro

ABSTRACT

Background and Objective

Spinal anaesthesia is a well known technique used in lower abdominal surgeries. Spinal anaesthesia is routinely performed with racemic 0.5% bupivacaine in the present anaesthesia practice. Levobupivacaine is a pure S enantiomer of bupivacaine and hence has less cardiac and central nervous system toxicity compared to bupivacaine. We attempted to compare onset and duration of sensory and motor blockade with intrathecal isobaric bupivacaine and levobupivacaine in patients posted for elective infraumbilical surgeries.

Methods

This one year double blind randomized controlled trial was conducted in the Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, during the period of June 2013 to June 2014. A total of 70 ASA I and II patients posted for elective infraumbilical were allocated into 2 groups. Group B received intrathecal 3 ml of 0.5 % isobaric bupivacaine and Group L received intrathecal 3 ml of 0.5% isobaric levobupivacaine. Onset and duration of sensory and motor blockage were compared between the two groups.

Results

In this study, both the groups were comparable with respect to sex, age and height. It was found that two groups were comparable in terms of onset for sensory block (5.2 ± 0.63 minutes versus 5.3 ± 0.66 minutes with p = 0.583); duration of sensory block (169.4 ± 13.04 minutes versus 170.6 ± 16.83 minutes

with p=0.691); onset for motor block (10.8±0.91 minutes versus 10.9±0.74 minutes with p=0.474); duration of motor (286.6 ± 13.92 minutes versus 284 ± 10.34 minutes with p=0.384). There was no statistical difference between the two groups. The two groups showed no difference in terms of hemodynamic parameters measured.

Conclusion and interpretation

Levobupivacaine is less cardio and cerebral toxic than bupivacaine. And from the above study we may conclude that intrathecal levobupivacaine is comparable to bupivacaine in terms of onset and duration of sensory and motor blockade. There is no significant hemodynamic variation between them.

Key Words: Bupivacaine ;Levobupivacaine; Motor block; Sensory block; Spinal anaesthesia;

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Chapter 1

Introduction

INTRODUCTION

In this current era of advanced medical sciences general anaesthesia has been replaced by regional anaesthesia in a wide range of surgeries. Fewer systemic side effects, possibility to use them in patients with comorbidities, easy usage in peripheral centers are few reasons for the increasing popularity of regional anaesthesia. With the introduction of nerve stimulators and ultrasound for achieving nerve blocks, nerve block as a technique has become more promising with less failure rates and shorter learning curve. Availability of newer local anaesthetics and adjuvants has further increased the effectiveness of regional anaesthesia

Spinal anaesthesia remains the most popular as well as effective technique for providing regional anaesthesia in cases of lower abdominal, perineal and lower limb surgeries. It provides fast onset and effective sensory and motor blockade. Less chances of failure of block and easy technique makes it a popular way of achieving regional anaesthesia.

Bupivacaine is a long acting amide local anaesthetic. Ever since its synthesis in 1957 by Ekenstam in Sweden, it has undergone various trails and has been widely accepted in virtually every area of local anaesthetic practice. It is one of the most commonly used local anaesthetic in the current clinical practice[1]

The major advantages are an increased duration of action, favorable potency to toxicity ratio, easy availability and low cost[1].

It has been used extensively in spinal anaesthesia because of its ability to produce long duration of sensory and motor blockade. It is available in two forms, an isobaric form with equal density to the spinal fluid and a denser hyperbaric form. Both forms have been widely used intrathecally.[2]

Stereoisomerism describes those compounds which have the same molecular formula and chemical structure, but the atoms are oriented in a different direction. There are two isomers, each a mirror image of the other, called enantiomers. They are also called optical isomers because they rotate the plane of polarized light either to the right referred to as +, dextro, d or D isomer, or to the left referred to as - , levo, l or L isomer[3].

More recently this classification has been replaced by the R-/S- notation, which describes the arrangement of the molecules around the chiral center (R is for rectus the Latin for right, and S for sinister, left). The R enantiomer rotates light to the right and the S enantiomer to the left[3].

Molecule of bupivacaine has an asymmetric carbon atom. For this reason, with this asymmetric carbon as a chiral center, bupivacaine exhibits the above phenomenon. Commercially available bupivacaine is a racemic mixture containing a 50:50 proportion: levobupivacaine, L (-) isomer, and dextrobupivacaine D (+) isomer[3].

Bupivacaine is associated with significant cardiac and CNS toxicity. This toxicity has been attributed mainly to its R isomer. And hence levobupivacaine, the pure S (−) enantiomer of bupivacaine, is a safer alternative for regional

anesthesia than its racemic parent. It demonstrated less affinity and strength of depressant effects onto myocardial and central nervous vital centers[4].

Few studies done have shown that isobaric levobupivacaine can be used as an effective alternative to isobaric bupivacaine in spinal anaesthesia. But since very few studies are done on Indian population to compare isobaric bupivacaine and isobaric levobupivacaine, we shall attempt to compare them with regard to onset and duration of motor and sensory blockade in infraumbilical surgeries under spinal anaesthesia.

Chapter 2

Objectives

OBJECTIVES

The objectives of the present study were to compare

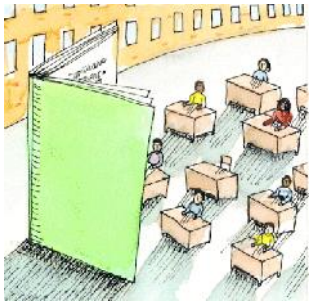
1) Onset and duration of sensory blockade

2) Onset and duration of motor blockade

between intrathecal isobaric 0.5% bupivacaine and 0.5% levobupivacaine in patients undergoing elective infraumbilical surgeries

Chapter 3

Review of Literature



REVIEW OF LITERATURE

Spinal anaesthesia also known as subarachnoid block has evolved a lot over years and has an extremely interesting history behind it. The first ever spinal anaesthesia was done accidentally by J. Leonard Corning, a neurologist from New York in 1885. While he was experimenting on a dog the action of local anaesthetic cocaine on the spinal nerves, the drug was injected in subarachnoid space due to accidental dural puncture between two lumbar vertebrae which let to paralysis of the hind limbs[6].

He later used this technique in various neurological disorders but did not use it for surgeries though he appreciated its potential use. He is thus credited with discovering spinal anaesthesia[6].

It took 14 years for next major development to take place. In 1898 Augustus Karl Gustav Bier and his assistant Dr .Hildebrandt both underwent spinal anaesthesia with cocaine by injecting each other. Bier experienced a shooting pain in his leg, a failed block , neural contact with needle leading to shooting pain in his leg and a postdural puncture headache (PDPH). While his assistant experienced a successful block[7].

On 16th of August 1898, first spinal anaesthesia was performed by Bier in Germany on a 34 year old male undergoing resection of a tuberculous ankle joint. He injected 15 mg of 0.5% cocaine intrathecally. Tough he went on to perform five more spinal anaesthesia procedures he soon abandoned the procedure due to increasing side effects and cocaine toxicity[8].

In 1905 a German surgeon by name Heinrich Braun, reported the use of procaine for intrathecal administration. It gained popularity in 1923 when Labat advocated the use of procaine and he said that transitory headache, abducens nerve palsy, retention of urine and anal incontinence which were noted before were transient and no permanent sequelae were found after its use[8].

Tetracaine was synthesized in 1931 and was introduced into clinical practice by Sise in 1935

The technique of spinal anaesthesia evolved later in expert hands and got eventually well accepted in clinical practice. Usage of finer bore and non cutting needles along with strict asepsis reduced complications due to technique. Availability of newer, safer local anaesthetics and better understanding of anatomy and physiology has led to fewer side effects and toxicity[9].

Spinal anaesthesia has many advantages like ease of administration, rapid onset of action and good muscle relaxation. Main disadvantages are its limited duration of action and hemodynamic instability.

Currently the local anaesthetic drugs like Bupivacaine and Ropivacaine are being used intrathecally for these surgical procedures. Opioid analogues have been used as additives in spinal anaesthesia to improve the onset of action, prolong the duration of block and to improve the quality of perioperative analgesia.[10]

Albright in 1979 published an alarming editorial which associated the long acting local anaesthetics bupivacaine and etidocaine with cardiac arrest during regional anaesthesia; he reported six cases of accidental intravascular

injection of either bupivacaine or etidocaine which caused sudden ventricular arrhythmias at the same time as convulsions. This flow of events acted as a catalyst for the development of newer local anaesthetic drug[11].

Reports of fatalities through cardiovascular toxic effects after regional anaesthesia with bupivacaine in the late 1970s (Albright 1979) triggered pharmacological research that emphasized the selective behaviour of the two enantiomers of racemic bupivacaine, ie, levo- or S (−) bupivacaine and dextro- or R (+) bupivacaine, once in contact with biological receptors in the body. Levo-enantiomer appeared to have a safer pharmacological profile than its dextro-partner. Efforts were intensified to synthesize a pure S (−) bupivacaine enantiomer which was approved by the United States Food and Drug Administration in 1999 for clinical use. Ropivacaine another pure S (−) enantiomer, also became available as an alternative to the racemic mixture for regional anesthesia.

Because of the small doses of local anesthetic used for subarachnoid administration, systemic toxicity is not a problem. Not surprisingly therefore, bupivacaine remains the most widely and cost-efficient long acting local anesthetic used in spinal anesthesia. A surgical sensory and motor block of similar characteristics and recovery over equal dose ranges of levobupivacaine and bupivacaine was demonstrated in healthy volunteers (Alley et al.) and confirmed in surgical patients (Glaser et al ; Lee et al ; Casati et al ; Fattorini et al) .

Glaser et al. in 2002 performed a prospective randomized double-blinded study to evaluate the anaesthetic potencies and hemodynamics of intrathecal

levobupivacaine compared with racemic bupivacaine. Eighty patients undergoing elective hip replacement received either 3.5 mL levobupivacaine 0.5% isobaric or 3.5 mL bupivacaine 0.5% isobaric. Intergroup differences between levobupivacaine and bupivacaine were insignificant with regard to the onset time and the duration of sensory and motor blockade. Both groups showed slight reductions in heart rate and mean arterial pressure, but there was no intergroup difference in hemodynamics. Thus they concluded that intrathecal levobupivacaine is equal in efficacy to, but less toxic than, racemic bupivacaine.[12]

Lee et al. in 2003 conducted a prospective, randomized, double-blind study to compare the clinical efficacy and motor block of 0.5% levobupivacaine with 0.5% racemic bupivacaine in spinal anaesthesia for urological surgery. Fifty patients were recruited. Spinal anaesthesia was achieved with 2.6 ml of study solution injected in the subarachnoid space. There were no significant differences between the two groups in the quality of sensory and motor block or in hemodynamic change. They concluded that 0.5% levobupivacaine can be used as an alternative to 0.5% racemic bupivacaine in spinal anaesthesia for surgery when a sensory block to at least T10 is required.[13]

Fattorini F et al. compared clinical and anaesthetic features of levobupivacaine and racemic bupivacaine when administered intrathecally in 60 patients undergoing major orthopaedic surgical procedures.3 ml of isobaric levobupivacaine 0.5% or 3 ml of isobaric bupivacaine 0.5% were administered. No statistically significant difference between groups were observed either in anaesthetic potencies or postoperative pain. They concluded that,

levobupivacaine can be a valid alternative to racemic bupivacaine for spinal anaesthesia.[14]

In a double-blinded, randomized, cross-over study done by Alley et al. eighteen healthy volunteers were randomized into three equal groups to receive two spinal anesthetics, one with bupivacaine and the other with levobupivacaine, of equal-milligram doses (4, 8, or 12 mg). Blockade quality and duration was assessed with pinprick, transcutaneous electrical stimulation, thigh tourniquet, abdominal and quadriceps muscle strength, modified Bromage scale, and time until achievement of discharge criteria. It was found that hyperbaric spinal levobupivacaine has equivalent clinical efficacy to racemic bupivacaine for spinal anesthesia in doses from 4 to 12 mg[15]

Casati et al. studied in 60 patients undergoing inguinal hernia repair the clinical profile of unilateral spinal anesthesia produced with either 8 mg of hyperbaric bupivacaine 0.5% , 8 mg of hyperbaric levobupivacaine 0.5% , or 12 mg of hyperbaric ropivacaine 0.5% . The onset time and intraoperative efficacy were similar in the three groups. They concluded that 8 mg of levobupivacaine or 12 mg of ropivacaine were acceptable alternatives to 8 mg of bupivacaine when used intrathecally.[16]

Comparison between 3 local anaesthetic- hyperbaric solutions of bupivacaine, levobupivacaine and ropivacaine under spinal anaesthesia for elective surgery were studied and it showed that, bupivacaine or levobupivacaine shows clinically indistinguishable effects whereas hyperbaric ropivacaine provides reliable spinal anaesthesia of shorter duration. Ropivacaine may be useful where prompt mobilization is required due to its faster recovery profile[17 18]

Lee et al. did a prospective, randomized, double-blind study in 50 patients undergoing urological surgery to compare the clinical efficacy, motor block and haemodynamic effects of using 2.6 mL of 0.5% levobupivacaine alone and 2.3 mL of 0.5% levobupivacaine with fentanyl 15 microg in 0.3 mL for spinal anaesthesia .There were no significant differences between the two groups with respect to haemodynamic changes, and quality of sensory and motor block. Anaesthesia was adequate and patient satisfaction was good in all cases. Side-effects were minor and infrequent with both regimes. The addition of fentanyl 15 μg demonstrated a sparing effect on the requirement of levobupivacaine while maintaining excellent clinical efficacy with less hemodynamic variation[19]

Chapter 4

Basic Sciences

BASIC SCIENCES

APPLIED ANATOMY

Subarachnoid block is a safe and effective alternative to general anaesthesia when the surgical site is located on the lower extremities, perineum, or lower abdominal wall. Spinal anaesthesia was the dominant form of neuraxial anaesthesia well into the 20th century[20]

Spinal anaesthesia produces intense sensory and motor blockade as well as sympathetic blockade. The goal of spinal anaesthesia is to install the desired medications into the cerebrospinal fluid (CSF). The block produced requires smaller doses of local anaesthetics (hence, local anaesthetic toxicity is rarely a concern) and is often more dense in character.

Advantages include avoidance of general anaesthesia and the airway management concerns that accompany general anaesthesia. Additional benefits may include reducing the metabolic stress response to surgery, reduction in blood loss, decrease in the incidence of venous thromboembolism, reduction in pulmonary compromise (particularly in patients with advanced pulmonary disease), and the ability to monitor the patient's mental status.

Strong contraindications include patient refusal, lack of patient cooperation, difficulties with positioning, and increased intracranial pressure. Other contraindications include situations that require some risk-benefit analysis, like spinal abnormalities, hypovolemia, coagulation disturbances, stenotic valvular heart disease, bacteremia, and infection at the site of needle insertion.

Spinal anaesthesia has also been noted to result in symptomatic deterioration in patients with multiple sclerosis.[20] Allergy to local anaesthetics may also be a

contraindication, but true allergies are usually found with ester-based local anaesthetics (tetracaine), not the amide-based local anaesthetics (bupivacaine)

ANATOMY

Sound knowledge of anatomy of vertebral column and its contents is essential to all the anaesthesiologists for safe and successful administration of spinal anaesthesia, not only in terms of performance but also in terms of spread of drug in CSF and level of block achieved.

Vertebral column

Main function of the vertebral column is to protect the spinal cord (figure 1). The vertebral column comprises of 33 vertebrae and includes[21]

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

Curves of spine

In adult, the vertebral column has four curves which have significant effect on spread of drugs in sub arachnoid space namely[21]

- Cervical and lumbar curve - Convex anterior
- Thoracic and sacral curve - Concave anterior

In adults the curves of the spine are important when patient is supine. The highest point of cervical and lumbar curves in supine position are at cervical (C) five and lumbar (L) five; lowest points of thoracic and sacral are at thoracic (T) five and sacral (S) two respectively.[21]

Vertebral ligaments[21]

Vertebral column is bound together by following ligaments which give stability and elasticity.

Supraspinous ligament*:* This is a strong fibrous cord which connects apices of spinous processes from where it continues as the ligamentum nuchae (Figure 2).

Interspinous ligament: This is a thin membranous ligament which connects spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament (Figure 2).

Ligamentum flavum: This ligament comprises yellow elastic fibres and connects adjacent lamina. Laterally this ligament begins at the root of articular processes and extends posteriorly and medially to the point where laminae join to form spinous process (Figure 2).

Longitudinal ligaments: There are two longitudinal ligaments (anterior and posterior) that bind vertebral bodies together (Figure 2).

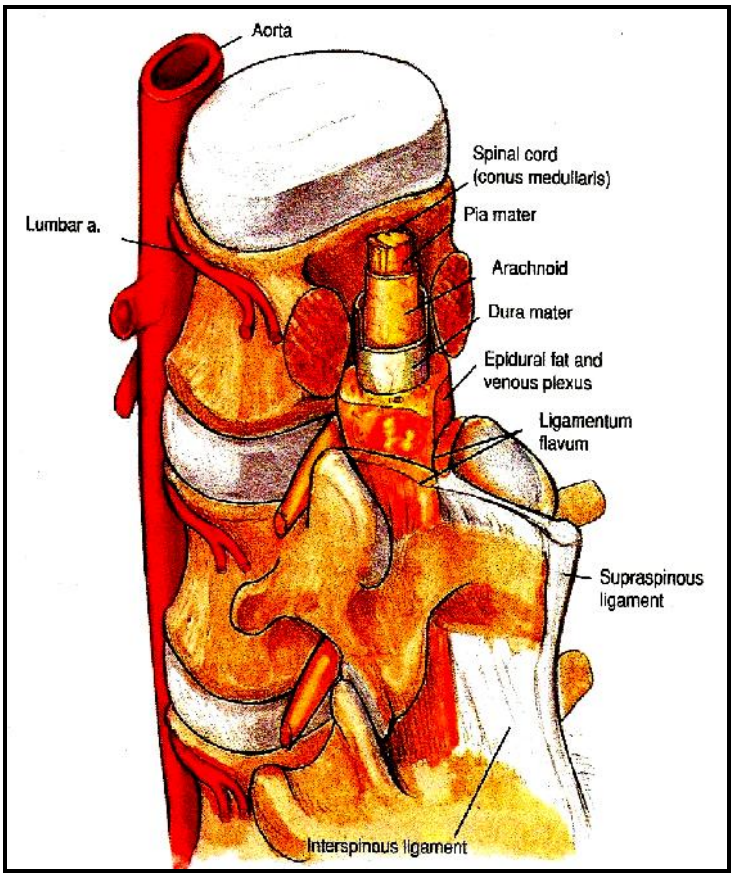


Figure 1. Vertebral Column

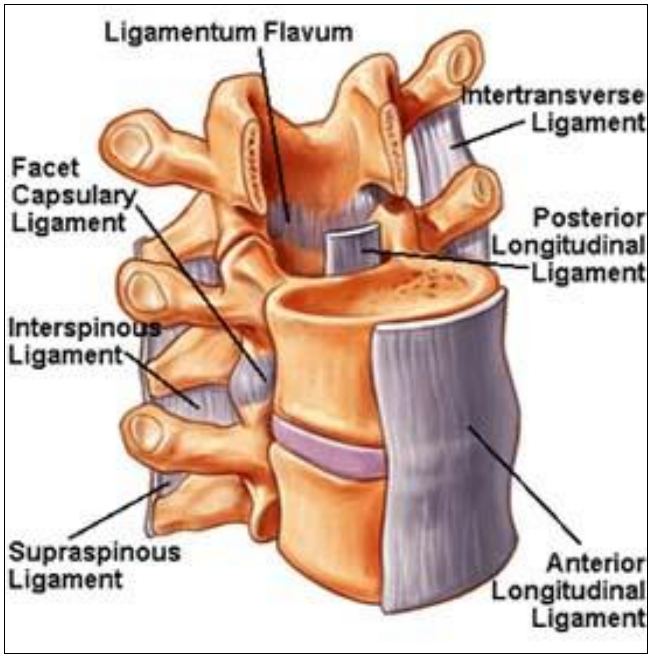


Figure 2. Spinal Ligaments

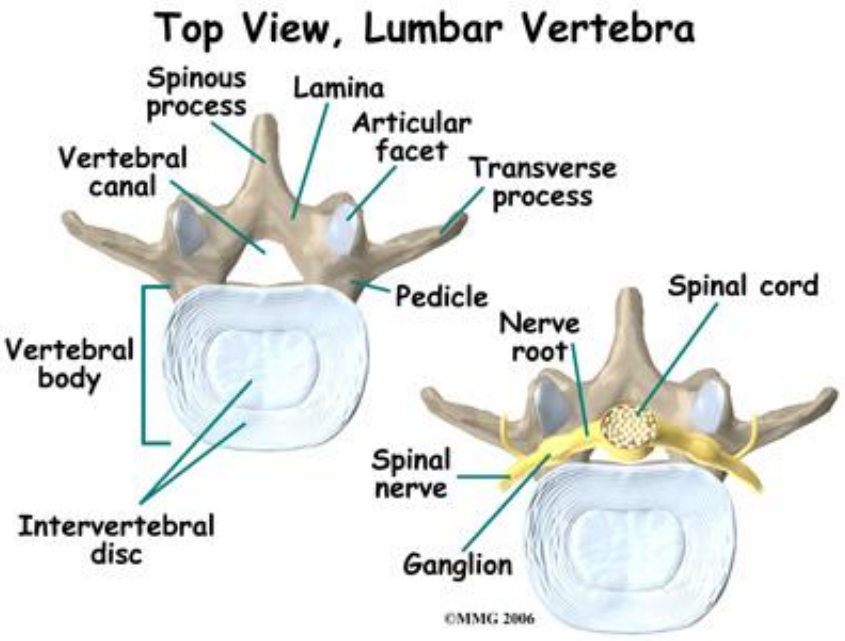


Figure 3. Typical Lumbar Vertebra

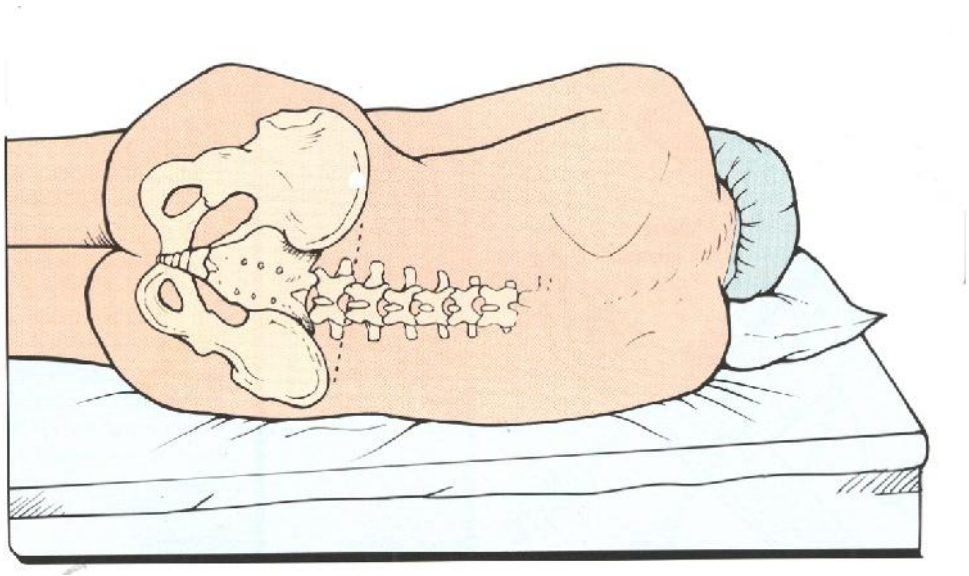


Figure 4. Line of Tuffier

Lumbar vertebrae[22]

A typical lumbar vertebra consists of (Figure 3);

- A kidney shaped body.
- Two pedicles directed backwards from the upper part of the body.
- Two transverse processes which are slender
- Two laminae meeting posteriorly and enclosing the triangular vertebral foramen.
- Spinous processes which are thick, broad and quadrilateral in shape.
- Two upper and lower articular processes which prevent rotation but allow limited flexion and extension between contiguous vertebrae.

Topographical Line of Tuffier[21]

This is a horizontal line across the back between the crests of the ilia passing over the spine of the 4th lumbar vertebra in the upright position. In a patient lying in the lateral position it may also pass through L4 and L5 interspaces. The superior iliac crest is used to identify the L4 and L5 interspace during spinal anaesthesia (Figure 4).

Vertebral canal

Vertebral canal is bounded posteriorly by spinous processes and interspinous ligaments, laterally by the pedicles and posterolaterally by the laminae and ligamentum flavum. This ends superiorly in the foramina magnum and inferiorly in the sacral hiatus. The vertebral canal contains the spinal cord, spinal membranes, adipose tissue, blood vessels, CSF and the roots of the spinal nerves.

Spinal cord[20]

The average length of the spinal cord in males is 45 centimeter (cm) and females it is 42 cm (figure 5).

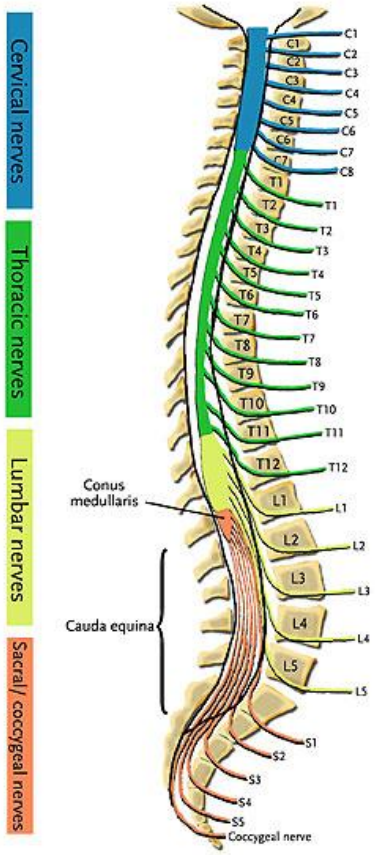


Figure 5. Spinal nerve roots

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

At birth spinal cord ends at the level of L3 but rises as age progresses and reaches the lower border of L1 in adults.

Blood Supply of Spinal Cord[20]

The spinal cord receives blood supply from three arteries, one anterior and two posterior spinal arteries (figure 6).

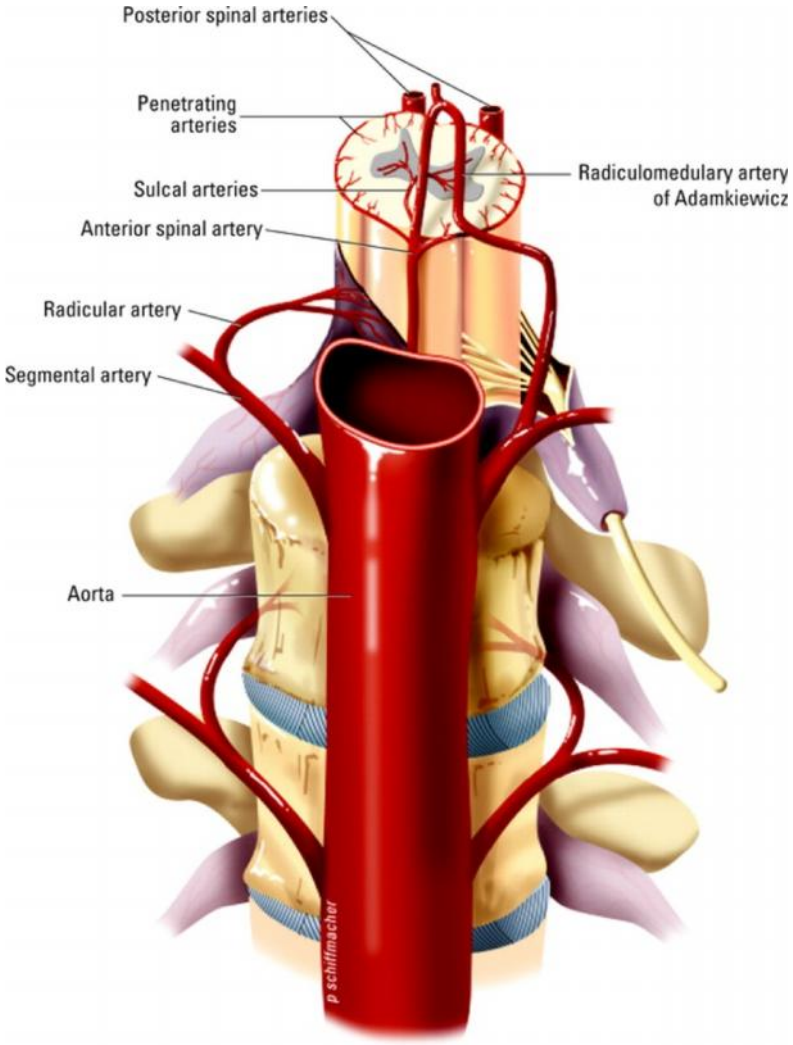


Figure 6. Blood Supply of Spinal Cord

Anterior spinal artery is a single vessel lying in the substance of pia matter overlying the anterior median fissure. It supplies the lateral and anterior columns, comprising three quarters of substance of the cord. Thrombosis of this artery causes anterior spinal artery syndrome.

There are two pairs of posterior spinal arteries, one pair on each side arising from posterior inferior cerebellar arteries at the level of foramen magnum. They supply posterior column of the cord.

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

Spinal Meninges[23]

Along with the bony vertebral column spinal cord is also protected with three connective tissue coverings called meninges.

Duramater[23]

This is a tough outermost fibro elastic covering consisting of outer endosteal layer and inner meningeal layer. Fibers of dura run longitudinally, thus it is important to insert the spinal needle so as to split these fibers and not to cut them. Dural sac ends at lower border of S2, where it is pierced by filum terminale.

Arachnoid Mater[23]

It is a delicate, non-vascular, middle covering and is closely attached to the dura. There is a capillary interval or potential space between dura and arachnoid mater called subdural space and contains serous fluid.

Pia Mater[23]

The pia mater, the innermost membrane is a vascular sheath which closely invests the brain and spinal cord.

Subarachnoid Space[23]

The space between the arachnoid and pia is called the subarachnoid space and is filled with cerebrospinal fluid and contains numerous arachnoid trabeculae which form delicate sponge like mass. . This space has three divisions which are free communication to each other: cranial (surrounding the brain), spinal (surrounding the spinal cord) and root (surrounding the dorsal and ventral nerve roots). In the spinal cord these nerve roots are covered only by pia and bathed in CSF. As these spinal nerve roots pass beyond the spinal dura and traverse the epidural space, they carry with them all the three meningeal layers and have a distinct epidural, subdural, subarachnoid and sub pial spaces. The subarachnoid space extends separately along both the dorsal and ventral roots to the level of dorsal root ganglion, where arachnoid and pia continue as perineural epithelium of peripheral nerve.

Cerebrospinal Fluid[23]

It is a clear colourless fluid found in the cranial and spinal subarachnoid spaces and in the ventricles. CSF is mainly formed by either secretion or ultrafiltration from the choroidal plexus of lateral ventricles. CSF flows from the lateral ventricles into the third ventricle through the foramina of Monro into the fourth ventricle through the Aqueduct of Sylvius into the cerebromedullary cisterna (cisterna magna) through foramen of Magendie and foramina of Luschka. From the cisterna magna, CSF enters subarachnoid space circulating around brain and spinal cord before being absorbed into the arachnoid granulations over the cerebral hemispheres.

Composition of cerebrospinal fluid

- Specific gravity : 1.003 to 1.009 at 37^0C.
- Volume : 120 ml to 150 ml (25 ml to 35ml in spinal space).
- CSF pressure : 60 to 80 mm Hg in lumbar space.
- pH : 7.27 to 7.37
- PCO_2 : 48 mm Hg
- HCO_3 : 23 mEq/L
- Sodium : 135 to 145 mEq/L
- Calcium : 2 to 3 mEq/L
- Phosphorous : 1.6 mg/dl
- Magnesium : 2 to 2.5 mEq/L
- Chloride : 15 to 20 mEq/L
- Proteins : 23 to 38 mg/dl

It is important to know that certain drugs alter the rate of formation of CSF. Carbonic anhydrase inhibitors like acetazolamide reduce the rate of CSF formation by as much as 50%. Furosemide in large doses may reduce the CSF formation. Inhalational anaesthetics like isoflourane and vasoconstrictors decrease the CSF formation. CSF formation is decreased when the serum osmolality increases and is increased when the serum is made hypotonic. During equilibrium, rate of formation equals the rate of absorption (500 mL/day).

PHYSIOLOGY OF SUB ARACHNOID BLOCK

The well recognized physiological effects of subarachnoid block are often wrongly termed as complications. The various factors, which control the different effects of a spinal anaesthetic technique are[24]

- Amount and type of drug
- Volume of solution
- Site of injection
- Rate of injection
- Specific gravity of solution – density and baricity
- Barbotage

The various factors which affect the spread of local anaesthetics include; [25, 26]

1) Patient factors:

- Age
- Height
- Position
- Spinal column configuration
- Cerebrospinal fluid volume

2) Technical factors

- Site of injection

- Direction of needle
- Local anaesthetic dose
- Local anaesthetic baricity
- Local anaesthetic volume

The sensory and motor blockade results from direct effects of local anaesthetic on the spinal nerve roots. The primary site of action is on both anterior and posterior nerve roots, affecting smaller nerve fibers first, and thick large motor fibers last. Generally, the sympathetic paralysis is more diffuse and will extend to two to four segments above motor block. The sympathetic fibers are affected first and are last to recover. On the other hand, motor nerve blockade is usually last to be affected and first to recover.

Sequence of spinal anaesthesia (SA) [27]

- Vasomotor block: Dilatation of skin vessels and increase cutaneous blood flow
- Temperature fibers: Cold first and then warmth
- Loss of temperature discrimination
- Pain – pin prick fibers first
- Loss of tactile sensation
- Motor paralysis
- Pressure sensation
- Proprioception and vibratory sensation.

Sympathetic blockade is the major determinant of physiologic response to spinal anaesthesia.

Sympathetic blockade

Because the level of sympathetic denervation determines the magnitude of cardiovascular responses to SAB, it might be anticipated that the higher the level of neural blockade, the greater would be the change in the cardio-circulatory parameters. In the presence of partial sympathetic blockade, a reflex increase in sympathetic activity occurs in sympathetically intact areas. The result is vasoconstriction that tends to compensate for the peripheral vasodilatation-taking place in the sympathetically denervated areas. This can be seen in the changes in the arterial pressure waveforms and in the cutaneous blood flow in the upper extremities in the presence of low or midthoracic sensory levels of spinal anaesthesia. Most cephalad preganglionic sympathetic fibers exit the spinal cord at the level of T1. Since sympathetic denervation is complete at the T1 level, cardiovascular changes are no greater with mid cervical sensory levels of anaesthesia than they are with T1 levels. Sympathetic fibers are blocked usually two to three segments higher than sensory fibers and sensory block is two segments higher than motor block.

Cardiovascular effects of spinal anaesthesia[28]

They are mediated by the combined effects of autonomic denervation and, with higher levels of neural blockade, added effects of vagal innervation. Spinal block can influence CVS in various ways.

a. Vasodilatation of resistance and capacitance vessels.

b. Block of cardiac efferent sympathetic fibers from T1-T4 resulting in loss of chronotropic and inotropic drive and fall in cardiac output.

c. Bainbridge reflex causing bradycardia.

d. Depression of vascular smooth muscle and beta adrenergic blockade of myocardium with fall in cardiac output following systemic absorption of local anaesthetic drug.

Block extending above T4 is associated with fall in BP. Slowing of HR is caused if any of anterior roots carrying sympathetic cardiac accelerator fibers are blocked as may happen in high spinals above T4-T5. Bradycardia may also be due to lowering of BP in the right atrium consequent to diminished venous return.

Theories of causation of fall in BP.

a. Diminished cardiac output due to reduction of venous return

b. Dilatation of post arteriolar capillaries and small venules

c. Paralysis of sympathetic nerve supply to heart.

d. Paralysis of sympathetic nerve supply to adrenal glands with consequent catacholamines depletion.

e. Ischemia and hypoxia of vital centres.

f. Compression of great vessels in abdomen by pregnant uterus or abdominal tumors.

Myocardial Oxygen Demand:

Myocardial oxygen demands decrease during hypotension associated with spinal anaesthesia due to decrease in afterload, preload and heart rate.

Cerebral Blood Flow

Cerebrovascular autoregulatory mechanisms maintain cerebral blood flow in humans at constant levels.

Respiratory System

Phrenic nerve paralysis can occur. During spinal analgesia breathing becomes quiet and tranquil. This is not only due to motor blockade but also due to differentiation with reduction of sensory input to the respiratory center. Lowered arterial and venous tone also lessens the work of the heart and tends to relieve any existing pulmonary congestion. The pulmonary gas-exchange is preserved. Intercostal paralysis is compensated for by increased descent of the diaphragm, which is made easier by a lax abdomen.

Gastrointestinal System

Pre-ganglionic sympathetic fibers from T5-Ll are inhibitory to the gut. There is no effect on oesophagus, the innervation of which is vagal. The small gut is contracted as sympathetic inhibitory impulses are removed, the vagus being dominant. Pressure within the bowel lumen is increased. Handling of small bowel by the surgeon may cause it to dilate, as may the injection of atropine before the operation. Nausea and vomiting due to the hypotension may occur and usually comes on in waves lasting a minute or so and passes away spontaneously. Relaxation of sphincters also occurs.

<u>Causes of Nausea and Vomiting</u>

- Hypotension
- Hypoxia
- Increased peristalsis
- Traction on nerve endings, especially vagus
- Presence of bile in stomach due to relaxation of pyloric sphincters
- Narcotic analgesics used in pre medication
- Psychological effects

Spleen

The spleen enlarges 2-3 times in high blocks when its sympathetic efferent fibers are paralyzed.

Liver

If the liver is diseased, a decrease in the mean arterial pressure (MAP) affects the liver blood flow and also the metabolism of amide anaesthetics.

Endocrine System

The stress response to surgery results in rise in blood sugar, cortisol and catecholamine level sufficiently high and prolonged spinal blockade can minimise or even prevent these changes.

Genitourinary System

Renal blood flow due to hypotension is decreased but does not cease until blood pressure has fallen to about 80 mm Hg. These changes are transient. The penis is often engorged and flaccid due to paralysis of nervi erigenti (S2 to S3) and this is also a positive sign of a successful block. Post spinal retention of urine may be moderately prolonged as S2 to S3 contain small autonomic fibers and their paralysis lasts longer that of larger sensory and motor fibers.

Uterus

The tone of uterus is not greatly altered after spinal analgesia in pregnancy. Block of nerves from T11 downwards results in painless labour.

Body Temperature

Vasodilatation favours heat loss, absence of sweating favours hyperpyrexia in hot environment, catacholamine secretion is depressed hence heat loss is prevented by metabolism. Spinal anaesthesia also reduces the threshold for shivering.

PHARMACOLOGY[29]

Local anaesthetics are drugs that produce reversible blockade of conduction of nerve impulses.

The primary desirable properties of an ideal local anaesthetic agent are:

1. Short latency
2. High potency or anaesthetic activity
3. Superior penetration or diffusion
4. Low toxicity
5. Complete reversibility of action
6. Prolonged duration of action
7. No tachyphylaxis
8. Stability and ability to withstand heat sterilization

Classification:

Clinically useful agents can be classified into two groups depending on the link between the aromatic portion and the intermediate chain. The aminoester groups 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.

Bupivacaine:[30]

Bupivacaine hydrochloride is 2-piperidine carboxamide, 1 butyl N-2, 6 dimethyl phenyl, monohydrochloride, monohydrate. Bupivacaine molecule is a tertiary amine

separated from an aromatic ring system that is a benzene ring by an intermediate chain. The tertiary amine is a base that is a proton acceptor. The chain contains an amide linkage (-NHCO-) therefore; it is classified as an aminoamide compound. This amide linkage contributes to the anaesthetic potency.

The aromatic ring system gives a lipophilic character to its portion of molecule whereas; the tertiary amine end is relatively hydrophilic.

Structure – Activity relationship

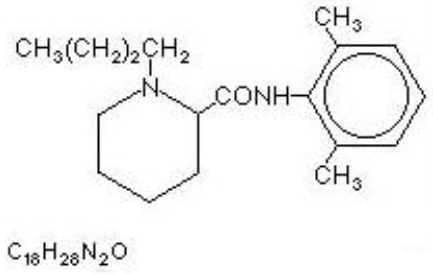


Figure 7 – Chemical structure of bupivacaine

Bupivacaine being more lipophilic (because of butyl group) it is very potent and produces longer lasting blocks.

pKa of any drug is defined as the hydrogen ion concentration specific for each drug at which the concentration of local anaesthetic base is equal to the concentration of charged cation. pKa of bupivacaine hydrochloride is 8.1 at 36ºC.

Anesthetic Potency

Hydrophobicity appears to be a primary determinant of intrinsic anesthetic potency and Bupivacaine is highly hydrophobic, hence is very potent.

Onset of Action

The onset of conduction blockade is dependent on the dose or concentration of the local anesthetic

Differential Sensory Motor Blockade

Bupivacaine in low concentration (0.125%) produces acceptable analgesia with only mild muscular weakness.

Pharmacokinetics

The concentration of Bupivacaine in blood is determined by the amount injected, the rate of absorption from the site of injection, the rate of absorption from the site of injection, the rate of tissue distribution and the rate of biotransformation and excretion of Bupivacaine.

Absorption

The site of injection, dose and addition of a vasoconstrictor determine the systemic absorption of Bupivacaine .The maximum blood level of Bupivacaine is related to the total dose of drug administered from any particular site. Absorption is faster in areas of high vascularity.

Distribution

The two-compartment model can describe this. The rapid distribution phase α is believed to be related to uptake by rapid equilibrating tissue i.e., tissues that have high vascular perfusion. The slow distribution phase β is mainly a function of distribution to slowly equilibrating tissue, biotransformation and excretion of the compound.

More highly perfused organs show higher concentrations of the drug. Bupivacaine is rapidly excreted by lung tissue. Though skeletal muscle does not show any particular affinity for bupivacaine it is the largest reservoir of the drug.

Distribution Characteristics

- T1/2 α 2-7 minutes (uptake by rapid equilibrium tissue)
- T1/2 β 28 minutes (distribution by slowly perfused tissues)
- T1/2 γ 3-5 hours (metabolism and elimination)
- VDSS 72 liters (volume of distribution at steady state)

Clinical Pharmacology

1. Anaesthetic potency: Hydrophobicity is a major determinant of intrinsic anaesthetic potency and bupivacaine being highly hydrophobic, is very potent.
2. Onset of action: It depends on the pH of the drug and its concentration.
3. Differential sensory/motor blockade:

Bupivacaine 0.25 to 0.75% produces adequate analgesia with less of motor blockade.

Factors influencing anaesthetic activity

1. ***Dosage of bupivacaine:*** As the dosage of bupivacaine is increased, the probability and duration of satisfactory analgesia will increase and the onset of block will be shortened. Administering either large volume or a more concentrated solution can increase the dosage.

2. ***Addition of vasoconstrictors:*** Addition of adrenaline does not significantly increase the duration of action of bupivacaine.

3. ***Site of action:*** The latency and duration are long when given for brachial block, epidural block and subarachnoid block.

4. ***Compounding of local anaesthetics:*** The basis for this practice is rapid onset of one agent. e.g., lidocaine and longer duration of action of other agent, e.g. bupivacaine.

5. ***Pregnancy:*** The spread and depth of spinal and epidural analgesia are greater in pregnant patients than in non-pregnant women.

6. ***Carbonation and pH adjustment:*** The success of any local anaesthetic depends upon the quantity of drug that can be absorbed on to the axon membrane of the target nerves. This in turn depends upon the ability of the drug to penetrate tissue barrier around the nerve. Alkalinisation of local anaesthetic solution improves the penetration power and more availability of diffusible base of the local anaesthetic. When pH of the solution is equal to pKa of local anaesthetic solution, half of the drug is present as ionized water-soluble cation and rest half as lipid soluble unionized base since this non-ionised soluble form is permeable to nerve cell membrane; it has a major role in penetration.

   Alkalinisation of local anaesthetic solution acts by

   - A direct depressant effect of CO_2 on the axon.
   - Concentrating local anaesthetic inside the nerve trunk (diffusion trapping).

- Converting local anaesthetic to the active cation through its effects on pH at the site of action inside the nerve.

The addition of sodium bicarbonate to bupivacaine increases the pH of the solution without affecting its chemical stability.

Actions

Central Nervous System

Bupivacaine readily crosses the blood brain barrier causing CNS depression following higher doses. The initial symptoms involve feeling of light-headedness and dizziness followed by visual and auditory disturbances. Disorientation and occasional feeling of lightheadedness may occur. Objective signs are usually excitatory in nature, which includes shivering, muscular twitches and tremors, initially involving muscles of the face (perioral numbness) and part of extremities. At still higher doses cardiovascular or respiratory arrest may occur. Acidosis increases the risk of CNS toxicity from Bupivacaine, since an elevation of $PaCO_2$ enhances cerebral blood flow, so that more anesthetic is delivered rapidly to the brain

Autonomic nervous system

Bupivacaine does not inhibit the Nor Adrenaline uptake and hence has no sympathetic potentiating effect. Myelinated preganglionic B fibers have a faster conduction time and are more sensitive to action of Bupivacaine. When used for conduction blockade, all local anesthetics, particularly Bupivacaine produces higher incidence of sensory than motor fibers.

Cardiovascular System

The primary cardiac electrophysiological effect of a local anesthetic is a decrease in the maximum rate of depolarization in Purkinje fibers and ventricular muscle. This action by Bupivacaine is far greater compared to Lignocaine. Also, the rate of recovery of block is slower with Bupivacaine. Therefore there is complete restoration of Vmax between action potential particularly at higher rates. Therefore Bupivacaine is highly arrythmogenic. Bupivacaine reduces the cardiac contractility. This is by blocking the calcium transport. Low concentration of Bupivacaine produces vasoconstriction whereas high doses cause vasodilatation.

Respiratory System

Respiratory depression may be caused if excessive plasma level is reached which in turn results in depression of medullary receptor center. Respiratory depression may be also caused by paralysis of respiratory muscles of diaphragm as may occur in high spinal or total spinal anesthesia.

Biotransformation And Excretion

Bupivacaine undergoes enzymatic degradation primarily in the liver. The excretion occurs primarily via the kidney. Renal perfusion and factors affecting urinary pH affect urinary excretion. Less than 5% of Bupivacaine is excreted via the kidney unchanged through urine. The major portion of injected agent appears in urine in the form of 2, 6 pipecolyoxylidine which is a de-alkylated metabolite of bupivacaine. Renal clearance of the drug is related inversely to its protein binding capacity and pH of urine.

Adverse effects are encountered in clinical practice mostly due to overdose, inadvertent intravascular injection or slow metabolic degradation.

Adverse Effects

CNS: Nervousness, dizziness, blurring of vision or tremors, drowsiness, convulsions and respiratory arrest.

CVS: Myocardial depression, hypotension, arrhythmia, ventricular type conduction defect, SA node depression and cardiac arrest.

Allergic reactions: Urticaria, bronchospasm, hypotension.

Other: Constriction of pupil and tinnitus.

Levobupivacaine[31]

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. Clinical efficacy of levobupivacaine has been shown to be comparable to bupivacaine.

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 C18H28N2O.

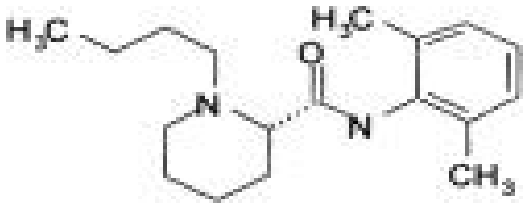


Figure 8 – Chemical structure of levobupivacaine

Mechanism of Action

Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. The drug binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization.

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. The pKa of levobupivacaine is 8.1, similar to the pKa of the racemic bupivacaine. 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.

Levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine or feces. In vitro studies using levobupivacaine showed that cytochrome (CYP) CYP3A4 isoform and CYP1A2 isoform mediate the metabolism of levobupivacaine to inactive metabolites, desbutyl levobupivacaine and 3-hydroxy levobupivacaine, respectively. In vivo, the 3-hydroxy levobupivacaine appears to undergo further transformation to glucuronide and sulfate conjugates, which are excreted in urine. Metabolic inversion of levobupivacaine to R(+) bupivacaine was not evident both in vitro and in vivo.

Clinical Utility

Levobupivacaine has increasingly been used in the clinical anesthesia practice since last few years because of its safer pharmacological profile.

Subarachnoid block

Levobupivacaine is an interesting alternative to bupivacaine for spinal anesthesia. Levobupivacaine produces subarachnoid block with similar sensory and motor characteristics and recovery like bupivacaine. The onset of sensory and motor block is hastened with the use of hyperbaric levobupivacaine as compared to isobaric levobupivacaine.

Epidural anesthesia

Levobupivacaine has been successfully used in providing epidural anesthesia and analgesia for surgical procedures, Equal doses of levobupivacaine and bupivacaine (15mL of 0.5%) provide similar onset of sensory block (8-30min), maximum cephalic spread (T7-T8) and duration of analgesia (4-6 h).

Post‑operative analgesia

Epidural analgesia

A continuous epidural infusion of low concentration of local anesthetics with or without adjuvants provides excellent post-operative analgesia. Equipotent doses of levobupivacaine, bupivacaine and ropivacaine provide comparable post-operative pain relief and recovery of sensory and motor function.A continuous infusion of 15 mg/h of levobupivacaine provides effective pain relief in the post-operative period[30].The quality of analgesia is also determined by the concentration of levobupivacaine, i.e., 0.25% solutionprovides better analgesia as compared to 0.125% or 0.0625% solutions.

Wound infiltration

Local anesthetic infiltration along the incision line is used frequently to provide post-operative analgesia. Post-incisional wound infiltration with 0.125% levobupivacaine provides more effective and longer duration of analgesia and early mobilization as compared to rectal paracetamol, in children after unilateral inguinal hernia surgery.Wound infiltration with levobupivacaine with or without tramadol provide good post-operative analgesia following a cesarean section or lumbar disc surgery.

Peripheral Nerve Blocks

Different studies have compared levobupivacaine, ropivacaine and bupivacaine in brachial plexus block for upper limb surgery. Levobupivacaine is a good substitute for bupivacaine. Compared to ropivacaine, levobupivacaine provides a significantly longer duration of analgesia.The return of motor activity is earlier with ropivacaine.The long duration of sensory block associated with good analgesia and less toxicity of levobupivacaine makes it a better choice for upper extremity blocks.

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.

Chapter 5

METHODOLOGY

METHODOLOGY

Study design

A one year hospital based randomized clinical study.

Study Period

One year from June 2013 to June 2014.

Place

The present study was conducted in the Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, attached to Jawaharlal Nehru Medical College, Belgaum.

Source of Data

Patients aged between 20 to 60 years of either gender, belonging to ASA Grade I and II, scheduled for elective infraumbilical surgeries under spinal anaesthesia were studied.

Sampling procedure

Based on the results of previous studies[12] considering onset of sensory blockade 13+/- 8 minutes for Bupivacaine and 11+/- 6 minutes for Levobupivacaine and based on the statistical formula the sample size was calculated as below.

$$\text{Sample Size (n)} = \frac{2 \text{ X } (Z\alpha + Z\beta)^2 (S_1^2 + S_2^2)}{(X_1 - \overline{X_2})^2}$$

Where,

Level of significance was considered as 5%

Power of the test used as 80%

Hence, $Z\alpha = 1.96$

$Z\beta = 0.84$

$S_1=8 \quad S_2=6$

$\overline{X}_1=13$

$\overline{X}_2=11$

With these values, the minimum sample size was obtained as 32.66 for each group. Hence the sample size was considered as 35 in each group.

Sample Size

A total of 70 patients distributed into two groups of 35 each undergoing elective infraumbilical surgeries under spinal anaesthesia were enrolled.

Selection Criteria

Inclusion criteria

- ASA Grade I and II patients.
- Aged between 20 to 60 years group.

Exclusion criteria

- Patient refusal.

- Contraindications to sub arachnoid block like coagulopathy, local skin infection, raised intracranial pressure, spinal deformity.
- ASA grade III or IV patients.
- Patient allergic to study drugs.

Ethical clearance

Prior to the commencement, the ethical clearance was obtained from Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belgaum.

Informed Consent

The patients fulfilling selection criteria were briefed about the nature of the study and interventions and a written informed consent was obtained (Annexure I).

Randomization

Patients were randomized based on computerized generated randomization into two groups.

- Group B (n=35)
- Group L (n=35)

Data collection

Demographic data of the patients like name, age, sex and history was obtained through an interview. The physical and medical examination conducted.

These findings were recorded on predesigned and pretested proforma (Annexure-II).

Procedure

Preanaesthetic Examination and Preparation

Overnight fasting status was confirmed. Anaesthetic techniques were standardized for all patients. Preanaesthetic check up was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations were recorded.

Before shifting to the operation theatre, I.V access was obtained with 18 Gauge I.V cannula and patients were preloaded with intravenous infusion of 10 mL/Kg of ringers lactate solution 30 minutes prior to surgery.

Preparation of operation room

Anaesthesia machine was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet and working suction apparatus were kept ready before the procedure.

Intervention

Group B

Under all aseptic precautions, L_{3-4} space identified, a 23G Quincke's spinal needle was inserted into L_{3-4} space and 3 ml of 0.5% Bupivacaine isobaric was injected into the space. Patients were turned immediately to supine position.

Group L

Under all aseptic precautions, L_{3-4} space identified and a 23G Quincke's spinal needle inserted into L_{3-4} space and 3ml of 0.5% levobupivacaine isobaric was injected into the space. Patients were turned immediately to supine position.

Outcome variables

- Sensory block: Sensory block was assessed bilaterally, using alcohol swab in mid axillary line. Sensory block onset was defined as the time taken to achieve T_{10} block level and duration of sensory block was defined as two dermatome regression of anaesthesia from the highest level. The surgery was allowed to start once sensory block reached at least T_{10} but general anaesthesia was induced if this did not occur after 15 minutes.

- Motor block: Motor block was assessed immediately after sensory block using a Modified Bromage Grade. Onset of motor block was defined as the time to reach Modified Bromage Grade 1 and Total duration of motor block was defined as the time for return to Modified Bromage Grade 0.

    - Bromage 0, free movement of legs and feet, with ability to raise extended leg.

- Bromage 1, inability to raise extended leg and knee flexion is decreased, but full flexion of ankle and feet is present.
- Bromage 2, inability to raise leg or flex knees, flexion of ankle and feet present.
- Bromage 3, inability to raise leg, flex knee or ankle, or move toes.

Blocks were assessed every minute for 10 minutes and then every 10 mintues duration till motor block reached bromage 0.

Intraoperative noninvasive monitoring of vitals (HR, SBP, DBP and SPO2) was done .

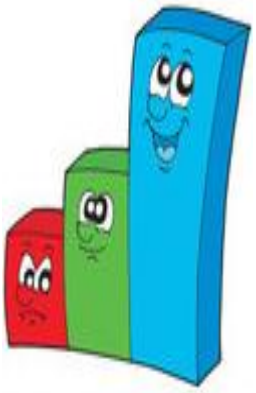
- Time to request for first post operative rescue analgesia – In the post anaesthesia care unit, time to request for first post-operative rescue analgesia was noted. Post-operative pain score was measured by using VAS of 'zero' to 'ten' where 'zero' indicated no pain and 'ten' indicated worst imaginable pain. Rescue analgesia of injection paracetamol 1gram intravenously was given if the VAS score was more than three.

Statistical Methods

The data was tabulated and master chart was prepared (Annexure IV). The categorical data was expressed as rates, ratios and percentages and the continuous data was expressed as mean ± standard deviation Significance was assessed at five percent level of significance. Student unpaired 't' test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups. Chi-square test was used to find association between the classes of variables.

Chapter 5

Results



RESULTS

The present one year clinical trial was conducted in the Department of Anaesthesiology, during the period of June 2013 to June 2014 at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum attached to Jawaharlal Nehru Medical College, Belgaum.

A total of 70 patients undergoing infraumbilical surgeries under spinal anaesthesia were randomly allocated into one of the two groups by computer generated randomization table.

- Group B (n=35) Patients received 3 ml of 0.5 % isobaric bupivacaine intrathecally.

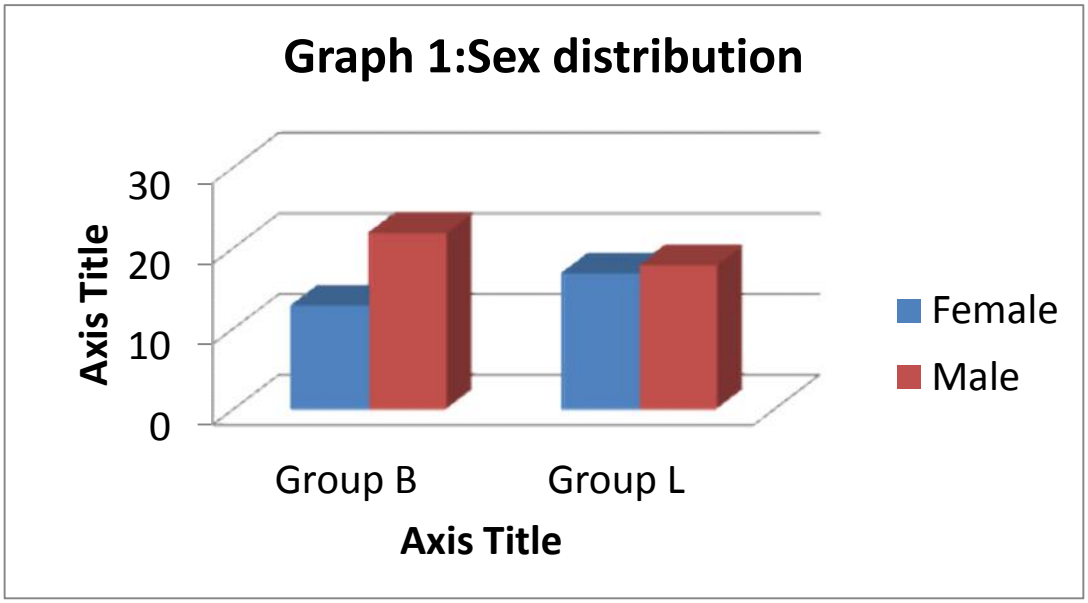
- Group L (n=35) Patients received 3 ml of 0.5 % isobaric levobupivacaine intrathecally.

Data obtained was coded and analyzed as below.

Table 1. Sex Distribution

Sex	Group B (n=35)		Group L(n=35)	
	Number	Percent	Number	Percent
Female	13	37.14	17	48.57
Male	22	62.85	18	51.43
Total	35	100.00	35	100.00

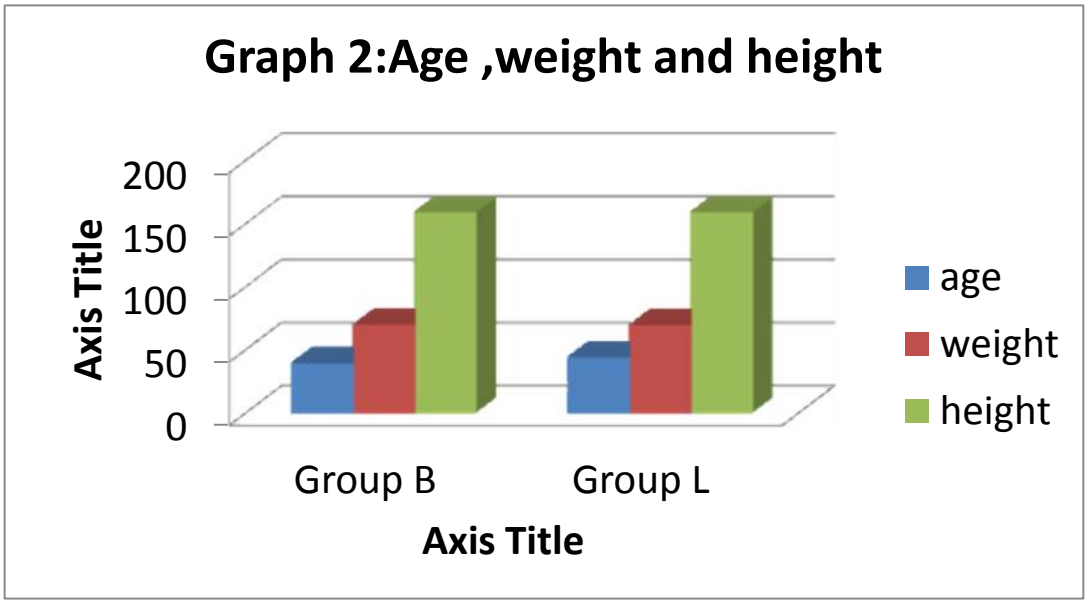
χ^2 =0.933 p=0.334



In this study 62.85% were males and 37.14% were female patients in group B and 51.42% were males and 48.57% were female patients in group L, suggesting both the groups had comparable demographic characteristics (p=0.334).

Table 2: Mean age , weight and height

Parameters	Group B		Group L		p value
	Mean	Standard deviation	Mean	Standard deviation	
Age (years)	40.4	14.98	45.2	14.07	0.169
Weight(kgs)	70.9	8.85	70.7	7.36	0.930
Height (cms)	160.1	5.70	160.1	5.98	1

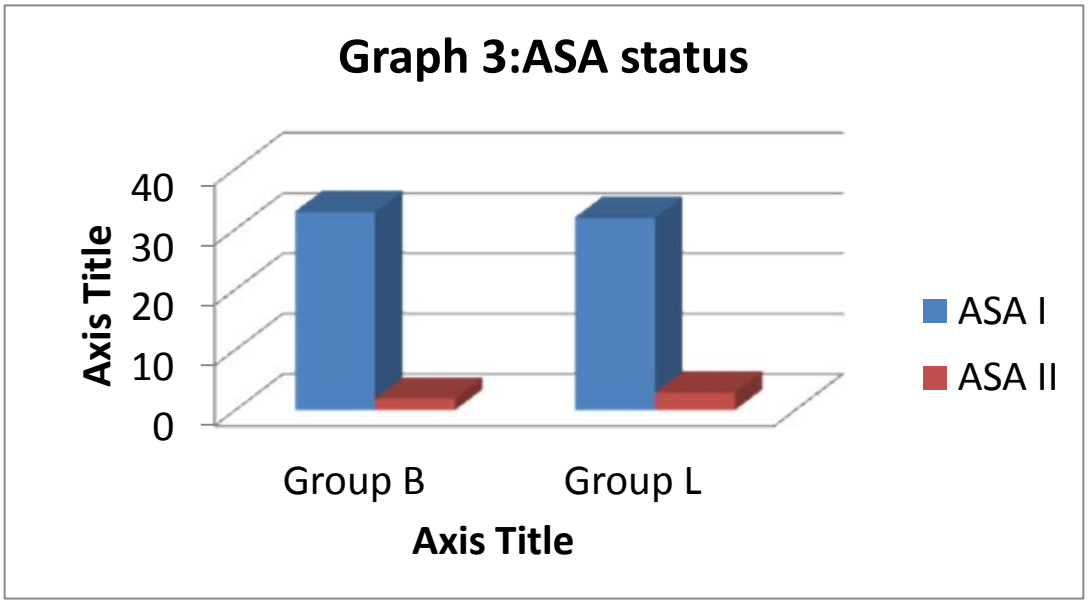


The mean age in group B was 40.4 ± 14.98 and in group L it was 45.2 ± 14.07 (p=0.169). The mean weight in group B was 70.9 ± 8.85 kgs and in group L it was 70.7 ± 7.36 kgs (p=0.930).The mean height in group B was 160.1 ± 5.70 cms and in group L it was 160.1 ± 5.98 cms (p=1), suggesting mean age, weight and height in both the groups were comparable.

Table 3. ASA grade

ASA grade	Group B (n=35)		Group L (n=35)	
	Number	Percent	Number	Percent
Grade I	33	94.3	32	91.4
Grade II	2	5.7	3	8.6
Total	35	100	35	100

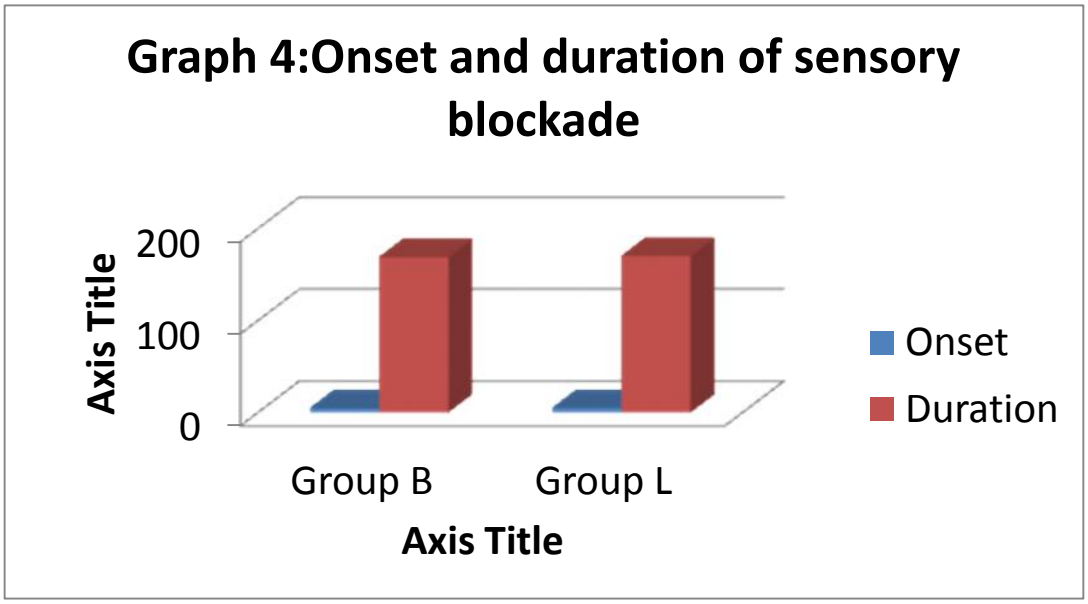
x^2=0 p=1



In group B, 94.3% patients were ASA I and in group L 91.4% patients were ASA I. Remaining being ASA II. Thus both the groups were comparable with p= 1.

Table 4. Onset and duration of sensory block

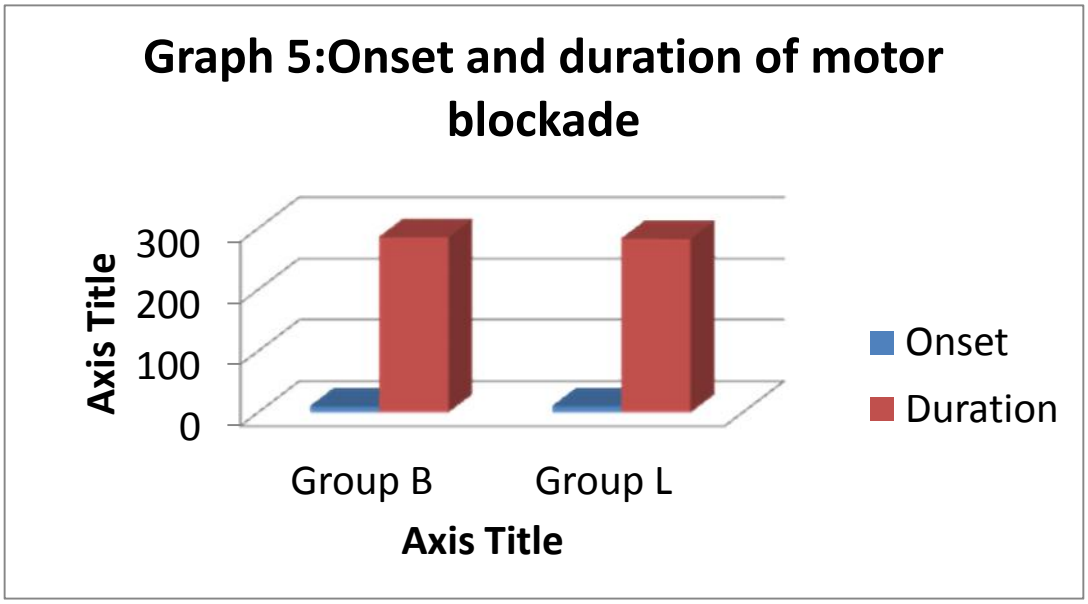
Group	Onset (minutes)		Duration(minutes)	
	Mean	Standard deviation	Mean	Standard deviation
Bupivacaine	5.2	0.63	169.4	13.04
Levobupivacaine	5.3	0.66	170.6	16.83
P	0.583		0.691	



The mean onset for sensory block in group B was 5.2 ± 0.63 minutes and in group L was 5.3 ± 0.66 minutes. The result was not statistically significant (p=0.583) and both groups had almost similar onset for sensory block. The mean duration of sensory block in group B was 169.4 ± 13.04 minutes and mean duration of sensory block in group L was 170.6 ± 16.83 minutes and the result was not statistically significant with p=0.691

Table 5. Onset and duration of motor block

Group	Onset (minutes)		Duration (minutes)	
	Mean	**Standard deviation**	**Mean**	**Standard deviation**
Group B	**10.8**	**0.91**	**286.6**	**13.92**
Group L	**10.9**	**0.74**	**284**	**10.34**
P	**0.474**		**0.384**	



The mean onset for motor block in group B was 10.8±0.91 minutes and in group L was 10.9±0.74 minutes. The result was statistically not significant with p =0.474. The mean duration of motor block in group B was 286.6 ± 13.92 minutes and mean duration of motor block in group L was 284 ± 10.34 minutes. This result signifies that statistical significant difference doesn't exist between the two groups with p=0.38.

Table 6 : Comparison of mean heart rate at different intervals (bpm)

Intervals	**Group B (n=35)**		**Group L (n=35)**		**P value**
	Mean	**SD**	**Mean**	**SD**	
Pre op	77.08	7.37	77.85	8.76	0.670
2 Minutes	77.20	9.69	75.50	7.65	0.387
4 Minutes	76.38	10.49	74.48	8.33	0.373
6 Minutes	75.55	9.22	72.58	6.61	0.102
8 Minutes	74.25	8.86	71.55	8.06	0.158
10 Minutes	73.28	7.92	70.35	8.40	0.113
15 Minutes	72.73	9.46	69.98	8.35	0.172
20 Minutes	70.63	7.78	69.05	6.69	0.335
25 Minutes	70.83	7.62	69.13	7.04	0.303
30 Minutes	70.30	8.65	69.20	6.89	0.531
45 Minutes	69.83	7.28	68.05	8.06	0.305
60 Minutes	70.75	8.38	68.45	5.72	0.156
75 Minutes	71.90	10.83	68.70	6.78	0.118
90 Minutes	70.70	10.56	67.76	7.67	0.158

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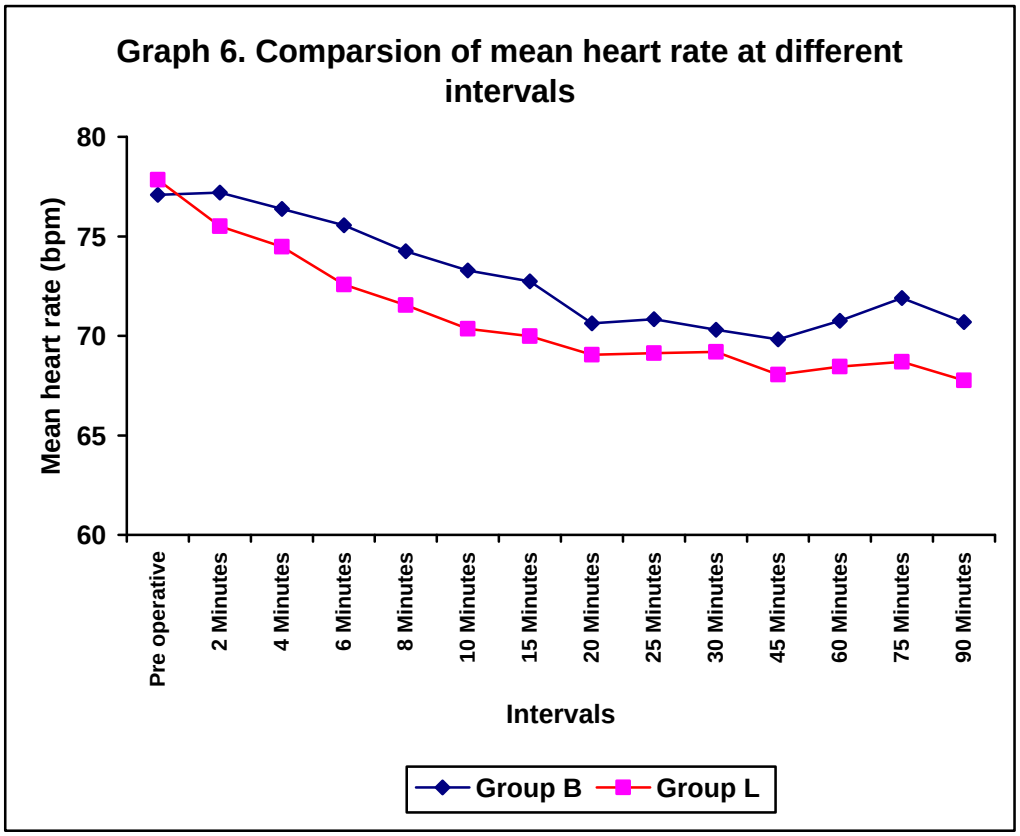
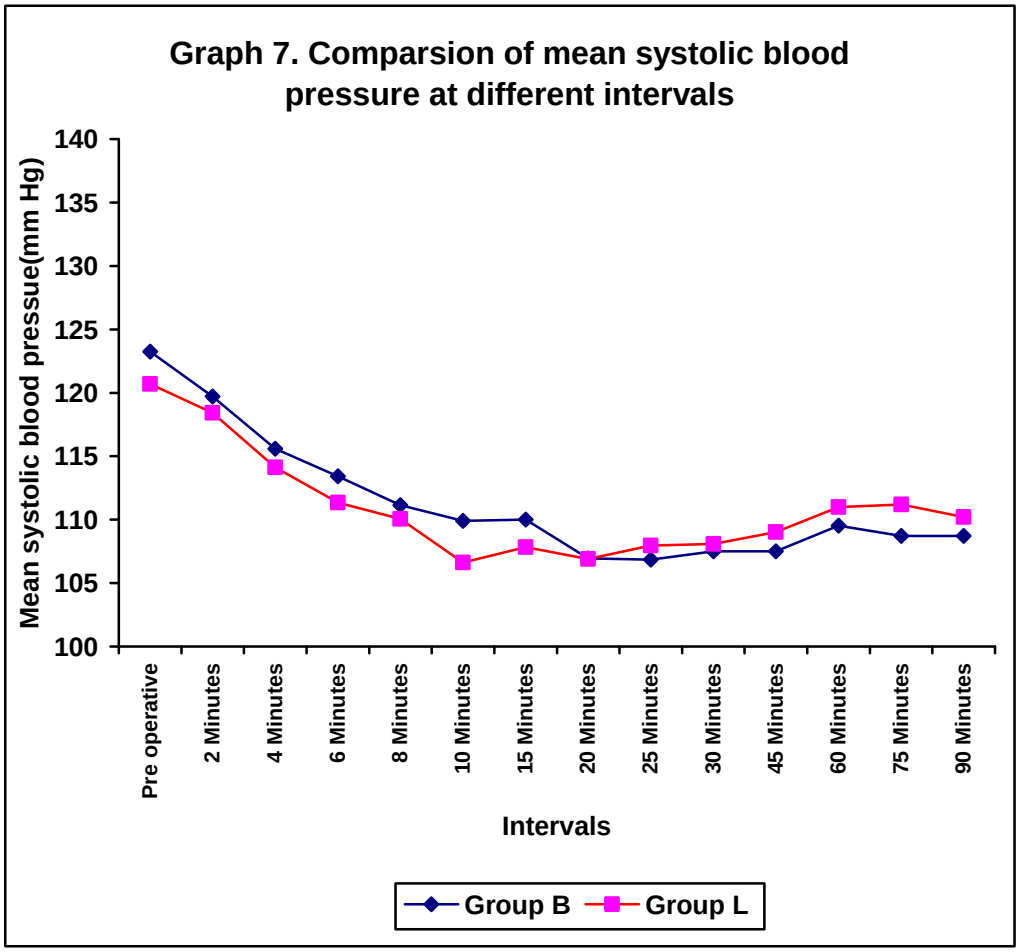


There was no statistically significant difference found between the two groups regarding changes in mean heart rate at various intervals ($p>0.05$)

Table 7. Comparison of mean systolic blood pressure at different intervals (mm Hg)

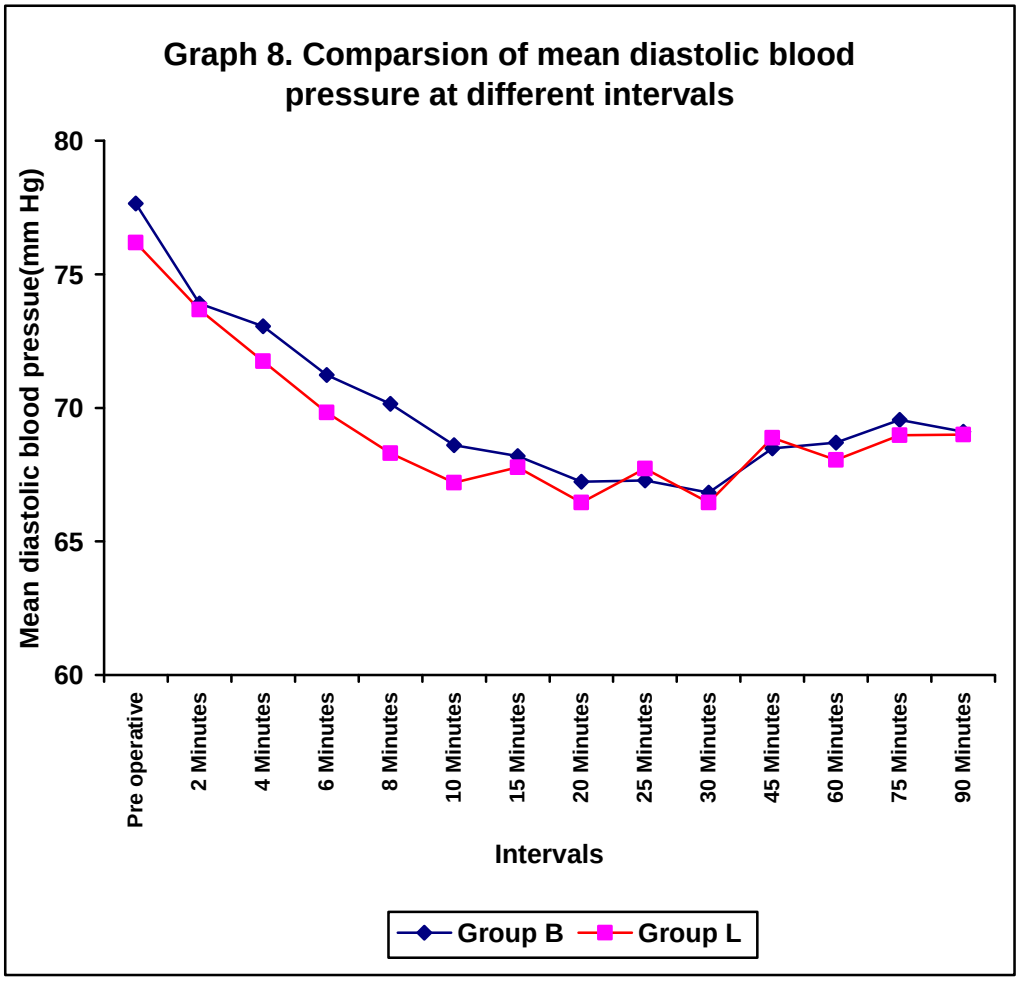
Intervals	Group B (n=35)		Group L (n=35)		p value
	Mean	**SD**	**Mean**	**SD**	
Pre op	123.25	10.19	120.70	8.29	0.223
2 Minutes	119.70	10.57	118.43	8.56	0.555
4 Minutes	115.58	12.71	114.13	9.38	0.563
6 Minutes	113.43	12.47	111.35	8.62	0.390
8 Minutes	111.15	10.74	110.05	10.36	0.642
10 Minutes	109.90	13.60	106.63	19.35	0.384
15 Minutes	110.00	12.76	107.83	11.10	0.419
20 Minutes	106.95	12.96	106.90	11.58	0.986
25 Minutes	106.85	15.58	107.95	10.47	0.712
30 Minutes	107.50	14.31	108.08	8.75	0.829
45 Minutes	107.50	12.91	109.03	10.05	0.557
60 Minutes	109.53	12.88	111.00	7.35	0.532
75 Minutes	108.73	11.16	111.20	7.64	0.251
90 Minutes	108.72	10.30	110.20	7.18	0.459



In the current study it was found that there was no statistically significant difference between group B and group L with respect to changes in systolic blood pressure in various intervals ($p > 0.05$)

Table 8. Comparison of mean diastolic blood pressure at different intervals (mm Hg)

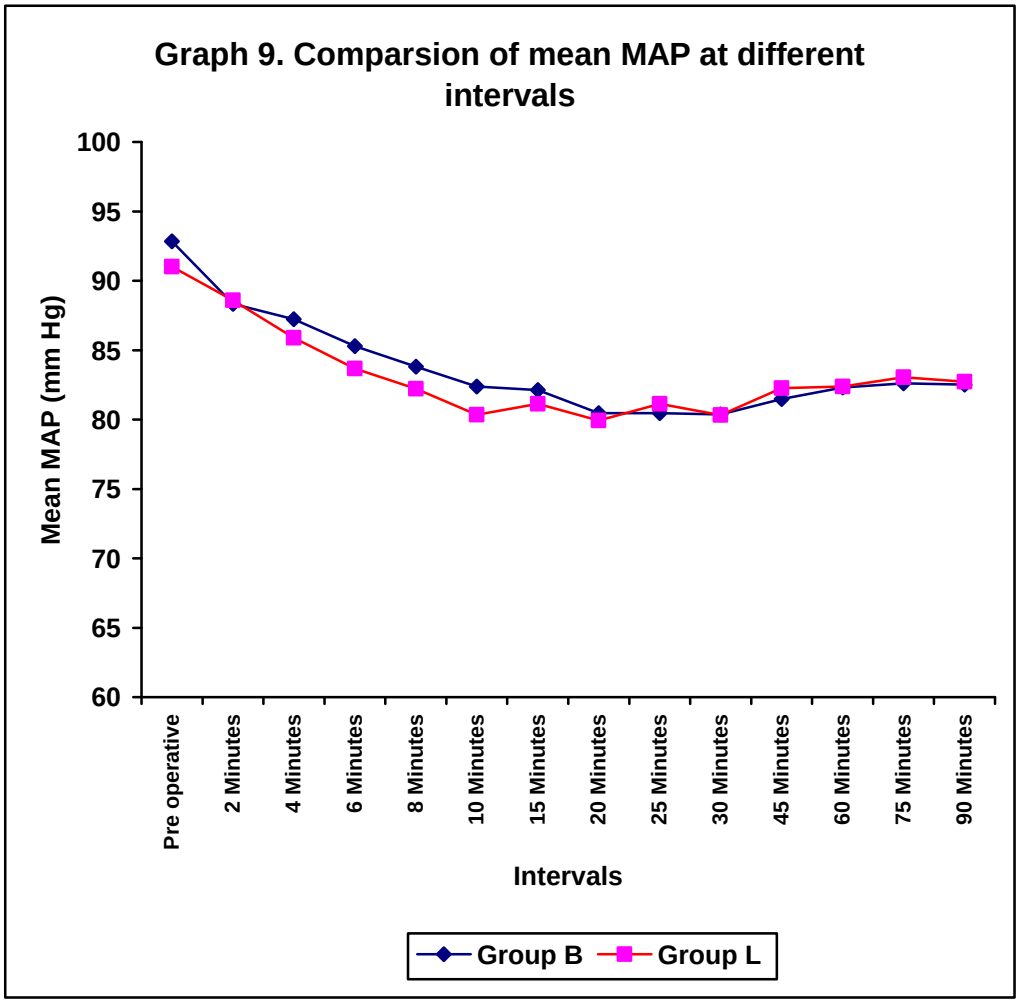
Intervals	Group B (n=35)		Group L (n=35)		p value
	Mean	**SD**	**Mean**	**SD**	
Pre op	77.65	7.12	76.18	6.28	0.329
2 Minutes	73.90	7.56	73.68	8.66	0.902
4 Minutes	73.05	9.09	71.75	8.12	0.502
6 Minutes	71.23	8.65	69.83	8.11	0.457
8 Minutes	70.15	7.62	68.30	7.81	0.287
10 Minutes	68.60	9.62	67.20	8.81	0.499
15 Minutes	68.20	10.11	67.78	11.12	0.858
20 Minutes	67.23	10.30	66.45	9.27	0.725
25 Minutes	67.28	11.28	67.73	7.83	0.836
30 Minutes	66.83	11.02	66.45	7.52	0.859
45 Minutes	68.48	9.61	68.88	8.25	0.842
60 Minutes	68.70	9.38	68.05	5.52	0.707
75 Minutes	69.55	8.97	68.98	6.27	0.741
90 Minutes	69.11	9.10	69.00	6.28	0.953



There was no significant difference with respect to variations in diastolic blood pressure between the two groups ($p > 0.05$)

Table 9. Comparison of mean MAP at different intervals (mm Hg)

Intervals	**Group B (n=35)**		**Group L(n=35)**		**P value**
	Mean	**SD**	**Mean**	**SD**	
Pre op	92.85	7.64	91.02	6.40	0.248
2 Minutes	88.34	10.09	88.59	8.04	0.903
4 Minutes	87.23	9.74	85.88	7.97	0.500
6 Minutes	85.29	9.56	83.67	7.57	0.402
8 Minutes	83.82	8.02	82.22	8.03	0.376
10 Minutes	82.37	10.26	80.34	10.28	0.381
15 Minutes	82.13	10.53	81.13	9.24	0.650
20 Minutes	80.47	10.72	79.93	9.28	0.813
25 Minutes	80.47	12.23	81.13	7.90	0.773
30 Minutes	80.38	11.60	80.33	6.94	0.978
45 Minutes	81.48	10.22	82.26	8.08	0.708
60 Minutes	82.31	10.12	82.37	5.30	0.974
75 Minutes	82.61	8.54	83.05	6.10	0.791
90 Minutes	82.51	9.00	82.73	5.97	0.896



In the current study statistically significant difference was not found between the two groups regarding changes in mean MAP ($p > 0.05$).Thus the two groups were comparable in terms of hemodynamic variations.

Chapter 6

Discussion

DISCUSSION

Subarachnoid block is the most extensively used anaesthetic technique in the present anaesthesia practice. Rapid onset, excellent relaxation, sufficiently long period of action especially with use of longer acting local anaesthetics as well as adjuvants, easy learning curve, comparatively less side effects makes it a very attractive anaesthetic technique for use .

Nevertheless it has its own disadvantages like limited duration and inadequate postoperative analgesia. Usage of neuraxial opiods and in dwelling catheters in subarahnoid space has to some extend decreased this disadvantage.

Bupivacaine hydrochloride a local anesthetic that is most widely used for spinal anesthesia, mainly as a hyperbaric or plain solution.It produces rapid onset, reliable duration and good muscle relaxation[32]. Its a long acting amide local anaesthetic most commonly used for spinal anaesthesia.

Albright described five cases of death resulting from accidental intravascular administration of long-acting amide local anesthetics, and the speculation was that bupivacaine hydrochloride is relatively more cardiotoxic than the shorter acting amide local anesthetic lidocaine. Both local anesthetic agents block cardiac sodium channels during the upstroke of the action potential, but the recovery from block during diastole proceeds slowly with bupivacaine compared with lidocaine. Bupivacaine, has a fast entry and slower release from the receptors. As a result of the slow recovery with the use of bupivacaine, a substantial frequency-dependent block accumulates at heart rates between 60 and 150 beats per minute (slow recovery from block during diastole).[33]

Pharmacological research that emphasized the selective behaviour of the two enantiomers of racemic bupivacaine, ie, levo- or S (−)-bupivacaine and dextro- or R (+)-bupivacaine, it was found that levorotatory forms are less cardiotoxic. Levobupivacaine is a pure S enantiomer of bupivacaine. Vanhouette F et al have demonstrated that levobupivacaine has less affinity and thus less inhibitory effect onto the inactivated state of cardiac sodium channels than the racemic parent or dextrobupivacaine in invitro animal tissue experimental studies[34.]It also showed less depressant effect on the atrioventricular conduction (Graf et al.)[35] and QRS complex duration (Mazoit et al.)[36], and provoked less impairment of the contractile function of the isolated animal heart (Simonetti and Fernandes)[37]. It was also less potent in blocking cloned human heart sodium and potassium channels (Valenzuela et al.)[38].The estimated mean (standard deviation) fatal dose through severe arrhythmias after intravenous administration of levobupivacine in sheep is 277 (51) mg, which is significantly larger than the fatal dose of bupivacaine of 156 (31) mg (Chang et al.)[39]

Levobupivacaine, the pure S (−)-enantiomer of bupivacaine, has emerged as a safer alternative for regional anesthesia than its racemic parent. It demonstrated less affinity and strength of depressant effects onto myocardial and central nervous vital centers in pharmacodynamics studies, and a superior pharmacokinetic profile. Clinically, levobupivacaine is well tolerated in a variety of regional anesthesia techniques both after bolus administration and continuous postoperative infusion.[40]

Levobupivacaine is said to have similar pharmacokinetic properties as racemic bupivacaine but many studies done in animals have shown that it was

faster protein binding rate which might reflect its reduced toxicity[7].Thus due to its reduced cardiovascular and cerebral toxicity makes levobupivacaine interesting alternative to bupivacaine in spinal anaesthesia despite the fact that less dose of the drug is used intrathecally.

Current literature comparing 0.5% levobupivacaine and 0.5% bupivacaine administered intrathecally are few and hence we compared the above drugs in patients posted for elective infraumbilical surgeries.

This one year randomized controlled trial was conducted in the Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of June 2013 to June 2014. A total of 70 patients undergoing infra umbilical surgeries under spinal anaesthesia were randomly allocated into one of the two groups by computer generated randomization that is, Group B (n=35; patients received 3 ml of 0.5 % isobaric Bupivacaine) or Group L (n=35; Patients received 3 mL of 0.5 % isobaric Levobupivacaine).

In this study demographic parameters like age, sex, weight and height were comparable between the two groups.

In this study onset of sensory block which was defined as as the time taken to achieve T_{10} block level was found to be 5.2 +/- 0.63 minutes for B group and 5.3+/- 0.66 minutes for L group. There was no statistical difference between the groups with p=0.583.

Similar results were found by J.F. Luck et al. They conducted a study on 60 ASA I – II patients undergoing elective surgeries under spinal anaesthesia.3ml of 0.5% hyperbaric bupivacaine was compared with 3ml of hyperbaric levobupivacaine and 3ml of 0.5 % hyperbaric ropivacaine and was found that onset of sensory block was median 5(2-8) minutes in all the 3 groups[17].

Duration of sensory block was defined as two dermatome regression of anaesthesia from the highest level. It was found to be 169.4+/- 13.04 in group B and 170.6+/- 16.83 in group L and with a p value of 0.691, there was no statistical difference in the 2 groups.

Monica del-Rio-Vellosillo et al. in a study done on 60 ASA I –II patients undergoing elective knee arthoscopy under spinal anaesthesia found similar results. Patients received 2.5 ml of isobaric 0.5% bupivacaine and 2.5 ml of 0.5% levobupivacaine and there was no difference between the 2 groups in terms of duration of sensory blockade. With a p value of 0.429 it was found to be median of 153 (20–312) minutes in bupivacaine group and median of 154 (52–317) minutes in levobupivacaine group[41]. Considering the fact that less dosage was used in their study duration is comparatively less compared to our current study.

Onset of motor block was defined as the time to reach Modified Bromage Grade 1.It was found to be 10.8+/- 0.9 minutes in bupivacaine group and 10.9 +/- 0.74 in levobupivacaine group. There was no statistical difference found between the 2 groups with p= 0.047

Total duration of motor block was defined as the time for return to Modified Bromage Grade 0. It was found to be 286.6+/- 13.92 in bupivacaine

group and 284+/- 10.34 in levobupivacaine group and with a p=0.877 there is no statistically significant difference

Glaser C et al. in a study done on 80 patients undergoing elective hip replacement surgeries found similar results. He compared 0.5 % isobaric bupivacaine with 0.5 % isobaric levobupivacaine and found that motor onset time was 9+/- 7 minutes for bupivacaine and 10+/- 7 minutes for levobupivacaine group. Duration of motor blockade was found to be 284+/- 80 minutes with bupivacaine and 280+/-84 minutes with levobupivacaine[12] .Thus these 2 groups were comparable in terms of onset and duration of motor blockade which is also similar to results obtained from the current study.

F.Fottorini et al. did a study on 60 patients undergoing elective orthopaedic surgeries and compared 0.5 % isobaric levobupivacaine and 0.5% bupivacaine. Onset of motor block was 8+/- 4 minutes and duration of motor block 245+/- 86 minutes with bupivacaine and onset of motor block 11+/- 6 minutes and duration 256+/-86 minutes with levobupivacaine[14]. Thus both groups were found to be comparable in terms of onset and duration of motor blockade.

Vanna O et al. studied 70 patients undergoing elective transurethral endoscopic surgery who received either 0.5% isobaric levobupivacaine or 0.5% hyperbaric bupivacaine intrathecally and found that the two groups were similar in terms of time to block suitable for surgery, duration of sensory block, time to two segments regression, time to T12 regression, time to onset and offset of motor block, verbal numeric pain scores at the start of the operation and adverse events[42].

Sahin S H et al. while doing study on 50 patients to know the effects of bupivacaine versus levobupivacaine on pulmonary function in patients with chronic obstructive pulmonary disease undergoing urologic surgery found that there were no significant differences between groups regarding sensory and motor onset times, maximal spread of sensory block, duration of sensory block and motor block, and time to L2 segment regression of spinal anesthesia[43].

Mean maximum upper spread was found to be same in both the groups. Maximum upper level of T8 was found in 24 patients in bupivacaine group and 25 patients in levobupivacaine group. Thus both groups were found to have similar upper level of sensory spread.

Similar results were obtained by F.Fottorini et al. 3ml of 0.5% isobaric levobupivacaine and bupivacaine were compared in 60 patients undergoing elective orthopaedic surgeries and maximum level of T8 was obtained in both the groups[14].

There was no statistically significant difference found in the hemodynamic variations between the two groups. Similar results were found in other studies[14,15,16].

Our study was done using isobaric solutions. In current clinical practice hyperbaric bupivacaine is most commonly used for intrathecal administration. It would be useful to do further studies comparing hyperbaric levobupivacaine and hyperbaric bupivacaine for intrathecal usage.

In the study both the drugs have comparable effects on sensory and motor blockade. It will be useful to do further studies with adjuvants added to it to study their effects.

Chapter 8

Summary

SUMMARY

Spinal anaesthesia remains a popular technique of choice for performing surgeries on abdomen, pelvis and lower limbs. It has fast onset of action and provides effective sensory and motor blockade. Spinal anaesthesia is routinely performed by administration of 0.5% bupivacaine. Commercially available bupivacaine is a racemic mixture containing a 50:50 proportion of levobupivacaine, L (-) isomer, and dextrobupivacaine D (+) isomer.Adverse effects found after inadvertent intraarterial administration of bupivacaine were mainly due to its R enantiomer. Levobupivacaine is a pure S enantiomer of bupivacaine and hence has less cardiac and central nervous system toxicity compared to bupivacaine. It has replaced bupivacaine in other regional anaesthetic procedures like nerve blocks and epidural block. We attempted to compare intrathecal isobaric levobupivacaine and bupivacaine in patients posted for elective infraumbilical surgeries

The current study was conducted in KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of June 2013 to June 2014 . Aim of the study was to compare onset and duration of sensory and motor blockade between intrathecal isobaric 0.5% bupivacaine and 0.5% levobupivacaine.

70 patients between the age group of 18-60 years of either gender, belonging to ASA Grade I and II scheduled for elective infraumbilical surgeries were enrolled in the study. They were randomised into 2 groups. Group B received intrathecal 3 ml of 0.5 % isobaric bupivacaine and Group L received

intrathecal 3 ml of 0.5% isobaric levobupivacaine. Onset and duration of sensory and motor blockage were compared between the two groups

It was found that the two groups were comparable in terms of onset for sensory (5.2 ± 0.63 minutes versus 5.3 ± 0.66 with p= 0.583); duration of sensory block (169.4 ± 13.04 minutes versus 170.6 ± 16.83 with p=0.691); onset for motor (10.8±0.91 minutes versus 10.9±0.74 with p=0.474); duration of motor (286.6 ± 13.92 minutes versus 284 ± 10.34 with p=0.384). There was no statistical difference between the two groups. The two groups showed no difference in terms of hemodynamic parameters measured.

Based on the study results it may be concluded that, intrathecal administration of 0.5% isobaric levobupivacaine has similar onset and duration of sensory and motor blockade compared to 0.5% isobaric bupivacaine.

Chapter 8

Conclusion

CONCLUSION

Based on the study results it may be concluded that, intrathecal administration of 0.5% isobaric levobupivacaine has similar onset and duration of sensory and motor block compared to 0.5% isobaric bupivacaine. However larger studies need to be conducted to confirm these findings.

Chapter 9

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Annexures

ANNEXURE I

ANNEXURE I – CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____ we are requesting you to enroll yourself in study titled "COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE WITH INTRATHECAL ISOBARIC BUPIVACAINE VERSUS ISOBARIC LEVOBUPIVACAINE FOR INFRAUMBILICAL SURGERIES- A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL", conducted by ----------, Post Graduate in M.D, Anaesthesiology under the guidance of ---------- Professor, Department of Anaesthesiology, J.N. Medical College, Belgaum under KLE university, Belgaum.

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

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

The purpose of research is to compare efficacy between bupivacaine and levobupivacaine on onset and duration of motor block, onset and duration of sensory block, hemodynamic changes in infraumbilical surgeries under spinal anaesthesia.

Procedure Involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history, then you will he clinically examined in detail and investigated accordingly. You will be randomly allocated either into study Group B or Group L, and be given the study drug as per the randomisation protocol. You will receive 3 cc of 0.5% bupivacaine isobaric or 3 cc of 0.5% levobupivacaine isobaric by spinal anaesthesia.

Risks and Benefits:

The benefits of taking part in this research are that we can avoid General Anaesthesia with good quality of Analgesia. The risks are minimal.

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E.S hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

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

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

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

Financial Incentives for participation:

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

Compensation:

In the event of injury related to the study, treatment will be made available through KLES Hospital & MRC, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact ----------, at Department of Anaesthesiology, KLES Hospital& MRC or by Ph. No: ----------.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact ----------, Department of Anaesthesiology, KLES Hospital and MRC, Ph. No. ---------- or phone

number: ----------. Or ----------, Professor, Dept. Of Anaesthesiology, KLES Hospital and MRC, Belgaum Ph.: ----------

If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli, Prof. & Head of Pathology as Chairman of J. N. Medical College Institutional Ethical Committee of Human Subjects Research, Phone No.---------- ext---------- at J. N. Medical College, Belgaum.

Consent for participation in research trial

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

Subject Name : _____

Signature or the Left Thumb Print of Subject :

_____ Date :

Witness Name : _____ Signature: _____ Date :

Investigators Name: _____Signature:_____ Date :

Place : _____

Annexures

Annexure II

ANNEXURE II – PROFORMA

STUDY: "COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE WITH INTRATHECAL ISOBARIC BUPIVACAINE VERSUS ISOBARIC LEVOBUPIVACAINE FOR INFRAUMBILICAL SURGERIES- A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"

Patient Name: **IP No.:**

Age: **Weight:**

Height: **Gender:**

Date of Operation: **Occupation:**

Address: **Anaesthesiologist:**

Preanesthetic Evaluation:

Chief Complaints:

Past History:

a. HTN / DM / Asthma / Epilepsy / Rx allergy
b. Drug therapy
c. Previous exposure to Anesthesia

Family history

General physical examination

Pallor / Icterus / Clubbing / Cyanosis / Lymphadenopathy / Edema

PR : BP :

RR : Temp :

Musculoskeletal disorders

Jaw movements : Teeth :

Airway assessment : Spine :

Systemic Examination

RS : CNS :

CVS : GIT :

Investigations

Hb : Total Count :

DC : BT :

Urine routine : CT :

Preoperative physical status: ASA Grade I, II, III, IV, V

Diagnosis

Proposed Surgery

Preoperative baseline values

HR: BP:

Monitors attached

Pulse oxymetry : NIBP :

ECG :

I. Group:

II. Vital parameters :

Time	**HR**	**Blood pressure**			**$Sp0_2$**
		SBP	**DBP**	**MAP**	
2 min					
4 min					
6 min					
8 min					
10 min					
1 5 min					
20 min					
25 mm					
30 min					
45 min					
60 min					
75 min					
90 min					
105min					
120min					

III. Sensory Block

a)	Onset (mins)	
b)	Maximum level	
c)	Duration (mins)	

IV. Motor Block

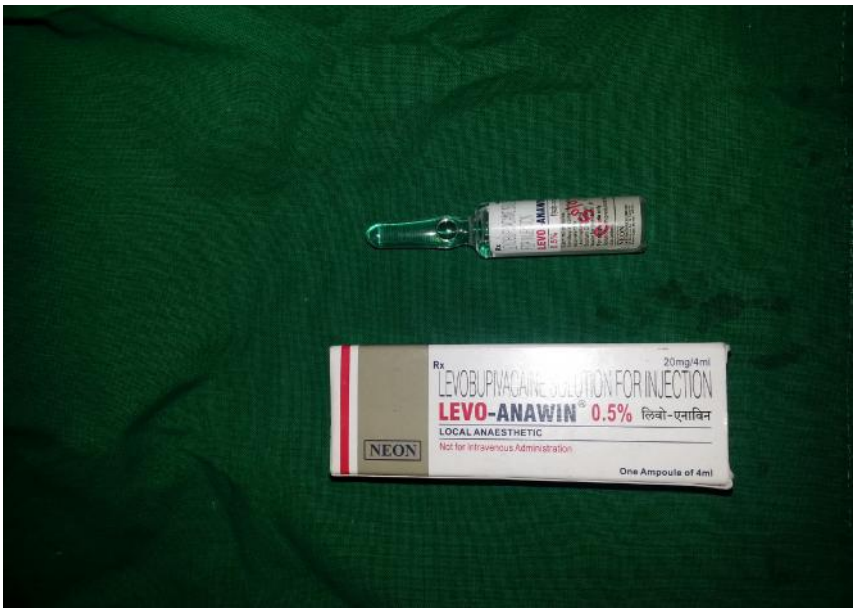
a)	Onset (mins)	
b)	Maximum level	
c)	Duration (mins)	

Annexures

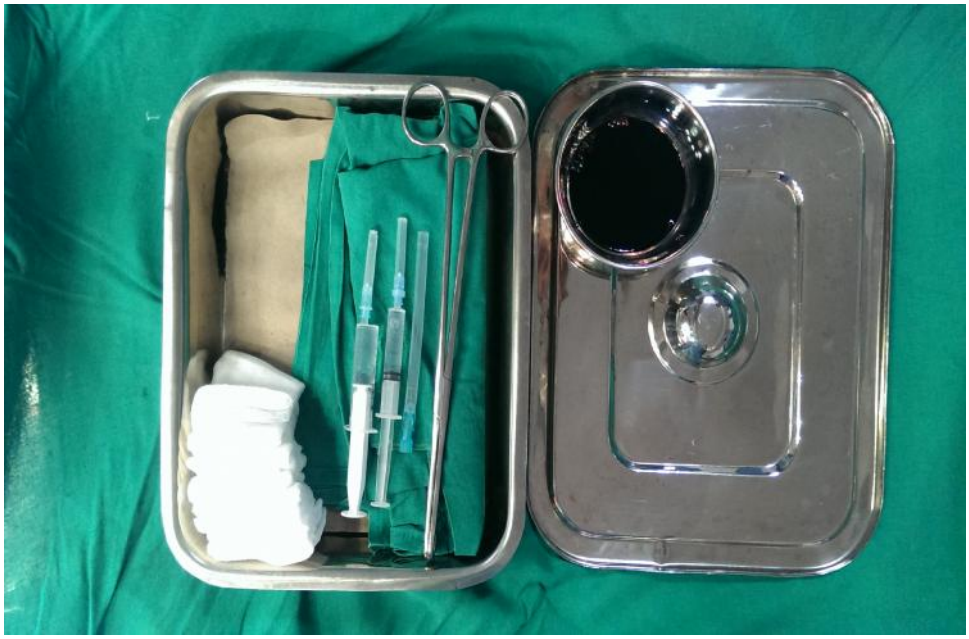
Annexure III

ANNEXURE III – PHOTOGRAPHS

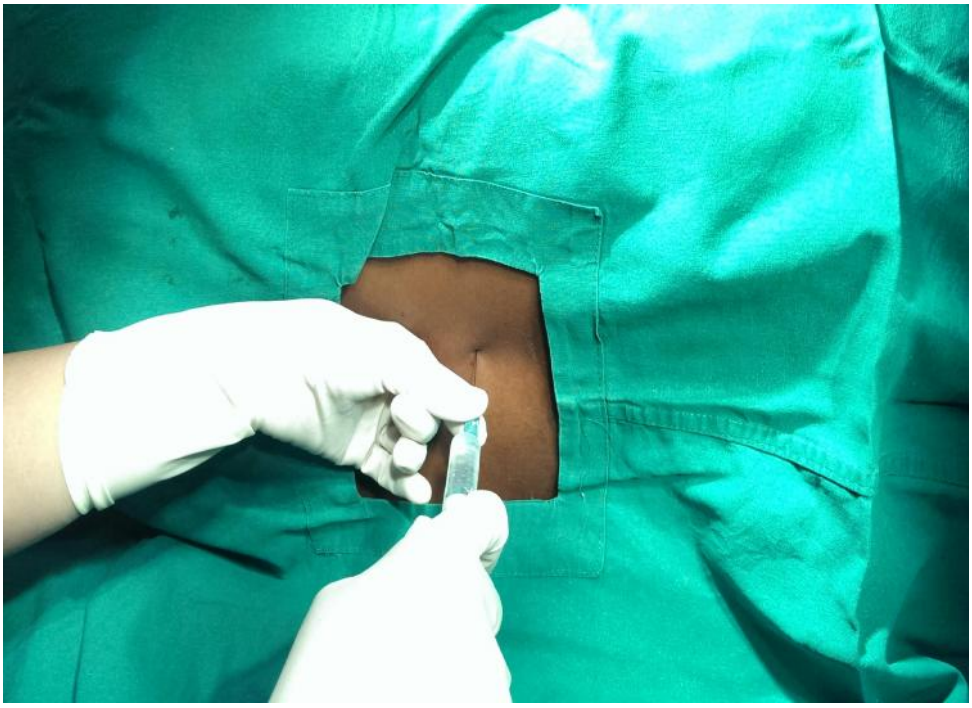
Photograph 1. 0.5% isobaric bupivacaine



Photography 2. 0.5% isobaric levobupivacaine



Photograph 3. Spinal tray



Photograph 4. Spinal anaesthesia

Photograph 5. Monitoring haemodynamic parameters

Annexures

Annexure IV

ANNEXURE IV – KEY TO MASTER CHART

ASA	-	American Society of Anaesthesiologists
BP	-	Blood pressure
Bpm	-	Beats per minute
Cms	-	Centimeters
F	-	Female
HR	-	Heart rate
Kgs	-	Kilograms
mm Hg	-	Millimeters of mercury
M	-	Male
SPO_2	-	Oxygen saturation

Annexures

Annexure III