"A RANDOMIZED CLINICAL TRIAL TO COMPARE 0.75% PLAIN ROPIVACAINE AND 0.5% PLAIN BUPIVACAINE IN LOWER ABDOMINAL SURGERIES UNDER SPINAL ANALGESIA AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"

By

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Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
ANAESTHESIOLOGY

Under the Guidance of

Dr. M. G. DHORIGOL MD
Professor

DEPARTMENT OF ANAESTHESIOLOGY,
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BELGAUM, KARNATAKA

MAY - 2012

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LIST OF ABBREVIATIONS USED

t½	-	Half life
ASA	-	American Society of Anaesthesiologists
C	-	Cervical
CNS	-	Central nervous system
CSF	-	Cerebrospinal fluid
CVS	-	Cardiovascular system
CYP450	-	Cytochrome P450
DBP	-	Diastolic blood pressure
ED	-	Effective dose
FDA	-	Food and Drug Administration
GA	-	General anaesthesia
HCO3	-	Bicarbonate
HR	-	Heart rate
IV	-	Intravenous
KCl	-	Potassium chloride
kg	-	Kilogram
L	-	Lumbar
m	-	Meters
MAP	-	Mean arterial pressure
mg	-	Milligram
Min	-	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
Yr	-	Year
α	-	Alpha
β	-	Beta
δ	-	Delta
μ	-	Micro

ABSTRACT

Background and Objectives

The selection of the local anaesthetic to be used for spinal anaesthesia is usually based on the expected duration of surgery and need for early patient discharge. Ropivacaine, a new amino-amide anaesthetic agent has been recently launched in India having various advantages like early onset and shorter duration of action and having lesser cardio toxicity as compared to bupivacaine. The present study was undertaken for comparison of isobaric ropivacaine and isobaric bupivacaine to determine clinical efficacy of ropivacaine.

Methods

This one year randomized clinical trial was undertaken to determine clinical efficacy of ropivacaine. This study was conducted in the Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, attached to Jawaharlal Nehru Medical College, Belgaum during the period of January 2010 to December 2010. A total of 100 patients scheduled for lower abdominal surgeries were randomly divided into two groups of 50 each (Group R received 2 ml of 0.75% isobaric ropivacaine, group B received 2 ml of 0.5% isobaric bupivacaine).

Results

There was no significant difference between the two groups in mean time to onset of sensory block at T10. Maximum sensory block attained in group R ranged between T4 and T6, where as in group B, it ranged between T6 and T8 which was statistically highly significant. Total duration of sensory block was

comparable in both the groups and was not significant. Mean time of onset of motor block was significantly delayed in group R. Duration of motor block was significantly less in group R.

Conclusion and interpretation

Intrathecal, plain solutions containing ropivacaine 15 mg is suitable for lower abdominal surgeries of approximately one hour duration.

Keywords: Bupivacaine; Motor block; Ropivacaine; Sensory block;

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INTRODUCTION

Central neuraxial blockade is probably the most widely used form of regional anaesthesia today. A number of clinical studies suggest that spinal anaesthesia may be superior to general or epidural anaesthesia for certain patients and for certain surgical procedures. The endocrine-metabolic response to surgery appears to be blunted when spinal anaesthesia is employed compared to the response during general anaesthesia (GA).[1]

The advantages of spinal anaesthesia are well established and widely accepted. In the underdeveloped and developing countries spinal anaesthesia still takes a major share in the anaesthesiologists work. Even in the well developed countries spinal anaesthesia technique is enjoying good support from the anaesthesiologists.

Since the development of spinal anaesthesia technique various local anaesthetics such as cocaine, procaine, etidocaine, tetracaine, lignocaine, bupivacaine were tried and studied for their effects. When these drugs were first developed bupivacaine was chosen to be marketed as a long acting local anaesthetic, its advantages compared to lignocaine being long duration of action and differential sensory-motor block. Little further work was carried out on the other drugs in the group.

Bupivacaine, an anilide compound, a most widely used drug for spinal anaesthesia presently, having longer duration of action and associated with few

adverse cardiac effects like arrhythmias and prolonged duration of sensory and motor blockade hence there is a need to overcome these problems.

However, with time, a number of deaths from cardiac arrest were reported in association with regional anaesthesia using bupivacaine. All appeared to be caused by accidental intravenous injection of these long acting local anaesthetics, and the doses required to produce cardiotoxicity seemed to be close to the convulsant doses. These deaths, and subsequent recommendations of the United States Food and Drug Administration (FDA) provided the impetus to develop a safer drug. It was possible that a less fat soluble drug than bupivacaine would be less cardiotoxic.[2]

Several investigators have reexamined the use of older short-acting local anaesthetics such as prilocaine or mepivacaine. Others have tested the efficacy of low dosages of bupivacaine. Hyperbaric 5% lidocaine has recently been reported to be associated with transient radicular irritation following single-dose spinal anaesthesia.

It was noted in 1977 that the propyl derivative of the pipecoloxylidides was less toxic than the butyl derivative (bupivacaine). Further work revealed that the nerve blocking properties of the R and S-enantiomers were similar but that the S-enantiomer was less cardiotoxic. Thus ropivacaine a single (S) stereoisomer was chosen for further development.[3]

Ropivacaine, structurally resembling bupivacaine, with a propyl group on the piperidine nitrogen atom of the molecule is a relatively new amino-amide anaesthetic agent, similar in chemical structure to bupivacaine has been recently

launched in India, for clinical evaluation having various advantages like early onset and shorter duration of action and having lesser cardio toxicity as compared to bupivacaine. The drug ropivacaine, relieves the psychological distress of being immobile for a longer period of time after lower abdominal surgeries.

In view of the above context the present study was undertaken for comparison of isobaric ropivacaine and isobaric bupivacaine to determine clinical efficacy of ropivacaine.

OBJECTIVES

Objectives of the present study were;

Primary objective

To compare the effect of 0.75% plain ropivacaine and 0.5% plain bupivacaine on the duration of motor block.

Secondary objectives

To compare the effects of 0.75% plain ropivacaine and 0.5% plain bupivacaine:

1. On the duration of sensory block.
2. Level of sensory block.

REVIEW OF LITERATURE

HISTORICAL REVIEW

Quincke in 1891 demonstrated a safe, predictable means of performing lumbar puncture. In 1899, August Bier used Quincke's technique to inject cocaine in order to produce operative anaesthesia in six patients, the first real spinal anaesthesia. The first phase in the history of spinal anaesthesia, from 1899 to 1905, was characterized by the use of only cocaine for spinal anaesthesia.[4]

In 1905, Heinrich Braun, a German surgeon, reported the use of procaine for operative spinal anaesthesia. Means for controlling levels of anaesthesia by making procaine solutions hyperbaric by adding glucose, was first reported by Barker in 1907 or hypobaric, by adding alcohol. Synthesis of tetracaine in 1931 and its introduction into clinical practice by Sise in 1935, synthesis of dibucaine and its introduction into clinical practice by Jones in 1930 popularized spinal anaesthesia. Continuous spinal anaesthesia was demonstrated by Lemmon in 1940 and Tuohy in 1945. In 1945, Prickett and associates published their report on the neurologic safety of intrathecal epinephrine to prolong the duration of spinal anaesthesia.[5]

By the mid 1940 spinal anaesthesia reached a peak of its popularity, a popularity soon followed by almost equally widespread avoidance and neglect. The pharmacologic explosion in anaesthesia between 1945 and 1965 made spinal anaesthesia appear unnecessarily demanding, inconvenient and tedious, as well as, at least medico legally unsafe.

Around 1965, spinal anaesthesia began a recovery that has persisted and even accelerated over the last 50 years.[6]

In 1979, Albright published an alarming editorial which associated the long acting local anaesthetics, bupivacaine and etidocaine with cardiac arrest during regional anaesthesia. Albright reported six cases of accidental intravascular injection of either bupivacaine or etidocaine which caused sudden ventricular arrhythmias at the same time as convulsions. Albright subsequently presented his findings to the United States Food and Drug Administration (FDA). This sequence of events provided the impetus to develop a new local anaesthetic drug.[7]

In a study, using isolated sheathed vagus and phrenic nerves of rats, showed that ropivacaine at low concentration (25-50μmol/L) produced a profound and rapid block of both Aδ and C fibres and was more potent than similar concentrations of bupivacaine in blocking these fibres. At higher concentrations had similar blocking activity.[8]

A study on plain bupivacaine by injecting 0.5% or 0.75% plain bupivacaine intrathecally in four groups of 10 patients, Group A received 0.75% bupivacaine 2.7 ml at L_{3-4} Group B 0.5% bupivacaine 4 ml at L_{3-4} Group C 0.7% bupivacaine 2.7 ml at L_{2-3} and Group D 0.75 bupivacaine 2 ml at $L_{3-4.}$ A wide range of height of block was found in each group.[9]

In 1989 a study was conducted to compare the in vitro potency, onset and recovery from block of ropivacaine and bupivacaine using an isolated rabbit vagus nerve model. The effect of varying concentration of ropivacaine and

bupivacaine and the compound action potential of A and C nerve fibres was assessed to determine, whether motor and sensory fibres have different sensitivities to the two agents. The results showed that depressant effect of bupivacaine was 16% greater than that of ropivacaine on motor fibres but only 3% greater on sensory fibres.[10]

In 1991, there appeared several reports of cauda equina syndrome in association with the use of spinal lidocaine, reawakening concern as to the potential toxicity of intrathecal local anaesthetics. Thereafter reports of transient neurologic symptoms (TNS) after the use of spinal lidocaine were followed. This syndrome was characterized by postoperative development (within 24 h) of bilateral aching pain or dysesthesia in the buttocks with radiation into sacral dermatomes of the legs. Symptoms typically abate within a week, although they may persist for longer in up to 10% of patients, and are not associated with other neurologic findings. The syndrome has been repeatedly demonstrated to occur in 10% to 20% of patients after spinal lidocaine, although it occurs only rarely with bupivacaine.[11]

In a study to find out the relative potencies of low dose hyperbaric spinal ropivacaine and bupivacaine and to assess the suitability of spinal ropivacaine for outpatient anaesthesia, ropivacaine and bupivacaine provided dose dependent prolongation of sensory and motor block.[12]

A study compared intrathecal ropivacaine to bupivacaine in 100 patients randomly assigned to receive either 10 mg isobaric bupivacaine or 15 mg isobaric ropivacaine scheduled for transurethral resection of bladder or prostate in the

ratio of 3:2. Onset and offset times for sensory and motor block, mean arterial pressure, pain at surgical site requiring supplemental analgesics were recorded. The study concluded that, 15 mg of intrathecal ropivacaine provided similar motor and hemodynamic effects but less potent anaesthesia than 10 mg of bupivacaine for endoscopic urological surgery.[13]

A study assessed efficacy and safety of two glucose free solutions of ropivacaine that is 7.5 and 10 mg/mL for intrathecal anaesthesia in patients undergoing total hip replacement. Both doses produced similar results in terms of onset and spread of analgesia. All patients achieved adequate sensory block.[14]

A study on clinical comparison of ropivacaine 0.75%, ropivacaine 1% or bupivacaine 0.5% for interscalene brachial plexus block for 45 healthy unpremedicated patients, undergoing elective shoulder surgery reported no differences in success rate between three groups. However seven patients receiving bupivacaine 0.5% required intraoperative analgesic supplementation, compared to one patient receiving ropivacaine 0.75% and two patients treated with ropivacaine 1%.[15]

A study compared extradural ropivacaine and bupivacaine. One hundred and ten patients were studied and received one of five solutions: 0.5, 0.75 or 1% ropivacaine or 0.5 or 0.75% bupivacaine. There was a little difference between the groups with respect to speed of onset or sensory block. The duration of analgesia was increased by increasing the concentration of both drugs, but this has minimal effect on onset time or extent of block.[16]

A study compared plain ropivacaine 5 mg/mL with bupivacaine 5 mg/ml in patients undergoing total hip arthoplasty. Onset of motor and sensory block was rapid with no significant differences between two groups. The median duration of complete motor block was significantly shorter in the ropivacaine group.[17]

Another study compared intrathecal isobaric bupivacaine-morphine and ropivacaine-morphine for caesarean delivery. Both provided effective sensory and motor block. Time to reach complete motor block was shorter and time to recovery from motor block was longer in the bupivacaine-morphine group than in the ropivacaine-morphine group.[18]

In a study a comparison of the effects of intrathecal ropivacaine, levobupivacaine and bupivacaine for caesarean section combined spinal epidural technique was used. Patients were given either isobaric bupivacaine 5 mg, isobaric levobupivacaine 8 mg or isobaric ropivacaine 12 mg, combined with sufentanyl 2.5 μg. It was found that bupivacaine 8 mg was associated with the significantly superior success rate to that observed in levobupivacaine group. It also provided a longer duration of analgesia and motor block.[19]

In a randomized, single-blinded study authors compared the effects of intrathecal ropivacaine with bupivacaine in a dose ratio of 2:1 for outpatient arthroscopic knee surgery. Ninety patients scheduled for outpatient arthroscopic knee surgery received 3 mL solution of either 15 mg of isobaric ropivacaine or 7.5 mg of isobaric bupivacaine and recorded the onset and offset times for sensory and motor block, highest level of sensory block, duration of the sensory

and motor block, first ambulation, urination, and discharge time, mean arterial pressure, and heart rate were recorded. Authors reported that, isobaric ropivacaine 15 mg provided a higher sensory block level and shorter sensorial onset and offset times than 7.5 mg of isobaric bupivacaine. 15 mg of ropivacaine intrathecally is adequate for lower extremity surgery of short duration. Hemodynamic changes were similar between the groups.[20]

In a dose-response study of spinal hyperbaric ropivacaine for caesarean section reported that, the maximum sensory block levels, duration of motor block and rate of hypotension, but not onset of anaesthesia, were significantly related to the ropivacaine dose. The ED50 and ED95 of spinal hyperbaric ropivacaine for caesarean delivery under the conditions of this study were 10.37 mg and 15.39 mg respectively. Study concluded that, ropivacaine is suitable for spinal anaesthesia in caesarean delivery.[21]

A comparison of plain ropivacaine, bupivacaine and levobupivacaine for lower abdominal surgery under spinal anaesthesia, intrathecal administration of either 15 mg bupivacaine, 15 mg ropivacaine, or 15 mg levobupivacaine was well-tolerated and provided similar, effective anaesthesia for lower abdominal surgery. In an equal milligram dose, ropivacaine produced a shorter duration of motor and sensory block than bupivacaine or levobupivacaine, even if this was not associated with a shorter home discharge time. So intrathecal ropivacaine may prove useful when surgical anaesthesia of a similar quality but of a shorter duration than that of bupivacaine or levobupivacaine is desired.[22]

BASIC SCIENCES

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[23]

The vertebral column comprises total of 33 vertebrae and includes 7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral and 4 coccygeal vertebrae. The vertebral column has 4 curves which have significant effect on spread of drugs in sub arachnoid space. Cervical and lumbar curves are convex anteriorly whereas thoracic and sacral curves are convex posteriorly. The highest point of cervical and lumbar curves in supine position are at C5 and L5; lowest points of thoracic and sacral are at T5 and S2 respectively. Main function of vertebral column is to protect the spinal cord.

Vertebral ligaments:[24] 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 sacrum to C5 where it is continued as the ligamentum nuchae.

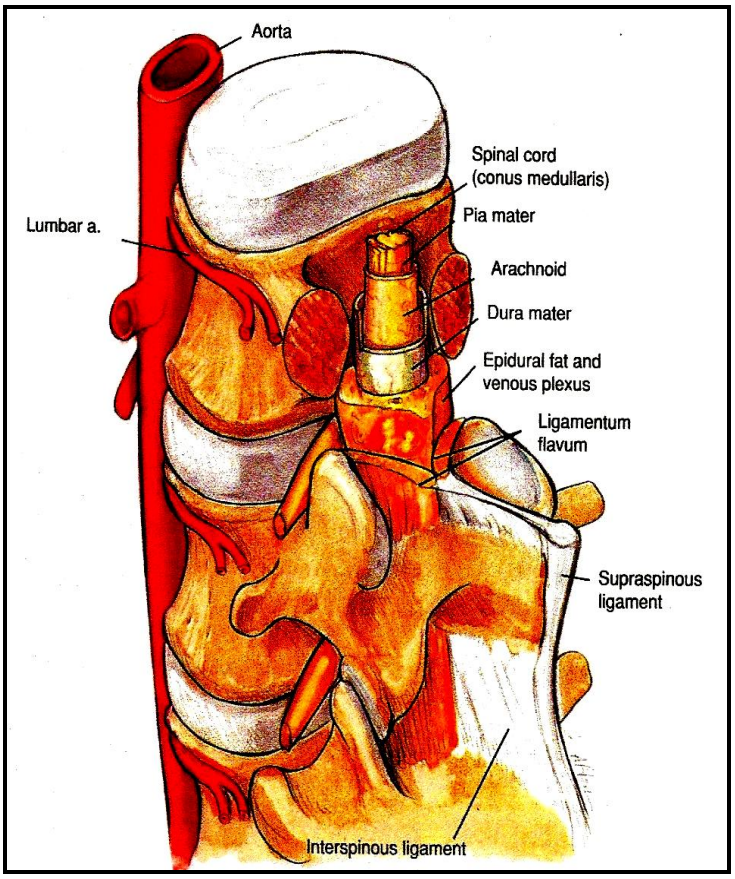


Fig 1: Anatomy of Vertebral Column

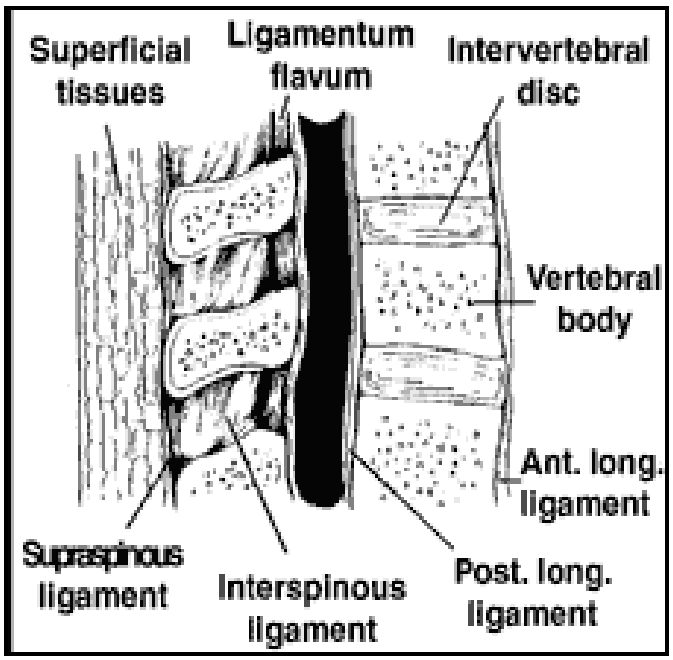


Fig. 2. Anatomy of vertebral column

Interspinous ligament

This is a thin membranous ligament which connects spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament.

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.

Longitudinal ligaments

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

Lumbar vertebrae[25]

A typical lumbar vertebrae consists of

1. A kidney shaped body.
2. Two pedicles directed backwards from the upper part of the body.
3. Two transverse processes which are slender
4. Two laminae meeting posteriorly and enclosing the triangular vertebral foramen.
5. Spinous processes which are thick, broad and quadrilateral in shape.

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

Vertebral canal[25]

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 consists of spinal cord, spinal membranes, adipose tissue, blood vessels, CSF and the roots of the spinal nerves.

Spinal cord[23]

The spinal cord which is the extension of central nervous system into the vertebral canal begins at the level of foramen magnum and ends below as the conus medullaris. At birth spinal cord ends at the level of L3 but rises as age progresses and reaches the lower border of L1 in adults. It measures about 42-45 cm.

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

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

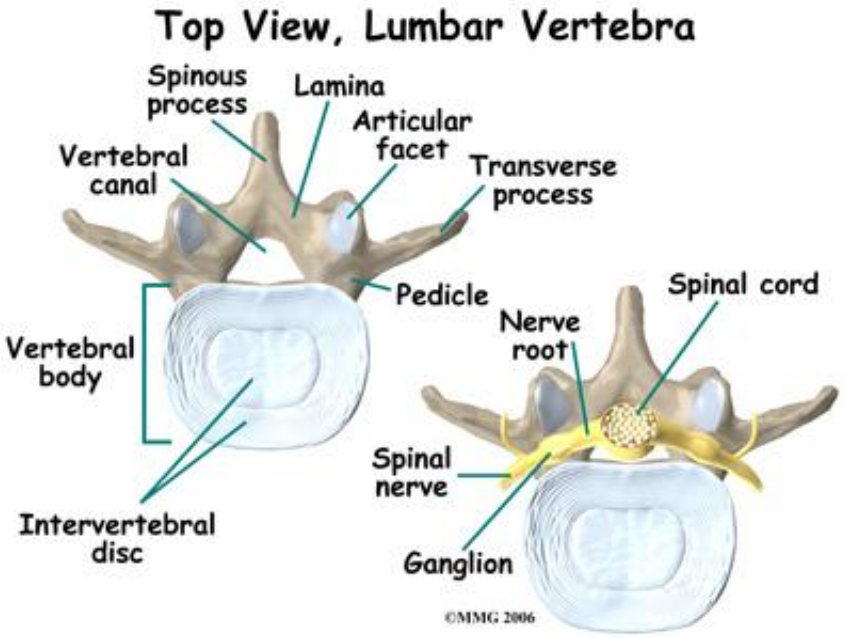


Figure 3: Typical Lumbar Vertebra

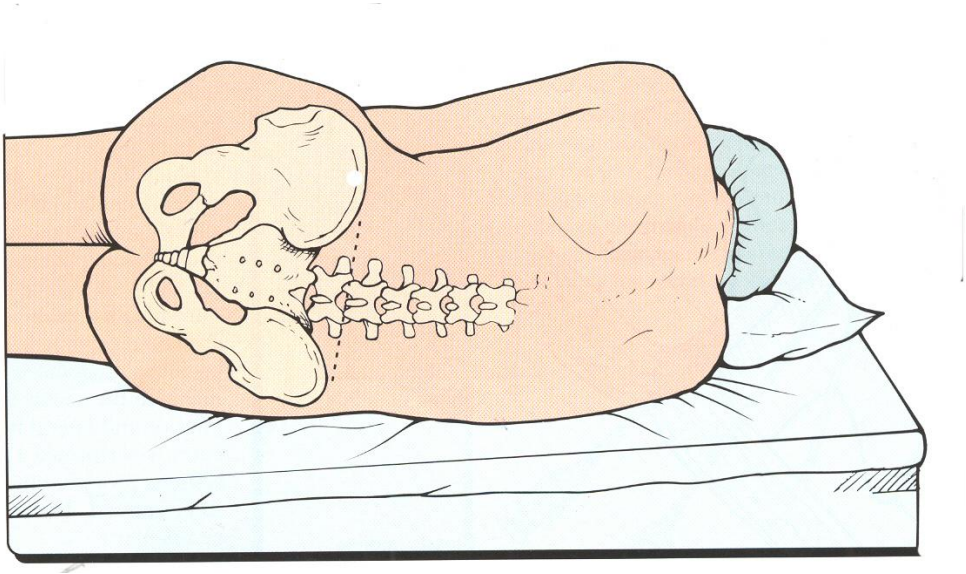


Fig 4: Line of Tuffier[26]

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.

Spinal meninges[27]

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

Dura mater[27]

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

Arachnoid mater[27]

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[27]

It is a delicate highly vascular covering closely investing the spinal cord and brain.

Subarachnoid space[27]

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[27]

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:[27]

Specific gravity:		1.003 to 1.009 at 37^0 c.
Volume	:	120 mL to 150 mL (25 mL to 35mL in spinal space).
CSF pressure	:	60 to 80 mm of Hg in lumbar space.
pH	:	7.27- 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	:	2.0 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 where as steroids have an inconsistent effect. Inhalational anaesthetics like isoflourane and vasoconstrictors decrease the CSF formation. CSF formation is decreased when the serum osmolality increases and increased when the serum is made hypotonic. During equilibrium, rate of formation equals the rate of absorption (500 mL/day).

PHYSIOLOGY OF SUBARACHNOID BLOCK[28]

Physiological responses to intra and extra dural blockade results from autonomic blockade with its effects on both vascular beds and cardiac action from addition of somatic pain and the reflex responses associated with it and from the effects of blockade of motor fibres.

1) Autonomic blockade

Order of blocking nerve fibres,

a) Autonomic pre ganglionic B fibres.

b) Temperature fibres.

c) Pin prick fibres.

d) Fibres conveying pain greater than pin prick.

e) Touch fibres.

f) Deep pressure fibres.

g) Somatic motor fibres.

h) Fibres conveying vibratory sense and proprioceptive impulses.

During recovery, return of sensations in the reverse order assumed, but it has been suggested that sympathetic activity returns before sensation.

In SAB sympathetic fibres are blocked two to three segments higher than sensory fibres and sensory block is two segments higher than motor block.

2) Effects of SAB on cardiovascular system

Spinal block can influence CVS in various ways.

a. Vasodilatation of resistance and capacitance vessels.
b. Block of cardiac efferent sympathetic fibres 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 fibres are blocked as may happen in high spinals above T4 to 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 to cardia and lack of muscular propulsive force in veins.
b. Dilatation of post arteriolar capillaries and small venules due to paralysis of vasoconstrictors.
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 tumours.

3) Effects of SAB on respiratory system

Due to motor blockade and deafferentation, with reduction of sensory input to respiratory centre, breathing becomes quiet during spinal anaesthesia. Intercostal paralysis is compensated by descent of diaphragm which is made easier by lax abdominal wall. This is not accompanied by hypoxia or hypercapnia although the ability to cough forcibly to expel secretions is impaired. Spinal anaesthesia as such does not interfere significantly with gas exchange.

Effects of SAB on gastrointestinal system

SAB up to T5 results in,

a) Narrowing of gut.

b) Active peristalsis.

c) Increase in intraluminal pressure.

d) Relaxation of sphincters.

e) Enlargement of spleen.

f) Nausea and vomiting.

4) Effects of SAB on 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.

5) **Effects of SAB on genito urinary system**

Kidney function is not affected unless severe hypotension is present. The

urinary bladder is relaxed and its spincter is contracted leading to retention of urine. Post spinal injury retention may be moderately prolonged as L2-L3 contains small autonomic fibres and their paralysis lasts longer than that of larger sensory and motor fibres.

The engorgement of flaccid penis due to paralysis of nervigentis is often the first sign of successful block. The tone of uterus is not greatly altered after spinal anaesthesia in pregnancy.

Factors affecting height of analgesia in SAB

a) Specific gravity of solution.

b) Position of patient during and after injection.

c) Volume of solution.

d) Concentration of drug.

e) Rate / force of injection.

f) The site of injection.

g) Pregnancy and intraabdominal tumours.

PHARMACOLOGY

Local anaesthetics are chemical compounds which are capable of reversibly inhibiting the propagation of impulses in nerve cells.

Classification

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

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.[29]

PHARMACOLOGY OF BUPIVACAINE HYDROCHLORIDE

$C_{18}H_{28}N_2o$, HCl

(±) –1–Butyl–N–(2,6–dimethyl phenyl)–2– piperidine–decarboxamide.

It was synthesized in 1957 by Ekemstan and hydrochloride monohydrate was first clinically used in 1963 by L.J.Telivuo.

Structural Formula

CH3CH2CH2CH2NC

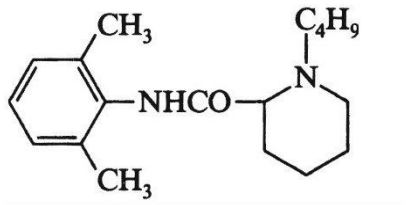


Fig : 5. Chemical structure of bupivacaine

PHYSICOCHEMICAL PROPERTIES

Molecular weight (free base) 342.9 (288.4)

pKa 8.1

Solubility

In alcohol 1 in 8

In water 1 in 25

Octanol / water partition coefficient 346.0

Protein binding 96%

Bupivacaine hydrochloride is a white, odourless, crystalline powder with a bitter, numbing taste. It is prepared by chemical synthesis. The hydrochloride salt is available in solution with and without epinephrine. A preparation marketed specifically for intrathecal use contains dextrose.[30]

Mechanism of action

Bupivacaine, like other local anaesthetics prevents the generation and the conduction of the nerve impulse. Their primary site of action is the cell membrane. Conduction block can be demonstrated in squid giant axons from which the axoplasm has been removed.

Local anaesthetics block conduction by decreasing or preventing the large transient increase in the permeability of excitable membranes to Na+ that normally is produced by a slight depolarization of the membrane. This action of local anaesthetics is due to their direct interaction with voltage gated Na+ channels. As the anaesthetic action progressively develops in a nerve the threshold for electrical excitability gradually increases, the rate of rise of the action potential declines, impulse conduction slows, and the safety factor for conduction decreases. These factors decrease the probability of propagation of the action potential, and nerve conduction eventually fails.[31]

Toxicity of Bupivacaine

It is relatively free of side effects if administered in an appropriate dosage. It is more cardiotoxic than lignocaine and this is made worse by hypoxia, hypercapnia and by pregnancy.

1. Central nervous system toxicity:

CNS is more susceptible to bupivacaine. The initial symptoms involve feeling of light headedness and dizziness followed by visual and auditory disturbance. Disorientation and occasional feeling of drowsiness may occur. Objective signs are usually excitatory in nature which includes shivering, muscular twitching and termors; 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 $PaCO_2$ enhance cerebral blood flow, so that more anaesthetic is delivered rapidly to the brain.[32]

2. Cardiovascular system toxicity:

Bupivacaine depresses rapid phases of depolarization (V_{max}) in purkinge fibres and ventricular musculature to a greater extent than lignocaine. It also decreases the rate of recovery from a dependent block than that of lignocaine. This leads to incomplete restoration of V_{max} between action potential at high rates, in contrast to complete recovery by lignocaine. This explains why lignocaine has antiarrhythmic property while bupivacaine has arrhythmogenic potential. High level of bupivacaine prolongs conduction time through various parts of heart and extremely high concentration will depress spontaneous pacemaker activity, resulting in bradycardia and arrest. Cardiac resuscitation is more difficult following bupivacaine induced cardiovascular collapse and hypoxia along with acidosis which markedly potentiates cardiac toxicity.

Bretylium but not lignocaine could raise the ventricular tachycardia threshold that was lowered by bupivacaine.

Pregnancy enhances the cardiotoxicity of bupivacaine. 0.75% is no longer recommended for use in labour analgesia.[33]

3. Respiratory system:

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

4. Autonomic nervous system:

Myelinated preganglionic beta fibres have a faster conduction time and are more sensitive to the action of local anaesthetic including bupivacaine. Involvement of preganglionic sympathetic fibres is the cause of widespread vasodilation and consequent hypotension that occurs in epidural and paravertebral block. When used for conduction blockade all local anaesthetic particularly bupivacaine produces higher incidence of sensory blockade than motor fibres.

Pharmacokinetics of Bupivacaine

Bupivacaine is rapidly absorbed from the site of injection, the rate of rise in plasma concentration and the peak plasma concentration depending on the particular local anaesthetic technique being used. There is also some inter

individual variation, and peak systemic concentrations may occur between 5 and 30 min after administration.

1. Absorption

The site of injection, dose and addition of a vasoconstrictor determine systemic absorption of bupivacaine. The maximum blood level of bupivacaine is related to the total dose of the drug administered from any particular site.

2. Distribution

This can be described by a two compartment model. The rapid distribution phase a) is believed to be related to uptake by rapid equilibrating tissue (i.e., tissues that have high vascular perfusion). The slow distribution phase B) 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 extracted by lung tissue. Though skeletal muscle does not show particular affinity for bupivacaine it is the largest reservoir of the drug.

Distribution characteristics of Bupivacaine

1. $T_{1/2}$ a (min) – 2.7
2. $T_{1/2}$ B (min) – 28
3. Volume of distribution at steady state (L) – 72.
4. Clearance (L/min) – 0.47.

3. Biotransformation and excretion

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

Dosage

Maximal dose is 2mg/kg body weight (25-30 mL 0.5% solution) and the strength used is 0.125% - 0.75%.[34]

PHARMACOLOGY OF ROPIVACAINE

Introduction

Ropivacaine is a new long acting local anaesthetic drug belonging to the amino amide group. Though it was synthesized by Ekenstam[35] in 1957 and belongs to the same group as that of bupivacaine and mepivacaine, pipecoloxylidides local anaesthetics, ropivacaine was introduced to clinical practice in 1996.

Historically Bupivacaine was used as it had a long duration of action,but subsequently it was found that "propyl derivatives" of pipecoloxylidides were less toxic than 'butyl derivatives' (bupivacaine). Thus Ropivacaine was developed after bupivacaine was noted to be associated with significant number of cardiac arrests.[7] Despite being in the market for close to three decades internationally, it was only introduced into the Indian market very recently.

It is the first local anaesthetic to be presented as an almost pure S-enantiomer (> 99% pure)[36] It is used as local anaesthestic including infiltration, nerve block, epidural and of late for intrathecal anaesthesia in adults and children over 12 years of age. It is also used for peripheral nerve blocks and caudal epidural in children 1 to 12 years of age for surgical pain relief.

CHEMICAL STRUCTURE

Ropivacaine is an amino-amide class of local anaesthetic chemically described as S-(-)-1-propyl-2',6'-pipecoloxylidide hydrochloride monohydrate. The International Union of Pure and Applied Chemistry name is (S)-N-(2,6-

dimethylphenyl)-1-propylpiperidine-2-carboxamide. The drug substance is a white crystalline powder, with a molecular formula of $C_{17}H_{26}N_2O$•HCl•H_2O and a molecular weight of 328.89. the chemical structure is given in the figure 5.

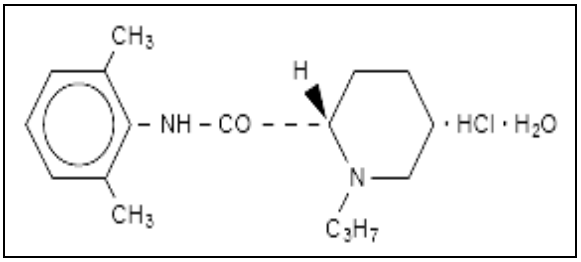


Fig : 6. Chemical structure of ropivacaine

Physical Properties

At 25°C ropivacaine HCL has a solubility of 53.8 mg/mL in water, a distribution ratio between n-octanol and phosphate buffer at pH 7.4 of 14:1 and a pKa of 8.07 in 0.1 M KCl solution. The pKa of ropivacaine is approximately the same as bupivacaine (8.1). However, ropivacaine has a lower lipid solubility owing to (substitution of pipecoloxylidine with a 3-carbon side chain instead of a 4–carbon side chain)[37] compared to bupivacaine and mepivacaine. Usually sodium hydroxide or hydrochloric acid is added to adjust pH of the compound. Ropivacaine is preservative free and is available in single dose containers in 2 (0.2%), 5 (0.5%), 7.5 (0.75%) and 10 mg/mL (1%) concentrations .The specific gravity of solutions range from 1.002 to 1.005 at 25°C.

Mechanism of Action

Ropivacaine reversibly interferes with the entry of sodium in nerve cell membranes, leading to decreased permeability to sodium and thus

a. Block generation and conductance of nerve impulses.

b. Slows propagation of nerve impulses

c. Reduce the rate of rise of action potential

Most local anaesthetics block the unmyelinated C and myelinated Aδ fibres that transmit pain impulses at the same rate. However the rate of blockade of Aα and Aβ (that carry motor impulses) depends on the physicochemical properties, Pka and lipid solubility of the individual local anaesthetic drugs. As ropivacaine is less lipid soluble when compared to bupivacaine , the blockade of Aα and Aβ is slow and hence produce less motor blockade than bupivacaine. Studies of lumbar epidural block in humans have confirmed that equal volumes and concentrations of bupivacaine and ropivacaine produce similar degree of sensory block while the motor block produced by ropivacaine is slower in onset, less in intensity and short in duration. Clinically the order of blockade of nerve fibres is autonomic, sensory and motor, while the disappearance occurs in reverse order. The order of the loss of nerve function is

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

Pharmacokinetics

Absorption

The systemic concentration of ropivacaine is dependent on the total dose and concentration of drug given, the route of administration, the patient's haemodynamic condition and the vascularity of the site of administration. Ropivacaine from the epidural space shows complete and biphasic absorption. The half lives of the 2 phases (mean ± SD) are 14±7 minutes and 4.2±0.9 h, respectively.

Distribution

After intravascular infusion, ropivacaine has a steady state of distribution of 41±7 litres. It is a 94% protein bound, mainly to α1-acid glycoprotein. Ropivacaine readily crosses the placenta.

Metabolism

Ropivacaine is extensively metabolized in the liver, predominantly by aromatic hydroxylation mediated by cytochrome P450 1A to 3-hydroxy ropivacaine. After a single IV dose, approximately 37% of the total dose is excreted in the urine as both free and conjugated 3-hydroxy ropivacaine. Low concentration of 3-hydroxy ropivacaine have been found in the plasma.An additional metabolite, 2-hydroxy-methyl-ropivacaine has been identified but not quantified. N-de-alkylated metabolite of ropivacaine and 3OH-ropivacaine are the major metabolites excreted in urine during epidural infusion.

Elimination

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

POTENCY[37]

Lipid solubility appears to the primary determinant of intrinsic anaesthetic potency. Chemical compounds which are highly lipophilic tend to penetrate the nerve membrane more easily, so that less molecules are required for conduction blockade resulting in enhanced potency. For this reason, a strict correlation between the lipid solubility of the local anaesthetic and its potency and toxicity exists. Mc Donald et al[12] compared three intrathecal doses of ropivacaine and bupivacaine (4, 6 and 8 mg) in healthy volunteers and reported that ropivacaine is half as potent as bupivacaine.

Using the same up-down sequential technique for determining the minimum local anaesthetic concentration (MLAC) producing adequate pain control in 50% of patients receiving an epidural for labour pain[38] and found nearly 50% higher MLAC values[39] for ropivacaine when compared to bupivacaine. A study[40] determined the minimum volume of local anaesthetic to produce an effective block of femoral nerve in 50% of patients within 20 min after the injection similar to that required when using 0.5% bupivacaine.

With ropivacaine 7.5 mg/mL a volume of two to three mL injected into the subarachnoid space (Dose 15 to 22.5 mg) results in a sensory block as high as T5 and T4 respectively. Anaesthesia to pin prick begins in the sacral dermatomes in two to three minutes extends to the T10 level in 10 to 13 minutes and last for approximately two hours.

Intrathecal administration

Intrathecal anaesthesia is useful for ambulatory anaesthesia, requirements of which are a sensory and motor block of adequate duration for the procedure and a fast regression of the motor block to assist mobilisation. The majority of data relating to the efficacy of intrathecal ropivacaine for regional anaesthesia to date are derived from studies of patients undergoing caesarean section or orthopaedic surgery. Ropivacaine has also shown efficacy in several trials in other types of surgery such as perineal surgery,[41] inguinal herniorrhaphy,[42] other lower abdominal or gynaecological procedures[43] and anorectal surgery.[44]

Adverse effects

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

a. Injection site pain

b. **Cardiovascular system toxicity:** Vasovagal reaction, syncope, postural hypotension, non-specific ECG abnormalities.

c. **Gastrointestinal system toxicity:** Fecal incontinence, tenesmus, nausea, vomiting.

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

e. **Liver and Biliary system toxicity:** Jaundice

f. **Metabolic disorders:** Hypomagnesemia

Management of complications

Discontinuation of ropivacaine should be done at the first sign of toxicity. As no specific antidote is available, symptomatic and supportive management should be done promptly. Any change in mentation need oxygen administration. Secure airway and provide assisted ventilation if any signs of respiratory depression are observed. Convulsions can be treated with barbiturates, specific anticonvulsants or neuromuscular blockers. In case of cardiac arrest ,prolonged resuscitative efforts might be required.

Drug interactions

Ropivacaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics, as these are additives. Strong inhibitors of cytochrome P4501A2, such as fluvoxamine can interact with ropivacaine leading to increased ropivacaine

plasma levels. Sixteen possible interactions with drugs known to be metabolized by CYP1A2 via competitive inhibition such as theophylline and imipramine may also occur.

Advantages over other local anaesthetics

Ropivacaine produces a more differential blockade allowing better separation between sensory and motor block and hence a better choice for use in labour analgesia and post op pain relief. When compared to bupivacaine it produces less motor blockade of shorter duration and hence permitting earlier mobilization and discharge. It has a low systemic toxicity than bupivacaine and a better cardiotoxic profile. Ropivacaine has been developed to offer a safer alternative to bupivacaine while retaining the desirable blocking properties of racemic bupivacaine.

The extensive clinical use of ropivacaine through various routes for a variety of surgeries have confirmed a long lasting block similar to that provided by racemic bupivacaine. Another clinically relevant advantage with ropivacaine is greater differentiation between sensory and motor blockade, that is particularly useful if early mobilization is needed to enhance postoperative recovery. Though 40 to 50% less potent than bupivacaine, ropivacaine in a equipotency ratio of 1.5:1 produces results in a similar clinical profile with good preservation of motor function. Ropivacaine is the only local anaesthetic that is specifically approved for use by infusion.[45]

METHODOLOGY

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 during the period of January 2010 to December 2010.

Source of Data

Patients between the age group of 20-50 years of either gender, belonging to ASA Grade I and II scheduled for lower abdominal surgeries were included.

Study design

A one year randomized clinical trial.

Study Period

One year from January 2010 to December 2010.

Sample Size and sampling procedure

By using rule of thumb, 50 samples in each group were considered. Hence, total sample size was 100 patients.

Randomization procedure

Based on the envelope method a total of 100 patients were allocated randomly into group R and group B that is 50 patients in each group.

Selection Criteria

Inclusion criteria

- ASA Grade I and II patients.
- Aged between 20 to 50 years group.
- Patients undergoing lower abdominal surgeries.

Exclusion criteria

- Patients with ASA Grade III and IV.
- Patients associated with cardiac diseases.
- Patients on anticoagulant therapy.

Procedure

The study was approved and ethical clearance was obtained from Human Ethics Committee, Jawaharlal Nehru Medical College, Belgaum. After finding the suitability according to selection criteria patients were selected for the study and briefed about the nature of the study, the interventions used and written informed consent was obtained (Annexure–I). Based on envelope method, patients were randomized into two groups, group R and group B. Further, descriptive data of the patients like name, age, sex, detailed history were obtained and recorded on predesigned and pretested proforma (Annexure-II).

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.

Patients were preloaded with intravenous infusion of 10 mL/Kg of ringers lactate solution 30 minutes prior to surgery.

Preparation of operation room

Boyle's 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. After shifting to the operation theatre, IV access was obtained on the forearm with 18 Gauge IV cannula and IV infusion started with ringer lactate.

Intervention

Group R

Under aseptic precautions, L_{3-4} interspinous space identified, a 25 G Quincke's spinal needle inserted into L_{3-4} subarachnoid space and 2 cc of 15 mg of 0.75% isobaric ropivacaine injected into the space after confirming free flow of clear CSF. Patients were turned immediately to supine position.

Group B

Under aseptic precautions, L_{3-4} interspinous space identified, a 25 G Quincke's spinal needle inserted into L_{3-4} subarachnoid space and 2 cc of 10 mg of 0.5% isobaric bupivacaine injected into the space after confirming free flow of clear CSF. Patients were turned immediately to supine position.

Supplementary oxygen was given through a facemask at 6 L/min.

The level of sensory anaesthesia, defined as the loss of pin prick sensation and was measured every minute until it reached the T10 dermatome level was achieved.

Study variables

Both the groups were monitored for;

- Development of the block.
- The extent of sensory block (Analgesia to pinprick with 27 swg shot bevel dental needle).
- Degree of lower limb motor block (Modified Bromage Scale).
- Non invasive blood pressure (NIBP) (SBP, DBP and MBP), peripheral O_2 saturation (SpO_2) and HR recorded at 2, 4, 6, 8, 10, 15, 20, 30, 40, 50 and 60 minutes.
- Time for onset of sensory block at T10, maximum level of block height, total duration of block were noted.

- Time for onset of motor block, duration of grade 3 block and total duration of motor block were assessed using the Bromage scale as follows;
    - 0 - Free movement of legs and feet
    - 1 - Just able to flex knees with free movement of feet
    - 2 - Unable to flex knees, but with free movement of feet
    - 3 - Unable to move legs or feet.

Hypotension was defined as 20% decrease in blood pressure from baseline values, and was treated with incremental intravenous boluses of mephetermine 6 to 12 mg.

Bradycardia was defined as heart rate less than 60 bpm and treated with IV atropine 0.6 mg.

Statistical Methods

The data was tabulated and master chart was prepared (Annexure IV). Mean and Standard Deviation were calculated for quantitative variables and results on categorical measurements were presented in numbers and percentages.

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 (Inter group analysis).

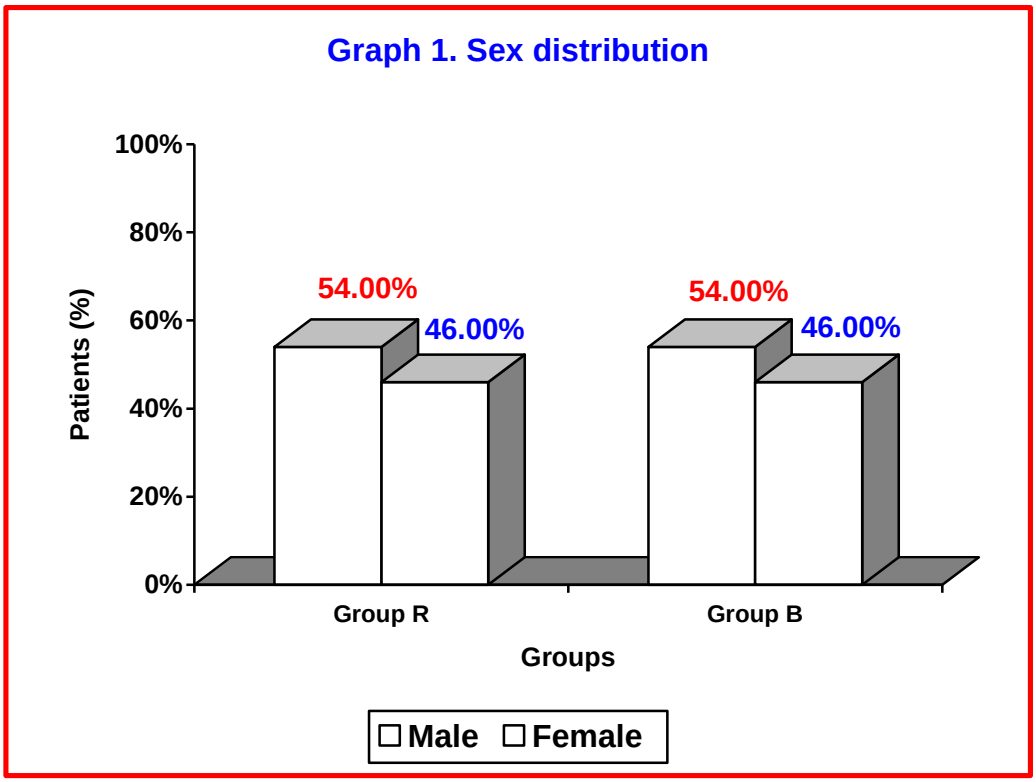
Chi-square test was used to find association between the classes of variables.

RESULTS

This one year randomized clinical trial was conducted in the Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, attached to Jawaharlal Nehru Medical College, Belgaum during the period of January 2010 to December 2010. A total of 100 scheduled for lower abdominal surgeries were randomly divided into two groups of 50 each (Group R received 2 ml of 0.75% isobaric ropivacaine, group B received 2 ml of 0.5% isobaric bupivacaine). The data obtained was tabulated and analysed as below.

Table 1: Sex distribution

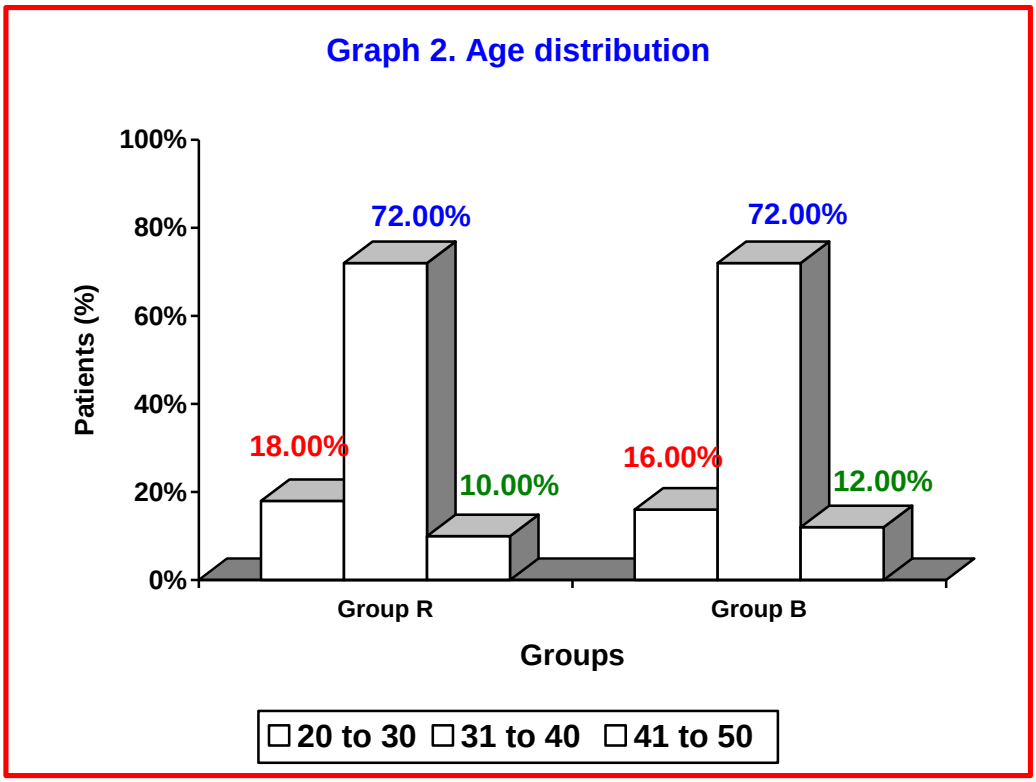
Gender	Group R (n=50)		Group B (n=50)	
	Number	**Percentage**	**Number**	**Percentage**
Male	27	54	27	54
Female	23	46	23	46
Total	**50**	**100**	**50**	**100**



In this study 54% were males and 46% were females in group R and B respectively with male to female ratio of 1.17:1. suggesting both the groups had comparable demographic characteristics. (p=1.00)

Table 2: Age distribution

Age group (Years)	Group R (n=50)		Group B (n=50)	
	Number	Percentage	Number	Percentage
20-30	9	18	8	16
30-40	36	72	36	72
40-50	5	10	6	12
Total	**50**	**100**	**50**	**100**

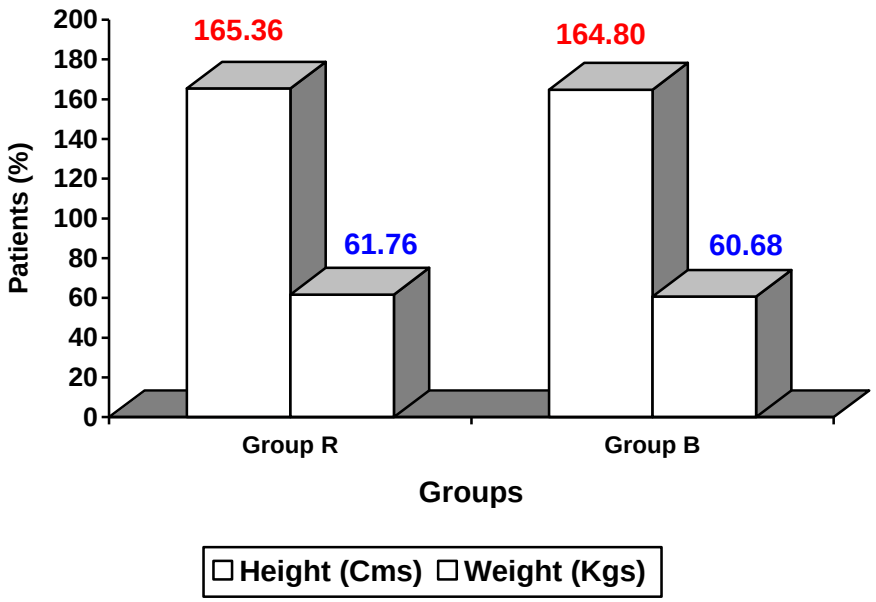


In group R and B most of the patients had age between 31 to 40 years. The mean age in group R was 34.42 ± 5.51 years and in group B was 35.4 ± 5.67 years suggesting both the groups had comparable demographic characteristics.(p=0.9279)

Table 3. Comparison of Height and Weight of patients studied

Variables	Group R (n=50)		Group B (n=50)	
	Mean	**S.D.**	**Mean**	**S.D,**
Height (Cms)	165.36	4.52	164.80	4.92
Weight (Kgs)	61.76	4.60	60.68	5.33

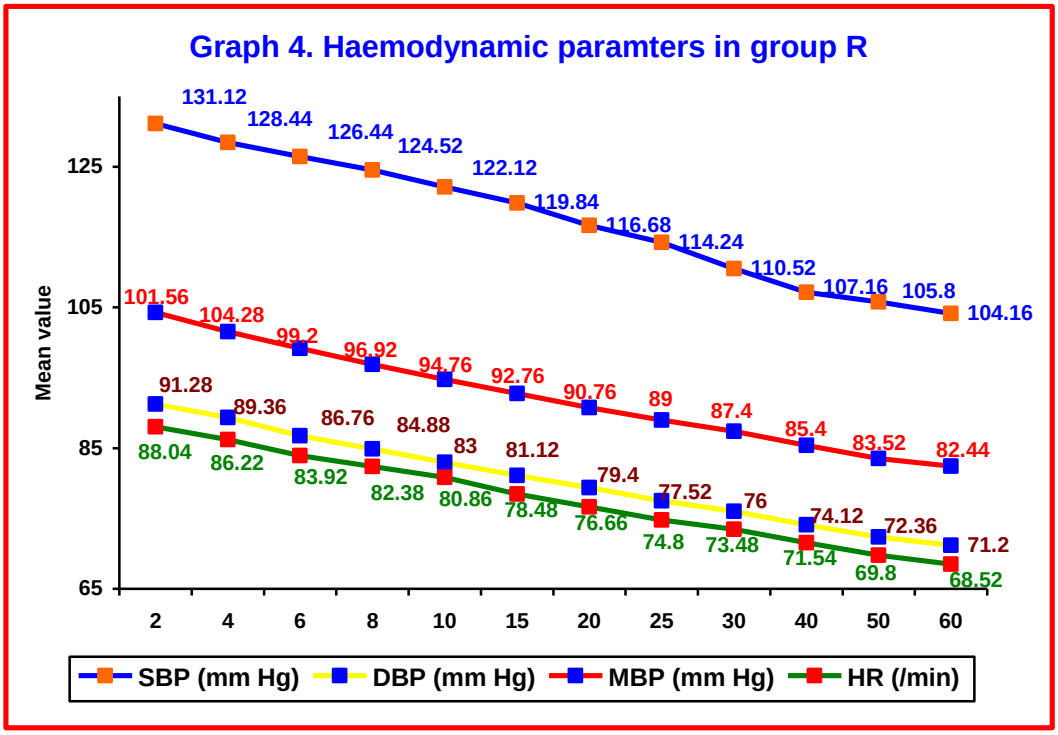
Graph 3. Comparison of Height and Weight of patients studied

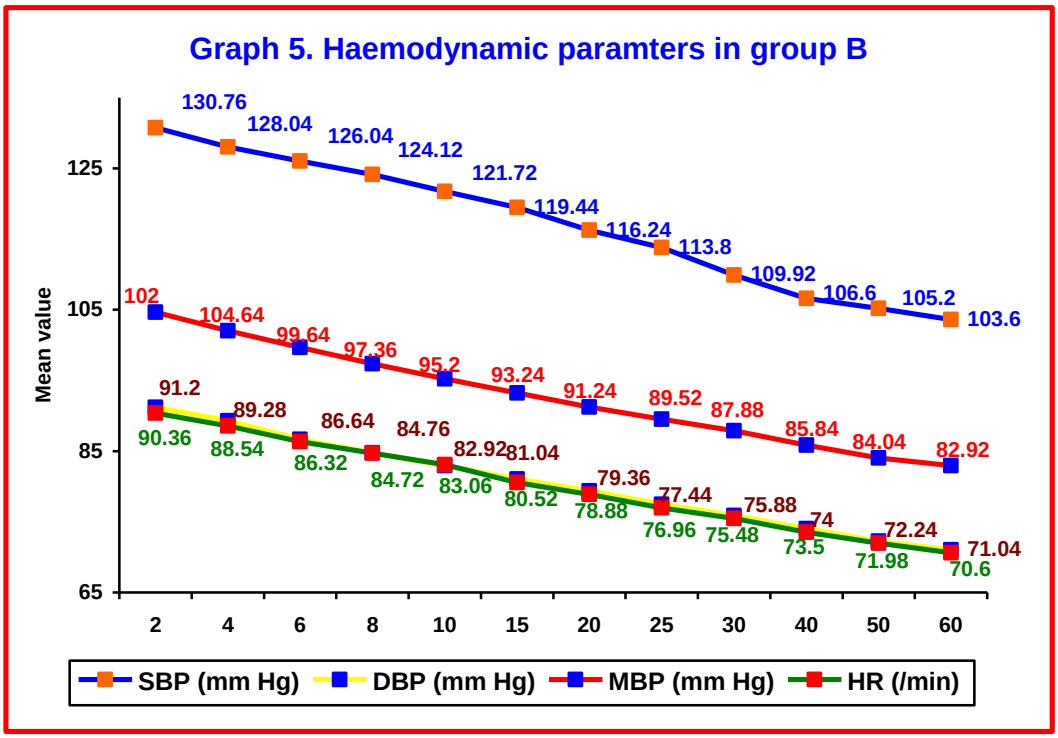


The mean height in group R was 165.36 ± 4.52 cms and in group B it was 164.80 ± 4.92 cms(p=0.5548). The mean weight in group R was 61.76 ± 4.60 Kgs and in group B it was 60.68 ± 5.33 Kgs(p=0.2807), suggesting mean weight and height in both the groups were comparable.

Table 4. Haemodynamic parameters

Time interval (Min)	SBP (mm Hg)		DBP (mm Hg)		MBP (mm Hg)		HR (/min)	
	Mean	**S.D.**	**Mean**	**S.D.**	**Mean**	**S.D.**	**Mean**	**S.D.**
Group R								
2	131.12	5.64	91.28	3.95	104.28	4.50	88.04	5.83
4	128.44	5.43	89.36	3.58	101.56	4.84	86.22	5.86
6	126.44	5.43	86.76	3.72	99.20	4.43	83.92	6.05
8	124.52	5.65	84.88	3.98	96.92	4.66	82.38	5.67
10	122.12	5.68	83.00	3.98	94.76	4.57	80.86	5.98
15	119.84	5.40	81.12	3.98	92.76	4.68	78.48	6.00
20	116.68	7.16	79.40	3.94	90.76	4.68	76.66	6.40
25	114.24	6.97	77.52	4.05	89.00	5.02	74.80	6.40
30	110.52	8.01	76.00	4.26	87.40	4.80	73.48	6.35
40	107.16	9.00	74.12	4.49	85.40	4.45	71.54	6.26
50	105.80	8.66	72.36	4.64	83.52	4.91	69.80	6.31
60	104.16	8.65	71.20	4.76	82.44	4.61	68.52	5.92
Group B								
2	130.76	5.83	91.20	3.94	104.64	4.30	90.36	5.45
4	128.04	5.65	89.28	3.56	102.00	4.61	88.54	5.44
6	126.04	5.65	86.64	3.71	99.64	4.21	86.32	5.90
8	124.12	5.75	84.76	3.98	97.36	4.51	84.72	5.67
10	121.72	5.81	82.92	3.98	95.20	4.43	83.06	5.82
15	119.44	5.53	81.04	4.03	93.24	4.61	80.52	5.91
20	116.24	7.20	79.36	3.97	91.24	4.61	78.78	6.18
25	113.80	6.99	77.44	4.04	89.52	4.96	76.96	6.09
30	109.92	8.15	75.88	4.21	87.88	4.79	75.48	6.37
40	106.60	9.06	74.00	4.39	85.87	4.37	73.50	6.34
50	105.20	8.73	72.24	4.58	84.04	4.92	71.98	6.60
60	103.60	8.64	71.04	4.61	82.92	4.61	70.60	6.24

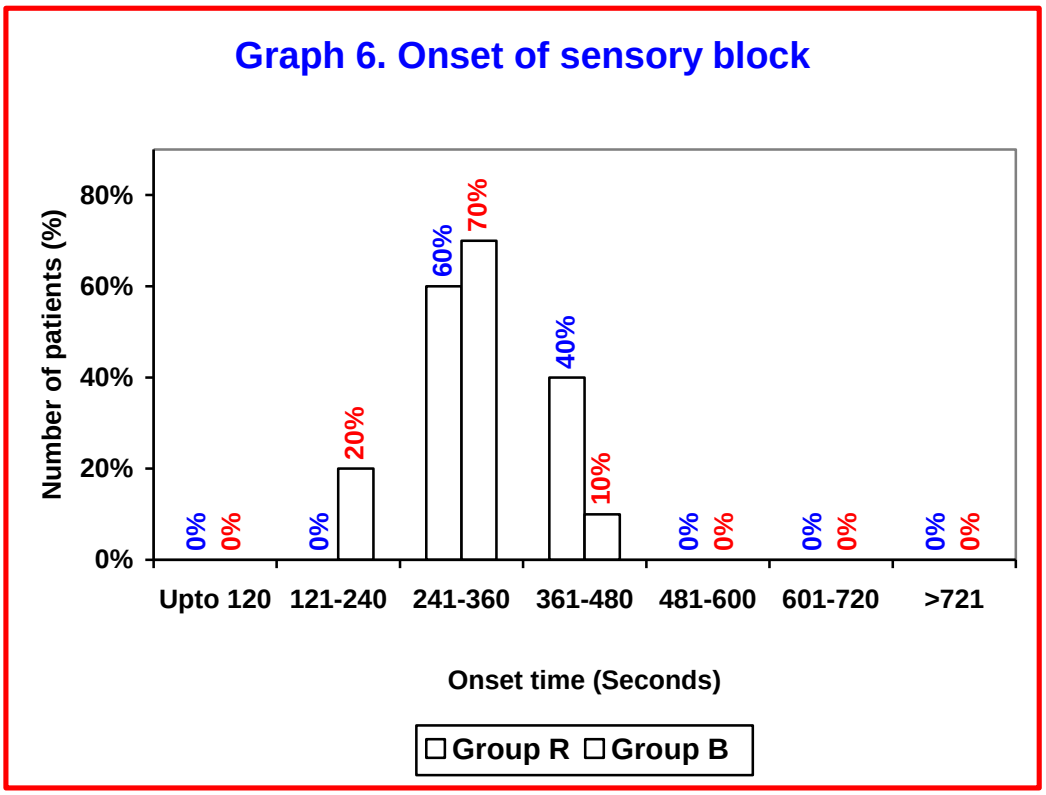




The haemodynamic parameters in group R and B were as shown in table 5 and graph 5, 6.

Table 5. Onset of sensory block

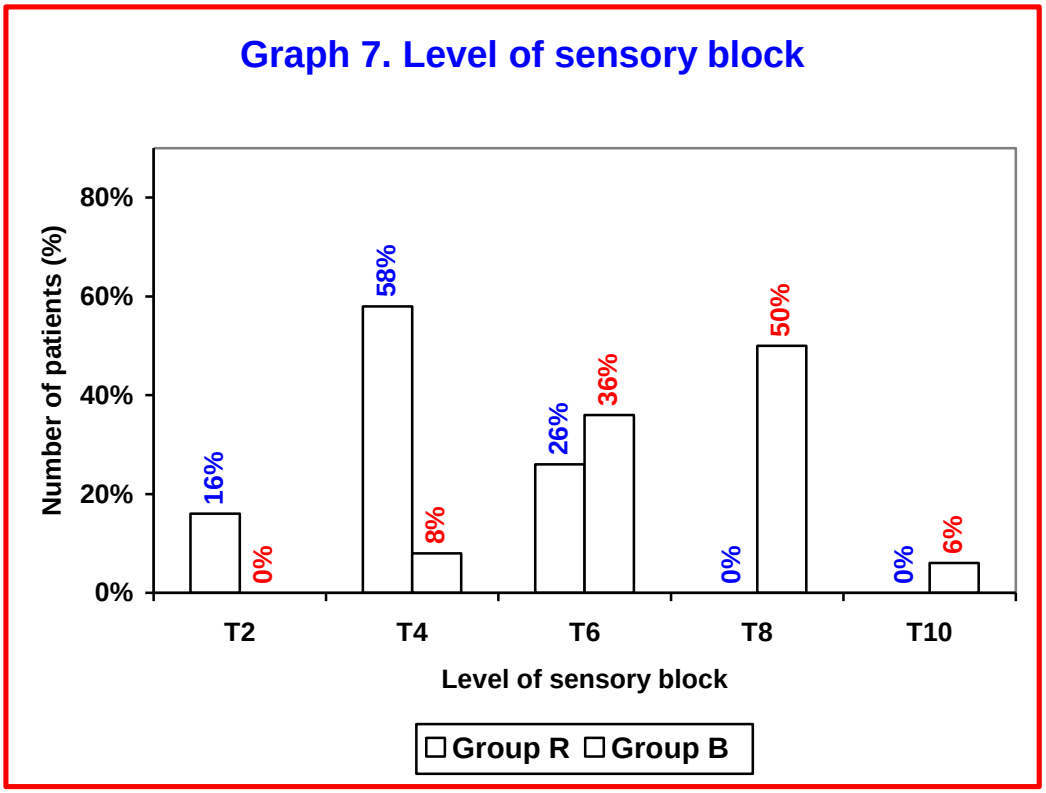
Onset (Seconds)	Group R (n=50)		Group B (n=50)	
	Number	Percentage	Number	Percentage
Upto 120	0	0	0	0
121-240	0	0	10	20
241-360	30	60	35	70
361-480	20	40	5	10
481-600	0	0	0	0
601-720	0	0	0	0
>721	0	0	0	0
Total	**50**	**100**	**50**	**100**



Onset of sensory blockade at T10 was achieved between 241 to 360 seconds in 60% of patients from group R and 70% of patients in group B, the remaining (40%) patients in group R had sensory blockade between 361 to 480 seconds but 20% of patients from group B had blockage between 121 to 240 seconds. The mean onset of sensory blockade at T10 in group R was more (374.40 ± 60.00 seconds) compared to group B (315.60 ± 59.4 seconds) and this difference was statistically significant ($p<0.0001$).

Table 6. Level of sensory block

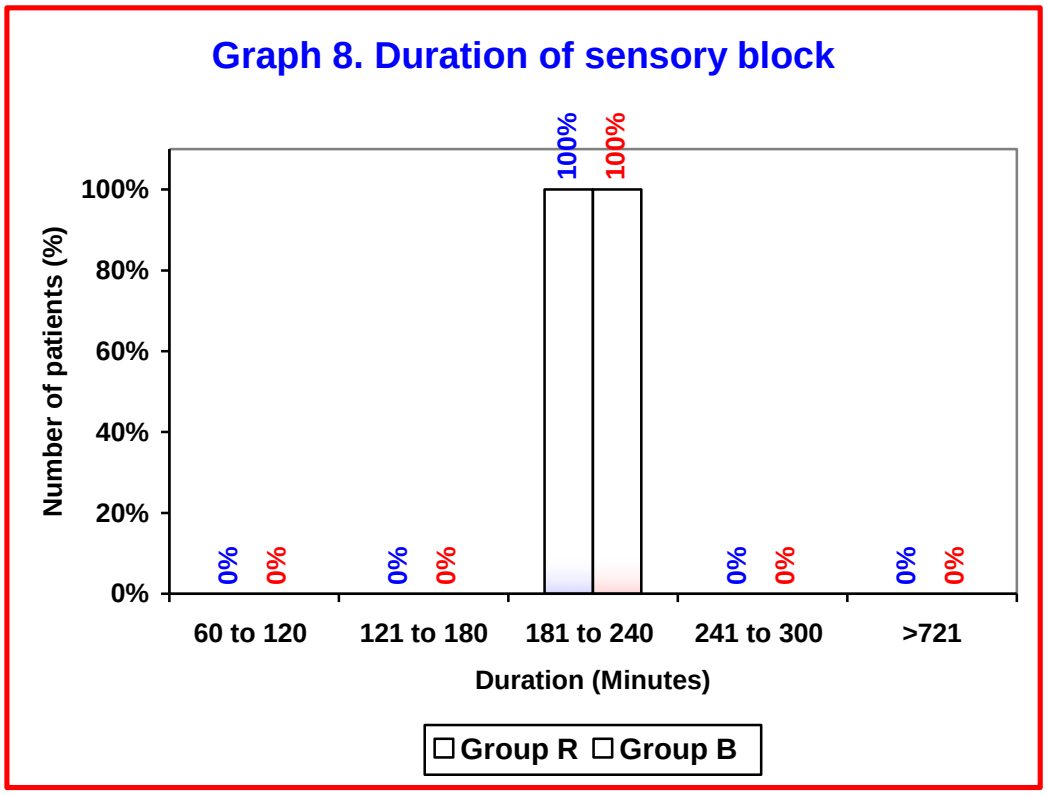
Level	Group R (n=50)		Group B (n=50)	
	Number	Percentage	Number	Percentage
T2	8	16	0	0
T4	29	58	4	8
T6	13	26	18	36
T8	0	0	25	50
T10	0	0	3	6
Total	**50**	**100**	**50**	**100**



Most of the patients (58%) in group R had T4 level of the sensory block compared to T8 in group B (50%). However in group R 26% patients had T6 and 16% had T2 levels of block compared to 36% with T6, 8% with T4 and 6% with T10.Higher block was achieved with group R which was statistically significant ($p<0.0001$)

Table 7. Duration of sensory block

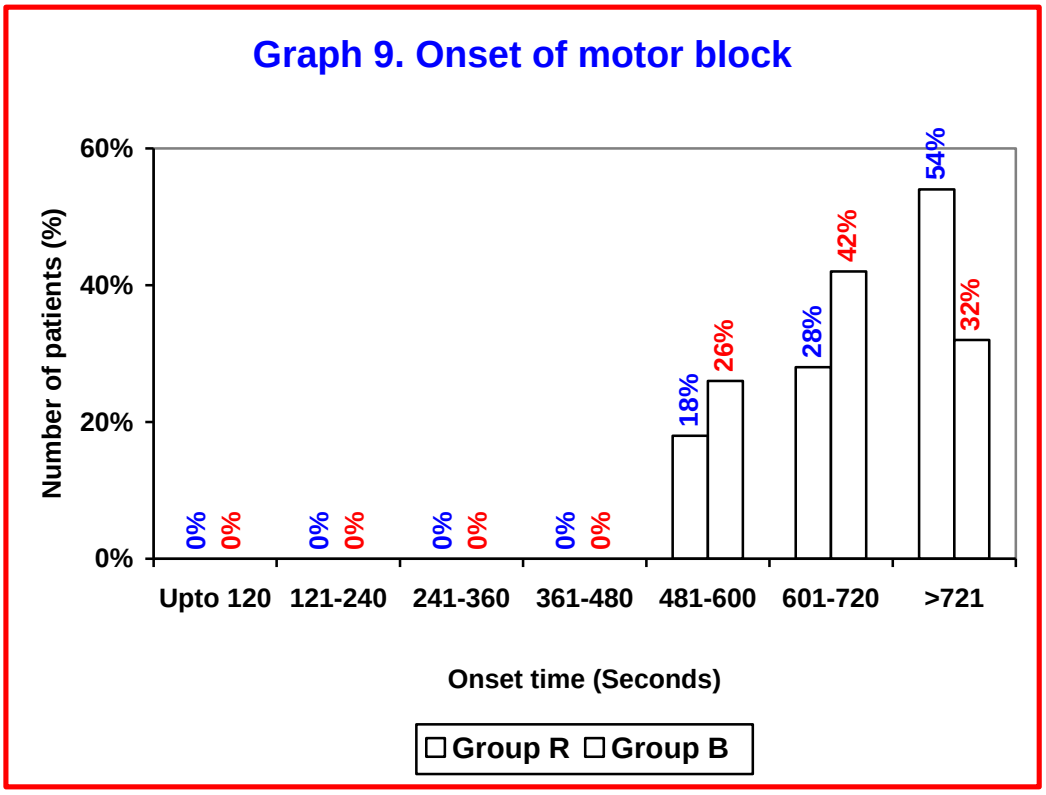
Duration (Minutes)	Group R (n=50)		Group B (n=50)	
	Number	Percentage	Number	Percentage
60-120	0	0	0	0
121-180	0	0	0	0
181-240	50	100	50	100
241-300	0	0	0	0
Total	**50**	**100**	**50**	**100**



In all the patients (100%), the duration of sensory block was between interval of 181 to 240 minutes in both the groups at T10. The mean duration of sensory block at T10 in group R was 191.24 ± 3.41 minutes which was almost similar when compared to group B (191.38 ± 3.56 minutes) (p=0.841).

Table 8. Onset of motor block

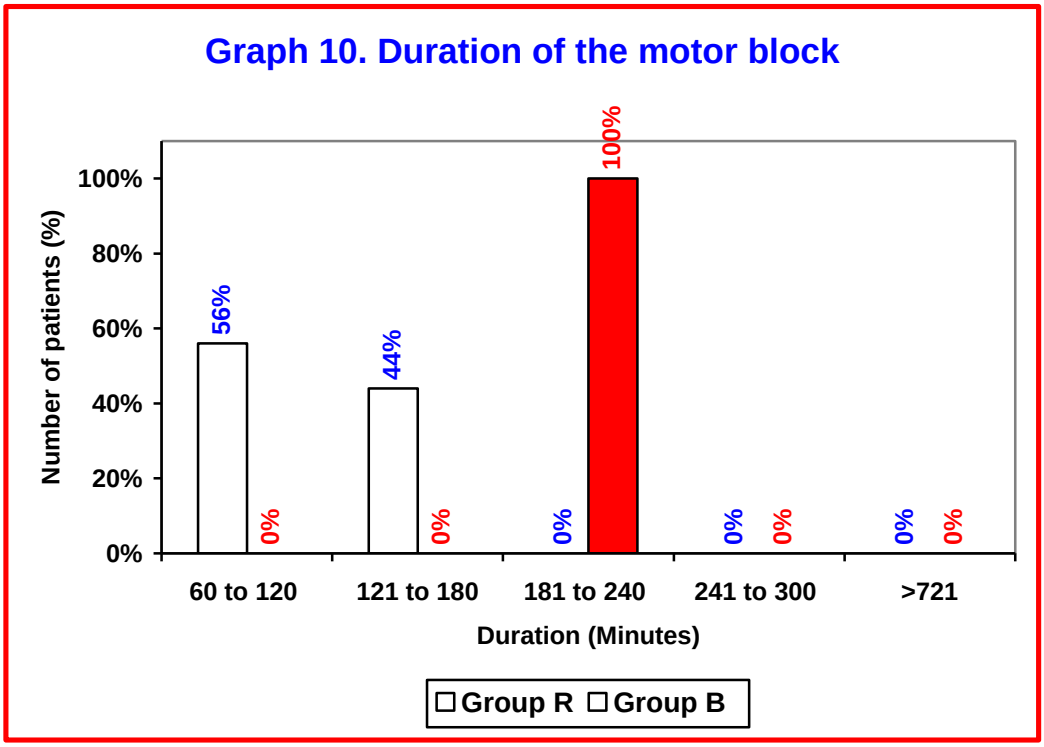
Onset (Seconds)	Group R (n=50)		Group B (n=50)	
	Number	Percentage	Number	Percentage
upto 120	0	0	0	0
121-240	0	0	0	0
241-360	0	0	0	0
361-480	0	0	0	0
481-600	9	18	13	26
601-720	14	28	21	42
>721	27	54	16	32
Total	**50**	**100**	**50**	**100**



Onset of motor blockade was achieved after 721 seconds in 54% of patients from group R and 42% of patients in group B had onset between 601 to 720 seconds. In the remaining patients of group R 28% had motor blockade between 601 to 720 seconds and 18% between 481 to 600 seconds but in group B 32% of patients had blockage after 721 seconds and 26% between 481 to 600 seconds. The mean onset of motor blockade in group R was more (790.80 ± 154.20 seconds) compared to group B (583.20 ± 101.40 seconds) and this difference was statistically significant ($p<0.0001$).

Table 9. Duration of the motor block

Duration (Minutes)	Group R (n=50)		Group B (n=50)	
	Number	Percentage	Number	Percentage
60-120	28	56	0	0
121-180	22	44	0	0
181-240	0	0	50	100
241-300	0	0	0	0
Total	**50**	**100**	**50**	**100**



The duration of motor block in 56% of patients from group R was between 60 to 120 minutes and 121 to 180 minutes in 44% patients whereas in group B among all the patients the duration of motor block was between 181 to 240 minutes. This was statistically significant ($p<0.0001$).

Table 10. Duration of mean motor block

Duration of motor block	Group R		Group B	
	Mean	**S.D.**	**Mean**	**S.D.**
Minutes	121.04	4.59	189.92	4.48

The mean duration of motor block in group R was 121.04 ± 4.59 minutes which was significantly less when compared to group B (189.92 ± 4.48 minutes) ($p<0.0001$).

DISCUSSION

The first clinical report of spinal anaesthesia was in the year 1899 by Dr August Bier, who described the intrathecal administration of cocaine.[4] Since then a lot of experience and data have been achieved on physiology, pharmacology, and clinical application of spinal anaesthesia. Moreover technological and pharmaceutic studies have enhanced our clinical practice while new approaches as well as special techniques have been developed to produce central neuraxial blocks. The greatest challenge of the technique is to control the spread of the local anaesthetic through the cerebrospinal fluid (CSF) in order to produce a block that is adequate for the proposed surgery without producing a needless extensive spread.

Subarachnoid block is a commonly employed anaesthetic technique for performing lower abdominal surgeries. It is a safe, inexpensive and easy-to-administer technique which also offers a high level of post–anaesthesia satisfaction for patients. The technique is simple, has rapid onset and is reliable. The risk of general anaesthesia including mishaps due to airway management are avoided by this technique.

The selection of the local anaesthetic to be used for spinal anaesthesia is usually based on the expected duration of surgery and need for early patient discharge. Because of the important changes in the health care system organization there is a surge in the number of surgical procedures performed on an outpatient basis and spinal anaesthesia has also become very popular for such procedures.

Lidocaine in doses ranging from 50 mg to 100 mg is widely used for surgical procedures lasting up to one hour.[46] For shorter surgery the dose can be reduced to 40 mg providing an adequate surgical block with times for complete regression of spinal block of about two hours and readiness for hospital discharge three hours after spinal injection.[47,48] The use of doses of spinal lidocaine as low as 20 mg has been described for outpatient procedures with high patient satisfaction and very rapid recovery and discharge, but only with the addition of small doses fentanyl (20 µg).[49]

However, in spite of its wide use and long history, the overwhelming evidence of transient neurologic symptoms associated with spinal lidocaine.[50,51] has raised strong concerns with its use, especially for day care surgery.[51] Mepivacaine is another amide local anaesthetic with a clinical profile similar to lidocaine. Nevertheless, it is associated with a similarly high incidence of transient neurologic symptoms.[52,53]

Theoretically, procaine and prilocaine could be good alternatives to lidocaine for short spinal anaesthesia.[50] but they are not extensively accessible for intrathecal administration around the world. A dose of 100 mg of procaine 10% provides similar onset time, shorter resolution of nerve block, and lower incidence of transient neurologic symptoms than the same dose of 5% lidocaine.[54] Nonetheless, spinal procaine has also been reported to be associated with a higher failure rate,[55,56] incidence of nausea and vomiting than lidocaine, with delayed home discharge times.[56] Prilocaine used in the same doses of lidocaine provides a similar clinical profile,[49] with the advantage of a lower incidence of transient neurologic symptoms.[57,58]

Recent studies have shown that a procaine derivative, 2-chloroprocaine (2-CP), shows ideal characteristics to be used in short outpatients procedures. 30 mg of 2-CP provides similar results to 80 mg of procaine on anaesthesia and patient tolerance.[59]

Doses ranging between 40 and 50 mg of 1% plain 2-chlorprocaine have been reported to provide adequate surgical block in outpatients undergoing lower limb surgery of 45-60 min duration, while reducing the dose of 2-chloroprocaine to 30 mg may be adequate only for very short procedures.[60] Comparing 50 mg of 1% lidocaine and 1% 2-chloroprocaine for outpatient knee arthroscopy, we recently reported that 2-chloroprocaine provided a faster onset of spinal anaesthesia, with a more rapid recovery of sensory/motor function, unassisted ambulation and a lower incidence of transient neurologic symptoms compared to spinal anaesthesia with lidocaine.[61]

Long acting agents such as bupivacaine (with doses ranging between 10 and 20 mg of either plain or hyperbaric solutions) and tetracaine (with doses ranging between 8 and 16 mg of either plain or hyperbaric solutions) are widely used to give spinal anaesthesia for surgical procedures lasting up to 2-2.5 hours.[50]

The use of long acting agents is associated with a lower risk for transient neurologic dysfunction.[50,52,53,57] With the increasing concerns on the incidence of neurologic dysfuntions after spinal lidocaine, the use of small doses of long acting agents has also been investigated to provide unfailing spinal anaesthesia for short procedures[62] 5 to 8 mg bupivacaine (used with plain, hypo- or hyperbaric solutions) have been demonstrated to provide reliable spinal

anaesthesia for outpatients with recovery times comparable to those of 40-60 mg lidocaine.[14,63,64]

The efficacy and safety of intrathecal administration of both plain and hyperbaric solutions of ropivacaine have been evaluated in different clinical settings including orthopaedic,[65] urological surgery,[66] caesarean section and labour pain.[38,67]

Bupivacaine is the local anaesthetic used rouitnely for surgeries because of its high potency and minimal neurological symptoms. Though cardiotoxicity is not a concern in subarachnoid block, the quality of sensory blockade, motor blockade, hemodynamic changes and side effect profile are some considerations in selecting a drug for spinal anaesthesia.

Ropivacaine, a S-enantiomer of bupivacaine is being increasingly used for spinal anaesthesia in caesarean section, lower abdominal and perineal surgeries including lower limb surgeries. Advantages claimed are shorter duration of motor block with similar sensory block properties compared to bupivacaine. Thus it minimizes the psychological discomfort of being immobile for long time. Also its major advantage is lesser cardiotoxic property compared to bupivacaine.

As for other agents, the use of hyperbaric solutions results in faster onset and higher maximum sensory level, with shorter duration of nerve block.[68] Hyperbaric ropivacaine provides a more consistent block, with a faster onset time and quicker mobilization than plain solutions.[12] Because of its lower lipophilicity, ropivacaine is also 40-60% less potent than bupivacaine.[2] A volunteer study[69] demonstrated that, when used in similar doses, ropivacaine is associated with a

shorter recovery than bupivacaine; thus the use of small doses of ropivacaine could potentially provide some advantages over bupivacaine for outpatient procedures. A study[70] compared the use of 8 mg ropivacaine with bupivacaine for outpatient knee arthroscopy and demonstrated that, ropivacaine provides earlier recovery of motor function and discharge than the same dose of bupivacaine. Similar findings have been also reported when comparing ropivacaine with levobupivacaine for different outpatient procedures.[2,71]

This one year randomized clinical trial was undertaken to determine clinical efficacy of ropivacaine. This study was conducted in the Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, attached to Jawaharlal Nehru Medical College, Belgaum during the period of January 2010 to December 2010. A total of 100 patients between the age group of 20 to 50 years of either gender, belonging to ASA Grade I and II scheduled for lower abdominal surgeries were assessed.

The equipotent ratio between Ropivacaine and Bupivacaine is considered to be 3:2 or 2:1.[2] In a dose finding study[72] of Ropivacaine for caesarean section, noted that ED50 of isobaric Ropivacaine for anaesthesia for caesarean section was 16.7 mg (14.1 – 18.8 mg) and ED 90 was 26.8 mg. Hence a equipotent dose of 15 mg of ropivacaine was used for the study.

In this study 54% were males and 46% were females in group R and B respectively with male to female ratio of 1.17:1. In group R and B most of the patients had age between 31 to 40 years. The mean age in group R was 34.42 ± 5.51 years and in group B was 35.4 ± 5.67 years suggesting both the groups had

comparable demographic characteristics. The mean height in group R was 165.36 ± 4.52 cms and in group B it was 164.80 ± 4.92 cms. The mean weight in group R was 61.76 ± 4.60 Kgs and in group B it was 60.68 ± 5.33 Kgs suggesting mean weight and height in both the groups were comparable.

In this study onset of sensory blockade was achieved between 241 to 360 seconds in 60% of patients from group R and 70% of patient in group B at T10. The remaining (40%) patients in group R had sensory blockade between 361 to 480 seconds but 20% of patient from group B had blockage between 121 to 240 seconds. The mean onset of sensory blockade at T10 in group R was more (374.40 ± 60.00 seconds) compared to group B (315.60 ± 59.4 seconds) and this difference was statistically significant ($p<0.0001$). These findings correlated well with a study[17] wherein authors reported the median time of onset of sensory block at the T10 dermatome was two minutes in ropivacaine and bupivacaine groups. In contrast, another study[73] reported that, the median onset of analgesia to T10 was 10 min, and this was reached in 24 (80%), 21 (70%), and 24 (80%) patients in the three groups namely ropivacaine 20 mg, ropivacaine 15 mg and bupivacaine 10 mg.

In the present study most of the patients (58%) in group R had T4 level of the sensory block compared to T8 in group B (50%). However in group R 26% patients had T6 and 16% had T2 levels of block compared to 36% with T6, 8% with T4 and 6% with T10 in group B. This higher level achieved with ropivacaine was statically significant($p <0.0001$) whereas, a study[73] reported the highest median extent of sensory block (n=90) did not differ significantly among groups: T7 (T4–T10), T7 (T4–T12), and T9/T10 (T6–T11) in the ropivacaine 20

mg, ropivacaine 15 mg, and bupivacaine 10 mg groups, respectively. Another study[74] noted that, the maximum level of sensory block attained was T7 with ropivacaine and T5 with bupivacaine when 15 mg of hyperbaric ropivacaine and bupivacaine were used for lower abdominal and lower limb surgeries.

In this study, among all the patients (100%), the duration of sensory block at T10 was between the interval of 181 to 240 minutes in both the groups. The mean duration of sensory block at T10 in group R was 191.24 ± 3.41 minutes which was almost similar when compared to group B (191.38 ± 3.56 minutes) (p=0.841). Similar findings were reported in a study[17] whereas another study[73] reported that, the median duration of analgesia at the level of at least T10 (*n*=69; 24 + 21 + 24 patients) was 170, 140, and 140 min, respectively, and with ropivacaine 20 mg, the sensory block lasted significantly longer than with bupivacaine 10 mg (p=0.005) or with ropivacaine 15 mg (p=0.009). In a study[69] authors noted that, time of regression of block to S1 was longer **(**188.56±28.2 min) in bupivacaine group when compared to ropivacaine group (162.56±20.2 min). Observations in another study[81] noted regression to S1 was comparable when either intrathecal isobaric bupivacaine or ropivacaine was used for caesarean delivery.

Onset of motor blockade was achieved after 721 seconds in 54% of patients from group R and 42% of patient in group B had onset between 601 to 720 seconds. In the remaining patients of group R 28% had motor blockade between 601 to 720 seconds and 18% between 481 to 600 seconds but in group B 32% of patient had blockage after 721 seconds and 26% between 481 to 600 seconds. The mean onset of motor blockade in group R was more

(790.80±154.20 seconds) compared to group B (583.20±101.40 seconds) and this difference was statistically significant ($p<0.0001$). In a study[73] the median onset of complete motor block was 20 min, with no significant difference among groups.

In this study, the duration of motor block in 56% of patients from group R was 60 to 120 minutes and 121 to 180 minutes in 44% patients whereas in group B among all the patients the duration of motor block was 181 to 240 minutes. The mean duration of motor block in group R was 121.04 ± 4.59 minutes which was significantly less when compared to group B (189.92 ± 4.48 minutes) ($p<0.0001$). These findings were consistent with a study[17] whereas in another study[73] the median duration of complete motor block was 100, 40, and 100 min, respectively, in the ropivacaine 20 mg, ropivacaine 15 mg, and bupivacaine 10 mg groups. The median offset of motor block was significantly faster in the ropivacaine 15 mg group, and this reached full recovery in 150 min, compared with 210 min in the ropivacaine 20 mg ($p=0.014$) and 210 min in the bupivacaine 10 mg ($p=0.005$) groups. A study[75] noted that duration of motor blockade was 118 min with 15 mg ropivacaine when used for caserean section. In another study[69] authors found shorter duration (120 min) of motor blockade with ropivacaine when compared to bupivacaine. Another study[72] noted shorter duration of motor block with 15 mg of ropivacaine for caesarean section.

The comparison of the duration of complete motor block of the lower extremities also confirms that ropivacaine is approximately 50% less potent than bupivacaine because a similar median duration was seen with ropivacaine 15 mg.

From practical clinical point of view the smaller dose of ropivacaine 15 mg proved beneficial because recovery of the motor block was the fastest.

CONCLUSION

Our study showed that 15 mg of isobaric ropivacaine (2 ml of 0.75%) when administered intrathecally provides adequate anaesthesia for lower abdominal surgeries. Onset of sensory blockade was similar to that of bupivacaine with level of sensory block significantly higher with ropivacaine.

However there was delayed onset of motor block and shorter duration of motor block with ropivacaine compared to bupivacaine. Hence intrathecal, plain solutions containing ropivacaine 15 mg is suitable for lower abdominal surgeries of approximately one hour duration. The major advantage of ropivacaine 15 mg, in particular is a faster motor recovery compared with bupivacaine 10 mg.

SUMMARY

A prospective randomized clinical trial was conducted involving 100 patients belonging to ASA grade I and II coming for lower abdominal surgeries. They were randomly divided into two groups of 50 each. Group R received 2ml of 0.75% isobaric ropivacaine, group B received 2 ml of 0.5% isobaric bupivacaine. Preanaesthetic evaluation was done and all patients were preloaded with 10 ml/kg of ringer lactate. Following institution of subarachnoid block sensory characteristics such as onset of sensory block, level of block, duration of sensory block were studied .Motor blockade characteristics such as onset of motor block, duration and quality of motor blockade were studied. Hemodynamic parameters like heart rate, NIBP and SpO_2 were monitored.

Demographic parameters in both groups were comparable. Onset of sensory block was comparable in both groups. Level of sensory block was significantly higher with group R.

Whereas total duration of sensory block at T10 was similar in both groups. Onset of motor blockade was slower and duration of motor blockade was also shorter with ropivacaine compared to bupivacaine. However all the patients in either groups attained complete motor blockade. Hemodynamic parameters were comparable in both the groups with magnitude of fall in blood pressure being similar.

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ANNEXURE I - INFORMED CONSENT

Your participation

A study "**A RANDOMIZED CLINICAL TRIAL TO COMPARE** 0.75% **PLAIN ROPIVACAINE AND 0.5% PLAIN BUPIVACAINE IN LOWER ABDOMINAL SURGERIES UNDER SPINAL ANALGESIA AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM"** is being conducted by Dr. Pradeepkumar Hiremath, Post Graduate in Anaesthesiology at J. N. Medical College, Belgaum, Karnataka under the guidance of Dr. M. G. Dhorigol. Professor, Department of Anaesthesiology at J. N. Medical College, Belgaum, under KLE University, Belgaum.

Respected _____ we request you to participate in our study as you are eligible to be included. During the study you will be asked questions regarding your present and past medical history and you are supposed to answer to the best of your knowledge.

Your participation in this study is voluntary. Your decision whether or not to participate in the study will not affect your relationship with JNMC. If you decide to participate, you are free to withdraw at any point of time. The purpose of the study is to assess the effect of 0.75% ropivacaine (plain) and 0.5% bupivacaine (plain) on onset and duration of sensory block, onset and duration of motor block, level of sensory block in lower abdominal surgeries under spinal analgesia.

Objective of the study

Objective of my study is to assess the effect of 2cc of 0.75% ropivacaine (plain) and 2cc of 0.5% bupivacaine (plain) on onset and duration of sensory

block, onset and duration of motor block, level of sensory block in lower abdominal surgeries under spinal analgesia.

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 receive 2cc of 0.75% plain ropivacaine / 2cc of 0.5% of plain bupivacaine injection.

Benefits and risks

The benefits of taking part in this research are that we can avoid GA with good quality of analgesia. The risks are minimal which include: hypotension, bradycardia, headache, backache, syncope, paraesthesia.

Voluntary participation/withdrawal

Taking part in the study is voluntary. You may choose not to enroll in this study. Your decision will not change present or future health care services offered to you at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Alternatives

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

Confidentiality

All information collected about you during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will

identify you in this study records and the information from this study may be published but your identity will be confidential in any publication.

Financial incentives for participation

No financial incentives are being offered to enroll 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 at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. No reimbursement, compensation or free medical care will be given by law.

Queries / Contact details

If you have any queries in future or in case of study related injury or illness you may contact. Dr. M. G. Dhorigol $_{MD}$, Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Belgaum Mobile No. 98447 78096 or Dr. Pradeepkumar Hiremath at Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum Ph No. 0831-2473777 or on phone 9901179333.

If you have any queries about your rights as a study subject you may call Dr. V. D. Patil, Principal and Chairman, J. N. Medical College Institutional Ethical Committee for Human Subjects Research, Ph. 0831-2473777 at J. N. Medical College, Belgaum.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

I Mr / Mrs. _____ voluntarily agree to take part in this study, by signing this consent form I am not giving up my legal rights. I may withdraw at anytime. I am signing after having read or been read to me in the vernacular language including risks and benefits and having all queries cleared.

Signature of Participant & Date

Witness Name :

Signature of Witness & Date :

Date :

Place :

Signature of the Investigator :

ANNEXURE II – PROFORMA

STUDY : "A RANDOMIZED CLINICAL TRIAL TO COMPARE 0.75% PLAIN ROPIVACAINE AND 0.5% PLAIN BUPIVACAINE IN LOWER ABDOMINAL SURGERIES UNDER SPINAL ANALGESIA AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM".

Patient Name : **IP No. :**

Age : **Wt :**

Ht: **Gender :**

Date of Operation : **Occupation :**

Address : **Anaesthesiologist:**

Preanaesthetic Evaluation :

Chief Complaints :

Past History :

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

Family history :

General physical examination :

Pallor / Icterus / Clubbing / Cyanosis / Kylonychia / Lymphadenopathy / Edema

PR : BP :

RR :

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 :

Preoperaiive baseline values :

HR: BP:

Monitors attached :

Pulse oxymetry : NIBP :

ECG :

I. Group : R

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					
40 min					
50 min					
60 min					

III. Sensory Block

a)	Onset at T_{10} (min)	
b)	Duration at T_{10} (min)	
c)	Level of sensory block	

IV. Motor Block

a)	Onset (min)	
b)	Grade III Block (min)	
c)	Total duration of motor block	

I. Group : B

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					
40 min					
50 min					
60 min					

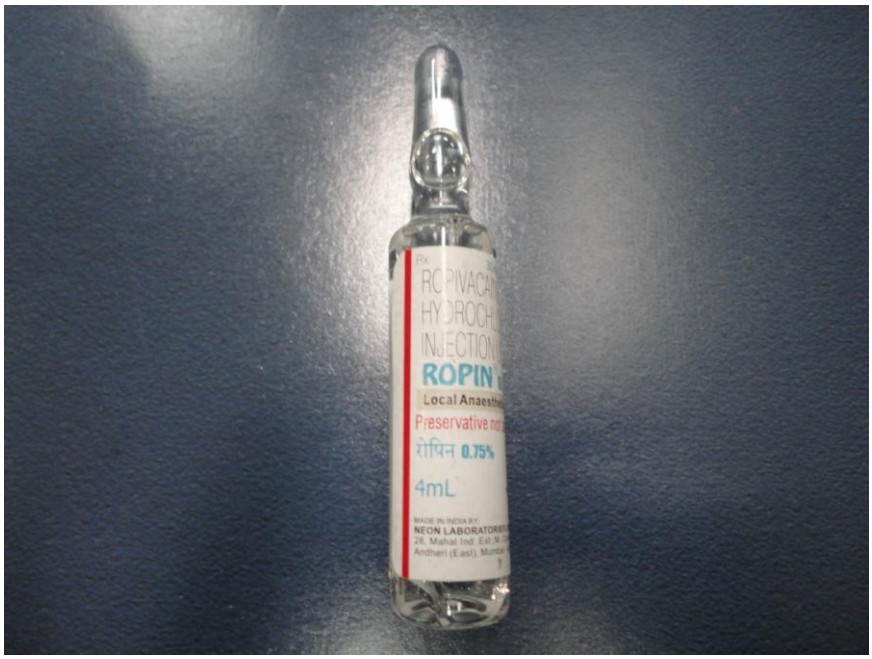
III. Sensory Block

a)	Onset at T_{10} (min)	
b)	Duration at T_{10} (min)	
c)	Level of sensory block	

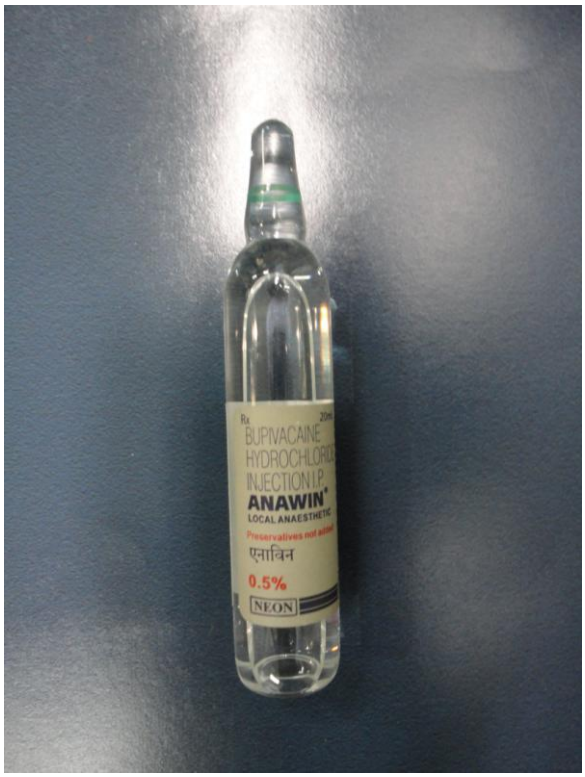
IV. Motor Block

a)	Onset (min)	
b)	Grade III Block (min)	
c)	Total duration of motor block	

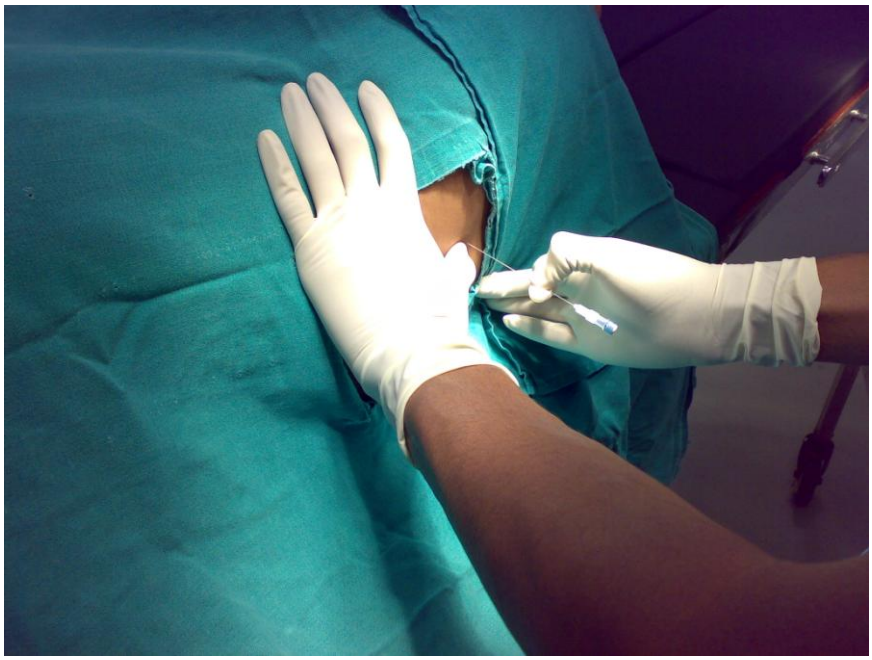
ANNEXURE III – PHOTOGRAPHS



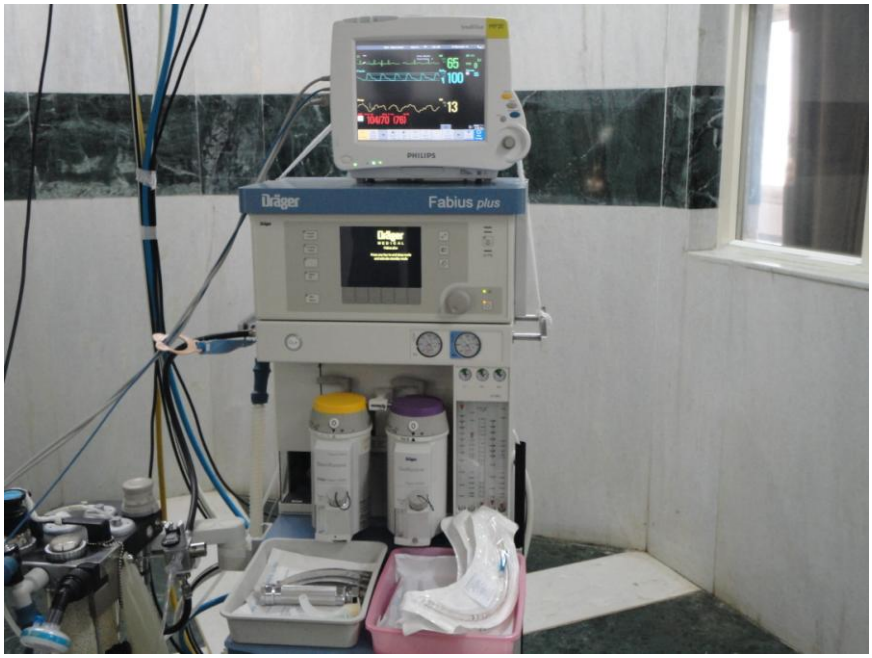
Photograph 1. Isobaric ropivacaine



Photograph 2. Isobaric bupivacaine



Photograph 3. Subarachnoid block



Photograph 4. Monitoring

ANNEXURE IV – KEY TO MASTER CHART

ASA	-	American Society of Anaesthesiologist
Cms	-	Centimeters
DBP	-	Diastolic blood pressure
F	-	Female
HR	-	Heart rate
Kg	-	Kilogram
M	-	Male
MBP	-	Mean blood pressure
Min	-	Minutes
mm Hg	-	Millimeters of mercury
SBP	-	Systolic blood pressure

ANNEXURE IV MASTER CHART - GROUP B

Serial Number	In Patient Number	Gender	Age (Years)	Weight (Kg)	Height (Cms)	ASA Grade	Surgery	Observations at regular intervals (Time in minutes)																																														Blockade					
								2				4				6				8				10				15				20				25				30				40				50				60				Sensory			Motor		
								SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	Onset (Min)	Duration (Min)	Level	Onset (Min)	Grade III Duration (Min)	Total Duration (Min)
1	312842	M	24	64	154	I	Fistula in ano	##	94	##	78	##	90	98	76	##	88	96	74	##	86	94	74	##	84	92	72	##	82	90	68	##	82	88	66	##	80	86	64	##	78	84	64	##	76	82	62	##	74	78	60	##	74	80	60	5	##	T6	8	##	##
2	312362	M	36	68	159	I	Fistula in ano	##	98	##	88	##	96	##	86	##	94	##	84	##	94	##	84	##	92	##	82	##	90	96	80	##	88	94	78	##	86	94	76	##	86	92	74	98	84	90	72	98	82	88	70	94	82	86	68	6	##	T8	9	##	##
3	321623	F	33	58	166	I	Vaginal hysterectomy	##	88	##	84	##	84	##	82	##	82	##	80	##	80	##	78	##	78	98	76	##	76	96	74	##	74	94	72	##	72	92	70	##	74	90	68	##	70	88	66	##	68	86	64	##	66	84	63	5	##	T4	7	##	##
4	323421	M	34	56	166	I	Haemorrhoids	##	90	##	96	##	88	##	94	##	86	##	92	##	84	##	90	##	82	##	88	##	80	98	86	##	78	96	84	##	76	94	82	##	74	92	80	##	72	90	78	##	70	88	76	##	70	88	74	6	##	T6	9	##	##
5	312642	M	25	64	165	I	Appendicitis	##	96	##	90	##	94	##	88	##	90	98	84	##	88	96	84	##	86	96	82	##	86	94	78	##	84	92	76	##	82	90	74	##	80	90	74	##	78	88	72	##	76	86	72	##	74	86	70	5	##	T8	8	##	##
6	316248	M	36	56	164	I	Fissure in ano	##	90	##	98	##	88	##	96	##	86	98	96	##	84	96	94	##	84	94	92	##	82	92	90	##	80	90	88	##	78	88	86	##	76	86	86	##	76	86	84	##	74	84	84	##	72	82	82	7	##	T8	10	##	##
7	312653	M	36	58	165	I	Appendicitis	##	96	##	82	##	94	##	80	##	92	##	78	##	90	##	76	##	88	##	74	##	86	##	74	##	84	##	72	##	82	98	72	98	80	96	70	98	78	92	68	96	78	92	66	96	74	90	64	4	##	T6	8	##	##
8	312698	M	36	55	166	I	Appendicitis	##	92	##	84	##	90	##	83	##	86	##	80	##	84	##	78	##	82	98	77	##	80	96	72	##	78	94	68	##	76	94	64	##	74	92	64	##	72	90	63	98	70	90	63	98	70	88	63	5	##	T6	9	##	##
9	326148	M	36	52	164	I	Fissure in ano	##	90	##	90	##	88	##	92	##	84	98	88	##	82	96	84	##	80	94	82	##	78	92	80	##	78	90	78	##	76	90	74	##	74	88	72	##	72	84	70	##	70	82	68	##	70	80	67	3	##	T8	8	##	##
10	328621	M	35	67	165	I	Haemorrhoids	##	86	##	84	##	84	##	82	##	82	##	80	##	80	##	78	##	78	98	76	##	76	96	74	##	74	94	73	##	72	92	74	##	70	90	70	##	70	88	68	##	68	86	66	##	68	84	66	4	##	T8	9	##	##
11	325862	F	35	64	167	I	Inguinal hernia	##	90	##	94	##	88	##	90	##	86	##	88	##	84	96	86	##	82	94	88	##	80	92	84	##	78	90	86	##	76	88	84	##	74	88	82	##	70	86	80	##	68	84	76	##	66	84	76	5	##	T8	10	##	##
12	324324	F	36	60	170	I	Acute appendicitis	##	84	##	88	##	86	##	86	##	82	98	84	##	80	96	84	##	78	92	82	##	76	90	80	98	74	88	78	96	72	84	76	94	70	82	74	90	68	82	72	88	66	80	70	86	64	80	68	6	##	T6	7	##	##
13	324321	F	35	58	160	I	Fistula in ano	##	90	98	84	##	88	96	82	##	86	94	80	##	84	90	78	##	84	88	76	##	82	86	74	##	80	84	72	##	78	82	70	##	76	80	68	96	76	78	66	98	74	76	64	96	72	74	63	4	##	T4	10	##	##
14	323351	M	38	59	158	I	Inguinal hernia	##	96	##	96	##	94	##	94	##	92	##	92	##	90	##	90	##	88	##	88	##	86	##	86	##	84	##	84	##	82	98	82	98	80	96	80	98	78	92	78	96	78	92	76	96	74	90	74	3	##	T6	8	##	##
15	326251	M	46	54	158	I	Fissure in ano	##	92	##	90	##	90	##	88	##	86	##	84	##	84	##	84	##	82	98	82	##	80	96	78	##	78	94	76	##	76	94	74	##	74	92	74	##	72	90	72	98	70	90	72	98	70	88	70	4	##	T8	9	##	##
16	324123	F	37	48	158	I	Vaginal hysterectomy	##	90	##	98	##	88	##	96	##	84	98	96	##	82	96	94	##	80	94	92	##	78	92	90	##	78	90	88	##	76	90	86	##	74	88	86	##	72	84	84	##	70	82	84	##	70	80	82	4	##	T8	7	##	##
17	323778	F	36	58	168	I	Fissure in ano	##	86	##	90	##	84	##	92	##	82	##	88	##	80	##	84	##	78	98	82	##	76	96	80	##	74	94	78	##	72	92	74	##	70	90	72	##	70	88	70	##	68	86	68	##	68	84	67	4	##	T8	9	##	##
18	323573	F	37	66	166	I	Vaginal hysterectomy	##	90	##	84	##	88	##	82	##	86	##	80	##	84	96	78	##	82	94	76	##	80	92	74	##	78	90	73	##	76	88	74	##	74	88	70	##	70	86	68	##	68	84	66	##	66	84	66	6	##	T6	8	##	##
19	326212	F	47	69	158	II	Fissure in ano	##	84	##	94	##	86	##	90	##	82	98	88	##	80	96	86	##	78	92	88	##	76	90	84	98	74	88	86	96	72	84	84	94	70	82	82	90	68	82	80	88	66	80	76	86	64	80	76	5	##	T8	10	##	##
20	324247	M	35	67	166	I	Appendicitis	##	90	98	88	##	88	96	86	##	86	94	84	##	84	90	84	##	82	88	82	##	82	86	80	##	80	84	78	##	78	82	76	##	76	80	74	96	74	78	72	98	74	76	70	96	72	74	68	7	##	T10	7	##	##
21	324575	F	35	63	166	I	Appendicitis	##	94	94	84	##	92	90	82	##	90	88	80	##	88	86	78	##	86	84	76	##	84	82	74	##	82	80	72	##	82	78	70	##	82	78	68	##	82	76	66	##	80	74	64	##	80	74	63	5	##	T8	9	##	##
22	324173	F	39	64	165	I	Fissure in ano	##	96	##	96	##	94	##	94	##	92	98	92	##	90	96	90	##	88	94	88	##	84	92	86	##	82	90	84	##	80	88	82	##	78	86	80	##	76	84	78	##	74	82	76	##	72	80	74	5	##	T6	11	##	##
23	323667	M	36	65	157	I	Hemorrhoids	##	94	##	90	##	90	98	88	##	88	96	84	##	86	94	84	##	84	92	82	##	82	90	78	##	82	88	76	##	80	86	74	##	78	84	74	##	76	82	72	##	74	78	72	##	74	80	70	6	##	T8	8	##	##
24	318637	F	36	64	159	I	Inguinal hernia	##	98	##	98	##	96	##	96	##	94	##	96	##	94	##	94	##	92	##	92	##	90	96	90	##	88	94	88	##	86	94	86	##	86	92	86	98	84	90	84	98	82	88	84	94	82	86	82	4	##	T10	12	##	##
25	318912	M	28	58	168	I	Acute appendicitis	##	88	##	84	##	84	##	82	##	82	##	80	##	80	##	78	##	78	98	76	##	76	96	74	##	74	94	72	##	72	92	70	##	74	90	68	##	70	88	66	##	68	86	64	##	66	84	63	5	##	T6	11	##	##
26	316824	F	38	56	165	I	Fistula in ano	##	90	##	96	##	88	##	94	##	86	##	92	##	84	##	90	##	82	##	88	##	80	98	86	##	78	96	84	##	76	94	82	##	74	92	80	##	72	90	78	##	70	88	76	##	70	88	74	6	##	T8	10	##	##
27	317981	F	39	64	167	I	Appendicitis	##	96	##	90	##	94	##	88	##	90	98	84	##	88	96	84	##	86	96	82	##	86	94	78	##	84	92	76	##	82	90	74	##	80	90	74	##	78	88	72	##	76	86	72	##	74	86	70	5	##	T6	9	##	##
28	317984	M	28	56	166	I	Hemorrhoids	##	90	##	98	##	88	##	96	##	86	98	96	##	84	96	94	##	84	94	92	##	82	92	90	##	80	90	88	##	78	88	86	##	76	86	86	##	76	86	84	##	74	84	84	##	72	82	82	4	##	T8	12	##	##
29	317199	F	22	58	169	I	Inguinal hernia	##	96	##	90	##	94	##	92	##	92	##	88	##	90	##	84	##	88	##	82	##	86	##	80	##	84	##	78	##	82	98	74	98	80	96	72	98	78	92	70	96	78	92	68	96	74	90	67	5	##	T8	11	##	##
30	318443	F	39	55	163	I	Acute appendicitis	##	92	##	84	##	90	##	82	##	86	##	80	##	84	##	78	##	82	98	76	##	80	96	74	##	78	94	73	##	76	94	74	##	74	92	70	##	72	90	68	98	70	90	66	98	70	88	66	6	##	T8	8	##	##
31	316925	M	39	52	168	I	Fistula in ano	##	90	##	94	##	88	##	90	##	84	98	88	##	82	96	86	##	80	94	88	##	78	92	84	##	78	90	86	##	76	90	84	##	74	88	82	##	72	84	80	##	70	82	76	##	70	80	76	6	##	T6	10	##	##
32	315624	M	29	67	166	I	Appendicitis	##	86	##	88	##	84	##	86	##	82	##	84	##	80	##	84	##	78	98	82	##	76	96	80	##	74	94	78	##	72	92	76	##	70	90	74	##	70	88	72	##	68	86	70	##	68	84	68	7	##	T8	11	##	##
33	305262	M	34	64	165	I	Fissure in ano	##	90	##	84	##	88	##	82	##	86	##	80	##	84	96	78	##	82	94	76	##	80	92	74	##	78	90	72	##	76	88	70	##	74	88	68	##	70	86	66	##	68	84	64	##	66	84	63	5	##	T6	12	##	##
34	325826	M	35	60	167	I	Fissure in ano	##	84	##	96	##	86	##	94	##	82	98	92	##	80	96	90	##	78	92	88	##	76	90	86	98	74	88	84	96	72	84	82	94	70	82	80	90	68	82	78	88	66	80	76	86	64	80	74	5	##	T8	12	##	##
35	325079	F	34	58	154	I	Tubectomy	##	90	98	90	##	88	96	88	##	86	94	84	##	84	90	84	##	82	88	82	##	82	86	78	##	80	84	76	##	78	82	74	##	76	80	74	96	74	78	72	98	74	76	72	96	72	74	70	6	##	T6	10	##	##
36	298652	F	49	59	170	II	Vaginal hysterectomy	##	94	94	98	##	92	90	96	##	90	88	96	##	88	86	94	##	86	84	92	##	84	82	90	##	82	80	88	##	82	78	86	##	82	78	86	##	82	76	84	##	80	74	84	##	80	74	82	6	##	T8	11	##	##
37	325039	M	33	54	174	I	Acute appendicitis	##	96	##	96	##	94	##	94	##	92	98	92	##	90	96	90	##	88	94	88	##	84	92	86	##	82	90	84	##	80	88	82	##	78	86	80	##	76	84	78	##	74	82	76	##	72	80	74	5	##	T4	12	##	##
38	323948	F	32	48	166	I	Fistula in ano	##	94	##	90	##	90	98	88	##	88	96	84	##	86	94	84	##	84	92	82	##	82	90	78	##	82	88	76	##	80	86	74	##	78	84	74	##	76	82	72	##	74	78	72	##	74	80	70	6	##	T6	8	##	##
39	324089	M	26	58	165	I	Inguinal hernia	##	98	##	98	##	96	##	96	##	94	##	96	##	94	##	94	##	92	##	92	##	90	96	90	##	88	94	88	##	86	94	86	##	86	92	86	98	84	90	84	98	82	88	84	94	82	86	82	7	##	T8	9	##	##
40	323942	M	31	66	164	I	Acute appendicitis	##	88	##	84	##	84	##	82	##	82	##	80	##	80	##	78	##	78	98	76	##	76	96	74	##	74	94	72	##	72	92	70	##	74	90	68	##	70	88	66	##	68	86	64	##	66	84	63	6	##	T6	10	##	##
41	324239	M	32	69	178	I	Fistula in ano	##	90	##	96	##	88	##	94	##	86	##	92	##	84	##	90	##	82	##	88	##	80	98	86	##	78	96	84	##	76	94	82	##	74	92	80	##	72	90	78	##	70	88	76	##	70	88	74	5	##	T8	9	##	##
42	325053	F	36	67	177	I	Tubectomy	##	96	##	90	##	94	##	88	##	90	98	84	##	88	96	84	##	86	96	82	##	86	94	78	##	84	92	76	##	82	90	74	##	80	90	74	##	78	88	72	##	76	86	72	##	74	86	70	5	##	T6	11	##	##

ANNEXURE IV MASTER CHART - GROUP B

Serial Number	In Patient Number	Gender	Age (Years)	Weight (Kg)	Height (Cms)	ASA Grade	Surgery	Observations at regular intervals (Time in minutes)																																																Blockade					
								2				4				6				8				10				15				20				25				30				40				50				60				Sensory			Motor		
								SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	SBP (mm Hg)	DBP (mm Hg)	MBP (mm Hg)	HR (/Min)	Onset (Min)	Duration (Min)	Level	Onset (Min)	Grade III Duration (Min)	Total Duration (Min)
43	325375	F	35	63	165	I	Vaginal hysterectomy	##	90	##	98	##	88	##	96	##	86	98	96	##	84	96	94	##	84	94	92	##	82	92	90	##	80	90	88	##	78	88	86	##	76	86	86	##	76	86	84	##	74	84	84	##	72	82	82	7	##	T8	12	##	##
44	325396	M	26	64	166	I	Fistula in ano	##	96	##	90	##	94	##	92	##	92	##	88	##	90	##	84	##	88	##	82	##	86	##	80	##	84	##	78	##	82	98	74	98	80	96	72	98	78	92	70	96	78	92	68	96	74	90	67	6	##	T6	13	##	##
45	324449	M	43	65	167	I	Appendicitis	##	92	##	84	##	90	##	82	##	86	##	80	##	84	##	78	##	82	98	76	##	80	96	74	##	78	94	73	##	76	94	74	##	74	92	70	##	72	90	68	98	70	90	66	98	70	88	66	5	##	T8	9	##	##
46	334212	F	39	64	166	I	Fissure in ano	##	90	##	94	##	88	##	90	##	84	98	88	##	82	96	86	##	80	94	88	##	78	92	84	##	78	90	86	##	76	90	84	##	74	88	82	##	72	84	80	##	70	82	76	##	70	80	76	6	##	T10	10	##	##
47	324321	M	38	58	166	I	Fissure in ano	##	86	##	88	##	84	##	86	##	82	##	84	##	80	##	84	##	78	98	82	##	76	96	80	##	74	94	78	##	72	92	76	##	70	90	74	##	70	88	72	##	68	86	70	##	68	84	68	5	##	T4	11	##	##
48	326212	F	44	63	164	II	Acute appendicitis	##	90	##	84	##	88	##	82	##	86	##	80	##	84	96	78	##	82	94	76	##	80	92	74	##	78	90	72	##	76	88	70	##	74	88	68	##	70	86	66	##	68	84	64	##	66	84	63	6	##	T6	12	##	##
49	325624	M	36	66	157	I	Fistula in ano	##	84	##	96	##	86	##	94	##	82	98	92	##	80	96	90	##	78	92	88	##	76	90	86	98	74	88	84	96	72	84	82	94	70	82	80	90	68	82	78	88	66	80	76	86	64	80	74	5	##	T8	14	##	##
50	323198	F	46	65	167	I	Appendicitis	##	90	98	90	##	88	96	88	##	84	94	84	##	82	90	84	##	80	88	82	##	78	86	78	##	78	84	76	##	76	82	74	##	74	80	74	96	72	78	72	98	70	76	72	96	70	74	70	5	##	T8	9	##	##