"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE BETWEEN INTRATHECAL 0.5% ISOBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL AND 0.5% HYPERBARIC BUPIVACAINE WITH 25 MICROGRMS FENTANYL FOR INFRAUMBILICAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"

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Endorsement

This is to certify that the dissertation entitled **"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE BETWEEN INTRATHECAL 0.5% ISOBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL AND 0.5% HYPERBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL FOR INFRAUMBILICAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"** is a bonafide research work done by **(REG NO. BA0116003).**

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LIST OF ABBREVIATIONS USED

ASA	-	American Society of Anaesthesiologists
C	-	Cervical
T	-	Thoracic
Mcg	-	Microgram
cc	-	Cubic centimeter
CNS	-	Central nervous system
CSF	-	Cerebrospinal fluid
CVS	-	Cardiovascular system
DBP	-	Diastolic blood pressure
ED	-	Effective dose
FDA	-	Food and Drug Administration
GA	-	General anaesthesia
HCO_3	-	Bicarbonate
HR	-	Heart rate
bpm	-	Beats per minute
IV	-	Intravenous
HCL	-	Hydrochloric Acid
KCl	-	Potassium chloride
kg	-	Kilogram
L	-	Lumbar
m	-	Meters
MAP	-	Mean arterial pressure
mg	-	Milligram
v/s	-	Versus

Mins	-	Minutes
ml	-	Millilitre
NIBP	-	Non invasive blood pressure
O_2	-	Oxygen
$PaCO_2$	-	Partial pressure of carbon dioxide
S	-	Sacral
SAB	-	Subarachnoid block
SBP	-	Systolic blood pressure
SD	-	Standard deviation
Sec	-	Second
SpO_2	-	Peripheral saturation of oxygen
TNS	-	Transient neurological symptoms
α	-	Alpha
β	-	Beta
δ	-	Delta
μ	-	Micro
cm	-	centimeter
G	-	Gauge
mEq	-	milliequivalents
Lt	-	litre
Dl	-	decilitre
V_{max}	-	maximum initial velocity or rate of a reaction

ABSTRACT

Background and Aims: There are two forms of commercially available bupivacaine; isobaric bupivacaine and hyperbaric bupivacaine. Opioids like fentanyl are used as adjuvants with local anaesthetics to improve analgesic intensity and to achieve faster onset and prolonged duration. This study aims at comparing isobaric bupivacaine - fentanyl and hyperbaric bupivacaine-fentanyl primarily, in terms of onset and duration of sensory and motor blockade and secondarily, in terms of hemodyamic changes and associated complications.

Methods: Eighty patients belonging to American society of Anaesthesiologists I and II undergoing infraumbillical surgeries under spinal anaesthesia were randomised into two groups. Group A received 3ml of 0.5% isobaric bupivacaine with 25 micrograms fentanyl, while Group B received 3ml of 0.5% hyperbaric bupivacaine with 25 micrograms fentanyl . Student's unpaired t-test and the $\chi 2$ test were used to analyse the results, using the SPSS version 11.5 software.

Results: The mean onset of sensory block was significantly faster in Group B (3.55 ± 0.96 min) than in Group A (5.70 ± 0.69 min). The mean duration of sensory block was significantly longer in Group B (189.65 ± 9.58 min) than in Group A (129.08 ± 3.47 min). The mean onset of motor block was significantly faster in Group B (4.78 ± 0.80 min) than in Group A (7.83 ± 0.78 min).The mean duration of motor block was significantly longer in Group B (204.55 ± 12.46 min) than in Group A (171.18 ± 4.31 min). Isobaric bupivacaine-fentanyl mixture was associated with better hemodynamic stability as compared with hyperbaric bupivacaine-fentanyl mixture.

Conclusion: Intrathecal isobaric bupivacaine-fentanyl mixture is associated with lesser duration of both sensory and motor blockade, thereby enabling quicker recovery from anaesthesia and also better haemodynamic stability as compared with hyperbaric bupivacaine fentanyl mixture for infraumbilical surgeries

Keywords: Bupivacaine, fentanyl, hyperbaric, isobaric, spinal anaesthesia

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INTRODUCTION

Spinal anaesthesia is a commonly performed procedure for infraumbilical surgeries. The advantages are an awake and spontaneously breathing patient, minimal drug costs, reduction of usage of multiple drugs. It is a simple, effective and safe technique. Hence it has become the method of choice for such surgeries.

Spinal anaesthesia is performed by injection of a local anaesthetic with or without adjuvant in the sub-arachnoid space producing sensory, motor and sympathetic blockade. Anaesthesiologists, across the world, have been trying to make spinal anaesthesia more effective by providing adequate intra-operative and post-operative analgesia and also promoting early post-operative ambulation.

Regional anesthesia techniques have seen numerous modifications over the last two decades with the advent of many new and safer local anesthetics. Presently, hyperbaric bupivacaine is the most commonly used drug for administration of spinal anaesthesia.[1]

There are two forms of commercially available bupivacaine; isobaric bupivacaine, a formulation with a specific gravity or density equal to cerebrospinal fluid, and hyperbaric bupivacaine, a formulation with density heavier than cerebrospinal fluid.

The importance of isobaric spinal anaesthesia is that distribution of drug is not dependent on the positioning of the patient during injection of drug unlike hyperbaric solution.

The aim of using adjuvants with local anaesthetics is to improve analgesic intensity, to increase duration of action, to achieve faster onset and to achieve acceptable, effective prolonged post - operative analgesia with lower drug doses and thus reduced risks of side-effects. Efforts to find an ideal adjuvant in regional anaesthesia have been going on since a long time. Thus opioids like fentanyl[16], buprenorphine[16], alpha-2 agonists ,clonidine[16] have been used intrathecally as adjuvants to the local anaesthetics for improvement in quality and extending the duration of spinal blockade.

Very few studies have been done comparing these two drugs with adjuvants. Hence with this study we attempt at comparing Isobaric bupivacaine-fentanyl and Hyperbaric buivacaine-fentanyl in terms of onset and duration of sensory and motor blockade for infraumbilical surgeries under spinal anaesthesia.

OBJECTIVES

The objectives of the present study were :

- **Primary Objective**: To compare the onset and duration of sensory and motor blockade between intrathecal 0.5% isobaric bupivacaine with 25 micrograms fentanyl and 0.5% hyperbaric bupivacaine with 25 micrograms fentanyl for infraumbilical surgeries.
- **Secondary objective**: To study the hemodynamic changes and evaluate associated complications.

REVIEW OF LITERATURE

Subarachnoid block is a form of regional anaesthesia where nerve roots are blocked by injecting a local anaesthetic into the subarachnoid space.

Spinal anaesthesia has come a long way since its discovery and its history is very interesting. In 1885 J. Leonard Corning, a neurologist from New York, was the first to administer spinal anaesthesia, when he accidentally pierced the duramater while experimenting with cocaine on the spinal nerves of a dog. Within a few minutes, the dog developed marked weakness in the hind legs. Corning then went on to inject cocaine into a man at the T_{11}-T_{12} inter-vertebral space into what he thought was subarachnoid space. He repeated the injection when he did not observe any effect. Ten minutes after the second injection, the patient informed of heaviness in his legs, but was able to stand and walk around. In his records, Corning never mentioned of cerebrospinal fluid flow. Therefore most likely he inadvertently gave an epidural rather than a spinal injection to the patient. He later used this technique in various neurological disorders but did not use it for surgeries though he appreciated its potential use.[7]

In 1891 Essex Wynter described dural puncture.[8] Six months later, Quincke demonstrated a safe and predictable method of performing lumbar puncture.[9]

The first planned spinal anaesthesia for surgery in man was performed in 1898 by August Karl Bier in Germany. Bier and his assistant Otto Hildebrandt both administered spinal anaesthesia by injecting cocaine to each other. Bier had to discontinue after experiencing post dural puncture headache (PDPH). Bier attributed his PDPH to the loss of CSF and felt the use of small-gauge needles would prevent

the headache. After injection of cocaine intrathecally into Hildebrandt, he reported minimal to no pain during the experiments. Bier then went on to administer cocaine in the subarachnoid space of six patients undergoing lower limb surgeries.[10]

In 1905, Heinrich Braun reported the use of procaine for administration into subarachnoid space. In 1907, Arthur Baker reported on the advancement of spinal techniques, including the use of a hyperbaric spinal local anaesthetic, emphasis on sterility and ease of midline route over paramedian for dural puncture.[11] In 1923 Gaston Labat popularized spinal anaesthesia in United States and performed studies on the effects of Trendelenburg position on blood pressure after spinal anaesthesia.

Tetracaine was synthesized in 1931 and was introduced into clinical practice by Lincoln Sise in 1935. Spinal anaesthesia became more popular as new developments occurred. In 1946, Adriani and Roman-Vega introduced saddle block. The popularity of spinal anaesthesia reached newer heights in the 1940's. Continuous spinal anesthesia was demonstrated by Lemmon in 1940 and Tuohy in 1945.[12]

The technique of spinal anaesthesia has evolved with time since its inception in the nineteenth century. Usage of a finer bore and dura separating pencil-point needle along with strict asepsis have reduced complications due to the technique.

Spinal anaesthesia has many advantages like ease of administration, rapid onset of action and good muscle relaxation. The major limitations are its limited duration of action hence the paucity of post-operative analgesia and hemodynamic instability.

Spinal anaesthesia is performed by injection of a local anaesthetic with or without adjuvants in the sub-arachnoid space producing sensory, motor and

sympathetic blockade. The aim of using adjuvants with local anesthetics is to improve the analgesic intensity, to increase the duration of action, to achieve faster onset of action and to achieve acceptable analgesia with lower drug doses and thus reduced risks of side-effects.[13]

The three most important factors determining the spread of local anaesthesia in the subarachnoid space are the baricity of the local anaesthetic solution, position of the patient during and immediately after the injection and dose of the drug injected. Hypobaric drugs are less dense than CSF and tend to rise against gravity. Isobaric drugs are as dense as CSF and tend to remain at the same level as injected. Hyperbaric drugs are denser than CSF and tend to follow gravity after injection. With isobaric drugs, injection can be made in any position and then the patient can be placed into the position required for the surgery. Gravity does not play a role in the spread of isobaric drugs, unlike with hypo or hyperbaric local anaesthetics.[14]

Ever since the development of the technique of spinal anaesthesia various local anaesthetics such as cocaine, procaine, etidocaine, tetracaine, lignocaine and bupivacaine have been tried and studied for their effects. Lignocaine was first used as a spinal anaesthetic in 1945. Earlier lignocaine 5% was commonly used for spinal anaesthesia, but its use has declined because of concerns about cauda equina syndrome and transient neurological symptoms.[15]

Since a few decades lignocaine has been almost replaced with bupivacaine and ropivacaine.

A study conducted by Madhusudan Upadya et al in January 2016 compared intrathecal hyperbaric bupivacaine-fentanyl mixture and isobaric bupivacaine-fentanyl

mixture in common urological procedures[2]. One hundred patients belonging to American society of Anaesthesiologists grade I and grade II undergoing urological procedures were randomized into two groups. Group 1 received 3ml of 0.5% bupivacaine with 25 micrograms fentanyl while group 2 received 3ml of 0.5% hyperbaric bupivacaine with 25 micrograms fentanyl. The parameters measured included onset and duration of motor and sensory blockade, heart rate, blood pressure, respiratory rate. They concluded that isobaric bupivacaine-fentanyl mixture was found to provide adequate anaesthesia with minimal incidence of haemodynamic instability.

Another study by Mochamat Helmi, et al in February 2014 compared intrathecal use of isobaric and hyperbaric bupivacaine during lower abdominal surgery [6]. Sixty patients with ASA I and II, undergoing elective lower abdominal surgeries with the estimation in duration no longer than 120 minutes were enrolled. Patients were randomized with sealed envelope method into 2 groups. Group I received 4ml of 0.5% isobaric bupivacaine while group 2 received 4ml of 0.5% hyperbaric bupivacaine. Neither the anaesthesiologist performing SAB and collecting perioperative data nor the patients were aware of the used solution.They concluded that isobaric bupivacaine produced more rapid onset and longer duration compared to hyperbaric bupivacaine.

Another study by Seewal R, et al in January 2007 evaluated effect of addition of different doses of fentanyl intrathecally to 0.5% hyperbaric bupivacaine on perioperative analgesia and subarachnoid block characteristics in lower abdominal surgery : A dose response study[5]. A population of 60 patients belonging to ASA I and II were randomized to receive a spinal anaesthetic with 2.2 ml of 0.5% hyperbaric bupivacaine saline (control group) or fentanyl 10,20,30 or 40 micrograms. The

conclusion was that in a non- obstetric population receiving spinal anaesthetic for lower abdominal surgery, addition of 10 micrograms fentanyl to 0.5% hyperbaric bupivacaine significantly improves the quality and duration of analgesia. No further advantage occurs if the dose of fentanyl is increased upto 40 icrograms

Another study by Amitaya Layek et al in 2015 compared between intrathecal isobaric ropivacaine-fentanyl and bupivacaine-fentanyl in elective infraumbilical orthopedic surgery: A randomized controlled study[3].Seventy-four patients belonging to American Society of Anaesthesiologists grade I and grade II undergoing lower limb orthopedic surgery under subarachnoid block were randomized to receive either 3ml 0.5% isobaric ropivacaine and 25 micrograms fentanyl (Group R) or 3ml 0.5% isobaric bupivacaine and 25 micrograms (Group B). The hemodynamic profiles, maximum upperlevel of sensory block height, time to reach peak block height, two dermatome regression time, and duration of motor block were recorded. They concluded that intrathecal isobaric bupivacaine-fentanyl combination produces a significantly longer duration of analgesia, sensory block and motor block than isobaric ropivacaine-fentanyl combination.

In conclusion, there are few studies comparing isobaric bupivacaine with fentanyl and hyperbric bupivacaine with fentanyl. So there exists a knowledge gap with regards to these two drugs and hence our study is being undertaken to compare the combination of these drugs with adjuvants in spinal anesthesia.

BASIC SCIENCES

Subarachnoid block is the choice of anaesthesia when the surgery is to be performed on the lower extremities, perineum, or lower abdominal wall. Spinal anaesthesia causes motor, sensory and sympathetic blockade.

The main advantages of spinal anaesthesia are avoidance of using multiple drugs and airway manipulation that accompany general anaesthesia. The other added benefits are reduction of metabolic stress response to surgery, reduction in blood loss, reduced incidence of venous thromboembolism, reduction in pulmonary compromise (particularly in patients with advanced pulmonary disease).

The absolute contraindications to spinal anaesthesia are patient refusal, lack of co-operation by patient, difficulties with positioning, and increased intracranial pressure. Other relative contraindications are spinal abnormalities, hypovolemia, coagulopathies, fixed cardiac output lesions, septicaemia, and local infection at the site of needle insertion. Allergy to local anaesthetics may also be a contraindication, but true allergies are usually found with ester-based local anaesthetics (tetracaine), not the amide-based local anaesthetics (bupivacaine, levobupivacaine and ropivacaine) that are more commonly used now-a-days.

ANATOMY

A detailed knowledge of anatomy of vertebral column, spinal cord and spinal nerves is essential to all the anaesthesiologists for safe and successful administration of spinal anaesthesia.

Vertebral column

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

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

Curves of spine

In adult, the vertebral column has four curves [21](Figure2):

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

In adults the curves of the spine are important when patient is supine. The highest point of cervical and lumbar curves in supine position are at cervical (C) five and lumbar (L) five; lowest points of thoracic and sacral are at thoracic (T) five and sacral (S) two respectively. The vertebral column curves, dose as well as the baricity of local anaesthetic and patient position determine the spread of local anaesthetic in the subarachnoid space.

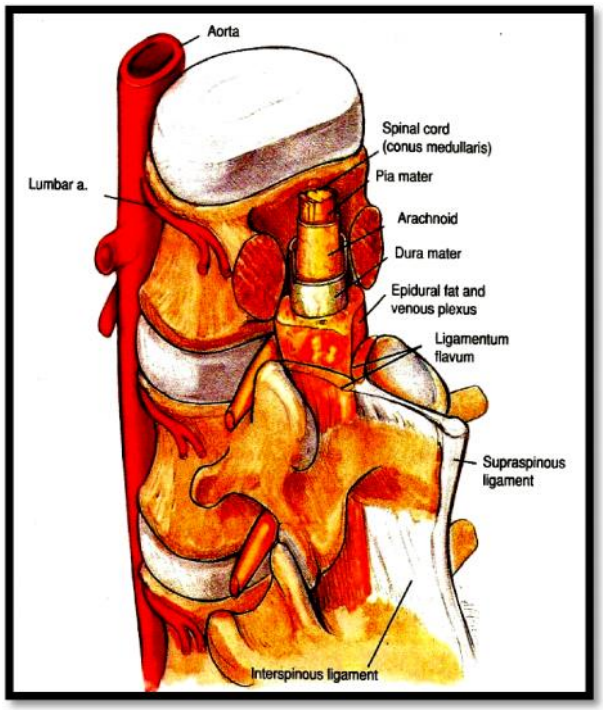


Figure 1: Vertebral Column

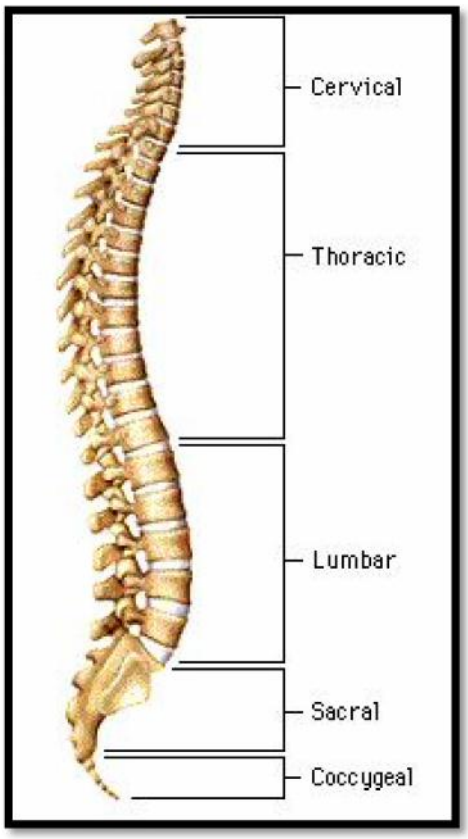


Figure 2 : Curves of the spine

Vertebral ligaments

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 the seventh cervical vertebra (C_7) to the sacrum. The supraspinous ligament is known as the ligamentum nuchae in the area above C_7

Interspinous ligament: This is a thin membranous ligament which connects spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament (Figure 3).

Ligamentum flavum: This ligament comprises yellow elastic fibres and connects adjacent lamina. Laterally this ligament begins at the root of articular processes and extends posteriorly and medially to the point where laminae join to form spinous process (Figure 3).

Longitudinal ligaments:There are two longitudinal ligaments (anterior and posterior) that bind vertebral bodies together (Figure 3).

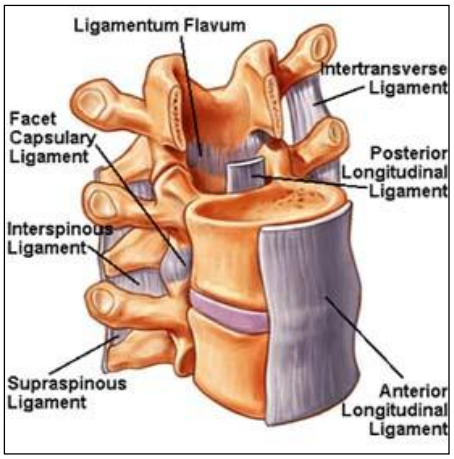


Figure 3: Spinal Ligaments

Lumbar vertebrae

A typical lumbar vertebra consists of (Figure 4);

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

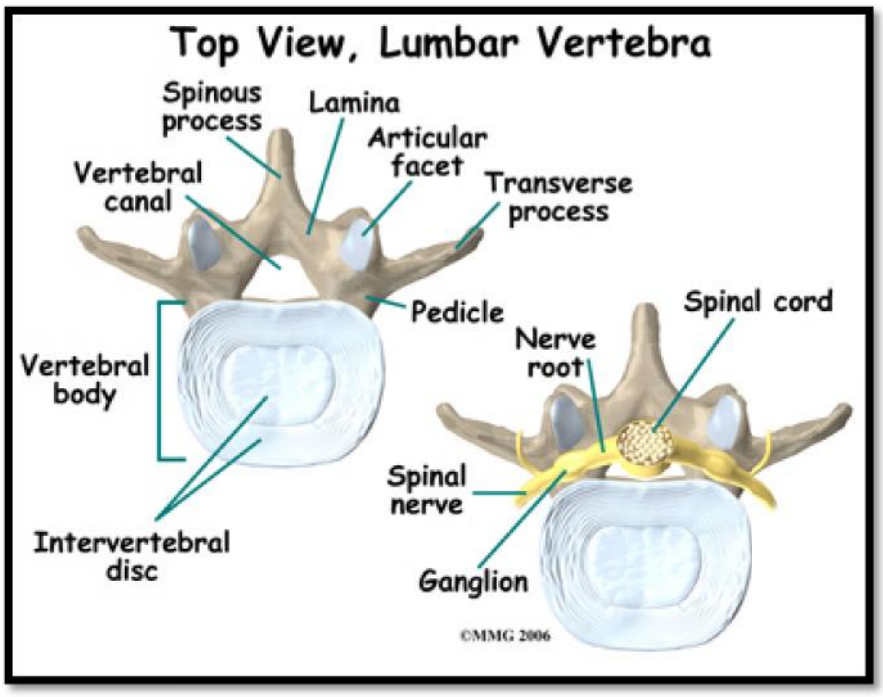


Figure 4 : Typical Lumbar Vertebra

Topographical Line of Tuffier[23]

An imaginary line that passes between the highest points of the iliac crests crossing the spine of the 4th lumbar vertebra in the upright position. In a patient lying in the lateral position it may also pass through L_4 and L_5 interspaces. The superior iliac crest is used to identify the L_4 and L_5 interspace during spinal anaesthesia (Figure 5).

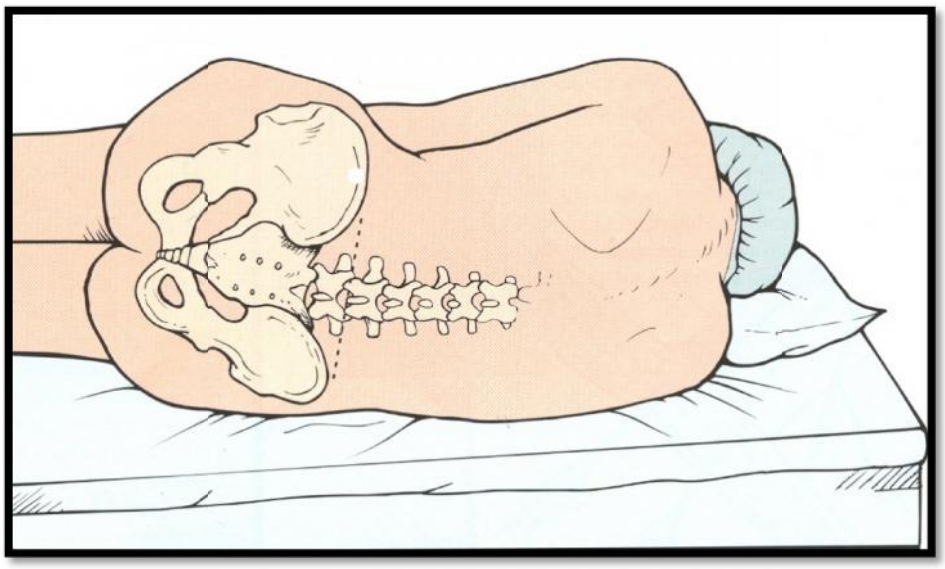


Figure 5: Line of Tuffier

Vertebral canal[7]

Vertebral canal is bound posteriorly by spinous processes and interspinous ligaments, laterally by the pedicles and posterolaterally by the laminae and ligamentum flavum. It terminates superiorly in the foramina magnum and inferiorly in the sacral hiatus. The vertebral canal contains the spinal cord, dorsal root ganglia and ventral rootlets, roots of the spinal nerves, sympathetic trunk, rami communicantes, adipose tissue, blood vessels, CSF and spinal membranes.

Spinal cord[21]

The average length of the spinal cord in males is 45 centimeter (cm) and females it is 42 cm (Figure 6).

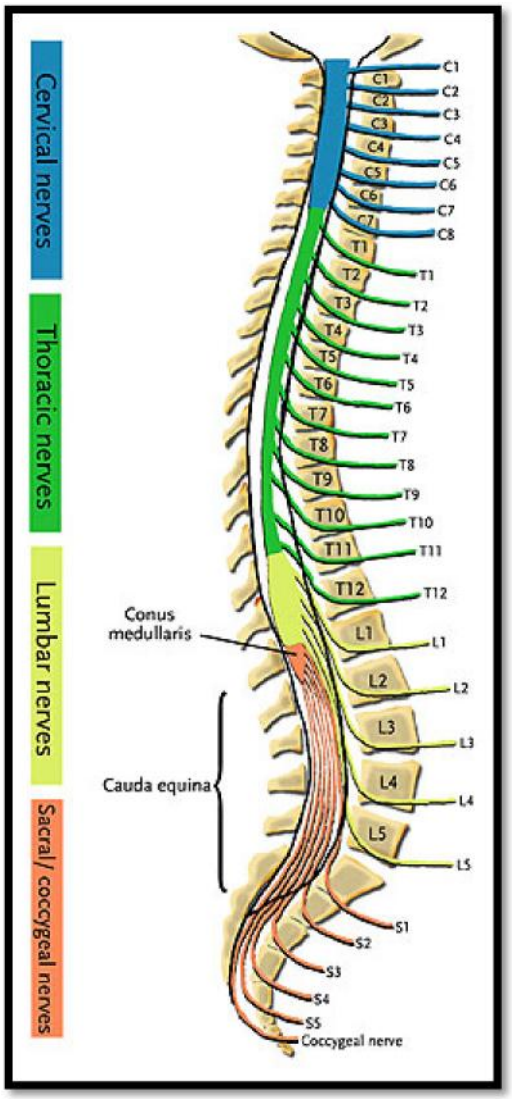


Figure 6: Spinal nerve roots

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

a continuation of the piamater. The length of the spinal cord differs according to age. In the first trimester, the fetal spinal cord extends up till the end of the spinal column. As the fetus grows, the vertebral column lengthens more than the spinal cord. At birth, the spinal cord ends approximately at L_3 space. In an adult it ends approximately at L_1 space.

Blood Supply of Spinal Cord[21]

The spinal cord receives blood supply from three arteries, one anterior and two posterior spinal arteries (Figure 7).

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

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

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

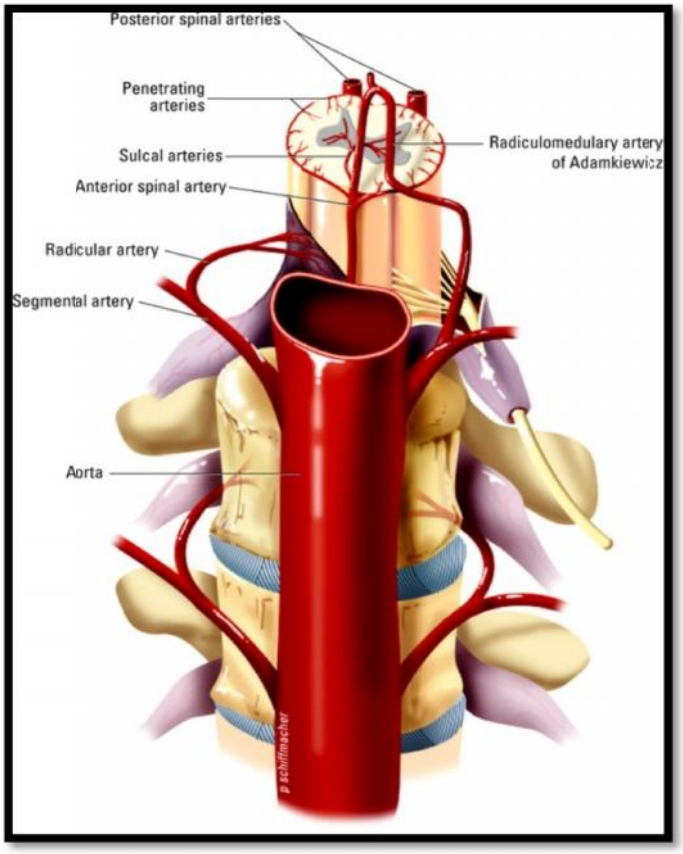


Figure 7: Blood Supply of Spinal Cord

Spinal Meninges[23]

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

Dura mater[24]

This is a tough outermost fibro-elastic covering consisting of outer endosteal layer and inner meningeal layer. Fibers of duramater run longitudinally, thus it is important to insert the spinal needle in such a way that its fibers are split and not cut. Dural sac ends at lower border of S_2, where it is pierced by filum terminale.

Arachnoid mater[24]

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

Pia mater[24]

The piamater, the innermost membrane is a vascular sheath which closely invests the brain and spinal cord. It continues till the coccyx as filum terminale.

Subarachnoid Space[24]

The space between the arachnoid and pia mater 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 in free communication with 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 mater 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[24]

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 cerebro-medullary cisterna (cisterna magna) through foramen of Magendie and foramina of Luschka. From the cisterna magna, CSF enters subarachnoid space circulating around brain and spinal cord before being absorbed into the arachnoid granulations over the cerebral hemispheres.

Composition of cerebrospinal fluid

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

PHYSIOLOGY OF SUB ARACHNOID BLOCK

The various factors, which control the different effects of a spinal anaesthetic technique, are: [25]

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

The various factors which affect the spread of local anaesthetics include: [26,27]

1) Patient factors:

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

2) Technical factors

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

The nerve roots as well as spinal cord take up local anaesthetics after injection into the subarachnoid space. More the surface area of exposure of the nerve root, greater is the uptake. There are two mechanisms for uptake of local anaesthetics. The first mechanism is by diffusion from CSF to the pia mater and into the spinal cord. This is a slow process and only the most superficial portion of spinal cord is affected by it. The second method of local anaesthesic uptake is by extension into the spaces of Virchow- Robin, which are areas of pia mater that surround the blood vessels that penetrate the CNS. These spaces connect with perineuronal clefts that surround the nerve cell bodies in the spinal cord. The site of action is on both anterior and posterior nerve roots, affecting smaller nerve fibers first, and thick large motor fibers last. Generally, the sympathetic paralysis is more diffuse and will extend to two to four segments above motor block. The sympathetic fibers are affected first and are last to recover. On the other hand, motor nerve blockade is usually last to be affected and first to recover. [28]

Sequence of spinal anaesthesia (SA) [29]

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

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

Sympathetic blockade

Since the level of sympathetic denervation determines the magnitude of cardiovascular responses to subarachnoid block, it might be anticipated that the higher the level of neural blockade, the greater would be the change in the cardio-circulatory parameters. Sympathetic fibers are blocked usually two to three segments higher than sensory fibers and sensory block is two segments higher than motor block

Cardiovascular effects of spinal anaesthesia[27]

The autonomic denervation accompanying spinal block influences cardiovascular system in the following ways:

a. Vasodilatation of resistance and capacitance vessels.
b. Block of cardiac efferent sympathetic fibers from T_1-T_4 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 T_4 is associated with fall in BP. Slowing of HR is caused if any of anterior roots carrying sympathetic cardiac accelerator fibers are blocked as may happen in high spinals above T_4-T_5. Bradycardia may also be due to lowering of BP in the right atrium consequent to diminished venous return.

Theories of causation of hypotension.

a) Diminished cardiac output due to reduction of venous return
b) Dilatation of post arteriolar capillaries and small venules
c) Paralysis of sympathetic nerve supply to heart.
d) Paralysis of sympathetic nerve supply to adrenal glands with consequent catacholamines depletion.

Cerebral Blood Flow

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

Respiratory System

During spinal anaesthesia breathing becomes quiet and tranquil. This is not only due to motor blockade but also due to differentiation with reduction of sensory input to the respiratory center. The pulmonary gas-exchange is preserved. Intercostal paralysis is compensated for by increased descent of the diaphragm, which is made easier by a lax abdomen.

Gastrointestinal System

Pre-ganglionic sympathetic fibers from T_5-L_l are inhibitory to the gut. There is no effect on oesophagus, the innervation of which is vagal. The small gut is contracted as sympathetic inhibitory impulses are removed, the vagus being dominant. Pressure within the bowel lumen is increased. Nausea and vomiting occur due to hypotension. Relaxation of sphincters also occurs.

Causes of Nausea and Vomiting

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

Genitourinary System

Renal blood flow due to hypotension is decreased but does not cease until blood pressure has fallen to about 80 mm Hg. These changes are transient. The penis becomes engorged and flaccid due to paralysis of nervi erigenti (S_2 to S_3). Post spinal retention of urine may be moderately prolonged as S_2 to S_3 contain small autonomic fibers and their paralysis lasts longer that of larger sensory and motor fibers.

Uterus

The tone of uterus is not greatly altered after spinal analgesia in pregnancy..

Body Temperature

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

PHARMACOLOGY

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

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

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

Classification:

Clinically useful agents can be classified into two groups depending on the link between the aromatic portion and the intermediate chain. The aminoester groups have an ester link and include procaine, chloroprocaine and amethocaine. The amino amides have an amide link between the aromatic head and the intermediate chain and include lignocaine, bupivacaine, levobupivacaine, mepivacaine, prilocaine, etidocaine and ropivacaine.

PHARMACOLOGY OF BUPIVACAINE [28,29] :

Local Anaesthetic Drugs : These drugs produce reversible conduction blockade of nerve conduction along the central and peripheral nerve pathways . When the concentration is increased gradually the transmission of autonomic.somatic sensory and somatic motor impulses are interrupted in the same sequence. This produces autonomic blockade ,sensory anaesthesia, and muscle paralysis in the area supplied . Gradual removal by absorption into systemic circulation causes the reversal of this blockade .

Molecular Structure: These drugs have two portions. One is lipophillic while the other is hydrophilic and the two are connected by a hydrocarbon chain. The hydrophilic portion is usually a tertiary amine while the lipophillic postion is an unsaturated aromatic ring.

This lipophillic potion is essential for anaesthetic activity.

BUPIVACAINE[30] : Bupivacaine is a long acting, amide-type local anaesthetic. It was prepared by A.F. Ekenstam in 1957 and introduced by Telivuo in 1963.

Chemically related to lignocaine and its structure is similar to that of Mepivacaine except that the amine-containing group is a butyl piperidine. Its potency is approximately four times that of lignocaine.

Its long duration of action plus its tendency to provide both sensory and motor block has made it a popular drug for providing prolonged analgesia during labor or the postoperative period.

By taking advantage of indwelling catheters and continuous infusions, bupivacaine can be used to provide several days of effective analgesia.

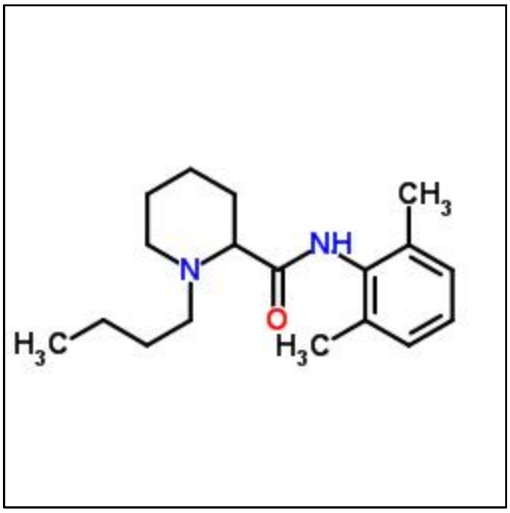


Figure 8 :Structure of Bupivacaine

Physiochemical Properties :

1. Chemical name : 1-N-butyl-DL-piperidine 2 carboxylic acid-2,6 dimethyl anillide hydrochloride
2. Molecular weight : 324.9

   Solubility : 28
3. pka : 8.1
4. Half life : 1.5 -5.5 hours in adults and 8.1 in neonates.
5. Specific gravity : 1.026 at 37°C
6. Volume of Distribution = 73 liters

Pharmacology[31] :

The addition of a butyl group to the piperdine Nitrogen of Mepivacaine makes Bupivacaine 35 time more lipid soluble

Potency :

It is approximately 3 to 4 times more potent tha Mepivacaine or Lignocaine

Onset and Duration :

The onset of action of Bupivacaine is between 5 and 7 minutes and maximum anaesthesia is achieved in between 15 and 25 minutes .

The duration varies according to the type of block ; average duration of epidural block is – 2.5 to 4 hours average duration of spinal block is – 2 to 3 hours

Mechanism of Action :

The mechanism of action of bupivacaine is similar to lignocaine.

Local Anaesthetics bind to specific site in the voltage gated sodium channels and block Na+ current and reduce the excitability of Neuronal, Cardiac or CNS Tissue.

The large transient increase in permeability to sodium ions necessary for popogation of the impulse is prevented.

Thus the resting membrane potential is maintained and depolarisation in response to stimulation is also prevented.

The mechanism of sodium conductance blockade :-

a) The cationic form of Local anaesthetics acts on the receptors within the Na+ Channel on the cell membrane and block it. The local anaesthetics can reach

the Na+ channel either via the lipophillic pathway directly across the lipid membrane or via the axoplasmic opening .

b) The second mechanism is a non specific action i.e. by membrane expansion .

Available concentrations of Bupivacaine: - 0.25% and 0.5%

Dosage of Bupivacaine: - Maximum dosage – 3mg /Kg body weightBupivacaine is less likely to produce vasoconstriction unless sufficiently dilute [32] . Adrenaline prolongs its action only marginally, if at all.

Tachyphylaxsis is much less likely than with Lignocaine .

Metabolism and Elimination :-

Bupivacaine gets metabolised by the following mechanisms–

a) Aromatic Hydroxylation
b) N- dealkylation
c) Amide Hydrolysis
d) Glucuronide – conjugation

The chief mechanism is N- dealkylation and the metabolite is N-desbutyl Bupivacaine .

The mean total of urinary excretion of Bupivacaine and its dealkylation and hydroxylation metabolites account for >40% of the total anesthetic dose.

Systemic Actions :-

Central Nervous System:-

Over dosage concentrations of Bupivacaine produce dizziness and light headedness followd by visual and auditory disturbances such as difficulty to focus and tinnitus .

Shivering , muscular tremors and tremors of facial muscles can occur.

The plasma concentration of Bupivacaine associated with seizures is 4.5 to 5.5 mcg/ml

Cardiovascular System :-

Usually cardiovascular system is more resistant to the toxic effects of high plasma concentrations of local anaesthetics.

Lignocaine concentration <5mcg/ml is devoid of adverse effects but causes decrease in automaticity. Lignocaine concentrations 5-10 mcg/ml can produce profound hypotension due to arteriolar vascular smooth muscle relaxation and direct myocardial depression.

Blockade of cardiac sodium channels by local anaesthetics contributes to anti dysrhythmic properties.

With increase in concentration more Na+ channels become blocked and conduction and automaticity become affected adversely [33].This is evident by prolongation of PR interval and QRS Complexes.

Accidental IV injection of bupivacaine may result in precipitous Hypotension , cardiac dysrhythmias and AV Heart block.

Most common dysrythmias include Widening of QRS Complex,Premature Ventricular contractions and Ventricular tachycardia[34].

Cardiotoxicity of Bupivacaine is seen when plasma concentrations are 8 – 10 mcg/ml [35]

Pregnancy may increase sensitivity to cardiotoxic effects of Bupivacaine [36] .

Cardiotoxic threshold of Bupivacaine may be decreased in patients being treated with drugs like digitalis,calcium channel blockers and beta blockers [37].

Epinephrine and phenylephrine can increase cardiotoxicity of Bupivacaine induced inhibition of catecholamine induced production of cyclic AMP [38].

Bupivacine blocks cardiac Na+ ion channels during systole but due to its high lipid solubility ,it gets dissociated during diastole. This explains its persistent depressant effect on Vmax and hence greater cardiotoxicity[39]. The R- enantiomer of Bupivacaine is more cardiotoxic.

Tachycardia can enhance frequency dependent blockade of cardiac sodium channels by Bupivacaine[40] .

Treatment :-

Bretyllium 20mg/Kg IV reverses Bupivacaine induced cardiac depression and hence increases the threshold for ventricular tachycardia[41] .

Lipid emulsion infusion is also used for Treatment of cardiotoxicity . Its use is recommended at the earliest sign of toxicity .

Initial bolus of 1.5 ml/Kg 20% lipid emulsion followed by 0.25ml/Kg/min. the infusion should be continued for atleast 10 minutes after circulatory stability is achieved.

Respiratory System :-

Local Anaesthetics in very high plasma levels depress medullary respiratory center which can precipitate decreased oxygenation

Toxicity :-

The toxic plasma concentration is >3mcg/ml [30]but cardiotoxicity of Bupivacaine becomes evident when plasma concentration are 8 – 10 mcg/ml.

Pharmacokinetics[30] :-

Levels of Bupivacaine are detectable in blood 5 minutes after infiltration. Peak blood concentrations depend on the total dosage given and range between 0.14-0.18mcg/ml.

These levels are from 5 mins to 2hrs and slowly reduce to 0.1 to 0.34 mcg/ml in approximately 4 hrs .

Being an amide the liver is the primary site of metabolism of Bupivacaine.

Bupivacaine is secreted in the breast milk and also crosses the placenta but in very less concentrations with feto-maternal concentration ratios ranging from 0.2-0.4[42]

ISOBARIC BUPIVACAINE: Dextrose free solutions of bupivacaine can be slightly hypobaric compared to CSF; the sitting position is likely to cause a greater cephalad spread.[9]

Baricity influences the distribution of local anesthetic solution in the CSF. It is defined as the ratio of density (mass/volume) of local anesthesia solution's density compared to CSF density at 37°C. Thus, baricity influences local anesthetic spread and block height since gravity causes hyperbaric solutions to flow downward in the CSF, whereas hypobaric solutions tend to rise. In contrast, gravity has no effect on the distribution of truly isobaric solution.

FENTANYL[34]

Fentanyl was synthesized by Janssen Pharmaceutica in the year 1960 with the emphasis on potency and safety.

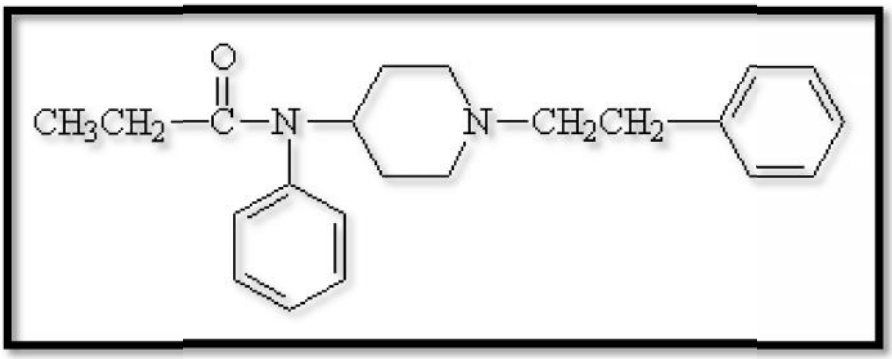


Figure 9: Chemical Structure of Fentanyl

Fentanyl citrate is a synthetic phenyl piperidine opioid analgesic and a chemical congener of the reversed ester of Pethidine (Meperidine)

Physiochemical properties

It occurs as a white crystalline powder. It is highly lipid soluble and sparingly soluble in water. The commercially available injections have a pH of 7 to 7.5. pKa value of 8.4. At physiologic pH of 7.4 less than 10% is unionized. Its plasma protein binding is 84%. It is 50 to 100 times more potent than Morphine. Injection should be protected from light and stored at 15 to 30° C. It is also available as intrabuccal, transdermal and aerosolized preparations.

Mechanism of action

Fentanyl is primarily a mu receptor agonist and these mu receptors are present in the brain (periaqueductal gray matter of brain stem, amygdala, corpus striatum and hypothalamus), spinal cord (substantia gelatinosa) and peripheral nerves. These receptors are involved with pain perception, integration of pain impulses and responses to pain.

Opioids act as agonists at stereospecific opioid receptors at pre-synaptic and post-synaptic sites. The most likely mechanism of these peripheral actions appears to be activation of opioid receptors on primary afferent neurons; Fentanyl mimics the actions of endogenous ligands by binding to receptors resulting in activation of pain modulating system. Opioid receptor activation leads to decrease in neurotransmission. This decrease occurs largely by presynaptic inhibition of neurotransmitter (acetylcholine, dopamine, norepinephrine, substance P) release.

Biochemical events on activation are increased potassium conductance leading to hyperpolarization and calcium channel inactivation or both. Fentanyl also binds to Kappa receptors to a lesser extent in the spinal cord and mediates sedation and miosis.

Pharmacokineties

Absorption

After I.V administration the onset of action is rapid with short duration of action. The effect site equilibration time between blood and the brain is 6.4 minutes.

Distribution

Fentanyl has high lipid solubility, so distributes widely throughout the body to inactive sites. Initially it distributes to vascular organs such as heart, lungs and brain, then to skeletal muscles and fat. Lungs also serve as inactive storage site with estimated 75% of initial dose undergoing first pass pulmonary uptake. Volume of distribution for Fentanyl after administration is 4 ± 0.4 Liters kg^{-1}.

Metabolism

- Fentanyl is extensively metabolized by N-demethylation producing Norfentanyl in the liver and hydrolysed to 4-N amilinopiperidine and proprionic acid.

- Lungs exert significant first pass effect and transiently take up 75% of injected dose of Fentanyl, 80% of Fentanyl is bound to plasma proteins, approximately 50% to α – acid glycoprotein.

Elimination

Fentanyl is excreted mainly in the urine as metabolite and less than 8% is excreted as unchanged drug. The mean clearance after i/v administration is between the range of 34-53 liters $hour^{-1}$ or approximately 13 ml min^{-1} kg^{-1}. Mean terminal half

lives are between 2.5 and 8 hours. Context sensitive half life (After continuous infusion for 4 hours) is 260 minutes and this reflects saturation of inactive tissues during infusion and

Adverse Reactions

Cardiovascular system: Hypotension, orthostatic hypotension, syncope and drug induced bradycardia.

Respiratory System: Dose dependent depression of ventilation which is characterized by reduced response of ventilator centres to carbon dioxide.

Central nervous system: In the absence of hypoventilation, fentanyl decreases cerebral blood flow and in turn decreases intracranial pressure. Myoclonus during administration may resemble generalized tonic clonic seizures. It can produce thoracic and abdominal skeletal muscle rigidity. Miosis may occur as most of mu and kappa agonists cause constriction of pupil by an excitatory action on the parasympathetic nerve innervating the pupils.

It causes pruritus when administered for central neuraxial blockade. . Pruritus produced by neuraxial opioids is likely due to cephalad migration of opioids in cerebrospinal fluid and subsequent interaction with opioid receptors in trigeminal nucleus. Pruritus is more likely to be localized to face, neck and upper thorax.

Biliary system

It produces increase in biliary duct pressure and sphincter of oddi tone which are dose dependent.

Gastrointestinal system

It delays gastric emptying time and it can also produce nausea and vomiting by directly stimulating chemoreceptor trigger zone.

Immune system

The overall effect appears to be suppressive leading to increased susceptibility to infection.

Allergic reactions

True allergic and anaphylactoid reactions are rare. More commonly local reactions may occur due to preservatives or histamine release

Tolerance and physical dependence

Tolerance can occur without physical dependence but the reverse does not seem to occur. Cross tolerance develops between all the opioids.

METHODOLOGY

The present study titled **"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE BETWEEN INTRATHECAL 0.5% ISOBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL AND 0.5% HYPERBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL FOR INFRAUMBILICAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL"** was conducted in the Department of Anaesthesiology, KLE's Dr. Prabhakar Kore Hospital and Medical Research Center, Nehru Nagar, Belagavi during the period of January 2017 to December 2017 .

Source of data

Patients between the age group of 18-60 yrs, belonging to ASA Grade I and II scheduled for elective infraumbilical surgeries at K.L.E`S Dr. Prabhakar Kore Hospital and Medical Research Center , Nehru Nagar, Belagavi between January 2017 to December 2017 were included.

Study Design:

A one year randomised controlled trial.

Study Period:

One year from January 2017 to December 2017.

Selection criteria

Inclusion:

- Patients undergoing elective infraumbilical surgeries
- Age: 18 to 60 years
- ASA Grade I and Grade II patients
- Patients providing consent
- Weight : 50 – 75 kgs
- Height : 150 – 165 cms.

Exclusion:

- Patients refused for the study
- Hypovolemic patients
- Unco-operative patients
- Patients with spinal deformities
- Contraindications to spinal anaesthesia .
- Pre-existing neurological deficits in the lower extremities, and cardiovascular,respiratory,neurological, psychological, hepatic, or renal disease.
- Pregnant patients

Sample size:

Total sample size is 80 patients.

0.5% Isobaric Bupivacaine with 25 micrograms Fentanyl . Group A= 40

0.5 % Hyperbaric Bupivacaine with 25 micrograms Fentanyl. Group B = 40

Randomisation was achieved by computer generated randomisation chart.

Sample size calculation:

Using the formula, sample size =

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

Level of significance was taken as 5%

Power of the test used was taken as 80%

type I error rate $\alpha = 0.05$ and

type II error rate $\beta = 0.2$

Taking the level of significance at 5%(α=0.05), power of the test as 80%(β=0.2), and using one sided test we get $Z\alpha$=1.65 and $Z\beta$=0.84

$S_1$was S.D of 0.5% Isobaric Bupivacaine

$S_2$was S.D of 0.5% Hyperbaric Bupivacaine

$X_1$was time for onset of sensory blockade at T_{10} with 0.75 % Ropivacaine[25]

$X_2$was time for onset of sensory blockade at T_{10} with 0.5 % Ropivacaine[23]

Hence, $Z\alpha = 1.65$

$Z\beta = 0.84$

$S_1 = 3.30$

$S_2 = 1.90$

$X_1 = 11.36$

$X_2 = 13.5$

$$\text{Sample Size} = \frac{2X(1.65+0.84)^2(3.30^2+1.9^2)}{(n)\quad (11.36-13.5)^2}$$

n = 39.27

For ease of calculations and sake of consistent result, sample size was taken as 40. There were thus two groups of 40 each.

Methodology

After obtaining the approval of ethical committee and written informed consent, a total of 80 patients undergoing elective infraumbilical surgeries under spinal anaesthesia were included in the study.

After having met inclusion and exclusion criteria and having obtained informed consent, patients were randomised based on computer generated randomization table into two groups.

Group A : 3ml of 0.5% isobaric bupivacaine with 0.5ml (25 micrograms) of fentanyl making a total volume of 3.5ml of drug.

Group B: 3ml of 0.5% hyperbaric bupivacaine with 0.5ml (25 micrograms) of fentanyl making a total volume of 3.5ml of drug.

A thorough Pre-Anaesthetic Evaluation was done. Detailed medical and personal history was obtained. A detailed physical examination was done. Patients were advised overnight fasting. Routine investigations such as Complete blood count, Random Blood Sugar, Serum Creatinine, Blood Grouping and Typing, Chest X-ray, Electrocardiography were carried out.

In the preoperative holding area, a wide bore i.v. access was secured and patients were preloaded with ringer lactate 10ml/kg half an hour before induction of anaesthesia. Anaesthetic techniques were standardized for all patients.

Inside the operation theatre , the patient were shifted onto the operating table. Standard non – invasive monitors were attached and baseline Heart Rate, BP , SpO_2 was recorded.

Patient were then put in left lateral position and under strict aseptic precautions, L3-L4 space was identified. Skin was infiltrated with 2ml 0f 2% lignocaine. Using 23G Quincke spinal needle L3-L4 subarachnoid space was identified after confirming free flow of clear CSF.

Group A : 3ml of 0.5% isobaric bupivacaine with 0.5ml (25 micrograms) of fentanyl making a total volume of 3.5ml of drug was injected in L3-L4 subarachnoid space.

Group B : 3ml of 0.5% hyperbaric bupivacaine with 0.5ml (25 micrograms) of fentanyl making a total volume of 3.5ml of drug was injected in L3-L4 subarachnoid space.

Patients were then immediately placed in supine position. Intraoperative and postoperative assessments were performed. The following parameters were monitored/measured:

A) **Sensory Blockade** was assessed by pinprick in mid axillary line every minute till T_{10} block occurs , following which it will be assessed at 10 minute intervals for next 2 hrs and at 15 minute intervals beyond 2 hrs till full regression occurs .

   Sensory block onset was taken as the time of administration of drug to the time taken for sensory blockade till T_{10} dermatome and highest sensory dermatome blocked was recorded. Duration of sensory block was taken as the

time for regression to two dermatomes from the highest dermatome reached and time for regression to S_2 would be recorded.

Surgery was allowed to start once T_{10} dermatome was blocked but GA was induced if this does not happen in 30 minutes. Such cases were labeled as Block failure and excluded from final analysis .

B) Motor Blockade was assessed immediately after sensory block assessment using a Modified Bromage scale.

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

Bromage 1:-inability to raise extended leg and knee flexion is decreased, but full flexion of ankle and feet is present.

Bromage 2:-inability to raise leg or flex knees, flexion of ankle and feet present.

Bromage 3:-inability to raise leg, flex knee or ankle or move toes.

Motor block onset was be taken as the time to reach modified Bromage score 3 and total duration of motor block will be taken as the time for return to modified Bromage score 0.

In case patient doesn't attain Bromage score of 3, the highest score attained was documented .

C) Post operative analgesia : Following surgery patient were not put on regular analgesics .

Time for first rescue analgesia was noted and were treated with inj.Diclofenac sodium 75mg added to 100 ml of normal saline.

D) Vitals : HR , BP , and SpO_2 were monitored throughout the surgery .

Blood pressure and Heart rate were recorded at 2, 4, 6, 8, 10, 15, 20, 25, 30 minutes and every 15 minutes till the end of surgery.

Hypotension was defined as decrease in systolic B.P by 20% from baseline values or a systolic B.P less than 90 mm of Hg and was treated with incremental intravenous boluses of mephentermin 5 to 10 mg and a bolus administration of 250ml of Ringer Lactate solution over 10 mins.

Bradycardia will be defined as decrease in heart rate less than 50 beats per minute and will be treated with intravenous Atropine 0.6 mg.

Supplementary oxygen was given through face mask.

E) Side effects: Any side effects which occurred were duly documented .

Statistical Analysis

The data was tabulated and master chart was prepared (Annexure V). The categorical data was expressed as rates, ratios and percentages while continuous data was expressed as mean $\pm$ standard deviation. Student unpaired ' t ' test was used to find significance of study parameters on continuous scale between the two groups. Chi - square test was used to find association between different classes of variables. A p – value < 0.05 was considered statistically significant.

RESULTS

This one year randomised clinical trial was conducted in the Department of Anaesthesiology, during the period of January 2017 to December 2017 at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Center, Nehru Nagar, Belagavi.

A total of 80 patients undergoing infraumbilical surgeries under spinal anaesthesia were randomly allocated into one of the two groups based on a computer generated randomisation chart :

Group A : 3ml of 0.5% isobaric bupivacaine with 0.5ml (25 micrograms) of fentanyl making a total volume of 3.5ml of drug was injected in L3-L4 subarachnoid space.

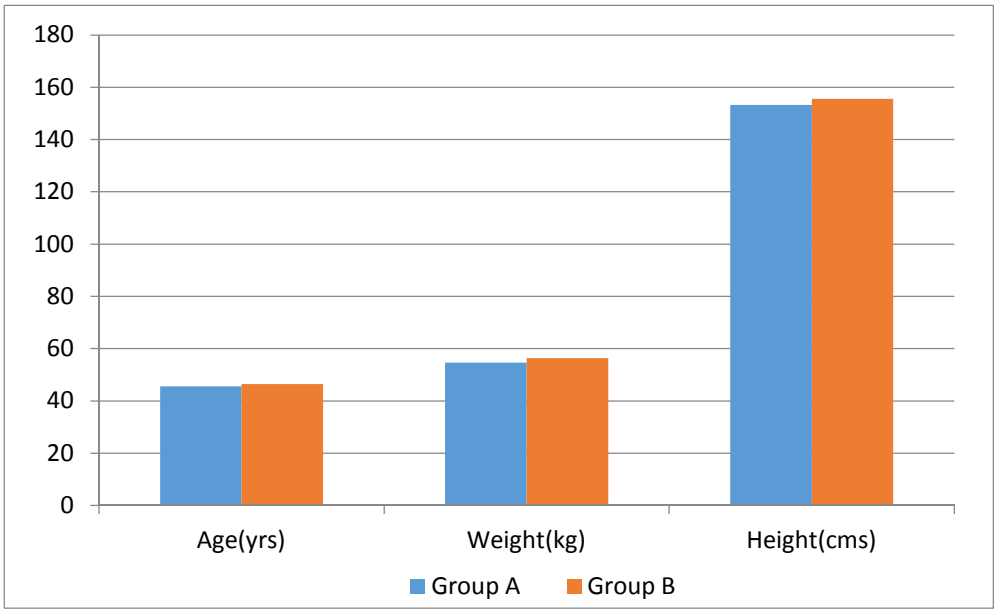
Group B : 3ml of 0.5% hyperbaric bupivacaine with 0.5ml (25 micrograms) of fentanyl making a total volume of 3.5ml of drug was injected in L3-L4 subarachnoid space.

Data obtained was coded and analysed as below.

Table 1: Mean Age, Weight and Height

	Group A		Group B		P value
	Mean	Standard Deviation	Mean	Standard Deviation	
Age(years)	45.55	13.34	46.38	11.26	0.7659
Weight(kgs)	54.58	4.02	56.38	4.47	0.0621
Height(cms)	153.30	4.52	155.57	3.57	0.0146

Graph 1 : Mean Age, Weight and Height



In the present study we found no statistically significant difference between group A and group B with regards to mean age (45.55 ± 13.34 and 46.38 ± 11.26 years respectively; p = 0.7659), mean weight (54.58 ± 4.02 and 56.38 ± 4.47 kgs respectively; p = 0.0621) and mean height (153.30 ± 4.52 and 155.57 ± 3.56 cms respectively; p =0.0237)

Table 2 : Sex Distribution

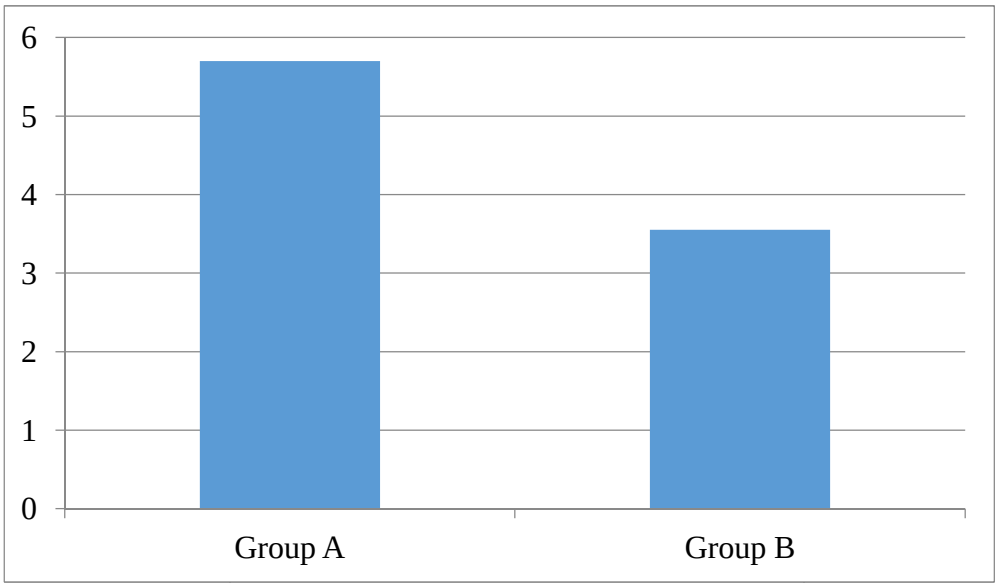
	Group A	%	Group B	%	Total
Female	9	22.5	5	12.5	14
Male	31	77.5	35	87.5	66
Total	40	100	40	100	80

In this study 77.5% were males and 22.5% were females in Group A and 87.5 % were males and 12.5% were females in Group B, suggesting both the groups had comparable demographic characteristics .

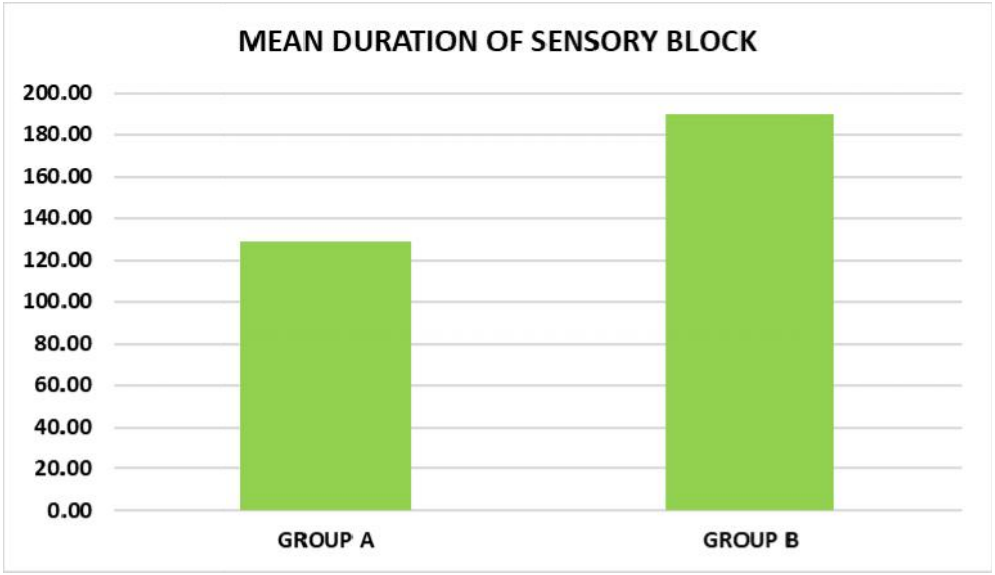
Table 3 Onset and duration of sensory block(Also refer Graphs 3,4)

	Onset(minutes)		Duration(minutes)	
	Mean	Standard Deviation	Mean	Standard Deviation
Group A	5.70	0.69	129.08	3.47
Group B	3.55	0.96	189.65	9.58
p value	< 0.001		< 0.001	

Graph 2 : Onset of sensory block



Graph 3: Duration of sensory block



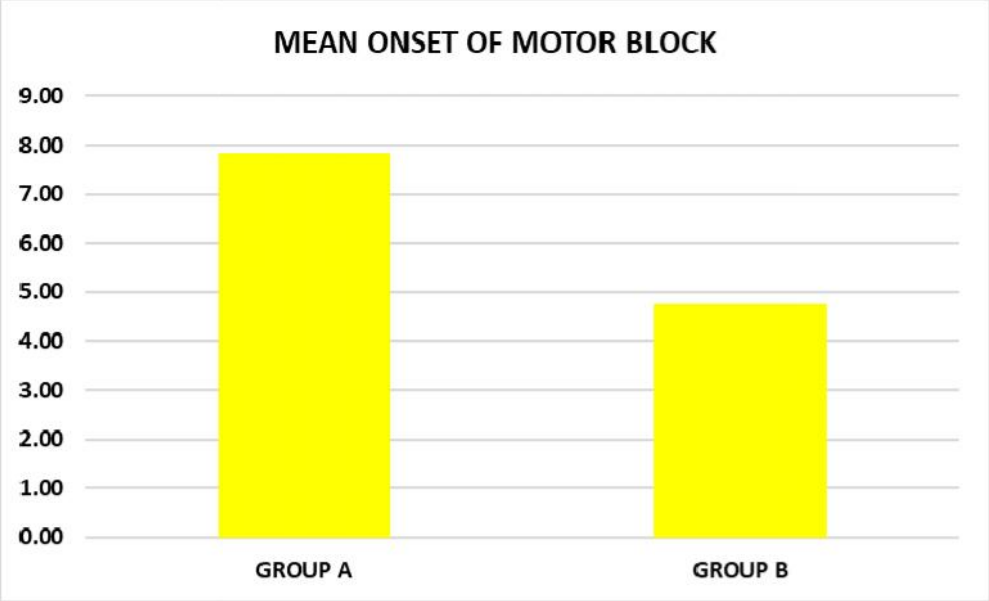
In our study, mean onset of sensory blockade was faster in Group B (3.55 $\pm$ 0.96min) than in group A (5.70 $\pm$ 0.69 min) and was statistically significant ($p < 0.001$).

The mean duration of sensory blockade was longer in group B (189.65$\pm$ 9.58 min) than in group A (129.08 $\pm$ 3.47min) and was statistically highly significant ($p < 0.001$)

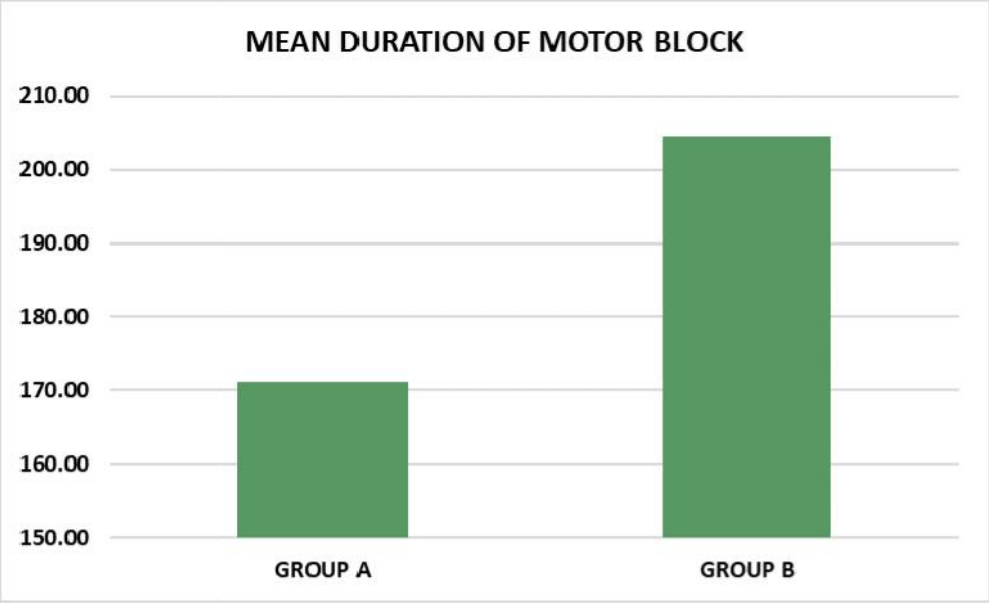
Table 4 : Onset and duration of motor block (Also refer graphs 5,6)

	Onset(minutes)		Duration(minutes)	
	Mean	Standard Deviation	Mean	Standard Deviation
Group A	7.83	0.78	171.18	4.31
Group B	4.78	0.80	204.55	12.46
p value	< 0.001		< 0.001	

Graph 4 : Onset of Motor Block



Graph 5 : Duration of Motor block



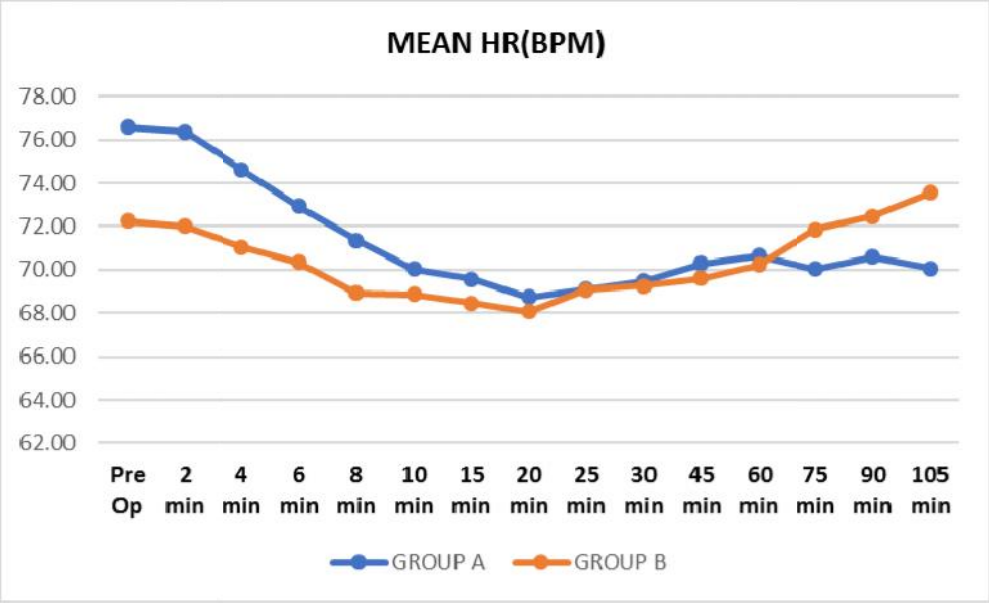
In the present study, mean onset of motor block was faster in group B (4.78±0.80 min) than group A(7.83 ± 0.78 min) and was statistically highly significant (p< 0.001).

The mean duration of motor block was longer in group B (204.55± 12.46 min) than group A (171.18 ± 4.31 min) and was statistically highly significant (p < 0.001)

Table 5: Comparison of mean heart rate at different time intervals (bpm)

Intervals(min)	Group A		Group B		p value
	Mean	SD	Mean	SD	
Pre op	76.60	6.74	72.28	6.47	0.0045
2	76.38	7.19	72.00	6.56	0.0057
4	74.63	6.82	71.05	6.40	0.0180
6	72.95	6.71	70.35	6.61	0.846
8	71.35	7.51	68.93	5.61	0.1060
10	70.05	7.72	68.85	7.16	0.4732
15	69.58	7.26	68.45	7.21	0.4889
20	68.75	8.45	68.05	7.21	0.6914
25	69.13	7.70	69.08	7.87	0.9772
30	69.48	7.53	69.28	7.23	0.9039
45	70.28	6.12	69.60	7.50	0.6605
60	70.65	6.60	70.23	7.10	0.7824
75	70.05	6.81	71.87	7.91	0.2830
90	70.61	7.32	72.47	7.06	0.2848
105	70.07	5.48	73.57	8.29	0.0706

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



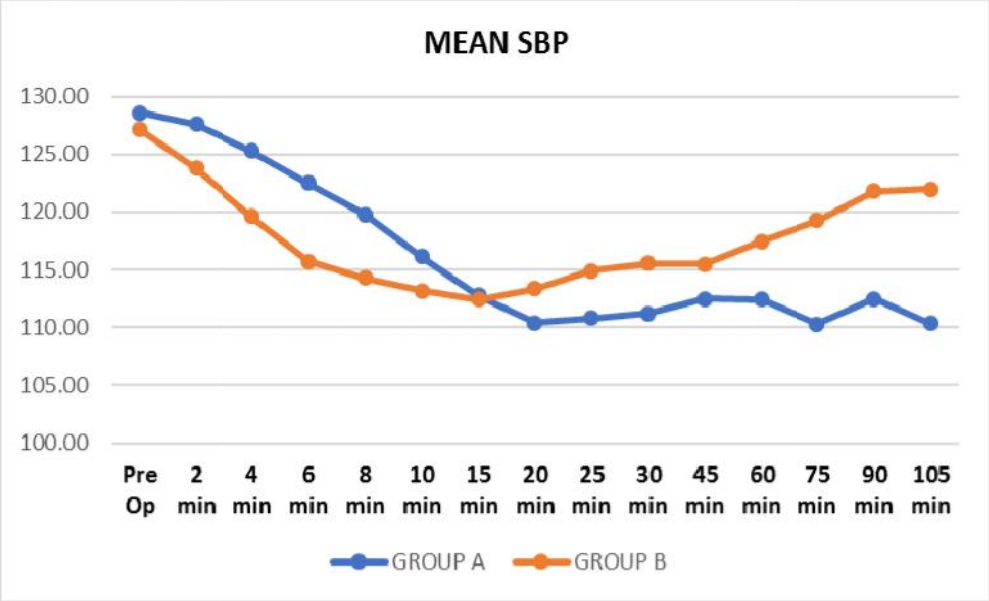
In this study the mean heart rate in the pre operative phase was 76.60 ±6.74 bpm in group A and 72.28 ± 6.47 bpm in group B and was comparable (p = 0.0045).

The heart rate fell to 70.65± 6.60 bpm at 60 minutes in group A while it fell to 70.23± 7.10 bpm at 60 minutes in group B.

Table 6: Comparison of systolic blood pressure at different time intervals (mm of Hg)

Intervals(min)	Group A		Group B		p value
	Mean	SD	Mean	SD	
Pre op	128.60	9.23	127.15	8.95	0.4779
2	127.58	8.83	123.78	10.79	0.0887
4	125.28	8.93	119.63	10.74	0.0125
6	122.50	9.17	115.75	11.83	0.0055
8	119.78	9.20	114.28	10.14	0.0130
10	116.13	9.05	113.20	10.56	0.1873
15	112.78	9.13	112.45	11.21	0.8873
20	110.40	7.82	113.35	10.69	0.1631
25	110.83	8.10	114.90	9.28	0.0397
30	111.23	7.31	115.55	9.98	0.0300
45	112.48	8.54	115.45	10.41	0.1629
60	112.40	8.54	117.45	8.86	0.0113
75	110.31	17.36	119.4	8.77	0.0064
90	112.47	8.48	121.81	9.02	0.0000
105	110.33	6.87	122.00	9.09	0.0000

Graph 7 : Comparison of systolic blood pressure at different intervals (mm of Hg)



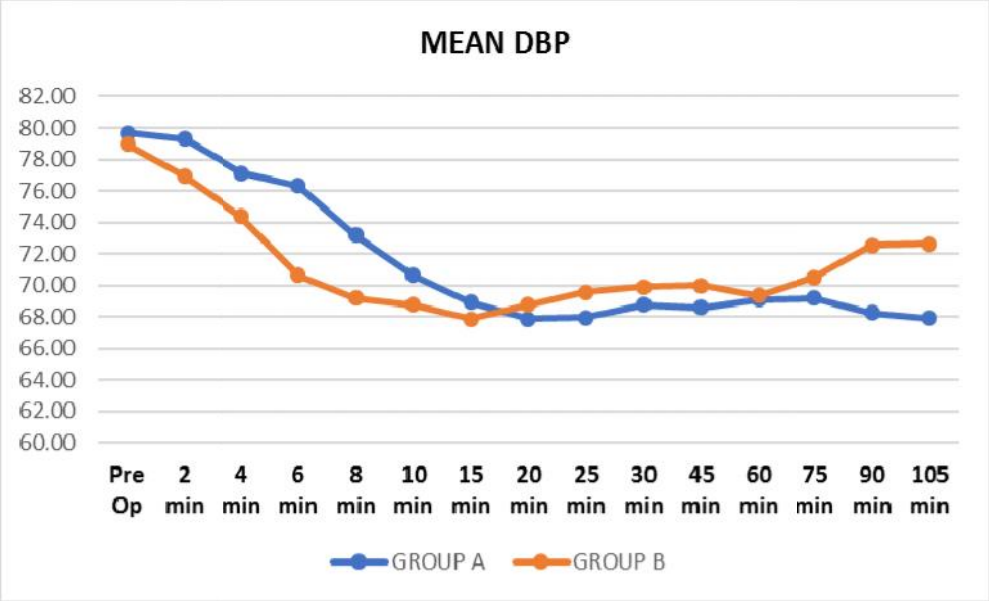
In this study the mean systolic BP in the pre operative phase was 128.60 ± 9.23 mm of Hg in group A and 127.15 ± 8.95 in group B and was comparable (p = 0.4779).

The systolic BP fell to 112.40 ± 8.54 mm of Hg at 60 minutes and 110.33 ± 6.87 mm of Hg at 105 minutes in group A while it fell to 117.45 ± 8.86 mm of Hg at 60 minutes and 122.00 ± 9.09 mm of Hg at 105 minutes in group B.

Table 7: Comparison of diastolic blood pressure at different time intervals (mm of Hg)

Intervals(min)	Group A		Group B		p value
	Mean	SD	Mean	SD	
Pre op	79.70	10.45	78.95	8.13	0.7211
2	79.30	10.17	76.90	8.90	0.2648
4	77.15	8.58	74.35	9.70	0.1755
6	76.33	9.00	70.65	8.52	0.0049
8	73.18	7.01	69.20	47.53	0.0168
10	70.63	6.42	68.78	7.33	0.2332
15	68.93	7.92	67.85	6.25	0.5024
20	67.88	6.77	68.75	5.67	0.5326
25	67.95	6.59	69.55	5.27	0.2341
30	68.78	5.48	69.90	5.92	0.3807
45	68.60	5.59	70.00	6.85	0.3198
60	69.10	5.66	69.35	4.52	0.8276
75	69.21	7.91	70.49	4.31	0.3871
90	68.24	6.66	72.53	4.11	0.0023
105	67.93	5.95	72.61	4.06	0.0022

Graph 8 : Comparison of diastolic blood pressure at different intervals (mm of Hg)



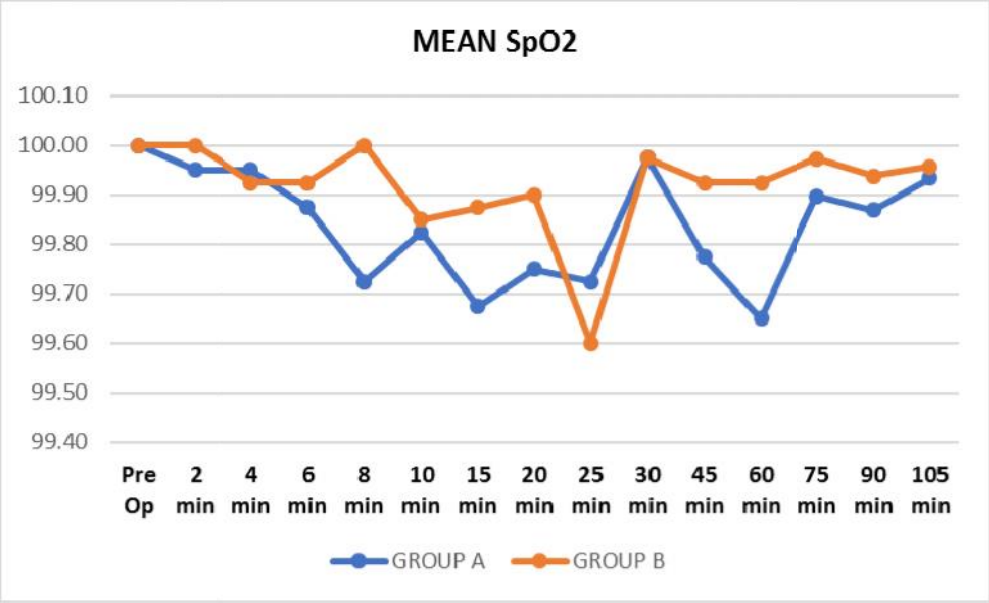
In this study the mean diastolic BP in the pre operative phase was 79.70 ± 10.45 mm of Hg in group A and 78.95 ± 8.13 mm of Hg in group B and was comparable (p =0.7211).

The diastolic BP fell to 69.10 ±5.66 mm of Hg at 60 minutes and 67.93 ±5.95 mm of Hg at 105 minutes in group A while it fell to 69.35 ± 4.52 mm of Hg at 60 minutes and 72.61 ± 4.06 mm of Hg at 105 minutes in group B.

Table 8: Comparison of SpO_2 at different time intervals (%)

Intervals(min)	Group A		Group B		p value
	Mean	SD	Mean	SD	
Pre op	100	0	100	0	-
2	99.95	0.22	100	0	0.1559
4	99.95	0.32	99.93	0.35	0.7383
6	99.88	0.33	99.93	0.27	0.4624
8	99.73	0.60	100.00	0.00	0.0048
10	99.83	0.50	99.85	0.48	0.8208
15	99.68	0.62	99.88	0.40	0.0898
20	99.75	0.59	99.90	0.30	0.1559
25	99.73	0.51	99.60	0.84	0.4230
30	99.98	1.39	99.98	0.16	1.000
45	99.78	0.58	99.93	0.27	0.1395
60	99.65	0.58	99.93	0.35	0.0121
75	99.90	0.31	99.97	0.16	0.1891
90	99.87	0.34	99.94	0.25	0.3444
105	99.93	0.25	99.96	0.21	0.7236

Graph 9 : Comparison of SpO_2 at different intervals (%)



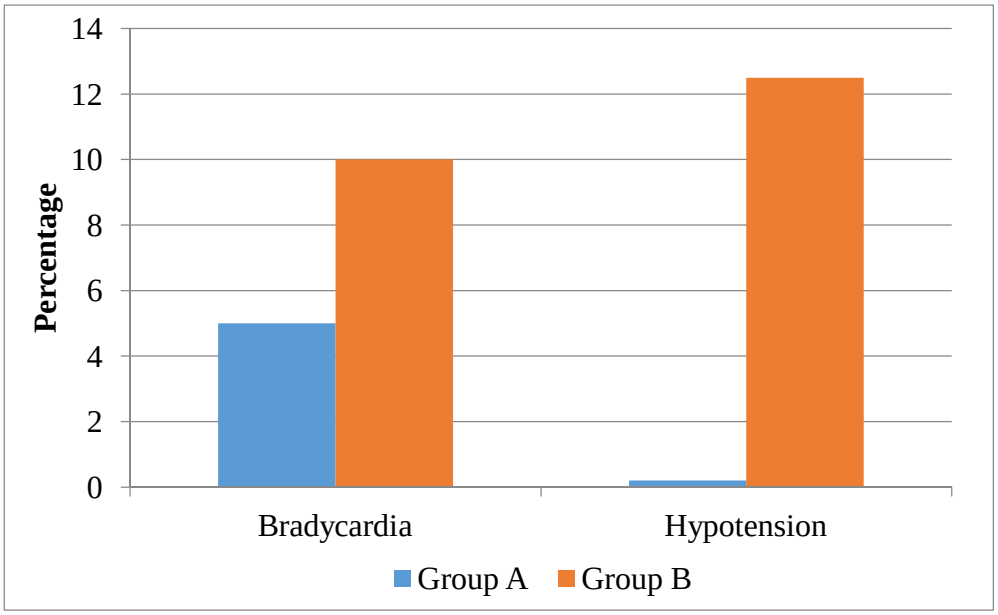
In this study the SpO_2 in the pre operative phase was 100 $\pm$ 0 % in both group A and group B and was thus identical.

The SpO_2 was comparable in both groups throughout the study period (p values > 0.05)

Table 9: Comparison of complications and side effects observed

	Group A	Percentage	Group B	Percentage
Hypotension	-	-	5	12.5
Nausea and vomiting	-	-	-	-
Bradycardia	2	5	4	10

Graph 10 : Complications/ Side effects observed (Percentage)



In the present study, 5 % of patients in group A and 10 % of patients in group B developed bradycardia.

12.5 % of patients in group B developed Hypotension.

None of the patients in either group developed Nausea and vomiting or respiratory depression

DISCUSSION

Spinal administration of local anaesthetics is the choice of anaesthesia technique for infraumbilical surgeries. Spinal anaesthesia has a quick onset, provides good relaxation with adequate sensory blockade. Hence it is one of the most commonly performed anaesthetic procedures in today's times.

With the advancement of technology and availability of better equipment, surgeries have become faster. However the patient's safety has always been the primordial importance. Hence research and development in the field of pharmacology has been encouraged for the discovery of newer, safer and better drugs.

Bupivacaine, the most commonly used local anaesthetic in spinal anaesthesia, is a racemic mixture (50:50) of its two enantiomers, levobupivacaine, S (−) isomer and dextrobupivacaine, R (+) isomer. Adverse reactions involving central nervous system and cardiovascular system have been reported in literature. These adverse reactions have been attributed to the R (+) isomer of bupivacaine.

The advantages of using opioids like fentanyl with local anaesthetics are sensory blockade can be achieved with fewer pulmonary complications, early return of bowel functions, early discharge from hospital.

In our study, the only variable was baricity, since dose, volume, and concentration were kept constant and even both solutions are produced by the same manufacturer. The isobaric bupivacaine (Anawin 0.5%) used in this study is an isotonic bupivacaine HCL 5 mg/mL, while the hyperbaric bupivacaine (Anawin

Spinal 0.5% Heavy) is an isotonic bupivacaine HCl 5 mg/mL and dextrose monohydrate 80 mg/mL.

Baricity influenced the distribution of local anesthetic solution in the CSF. It is defined as the ratio of density (mass/volume) of local anesthesia solution's density compared to CSF density at 37°C. Thus, baricity influences local anesthetic spread and block height since gravity causes hyperbaric solutions to flow downward in the CSF, whereas hypobaric solutions tend to rise. In contrast, gravity has no effect on the distribution of truly isobaric solution.

In the present study, hemodynamic stability was better in Group A compared to Group B. The time of onset of sensory blockade and motor blockade was faster in Group B compared to Group A. The duration of sensory and motor blockade were prolonged in Group B compared to Group A which was clinically significant.

A study conducted by Madhusudan Upadya et al in January 2016 compared intrathecal hyperbaric bupivacaine-fentanyl mixture and isobaric bupivacaine-fentanyl mixture in common urological procedures[2]. One hundred patients belonging to American society of Anaesthesiologists grade I and grade II undergoing urological procedures were randomized into two groups. Group 1 received 3ml of 0.5% bupivacaine with 25 micrograms fentanyl while Group II received 3ml of 0.5% hyperbaric bupivacaine with 25 micrograms fentanyl. The parameters measured included onset and duration of motor and sensory blockade, heart rate, blood pressure, respiratory rate . They concluded that isobaric bupivacaine-fentanyl mixture was found to provide adequate anaesthesia with minimal incidence of haemodynamic instability. The results were similar to our study.

Hallworth *et al*.[14] studied the effect of position and baricity on the spread of intrathecal bupivacaine. The patients were given 10 mg of hyperbaric, isobaric or hypobaric bupivacaine in combined spinal epidural technique either in sitting or right lateral position. They found that baricity had no effect on spread of sensory levels in lateral position compared to sitting position. In the sitting position hypobaric bupivacaine produced higher sensory levels (T_2) than hyperbaric bupivacaine.

Increased baricity produced less motor blockade which was evident in lateral position. The isobaric mixture was injected in the L_{3-4} space getting a median maximum sensory level of T_2 and for hyperbaric it was T_3. The isobaric mixture was not affected by posture unlike the hyperbaric or the hypobaric mixture.[14] Based on this study we decided to keep the left lateral position as the standard position for the spinal anaesthesia procedure. Unlike the study above, we were able to observe only a mean maximum sensory block level of T_{10} in the majority (52%) of our cases with no cases ascending up to a T_4 level using the isobaric mixture.

The isobaric solution produced a mean spread of analgesia to T_2 which was quite unlike our study where T_{10} was the mean. There was variation in the level of hyperbaric spread, which was T_3 in the above study, while it was T_6 in our study. The difference could be attributed to the use of combined spinal epidural technique used in the above mentioned study and also may be due to the variation in the drug dosage and addition of fentanyl to the study drug. The isobaric solution produced a more predictable level of blockade compared to the hyperbaric solution. Placing the patient in the lithotomy position did not show any significant difference in the level of sensory blockade.[14]

Another study by Seewal R, et al in January 2007 evaluated effect of addition of different doses of fentanyl intrathecally to 0.5% hyperbaric bupivacaine on perioperative analgesia and subarachnoid block characteristics in lower abdominal surgery : A dose response study[5]. A population of 60 patients belonging to ASA I and II were randomized to receive a spinal anaesthetic with 2.2 ml of 0.5% hyperbaric bupivacaine saline (control group) or fentanyl 10,20,30 or 40 micrograms. The conclusion was that in a non- obstetric population receiving spinal anaesthetic for lower abdominal surgery, addition of 10 micrograms fentanyl to 0.5% hyperbaric bupivacaine significantly improves the quality and duration of analgesia. No further advantage occurs if the dose of fentanyl is increased upto 40 icrograms

Another study by Mochamat Helmi, et al in February 2014 compared intrathecal use of isobaric and hyperbaric bupivacaine during lower abdominal surgery [6]. Sixty patients with ASA I and II, undergoing elective lower abdominal surgeries with the estimation in duration no longer than 120 minutes were enrolled. Patients were randomized with sealed envelope method into 2 groups. Group I received 4ml of 0.5% isobaric bupivacaine while group 2 received 4ml of 0.5% hyperbaric bupivacaine. Neither the anaesthesiologist performing SAB and collecting perioperative data nor the patients were aware of the used solution.They concluded that isobaric bupivacaine produced more rapid onset and longer duration compared to hyperbaric bupivacaine. This was contrary to our findings where hyperbaric bupivacaine had a faster onset and a longer duration of analgesia.[6]

In a study comparing intrathecal isobaric/hyperbaric bupivacaine combined with fentanyl or morphine for patients undergoing caesarean section, isobaric bupivacaine 9 mg with either 200 µg morphine or 25 µg fentanyl and hyperbaric

bupivacaine 12.5 mg with either 200 µg morphine or 25 µg fentanyl were administered. It was found that there was a significant drop in BP in 1st min in all the four groups. Intrathecal morphine with isobaric bupivacaine had the longest duration of analgesia. The visual analogue scale score in post-operative period was highest for intrathecal fentanyl with isobaric bupivacaine and was lesser for hyperbaric bupivacaine fentanyl group. This was similar to our findings where duration of analgesia was longer for hyperbaric bupivacaine fentanyl group[17].

In another study comparing intrathecal isobaric and hyperbaric bupivacaine anaesthesia for lower abdominal surgeries, 20 mg bupivacaine was used without additives. There was no statistically significant haemodynamic variation between the two groups. It was found that the onset of analgesia and motor blockade was faster with isobaric bupivacaine and the duration of analgesia was prolonged with isobaric bupivacaine, which was contrary to our findings where hyperbaric bupivacaine had a faster onset and a longer duration of analgesia. [6]

In a Cochrane analysis comparing six studies including 394 patients with intrathecal hyperbaric and isobaric bupivacaine,[5] the results were almost similar to our study. It was found that hyperbaric bupivacaine had rapid onset of analgesia and requirement for supplemental analgesia were also less. However variability in the dose, use of adjuvant drugs and differences in the technique used for regional anaesthesia should be taken into consideration[18].

In another study comparing isobaric and hyperbaric bupivacaine 10 mg, with 25 µg fentanyl for elective caesarean sections, it was found that there was no statistically significant difference in the onset of sensory blockade and time to reach maximal (T4) level. However, isobaric bupivacaine took more time for two

dermatomes sensory level regression below T4 and resulted in prolonged block duration, as against our findings where hyperbaric drug had a longer duration of blockade.[19]

Dextrose free solutions of bupivacaine can be slightly hypobaric compared to CSF; the sitting position is likely to cause a greater cephalad spread.[20] Under controlled clinical conditions, for example, Axelsson et al. found that decreasing the volume of drug injected decreased the level of anaesthesia to T10-11 level, but a volume <1.5 ml was not associated with a further decrease in level of anaesthesia.[4] With increasing volume there was an increase in the duration of analgesia and the onset time for complete motor blockade was less. Time to maximum cephalad spread took about 15–18 min in all groups. Time for 2–3 segment regression was on an average between 1.5 and 2 h and the rate of regression was similar in all groups (while using 3 ml the rate of regression was 101 ± 15.4 min to reach a T10 level). Based on this study we took 3 ml as standard volume of bupivacaine in our study. Though we added 25 µg of fentanyl to the mixture, we did not find considerable difference in the results.

Our study results correlated with the studies by Madhusudan Upadya et al.[2] Hemodynamic stability was better with isobaric bupivacaine-fentanyl group compared to Hyperbaric bupivacaine-fentanyl group.

Our study results also correlated with Chambers et al. and Møller et al.[19,20] There was a similar fall in SBP following the administration of spinal anaesthesia with the hyperbaric mixture.[20] In our study, the duration of action of bupivacaine was less with the isobaric group. In general, 3 ml of bupivacaine injected into the lumbar subarachnoid space produces anaesthesia to T7-8 level and making the volume of

drug above or below this produces proportionately higher or lower level of anaesthesia. [4,19,20,35]

Hypobaricity of plain or glucose-free bupivacaine solutions has been demonstrated in studies[11] but frequently they are referred to as 'isobaric' in literature.[31,32] More recently, several studies using high precision equipment to accurately measure the density of commonly used intrathecal drugs and human CSF at 37°C have confirmed that plain bupivacaine is indeed hypobaric in comparison with human CSF.[33]

In another study comparing ropivacaine (12 mg) and bupivacaine (8 mg) with 20 µg fentanyl, it was found that lower doses of local anaesthetics provide effective analgesia when supplemented with additives. In our study, we decided to use 15 mg of drug, as it was the basic dose used in our daily practice as an academic hospital, where the duration of surgery is unpredictable. The study subjects in our study belonged to ASA 1-2 whereas in the other study it was geriatric patients of ASA 2-3 which required lesser dosage in view of the possible adverse effects.[36]

CONCLUSION

Our study showed that 0.5% hyperbaric bupivacaine with fentanyl is significantly more potent than 0.5% isobaric bupivacaine with fentanyl in terms of onset and duration of sensory and motor block in patients undergoing infraumbilical surgery under spinal anaesthesia.

The haemodynamic parameters including HR, SBP and DBP are more stable in 0.5% isobaric bupivacaine with fentanyl than 0.5% hyperbaric Bupivacaine with fentanyl, which is a highly desirable feature.

Intrathecal isobaric bupivacaine-fentanyl mixture is associated with lesser duration of both sensory and motor blockade thereby enabling quicker recovery from anaesthesia and also with better haemodynamic stability for infraumbilical surgeries as compared with hyperbaric bupivacaine fentanyl mixture.

SUMMARY

Spinal anaesthesia is the choice of anaesthesia technique for infraumbilical surgeries. Spinal anaesthesia has a quick onset, provides good relaxation with adequate sensory as well as motor blockade. It has been well documented that the combination of opioids and local anesthetics administered intrathecally has a synergistic analgesic effect. Fentanyl, itself a short acting opioid, potentiates afferent sensory blockade of local anaesthetic and provides an acceptable surgical anaesthesia. Moreover, the adjuvant fentanyl does not prolong recovery.

This one year randomized controlled trial was conducted in the Department of Anaesthesiology, KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, during the period January 2017 to December 2017. A total of 80 patients undergoing infraumbilical surgeries under spinal anaesthesia were allocated into two groups namely, Group A (n =40 , Patients received 3.0 ml of 0.5 % isobaric bupivacaine with 0.5 ml (25mcg) fentanyl intrathecally) and Group B (n =40 , Patients received 3.0 ml of 0.5 % hyperbaric bupivacaine with 0.5 ml (25 mcg) fentanyl intrathecally). Sensory and motor block characteristics like onset and duration were studied. Hemodynamic parameters like heart rate, blood pressure and oxygen saturation were monitored continuously.

Demographic parameters were comparable in both the groups. In this study, onset of sensory block was significantly faster in Group B (3.55 ± 0.96 min) than in Group A (5.70 ± 0.69 min). Duration of sensory block was significantly longer in Group B (189.65 ± 9.58 min) than in Group A (129.08 ± 3.47 min). Onset of motor block was significantly faster in Group B (4.78 ± 0.80 min) than in Group A (7.83 ±

0.78 min). Duration of motor block was significantly longer in Group B (204.55 ± 12.46 min) than in Group A (171.18 ± 4.31 min). Isobaric bupivacaine-fentanyl mixture was associated with better hemodynamic stability as compared with hyperbaric bupivacaine-fentanyl mixture.

Overall, based on the findings of this study it may be concluded that Intrathecal isobaric bupivacaine-fentanyl mixture is associated with lesser duration of both sensory and motor blockade, thereby enabling quicker recovery from anaesthesia and also better haemodynamic stability as compared with hyperbaric bupivacaine fentanyl mixture for infraumbilical surgeries

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ANNEXURE I : CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____ we are requesting you to enrol in study titled **"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE BETWEEN INTRATHECAL 0.5% ISOBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL AND 0.5% HYPERBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL FOR INFRAUMBILICAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROL TRIAL"** conducted by Department of Anaesthesiology, J.N. Medical College, Belagavi under KLE University, Belagavi.

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

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

Purpose of the study:

The purpose of this study is to compare onset and duration of sensory and motor blockade between intrathecal 0.5% isobaric bupivacaine with 25 micrograms fentanyl and 0.5% hyperbaric bupivacaine with 25 micrograms fentanyl for infraumbilical surgeries.

Procedure Involved:

If you agree to enrol yourself in my study, you will be interviewed regarding your present, past and family history. You will then be clinically examined in detail and investigational procedures will be performed. You will be randomly allocated either into Group A who receive 0.5% isobaric bupivacaine with 0.5ml(25 micrograms) of fentanyl or Group B who receive 0.5% hyperbaric bupivacaine with 0.5ml(25 micrograms) of fentanyl and the block will be performed as per randomisation protocol.

Risks:

The risks of the procedure are minimal but can include hypotension, bradycardia, nausea, vomiting, postspinal headache, postoperative shivering.

Benefits:

The benefits of the study are that we can avoid general anaesthesia with good quality of analgesia during and after the study.

Voluntary Participation/Withdrawal:

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

Alternatives:

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

Privacy and Confidentiality:

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

1. In emergency to protect your rights and welfare.

2. If required by law.

Authorization to Publish Results:

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

Financial Incentives for participation:

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

Compensation:

In the event of injury related to the study, treatment will be made available through KLES' Hospital & MRC, Belagavi. There is no compensation or payment for such medical treatment by law.

Questions:

If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli, Professor, Department of Pathology and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number-9480275601, or extension 4052 at J.N. Medical College, Belagavi.

CONSENT FOR PARTICIPATION IN RESEARCH TRIAL:

"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE BETWEEN INTRATHECAL 0.5% ISOBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL AND 0.5% HYPERBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL FOR INFRAUMBILICAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROL TRIAL" I, Mr/Ms/Mrs _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print : _____

Date:

Witness Name : _____ Signature:_____

Date:

Investigators Name: _____ Signature:_____

Date:

Place : _____

ANNEXURE-II

ANNEXURE II – PROFORMA

"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE BETWEEN INTRATHECAL 0.5% ISOBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL AND 0.5% HYPERBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL FOR INFRAUMBILICAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMISED CONTROL TRIAL"

Patient Name:	IP NO:
Age:	Gender:
Height:	Weight:
Date of Operation:	Occupation:
Address:	Anaesthesiologist:

Pre-Anaesthetic Evaluation

Chief Complaints:

Past History:

- History of Diabetes Mellitus/Asthma/Tuberculosis/Congenital anomalies:
- Drug therapy:
- Previous Anaesthetic procedure/Previous surgeries:
- History of renal disease, hepatic disease and neurological diseases:

Family History:

General Physical Examination

Weight: Pallor:

Icterus: Lymphadenopathy:

Clubbing: Edema:

Pulse rate: BP:

Resriratory rate: Temperature:

Airway Assessment:

Mouth Opening: Jaw movements:

Teeth: M.P Grading:

Systemic examination:

Respiratory System:

Cardiovascular System:

Central Nervous System:

Per Abdomen:

Spine Assessment:

Investigations:

Blood group: Hb:

Total leukocyte count: RBS:

Platelet count: Serum creatinine:

ECG: chest x-ray:

Urine R/M: Others:

ASA GRADE: 1 2

Diagnosis:

Proposed surgery:

Selection criteria

Inclusion:

- Patients undergoing elective infraumbilical surgeries lasting 60 to 120 mins.
- Age: 18 to 60 years
- ASA Grade I and Grade II patients
- Patients providing consent
- Weight : 50 – 75 kgs
- Height : 150 – 165 cms.

Exclusion:

- Patients who refused SAB
- Hypovolemic patients
- Unco-operative patients
- Patients with spinal deformities
- Contraindications to spinal anaesthesia .
- Pre-existing neurological deficits in the lower extremities, and cardiovascular,respiratory,neurological, psychological, hepatic, or renal disease.
- Pregnant patients

Methodology

After obtaining the approval of ethical committee and written informed consent, a total of 40 patients undergoing elective infraumbilical surgeries under spinal anaesthesia will be included in the study.

After having met inclusion and exclusion criteria and having obtained informed consent, patients will be randomized based on computer generated randomization table into one of the two groups.

- Group A
- Group B

A thorough Pre-Anaesthetic Evaluation will be done. Detailed medical and personal history will be obtained. A detailed physical examination will be done. Patients will be advised overnight fasting. Routine investigations such as Complete blood count, Random Blood Sugar, Serum Creatinine, Blood Grouping and Typing, Chest X-ray, Electrocardiography will be carried out.

In the preoperative holding area, a wide bore i.v. access will be secured and patients will be preloaded with ringer lactate 10ml/kg half an hour before induction of anaesthesia. Anaesthetic techniques will be standardized for all patients.

Inside the operation theatre , the patient will be shifted onto the operating table. Standard non – invasive monitors will be attached and baseline Heart Rate, BP , SpO_2 will be recorded.

Under strict aseptic precautions the following procedure will be carried out.

Moniters such as pulseoximeter, ECG, non-invasive BP are connected. Patient will be then put in left lateral position and under strict aseptic precautions, L3-L4 space will be identified. 2ml 0f 2% lignocaine will be injected in L3-L4 space.

Group A : Using 23guage Quincke spinal needle 3ml of 0.5% isobaric bupivacaine + 25 micrograms of fentanyl making a total volume of 3.5ml of drug will be injected in L3-L4 subarachnoid space after confirming free flow of CSF.

Group B : Using 23guage Quincke spinal needle 3ml of 0.5% hyperbaric bupivacaine + 25 micrograms of fentanyl making a total volume of 3.5ml of drug will be injected in L3-L4 subarachnoid space after confirming free flow of CSF.

Patient will then be immediately placed in supine position. Intraoperative and postoperative assessments will be performed.

The following parameters will be monitored/measured :

A) Sensory Blockade will be assessed by pinprick in mid axillary line every minute till T_{10} block occurs , following which it will be assessed at 10 minute intervals for next 2 hrs and at 15 minute intervals beyond 2 hrs till full regression occurs .

Time taken for sensory blockade till T_{10} dermatome , highest sensory dermatome blocked , time for regression to 2 dermatomes from the highest dermatome reached and time for regression to S_2 would be recorded.

Surgery would be allowed to start once T_{10} dermatome has been blocked but GA will be induced if this does not happen in 30 minutes. Such cases will be labeled as Block failure and excluded from final analysis .

B) Motor Blockade will be assessed immediately after sensory block assessment using a Modified Bromage scale.

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

Bromage 1:-inability to raise extended leg and knee flexion is decreased, but full flexion of ankle and feet is present.

Bromage 2:-inability to raise leg or flex knees, flexion of ankle and feet present.

Bromage 3:-inability to raise leg, flex knee or ankle or move toes.

Motor block onset will be taken as the time to reach modified Bromage score 3 and total duration of motor block will be taken as the time for return to modified Bromage score 0.

In case patient doesn't attain Bromage score of 3, the highest score attained would be documented .

C) Post operative analgesia : Following surgery patient will not be put on regular analgesics .

Time for first rescue analgesia will be noted and will be treated with inj.Diclofenac sodium 75mg added to normal saline.

D) Vitals : HR , BP , and SpO_2 will be monitored throughout the surgery .

Blood pressure and Heart rate will be recorded at 2, 4, 6, 8, 10, 15, 20, 25, 30 minutes and every 15 minutes till the end of surgery.

Hypotension will be defined as decrease in systolic B.P by 20% from baseline values or a systolic B.P less than 90 mm of Hg and will be treated with incremental intravenous boluses of mephentermin 5 to 10 mg and a bolus administration of 250ml of Ringer Lactate solution over 10 mins.

Bradycardia will be defined as decrease in heart rate less than 50 beats per minute and will be treated with intravenous Atropine 0.6 mg.

Supplementary oxygen will be given through face mask.

E) Side effects : Any side effects which occur will be duly documented .

Preoperative baseline values:

HR: SBP: DBP: MAP:

Monitors attached:

Pulseoximetry: ECG:

NIBP

:

II. Vital parameters:

Time	HR	Blood Pressure			SPO2
		SBP	DBP	MAP	

Time (mins)	Sensory Blockade	Motor Blockade
0 mins		
5 mins		
10 mins		
15 mins		
20 mins		
30 mins		
45 mins		
60 mins		
75 mins		
90 mins		
Till recovery from spinal anaesthesia		

Side effects:

Hypotension treated with vasopressors:

Postoperative shivering:

Bradycardia treated with atropine:

Nausea/vomiting/post spinal headache:

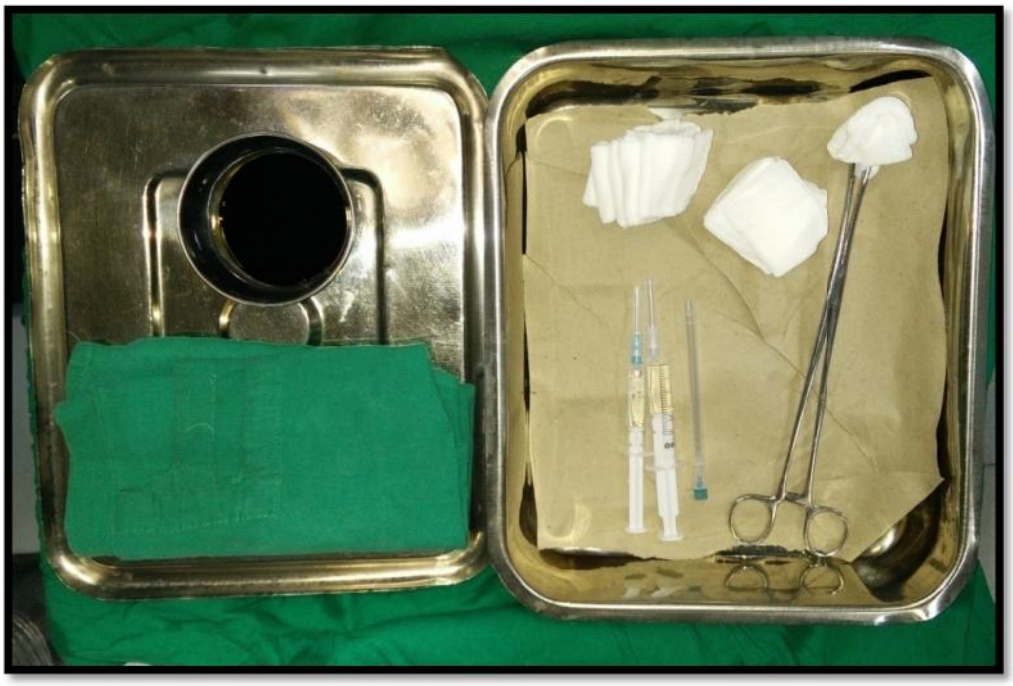
ANNEXURE III: PHOTOGRAPHS

Photograph 1: 0.5% Isobaric bupivacaine ampoule

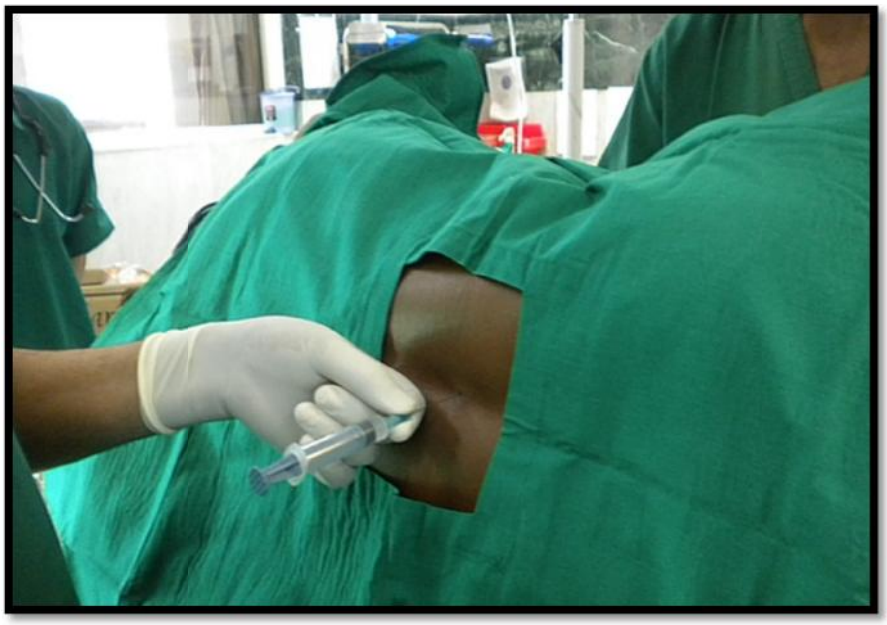
Photograph 2: 0.5% Hyperbaric bupivacaine ampoule

Photograph 3 : Fentanyl ampoule

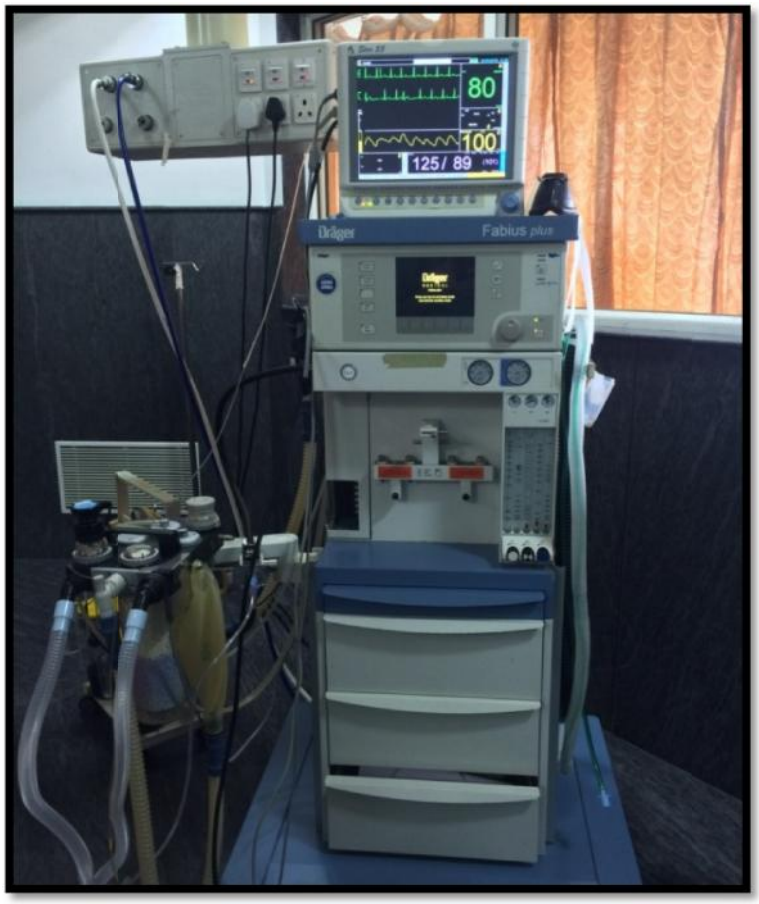
Photograph 4 : Spinal tray



Photograph 5 : Procedure of spinal anaesthesia



Photograph 6 : Monitoring during surgery



ANNEXURE-IV

KEY TO MASTER CHART

ASA	-	American Society of Anaesthesiologists
F	-	Female
HR	-	Heart Rate (bpm)
SBP	-	Systolic Blood Pressure (mm Hg)
DBP	-	Diastolic Blood Pressure (mm Hg)
SpO_2	-	Saturation of peripheral oxygen (%)
T	-	Thoracic sensory dermatomal level
mcg.	-	Micrograms
min.	-	Minutes
kgs.	-	Kilograms
cms.	-	Centimeters

GROUP A - 0.5% Isobaric bupibacaine with 25mcg Fentanyl

S.No.	Randomisation No	IP No.	ASA	Age(yrs)	Sex	Weight	Height	Sensory(minutes)		Motor(minutes)		Highest Sensory Level	Highest Bromage Score	Time for rescue analgesia (min)	Total Inj. Fentanyl(mcg)	Preoperative Vitals				Vitals At 2 min.				Vitals at 4 min.				Vitals At 6 Min.				Vitals at 8 min				Vitals at 10 min			
						(kgs.)	(cms.)	Onset	Duration	Onset	Duration					HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2
1	1	814353	2	58	M	56	153	6	127	8	170	T6	3	190	25	76	130	70	100	80	130	72	100	84	128	70	100	84	128	74	100	82	129	73	100	88	124	72	100
2	3	814432	2	52	M	60	152	5	135	7	180	T6	3	180	25	80	120	74	100	88	120	70	100	84	124	72	100	84	128	80	100	84	130	70	99	86	130	74	100
3	6	816012	1	43	M	53	151	5	120	7	180	T7	3	190	25	72	130	74	100	74	130	70	100	71	130	70	100	70	128	70	100	65	126	80	100	66	116	68	100
4	10	815496	1	30	F	50	156	6	135	8	170	T6	3	160	25	72	138	74	100	74	136	74	100	70	130	70	100	72	120	70	100	60	110	68	98	62	110	64	98
5	12	815948	2	60	M	58	156	8	130	10	172	T6	3	180	25	80	130	70	100	80	128	70	100	78	126	68	100	76	124	96	100	82	124	78	98	74	118	70	98
6	13	814448	2	55	F	59	151	7	135	8	176	T7	3	180	25	80	130	68	100	80	130	78	100	78	128	70	100	74	126	70	100	72	124	70	99	73	120	72	100
7	15	814458	1	28	M	53	151	6	134	8	170	T6	3	200	25	77	140	86	100	77	140	84	99	79	140	88	98	70	136	80	100	65	130	80	100	66	120	74	100
8	16	814423	2	60	M	53	152	5	132	8	175	T6	3	200	25	82	118	72	100	82	116	74	100	81	114	72	100	82	116	70	100	81	116	70	100	80	114	70	100
9	17	814580	2	52	M	58	154	5	124	8	168	T6	3	160	25	92	122	74	100	90	120	74	100	89	118	76	100	88	116	78	100	85	118	74	100	87	120	70	100
10	18	814323	2	60	M	56	152	6	126	8	172	T6	3	200	25	84	130	92	100	82	128	90	100	80	126	76	100	80	120	74	100	76	118	74	100	74	102	64	100
11	20	814713	1	36	M	54	155	5	124	7	168	T7	3	190	25	70	140	100	100	70	138	100	100	68	136	98	100	70	134	94	100	66	130	92	100	64	130	90	100
12	24	816897	2	58	M	56	154	6	128	8	170	T6	3	190	25	96	130	70	100	96	130	70	100	90	120	72	100	80	118	70	100	80	122	70	100	77	116	70	100
13	26	816724	2	59	M	51	152	6	130	9	170	T6	3	200	25	72	120	70	100	73	120	70	100	73	110	70	100	71	110	70	100	64	108	70	100	62	104	64	100
14	28	817037	1	32	F	50	150	5	132	7	168	T6	3	200	25	86	134	78	100	86	130	80	100	80	120	78	100	72	114	70	100	72	108	68	100	70	110	64	100
15	30	817152	1	45	M	53	150	6	128	8	172	T6	3	190	25	73	130	80	100	70	130	80	100	69	128	80	100	65	124	78	100	63	122	76	100	69	120	76	100
16	32	817273	2	56	M	58	154	7	126	10	170	T7	3	190	25	74	116	70	100	70	116	70	100	68	114	68	100	66	108	66	100	64	108	66	100	66	106	68	99
17	34	817696	1	32	F	58	156	5	130	7	166	T6	3	180	25	68	130	72	100	68	130	70	100	66	128	70	100	66	126	68	100	74	124	70	100	72	120	78	100
18	36	817718	1	36	M	58	152	6	128	8	166	T7	3	200	25	72	128	70	100	70	126	70	100	72	124	70	100	68	122	66	100	66	118	70	100	64	112	70	100
19	38	817152	1	45	F	60	156	6	130	8	170	T6	3	170	25	72	110	72	100	70	110	70	100	70	108	68	100	68	106	68	100	68	104	66	100	66	104	70	100
20	39	817889	1	50	M	52	150	5	128	7	168	T7	3	200	25	78	130	88	100	78	130	96	100	76	128	86	100	76	126	84	100	75	124	82	100	72	110	62	100
21	40	818190	1	54	M	60	155	6	126	8	166	T6	3	180	25	70	110	70	100	68	110	70	100	68	110	70	100	66	108	66	100	66	106	64	100	64	104	64	99
22	42	818193	1	20	M	42	134	5	130	7	164	T6	3	180	25	88	120	86	100	88	118	80	100	86	114	80	100	85	110	74	100	84	108	68	100	80	106	64	100
23	44	818192	2	60	F	59	150	6	127	8	166	T6	3	160	25	80	140	100	100	80	138	98	100	78	136	94	100	78	134	90	100	84	130	90	100	82	126	80	100
24	46	818172	2	56	M	52	156	5	135	7	172	T7	3	160	25	80	120	74	100	80	118	70	100	78	116	72	100	76	112	70	100	76	110	70	100	72	110	72	100
25	49	813282	1	35	M	54	156	6	126	8	170	T6	3	180	25	72	130	88	100	70	130	86	100	68	126	84	100	68	122	80	100	66	120	78	100	66	118	76	100
26	52	818426	1	20	M	50	156	5	127	8	170	T6	3	160	25	82	140	100	100	82	140	100	100	80	138	90	100	81	136	84	100	79	138	80	100	77	136	78	100
27	54	817616	1	24	F	53	150	6	130	8	176	T7	3	200	25	84	130	70	100	84	130	70	100	82	128	70	100	80	124	68	100	80	122	70	100	78	120	70	100
28	55	818218	2	57	M	50	150	5	128	8	166	T6	3	210	25	70	140	88	100	70	140	90	100	68	140	84	100	66	138	82	99	66	130	80	98	64	126	76	100
29	56	818654	2	59	M	51	150	6	126	8	174	T6	3	200	25	72	130	70	100	70	130	70	100	70	130	70	100	66	128	70	99	66	126	68	100	65	122	66	100
30	57	818283	2	60	M	52	150	5	130	7	166	T6	3	180	25	78	130	90	100	76	130	90	100	75	128	88	100	74	126	90	100	72	122	80	100	70	120	78	100
31	60	818498	1	30	M	52	152	6	127	8	170	T6	3	210	25	80	128	78	100	80	126	78	100	78	124	76	100	78	122	74	100	74	120	66	99	70	118	68	100
32	62	818629	2	60	M	58	156	5	134	7	174	T7	3	200	25	72	130	70	100	72	130	70	100	70	130	68	100	70	126	68	100	68	120	68	100	66	110	60	100
33	63	817381	1	38	F	58	152	6	128	8	170	T6	3	200	25	82	130	90	100	82	130	88	99	80	130	86	100	78	128	88	100	70	126	84	100	68	122	80	100
34	68	818055	1	44	M	59	151	6	130	8	172	T6	3	210	25	72	140	100	100	72	136	96	100	70	132	90	100	70	130	90	99	68	124	66	99	66	120	66	100
35	71	819354	2	55	M	51	159	6	125	8	180	T7	3	210	25	71	130	90	100	70	128	88	100	71	128	84	100	68	124	88	99	70	122	80	100	70	120	78	100
36	72	818841	2	60	M	59	161	6	132	9	176	T6	3	200	25	68	110	70	100	68	110	70	100	66	110	68	100	67	108	60	100	65	104	60	99	61	100	60	100
37	75	819430	1	28	M	51	160	5	126	6	174	T6	3	210	25	78	138	86	100	78	136	84	100	72	130	80	100	70	128	78	100	68	124	70	100	69	120	68	100
38	76	819421	1	23	M	58	160	6	132	8	166	T6	3	200	25	71	110	70	100	71	110	70	100	70	110	70	100	70	104	70	100	68	100	68	100	61	100	64	100
39	77	790933	1	47	F	58	157	5	130	7	180	T6	3	210	25	68	142	94	100	66	136	92	100	65	132	90	100	65	124	88	100	63	112	72	100	59	108	70	100
40	80	839934	2	45	M	50	160	6	132	8	174	T6	3	200	25	70	140	80	100	70	139	80	100	64	139	80	100	60	138	79	99	57	134	78	100	56	133	77	99

S.No.	Vitals at 15 Min.				Vitals at 20 Min.				Vitals at 25 Min.				Vitals at 30 Min.				Vitals at 45 Min.				Vitals at 60 Min.				Vitals at 75 Min.				Vitals at 90 Min.				Vitals at 105 Min.				Vitals at 120 in				Inj.Atropine given(Y/N)	Inj. Mephentermine given(Y/N)
	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2		
																																									N	N
1	83	128	68	100	81	129	69	100	79	128	72	100	82	130	69	100	83	140	70	100	87	130	72	100	91	140	74	100	90	130	76	100									N	N
2	86	128	76	100	92	128	75	100	78	127	69	100	84	123	72	100	82	122	80	98	85	122	70	100	83	120	69	100	88	128	65	100	81	130	74	100					N	N
3	63	108	64	100	61	108	62	100	62	110	66	100	69	108	64	100	70	106	62	100	71	108	64	99	73	110	66	99	71	108	64	100	69	110	66	100					N	N
4	68	110	64	100	72	110	68	100	74	114	74	100	70	116	72	100	68	118	70	100	66	120	74	100	64	22	80	100	70	120	74	100									N	N
5	76	120	68	99	75	112	70	100	77	114	68	100	79	116	70	100	81	114	68	100	79	116	70	100	77	118	68	100	80	120	64	100	75	116	66	100					N	N
6	68	116	70	100	61	110	74	100	63	108	60	100	60	106	60	100	65	110	62	98	69	108	64	98	67	110	66	100	68	112	68	100	71	108	64	100					N	N
7	66	108	70	100	63	108	70	100	65	110	74	100	66	112	74	100	70	116	68	100	67	110	64	100	69	110	68	100	64	118	72	100	69	120	74	100					N	N
8	73	108	64	100	72	100	62	100	68	100	64	99	66	100	62	100	64	110	68	100	71	114	64	100	68	106	60	100	72	106	62	99	71	108	64	100					N	N
9	86	110	68	100	82	114	64	99	80	116	68	100	79	118	70	100	81	120	68	100	83	122	66	100	84	118	68	100	86	120	64	100	80	114	68	100					N	N
10	70	100	60	100	68	100	62	100	65	100	60	100	65	102	64	100	65	100	70	100	67	110	70	100	61	108	64	100	69	106	66	100	69	108	70	100					N	N
11	62	128	96	100	60	124	82	100	62	122	80	100	68	110	68	100	66	108	68	100	63	100	70	100	62	100	68	100	67	108	68	99	63	110	70	100					N	N
12	77	114	70	100	79	112	70	100	77	110	68	100	75	116	70	100	80	118	70	100	81	114	78	100	83	116	78	100	85	112	76	100	79	110	68	100					N	N
13	63	100	62	98	65	100	62	98	63	100	60	99	68	106	64	100	67	108	68	100	70	106	70	100	66	110	72	99	65	108	64	100	63	106	68	100					N	N
14	68	108	64	100	66	106	70	98	65	110	70	99	69	108	68	99	71	110	68	100	73	112	70	100	71	108	68	100	69	106	70	100	77	110	66	100					N	N
15	69	116	72	100	73	112	70	100	71	110	72	100	65	108	70	100	68	108	68	99	63	110	70	100	67	108	70	100	71	108	62	100	73	106	68	100					N	N
16	66	110	70	98	65	108	70	100	64	110	68	100	63	108	70	100	64	106	74	100	66	100	66	100	69	100	64	100	65	104	60	100	70	106	70	100					N	N
17	70	116	68	100	70	114	70	100	68	110	68	100	74	118	74	100	76	116	72	100	76	118	70	100	70	116	80	100	72	110	70	100									N	N
18	63	106	58	100	60	110	70	100	64	110	74	100	70	114	70	100	72	110	68	100	74	110	72	100	70	104	70	100	68	106	72	100	66	116	78	100					N	N
19	66	110	70	100	64	110	72	100	66	108	70	100	65	110	68	100	66	108	70	100	69	114	72	99	70	114	78	100	68	116	80	99	67	118	74	100					N	N
20	70	108	60	100	72	108	64	100	70	110	70	100	70	114	70	100	72	112	70	100	68	114	70	99	66	110	74	100	68	110	64	100	70	110	66	99					N	N
21	66	100	70	99	66	102	64	100	68	110	74	100	67	110	70	100	66	100	68	100	65	104	64	99	70	106	70	100	64	108	68	100									N	N
22	78	104	68	100	76	110	76	100	72	112	68	99	70	110	70	99	72	108	68	100	68	104	62	100	66	110	70	100	68	108	72	100	70	110	74	100					N	N
23	82	124	82	100	81	126	78	100	83	128	76	99	77	128	82	100	79	130	80	100	79	130	84	100	75	130	82	100	81	128	76	100									N	N
24	74	108	68	100	78	110	72	100	88	126	84	100	86	120	82	100	74	130	72	100	76	134	80	100	74	138	90	100	72	130	74	100									N	N
25	68	110	68	100	70	104	68	100	66	110	60	99	66	108	68	98	68	110	70	100	64	104	70	100	65	102	60	100	67	102	80	100	71	104	76	100					N	N
26	81	130	90	100	82	128	88	100	89	124	80	98	88	128	80	100	84	130	88	99	85	134	84	100	83	138	92	100	79	136	90	100	77	128	84	100					N	N
27	76	114	62	100	74	112	64	100	70	108	62	99	70	104	70	99	74	106	68	98	72	104	74	100	70	104	66	100	72	108	62	100	80	110	68	100					N	N
28	66	120	74	100	64	114	72	98	66	110	70	99	68	110	68	100	70	108	70	100	70	114	68	100	70	112	60	100	68	116	70	100									N	N
29	66	118	70	98	68	110	70	99	66	108	60	100	68	106	60	100	68	106	60	100	66	108	62	99	64	108	64	100	68	110	68	100	70	110	64	100					N	N
30	68	110	68	100	66	102	60	99	65	102	60	99	66	102	60	100	66	110	60	100	64	110	70	99	64	110	60	100	60	108	62	100	64	104	60	100					N	N
31	68	116	70	99	66	114	70	100	70	114	70	100	64	110	70	99	64	110	70	100	66	110	68	100	66	108	66	100	66	106	66	100	68	110	70	100					N	N
32	66	108	60	100	63	108	58	100	64	108	64	100	65	112	66	100	64	112	60	100	66	114	60	99	64	116	64	100	66	112	68	100	64	110	68	100					N	N
33	70	118	78	100	68	110	60	100	70	114	70	100	70	112	70	100	68	118	68	100	66	114	70	100	68	116	70	100	72	114	70	99									N	N
34	66	110	64	100	64	110	66	100	65	108	66	100	66	108	66	100	68	110	66	100	70	112	60	99	68	114	64	99	66	110	62	99	64	110	60	100					N	N
35	68	118	76	100	70	116	74	100	68	114	70	100	66	108	70	99	66	110	70	100	64	110	66	99	65	108	64	100	63	106	62	100	64	104	60	100					N	N
36	60	100	58	100	60	100	58	100	60	98	60	100	61	100	62	100	61	100	58	100	70	110	70	99	70	108	58	100	68	104	60	100	66	100	60	99					N	N
37	70	114	68	99	66	112	64	100	64	110	66	100	61	108	64	99	65	106	64	100	63	104	66	100	61	110	60	99	61	108	62	100	67	102	60	100					N	N
38	66	100	60	99	66	102	62	100	65	110	70	100	68	112	70	99	70	110	72	100	66	108	70	100	68	112	72	100	66	104	60	100	64	102	60	100					Y	N
39	55	100	64	99	52	100	56	100	50	98	50	100	49	100	58	108	64	108	62	99	68	100	60	98	70	104	62	100													N	N
40	56	137	77	99	49	103	59	99	75	94	63	100	76	110	76	100	69	117	68	100	70	110	70	100																		

GROUP B: 0.5% Hyperbaric Bupivacaine with 25mcg Fentanyl

S.No.	Randomisation No	IP No.	ASA	Age(yrs)	Sex	Weight	Height	Sensory(minutes)		Motor(minutes)		Highest Sensory Level	Highest Bromage Score	Time for rescue analgesia(min)	Total inj. Fentanyl(mcg)	Preoperative Vitals				Vitals At 2 min.				Vitals at 4 min.			
						(kgs.)	(cms.)	Onset	Duration	Onset	Duration					HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)
1	2	814092	2	52	M	60	156	2	185	4	200	T6	3	2oo	25	66	114	74	100	66	100	66	100	65	98	60	100
2	4	813805	1	51	M	59	156	3	182	4	198	T7	3	190	25	74	130	70	100	74	130	70	100	75	130	74	100
3	5	814090	2	56	M	58	158	3	180	5	194	T7	3	190	25	69	130	72	100	69	126	70	100	67	120	70	100
4	7	814328	1	24	M	54	150	2	184	5	200	T7	3	200	25	70	120	72	100	74	116	70	100	68	110	70	100
5	8	810884	1	44	M	66	160	5	200	6	210	T6	3	210	25	72	130	92	100	72	132	90	100	71	126	90	100
6	9	814428	1	45	M	62	158	6	180	8	200	T7	3	220	25	72	132	90	100	71	130	90	100	70	128	88	100
7	11	814954	2	58	M	66	158	6	200	6	220	T7	3	200	25	66	144	92	100	65	130	94	100	64	128	94	100
8	14	814811	2	39	M	54	150	4	185	5	200	T7	3	220	25	65	130	90	100	64	125	82	100	64	124	70	100
9	19	815169	1	54	F	51	150	3	180	4	198	T6	3	230	25	84	138	78	100	80	136	76	100	79	134	74	100
10	21	814830	2	58	M	66	158	5	200	5	220	T7	3	200	25	68	140	88	100	68	132	90	100	67	126	88	100
11	22	815290	1	22	M	58	159	4	190	5	200	T6	3	220	25	70	130	90	100	67	130	92	100	72	114	76	100
12	23	808922	2	59	M	52	152	3	200	5	220	T7	3	240	25	96	110	70	100	98	110	70	100	96	110	68	100
13	25	815333	1	42	M	58	158	4	190	5	200	T7	3	220	25	78	140	80	100	80	136	80	100	82	130	90	100
14	27	815230	1	40	M	58	158	3	188	5	190	T7	3	210	25	66	130	78	100	68	130	70	100	67	110	70	100
15	29	815232	2	53	M	54	152	4	190	5	200	T6	3	200	25	70	130	72	100	74	130	70	100	70	128	70	100
16	31	813493	1	44	M	59	158	3	186	4	200	T7	3	220	25	67	130	82	100	67	130	70	100	66	128	70	100
17	33	815397	2	56	F	50	152	4	190	5	210	T6	3	230	25	69	140	80	100	69	140	80	100	72	130	90	98
18	35	815364	2	57	M	58	154	3	185	4	198	T7	3	220	25	74	130	74	100	70	130	70	100	74	130	68	100
19	37	815609	2	55	M	64	156	4	210	5	240	T7	3	210	25	68	134	90	100	66	132	92	100	65	130	90	100
20	41	815564	1	21	M	52	152	4	200	5	220	T7	3	230	25	76	128	86	100	75	126	84	100	74	125	82	100
21	43	814240	1	45	M	60	150	3	180	4	190	T7	3	220	25	80	128	70	100	78	120	76	100	80	110	70	100
22	45	815771	1	51	M	58	158	4	184	5	196	T7	3	210	25	70	130	90	100	74	130	90	100	72	128	88	100
23	47	815656	2	60	F	56	158	3	180	4	190	T8	3	220	25	74	120	78	100	68	116	80	100	68	110	70	100
24	48	814218	1	35	M	50	158	4	190	5	200	T6	3	200	25	70	130	90	100	70	124	80	100	72	110	70	100
25	50	815938	1	41	M	60	156	5	230	6	250	T7	3	210	25	66	114	74	100	66	100	66	100	65	98	60	100
26	51	816506	1	36	M	56	150	3	188	4	200	T7	3	230	25	76	132	90	100	72	130	90	100	71	120	84	99
27	53	815966	2	55	M	52	150	4	190	5	200	T7	3	200	25	72	130	80	100	70	130	70	100	68	128	70	100
28	58	815428	2	57	M	55	150	3	185	4	202	T6	3	210	25	82	130	80	100	84	130	78	100	80	130	74	100
29	59	816326	2	56	M	54	152	4	188	5	210	T7	3	200	25	72	130	92	100	70	132	90	100	68	126	90	100
30	61	816449	2	55	M	52	153	3	190	4	200	T7	3	230	25	84	118	70	100	82	110	68	100	80	110	66	100
31	64	816390	2	56	M	58	157	4	200	5	210	T7	3	220	25	70	110	70	100	70	110	70	100	68	110	68	100
32	65	816811	1	36	M	51	156	3	185	5	200	T7	3	220	25	68	110	70	100	70	104	66	100	68	100	60	100
33	66	814478	2	56	M	52	160	2	182	4	190	T7	3	210	25	84	114	74	100	84	100	66	100	80	98	60	100
34	67	816926	1	39	M	54	158	3	190	5	210	T8	3	240	25	70	128	70	100	70	128	72	100	68	128	70	100
35	69	816912	2	56	M	51	160	4	188	5	200	T7	3	220	25	68	138	74	100	70	138	74	100	68	136	72	100
36	70	817002	2	56	F	58	160	3	190	4	210	T7	3	230	25	68	128	80	100	68	120	78	100	66	118	74	100
37	73	817014	1	43	M	51	160	2	185	4	200	T7	3	230	25	72	124	70	100	72	124	70	100	71	122	70	100
38	74	816927	1	32	M	58	160	3	190	5	210	T7	3	210	25	68	110	70	100	68	110	70	100	66	108	68	100
39	78	817893	1	28	M	53	154	3	184	4	200	T7	3	220	25	69	124	72	100	69	120	72	100	68	116	68	100
40	79	817726	2	32	F	57	158	4	182	4	196	T7	3	210	25	68	128	74	100	68	124	74	100	67	120	70	100

S.No.	Vitals At 6 Min.				Vitals at 8 min				Vitals at 10 min				Vitals at 15 Min.				Vitals at 20 Min.				Vitals at 25 Min.				Vitals at 30 Min.			
	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)
1	65	92	54	100	64	108	60	100	62	110	72	100	62	112	70	100	60	110	74	100	61	108	72	100	62	106	70	100
2	75	126	70	100	73	122	72	100	69	120	70	100	71	124	70	100	73	122	68	100	71	120	64	100	70	124	68	100
3	67	110	72	100	66	108	68	100	70	100	60	100	63	98	66	100	59	100	60	100	64	110	70	100	61	112	74	100
4	66	100	60	100	66	100	58	100	70	100	60	100	74	104	58	100	66	100	60	100	84	110	68	100	78	120	70	100
5	70	110	70	100	70	110	70	100	69	104	64	100	69	100	58	100	62	90	58	100	60	108	62	100	58	100	56	100
6	70	127	87	100	68	127	86	100	67	125	85	100	66	122	82	100	65	120	82	100	64	118	80	100	63	116	76	100
7	64	126	90	100	63	124	86	100	60	122	84	98	58	118	76	100	66	116	68	100	78	100	58	98	85	96	52	100
8	63	123	72	100	62	96	61	100	61	94	60	100	60	92	60	100	62	100	60	99	76	114	70	97	69	118	68	100
9	77	130	76	100	80	128	74	100	81	126	74	100	75	128	72	99	77	130	78	100	78	128	76	99	79	126	78	100
10	66	110	74	99	65	104	68	100	64	98	50	100	64	110	72	100	63	112	70	100	60	114	72	100	62	112	70	100
11	68	110	76	100	69	110	78	100	64	110	74	100	66	108	68	100	69	108	68	99	67	112	70	100	65	106	74	100
12	98	110	70	100	88	110	70	100	100	108	72	100	96	110	74	100	94	106	76	99	96	110	74	98	89	106	70	100
13	78	124	80	100	71	110	70	100	70	108	72	99	68	100	60	100	68	110	72	100	70	114	74	100	66	122	80	100
14	63	120	68	100	63	118	70	100	61	116	72	100	60	114	68	99	57	116	70	100	59	118	68	100	63	118	70	100
15	71	126	64	100	71	124	68	100	69	120	70	100	67	130	68	100	75	128	66	100	73	130	70	100	71	130	68	100
16	65	130	68	100	65	130	70	100	66	130	68	100	63	128	70	100	61	126	68	100	60	128	72	98	70	130	70	100
17	70	124	80	100	66	120	78	100	70	110	70	100	70	106	66	100	74	100	60	100	73	100	64	100	71	106	70	100
18	72	124	74	99	68	126	71	100	76	128	74	100	74	130	76	100	76	134	74	100	72	130	76	98	72	138	72	100
19	65	128	88	100	64	126	86	100	64	125	84	98	62	124	82	100	62	122	80	100	62	120	78	100	63	118	76	100
20	72	124	81	100	70	122	80	100	70	120	76	100	68	120	74	100	66	118	70	99	68	116	72	98	66	114	72	99
21	82	100	62	100	68	100	60	100	70	98	60	100	70	102	60	100	72	110	70	100	74	136	74	100	78	128	80	100
22	72	136	80	100	71	130	80	100	73	134	78	100	77	128	76	100	69	126	76	100	67	128	80	100	73	130	74	100
23	64	104	60	100	60	100	60	100	62	108	70	100	64	106	70	100	66	108	70	100	64	106	70	100	66	108	70	100
24	72	100	60	100	74	104	60	100	68	108	64	100	66	110	70	100	66	112	68	100	67	118	64	100	67	120	82	100
25	65	92	54	100	64	108	60	100	62	112	70	100	60	110	74	100	61	108	72	100	62	106	72	100	62	104	68	100
26	70	110	72	100	73	104	70	100	75	100	60	100	76	104	60	100	74	100	62	100	72	108	68	100	70	110	70	100
27	68	126	70	100	66	128	70	100	70	128	68	100	72	126	68	100	70	130	74	100	70	130	72	100	68	128	74	100
28	78	128	72	100	78	126	70	100	78	120	68	100	76	124	66	100	80	124	68	100	80	120	68	100	84	128	70	100
29	68	110	70	100	69	104	64	100	66	100	58	100	62	90	58	100	58	100	58	100	56	100	56	100	70	102	58	100
30	80	114	68	99	79	116	70	100	73	116	70	100	77	118	68	100	75	116	70	100	77	110	70	100	81	110	72	100
31	67	110	68	100	65	110	70	100	68	112	70	100	69	108	68	100	71	108	70	100	73	106	70	100	71	108	68	100
32	67	108	70	100	66	106	70	100	65	112	68	100	66	108	68	98	61	106	70	100	65	108	68	100	63	106	70	100
33	78	92	54	100	78	108	60	100	80	110	72	100	82	112	70	99	74	124	68	100	76	120	62	100	75	116	66	100
34	70	124	70	100	70	122	68	100	67	120	68	99	66	120	66	100	69	130	68	100	68	126	68	100	70	124	68	100
35	68	134	70	100	66	128	68	100	67	132	70	100	71	130	66	100	73	124	68	100	65	122	66	98	63	128	68	100
36	67	108	72	100	66	110	70	100	65	106	74	100	63	100	60	100	61	104	70	100	62	108	74	100	62	110	70	100
37	73	120	68	100	70	120	64	100	69	120	66	100	71	118	70	100	70	114	70	100	71	112	70	100	69	116	70	100
38	67	108	78	100	65	100	60	100	63	102	64	100	61	106	66	100	62	110	64	100	70	108	66	100	61	106	64	100
39	67	114	64	100	70	114	60	100	67	112	60	100	69	100	60	100	70	108	68	100	67	106	64	100	68	108	62	100
40	66	118	70	100	67	110	70	100	63	104	62	100	64	100	60	100	65	104	64	100	61	110	70	100	67	114	68	100

S.No.	Vitals at 45 Min.				Vitals at 60 Min.				Vitals at 75 Min.				Vitals at 90 Min.				Vitals at 105 Min.				Vitals at 120 Min.				Inj.Atropine given(Y/N)	Inj.Mephentermine given(Y/N)
	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2(%)	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2		
1	62	104	68	100	60	104	66	100	88																N	Y
2	65	122	64	100	74	128	62	100	73	130	74	100	77	124	72	100	71	120	74	100					N	N
3	62	128	72	100	63	120	68	100	62	118	74	100	61	124	70	100	61	122	76	100					Y	N
4	76	120	74	100	77	120	78	100	75	130	70	100	72	126	74	100									N	N
5	75	102	58	100	80	100	58	100	82	108	56	100	92	110	71	100	93	114	70	100					N	N
6	62	115	74	100	60	114	72	100	60	112	70	100													Y	N
7	84	90	48	100	82	110	72	100	80	112	70	100	78	114	70	100									Y	Y
8	67	110	70	100	70	120	74	98	71	118	68	100	73	120	76	100	78	120	74	100					N	N
9	83	130	74	100	75	128	76	100	77	130	78	100	79	128	78	100	84	130	80	100					N	N
10	61	110	68	99	62	112	68	100	64	114	70	100	65	128	80	100	67	130	78	100					N	Y
11	69	108	74	100	69	110	72	100	71	110	70	99	69	108	68	99	70	110	70	100					N	N
12	93	104	70	100	91	108	68	100	90	108	74	100	89	106	72	100	91	108	72	100					N	N
13	68	120	78	99	70	118	74	100	70	110	70	100													N	N
14	64	116	70	100	66	114	68	100	61	112	70	100	70	118	70	100	71	120	68	100					N	N
15	72	128	72	100	71	128	70	100	69	132	74	100	71	132	76	100	73	128	74	100					N	N
16	69	126	80	100	67	128	70	100	66	128	70	100	72	130	72	100	68	136	80	100					N	N
17	64	110	70	100	74	112	70	100	75	118	76	100	76	136	78	100	70	134	80	100					N	N
18	70	140	76	100	72	132	70	100	70	128	70	100	70	134	68	100									N	N
19	62	116	74	100	60	114	72	100	60	114	72	100													N	N
20	64	112	70	100	66	110	68	100																	N	N
21	77	128	74	100	75	126	70	100	77	128	74	100	79	126	80	100									N	N
22	71	130	74	100	71	130	78	100	72	136	74	100	70	138	72	100	77	136	74	99	69	138	72	99	N	N
23	64	106	68	100	62	104	64	100	68	110	64	100	64	110	64	99	64	118	68	100	68	108	64	100	N	N
24	69	122	80	100	71	124	72	100	73	120	76	100	73	122	78	100									N	N
25	60	104	66	100	64	128	72	100	71	130	70	100	69	130	74	100	75	132	72	100					N	Y
26	69	112	74	100	68	126	70	100	72	126	74	100	68	120	70	100	69	128	72	100					N	N
27	66	126	72	100	64	128	70	100	68	130	74	100	70	128	72	100	74	128	70	100	70	126	68	100	N	N
28	82	126	88	100	80	124	70	100	80	128	68	100	78	124	78	100									N	N
29	80	100	58	100	82	108	56	100	92	110	72	100													Y	N
30	80	118	70	100	77	116	70	100	75	118	68	100	79	116	70	100	78	112	70	100					N	N
31	72	110	70	100	67	110	68	100	66	108	70	100	65	110	68	100	67	112	68	100	68	110	70	100	N	N
32	66	108	68	100	67	110	66	100	66	110	68	100	69	108	70	100									N	N
33	73	118	66	99	81	112	68	100	83	118	70	100	84	120	70	100	86	118	74	100	84	128	70	100	N	Y
34	71	118	68	100	73	130	70	100	70	124	68	100	69	126	70	100	67	128	70	100					N	N
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37	68	118	60	100	70	116	70	99	67	114	68	100	66	110	70	100	70	108	70	100	71	108	66	100	N	N
38	63	100	68	100	65	108	64	100																	N	N
39	67	110	64	100	66	108	66	100	63	106	62	100													N	N
40	69	114	66	100	66	112	68	100	67	114	66	100	66	116	70	100	68	114	66	100					N	N

ANNEXURE VI – ETHICAL CLEARANCE CERTIFICATE

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

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Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 42 **Date: 17/10/2016**

To,

[redacted]
J.N.Medical College,
BELAGAVI.

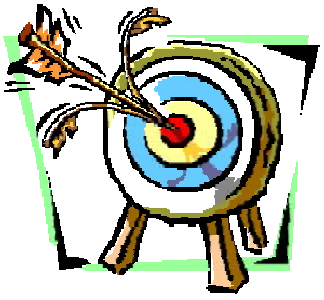
Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"COMPARISON OF ONSET AND DURATION OF SENSORY AND MOTOR BLOCKADE BETWEEN INTRATHECAL 0.5% ISOBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL AND 0.5% HYPERBARIC BUPIVACAINE WITH 25 MICROGRAMS FENTANYL FOR INFRAUMBILICAL SURGERIES – A ONE YEAR HOSPITAL BASED RANDOMISED CONTROL TRIAL "**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Ganga Pilli)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

Introduction



Objectives

Review of Literature

Basic Sciences

Methodology

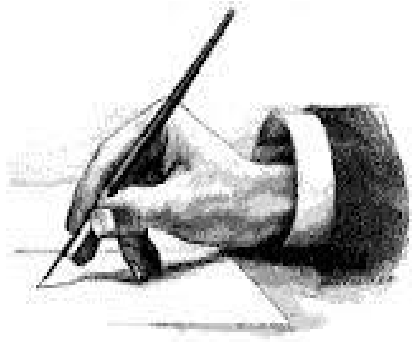
Results

Discussion

Conclusion

Summary

Bibliography



Annexure-I

Annexure-II

Annexure-III

Annexure-IV

Annexure-V

Annexure-VI