COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH NALBUPHINE FOR SUBARACHNOID BLOCK IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES, A ONE YEAR RANDOMISED CONTROLLED TRIAL.

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ENDORSEMENT

This is to certify that the dissertation entitled **"COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH NALBUPHINE FOR SUBARACHNOID BLOCK IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES, A ONE YEAR RANDOMISED CONTROLLED TRIAL.''** is a bonafide research work done by

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ABSTRACT

Backgrounds:

Spinal anaesthesia is a popular anaesthetic technique for lower abdominal surgeries and offers many advantages over general anaesthesia. Opioid analgesics which are common adjuvant to the local anaesthetics are associated with sedation, respiratory depression and postoperative nausea and vomiting. Nalbuphine however has a reduced incidence of respiratory depression and has been used to antagonize the side-effects of spinal opiates. In our study we investigated the effects of addition of nalbuphine (400mcg) to intrathecal hyperbaric bupivacaine.

Objective:

The objectives of the study were to compare onset, duration of sensory and motor blockade, duration of postoperative analgesia between hyperbaric bupivacaine and hyperbaric bupivacaine with nalbuphine (400mcg) in patients undergoing lower abdominal surgeries under spinal anaesthesia.

Methods:

This one year randomized controlled trial was conducted in the Department of Anaesthesiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period January 2016 to December 2016

After institutional ethical committee clearance and written informed consent 60 ASA physical status I and II patients undergoing lower abdominal surgeries under spinal anaesthesia were randomly allocated into two groups. Group A received 3ml of 0.5%

hyperbaric bupivacaine with 400 mcg inj. Nalbuphine. Group B received 3ml of 0.5% hyperbaric bupivacaine with 0.5 ml of normal saline.

Results:

In our study, the mean onset of sensory blockade and motor blockade in nalbuphine group were 3.76+/- 0.86 min and 6.33+/-12 min and in control group were 3.53+/- 0.75 min and 6.42+/-0.86 min respectively. The difference was statistically insignificant. The mean duration of sensory blockade and motor blockade in nalbuphine group were 118.93+/- 8.37 min and 144.28+/- 8.94 min and in control group 96.93+/- 7.10min and 121.21+/- 5.19 min respectively. The difference was statistically significant.

The mean duration of postoperative analgesia was 222.93+/- 19.75 min in nalbuphine group as compared to 151.64+/-10.61 min in control group which was highly significant. Hemodynamic parameters were comparable between the two groups with no major side effects / complications observed.

Conclusion:

In conclusion, administration of 400 mcg nalbuphine intrathecally along with 0.5% hyperbaric bupivacaine has similar onset of sensory and motor blockade and significantly prolongs duration of blockade and postoperative analgesia without major adverse effects or hemodynamic changes.

Key words:

Spinal anaesthesia, bupivacaine, nalbuphine, postoperative analgesia.

LIST OF ABBREVIATIONS USED

ASA	American Society of Anaesthesiologists
Bpm	Beats per Minute
CBC	Complete Blood Count
cm	Centimeter
CNS	Central Nervous System
CVS	Cardiovascular System
DBP	Diastolic Blood Pressure
dl	Decilitre
ECG	Electrocardiography
ED	Effective Dose
G	Gauge
GA	General Anaesthesia
HR	Heart Rate
I.V.	Intravenous
Kg	Kilogram
L	Lumbar
LA	Local Anaesthetic
LFT	Liver Function Test
lt	Litre
MAP	Mean Arterial Pressure
mcg	Microgram
meq	Milliequivalant
mg	Milligram
min	Minutes

ml	Millilitre
NBM	Nill By Mouth
NIBP	Non Invasive Blood Pressure
O_2	Oxygen
RFT	Renal Function Test
SD	Standard Deviation
sec	Second
Spo_2	Peripheral hemoglobin Saturation of Oxygen
V/S	Versus
V_{max}	Maximum Initial Velocity Or Rate Of A Reaction

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INTRODUCTION

Spinal anaesthesia remains the anaesthetic procedure of choice especially in surgeries on lower abdomen and lower limbs.[1] The advantages of spinal anaesthesia are reduced risk of respiratory complications, superior muscle relaxation, less bleeding, quick restoration of bowel function and reduced incidence of coagulation disorders.

In spite of many recent advances in general anaesthesia complications like nausea, vomiting, prolonged sedation, respiratory depression and airway related morbidity persists. Spinal anaesthesia is simple, effective and safe technique and hence remains the preferred choice among many anaesthesiologists.

There have been various modifications over the last two decades in spinal anaesthesia with the advent of many newer and safer local anaesthetics. Bupivacaine which was introduced into clinical practice in the year 1957 still remains the most commonly used drug for spinal anaesthesia.[2] However, the disadvantage is its inadequate duration of analgesia. Hence postoperative pain management under spinal anaesthesia remains a challenge for the anaesthesiologists.

Various adjuvants with local anaesthetics have been tried with the aim to achieve faster onset, improved analgesic intensity, increased duration of action and provide effective prolonged duration of postoperative analgesia with lower drug dose and thus reducing the side effects.

Drugs namely opioids (eg, fentanyl[3], morphine), alpha 2-agonists (eg: clonidine[4]), benzodiazepines (midazolam), anticholinergics (neostigmine) have been used intrathecally as adjuvant to local anaesthetics for subarachnoid block. They have however been associated with adverse effects like nausea, vomiting, hypotension, bradycardia, pruritis, respiratory depression etc.

Hence, the search for an ideal adjuvant to local anaesthetic for subarachnoid block remains elusive.

Nalbuphine is an opioid, structurally related to oxymorphone. It is highly lipid soluble with an agonist action at the kappa and an antagonist activity at the mu opioid receptors. Nalbuphine and other kappa agonists provide reasonably potent analgesia in certain models of visceral nociception.[5]

Nalbuphine has a moderate duration of action consistent with its lipid solubility and rapid clearance compared with other opioids like morphine

Nalbuphine is recently introduced into clinical practice in India. There are very few studies in literature of nalbuphine use for subarachnoid block. Therefore, an attempt is being made to study the effect of nalbuphine on addition to hyperbaric bupivacaine in patients undergoing lower abdominal surgeries under spinal anaesthesia.

AIMS OF THE STUDY

The objectives of the study were to evaluate

1. onset, duration of sensory and motor blockade.
2. duration of postoperative analgesia.
3. associated side effects if any.

between 0.5% hyperbaric bupivacaine (3ml) and 0.5%hyperbaric bupivacaine (3ml) with nalbuphine (400 mcg) in patients undergoing lower abdominal surgeries under spinal anaesthesia.

HISTORICAL REVIEW

The first spinal anaesthetic was administered accidentally by J. Leonard Corning, a neurologist from New York In 1885, while experimenting with the action of cocaine on the spinal nerves of a dog when he accidentally breached the dura between two lumbar vertebrae, causing paralysis of the hindquarters, and hence inadvertently performed the first spinal anaesthetic.[6]

On 16 August 1898, Bier performed the first operation under spinal anaesthesia at the Royal Surgical Hospital of the University of Kiel. Bier injected 15 mg of cocaine intrathecally in a patient scheduled for segmental resection of his left ankle.[7]

Ever since the development of the technique of spinal anaesthesia various anaesthetic agents such as cocaine, tetracaine, procaine, lignocaine and bupivacaine have been used and studied for their effects.Lignocaine was first synthesized by a Swedish chemist Nils Lofgren in 1943. Bupivacaine is the most common drug used for spinal anaesthesia was discovered in the year 1957. Arthur baker in 1907 first used hyperbaric local anaesthetics for performing spinal anaesthesia.[8]

Nicolae Racoviceanu-Piteşti a Romanian surgeon was the first to use opioids for intrathecal analgesia,in 1901.[9] In 1979 Behar and his colleagues were first to publish the report on epidural use of morphine for pain relief.[9]

The adjuvant Nalbuphine is a newer drug introduced for clinical use and hence its use mandates for further research and knowledge about the drug and its usage with local anaesthetics for subarachnoid block.

In a Study by Rashmi Dubey et al,on the effect of addition of Nalbuphine to intrathecal bupivacaine in elderly patient in lower abdominal surgeries under Spinal

Anaesthesia observed that there was no significant difference on addition of 0.5mg of nalbuphine to 3ml of hyperbaric bupivacaine compared to control group in the onset of motor and sensory blockade. The mean onset of sensory block in the study group was 58sec while in control group it was 60 sec. The mean onset of motor block in both the groups was 110 sec. However, mean time of postoperative analgesia in study group was 8hrs +/- 55min. which was highly significant than control group. No patient in the study developed any side effects. Thus, the authors concluded thatNalbuphine provides better quality of block as compared to bupivacaine alone.[10]

Tiwari AK et al, in a study evaluated the effects of 2 different doses of intrathecal nalbuphine. Patients in one group received 200 µg nalbuphine added to 2.5 ml of hyperbaric bupivacaine and patients in other group received 400 µg nalbuphine added to 2.5ml of hyperbaric bupivacaine. Two segment regression time of sensory blockade and duration of analgesia were maximally prolonged in group receiving 400mcg of nalbuphine intrathecally (190 $^{+}$/-10 min). Visual analogue score was more in control group while it was least in a group receiving 400 mcg of nalbuphine intrathecally. Thus, in the studythey observed that nalbuphine (400 µg) significantly prolongs the duration of sensory blockade and postoperative analgesia without any side effect or complication when introduced intrathecally along with hyperbaric bupivacaine.[11]

In a similar study conducted by Jyothi B et al to compare analgesic effect of addition of different doses of intrathecal nalbuphine namely0.8 mg, 1.6mg and 2.4 mg with3 ml of 0.5% bupivacaine and 3ml of 0.5% bupivacaine with normal saline for lower abdominal and orthopedic surgeries observed that the mean onset of sensory and motor block was comparable in both study group and control group (3.5 min +/-0.2). The 2segment regression of sensory block was more in the study group (122^{+}/-5.3

min) compared to control group (86^{+}/- 4.2min). The mean duration of analgesia was more in the study group (320^{+}/- 39.2 min) as compared with control group(190^{+}/- 20min). In study patients,there were no serious complications like nausea, vomiting,urinary retention, shivering, pruritis, hypotension, or respiratory depression. The study concluded that addition of 0.8 mg nalbuphine to 0.5% bupivacaine had a ceiling effect on the quality and duration of analgesia without any side effects.[12]

Mukherjee et al, conducted a study to find out effective dose of intrathecal nalbuphine as an adjuvant to subarachnoid block. 100 ASA I and II patients undergoing lower limb orthopedic surgery under subarachnoid block (SAB), were randomly allocated to four groups A, B, C and D, to receive 0.5 ml normal saline (NS) or 0.2mg, 0.4mg and 0.8 mg nalbuphine made up to 0.5 ml with NS and added to 0.5% hyperbaric bupivacaine 12.5 mg (total volume 3 ml), respectively. In the study, it was observed that onset time of sensory and motor block were similar in all the 4 groups (1.7^{+}/-0.27 min). The two segment regression time for sensory block was prolonged progressively in group A (120^{+}/- 6.8min), B(134^{+}/6.9 min), C(141^{+}/- 5.8min), D(151^{+}/- 5.6 min). The duration of analgesia was progressively prolonged in groups B, C and D as compared with group A. Group D recorded the longest duration of analgesia with a mean of 278.5 min compared with 237.3 min in group C. Duration of motor blockade was comparable in all the four groups.However, the side effects like hypotension, bradycardia, nausea, vomiting were significantly higher in group receiving 800 mcg nalbuphine.[13]

In a similar study by Mostafa H. et al,comparing post-operative analgesia between intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section, sixty female patientsof ASA grades I and II presented for

elective cesarean deliveries under spinal anaesthesiawere randomly allocated to 2 equal groups; Group F: 30 patients received intrathecal injection of 2 ml of 0.5% hyperbaric bupivacaine plus 0.5 ml fentanyl (25 μg); Group N: 30 patients received intrathecal injection of 2 ml of 0.5% hyperbaric bupivacaine plus 0.5 ml nalbuphine (0.8 mg). The study concluded that the onset of complete motor block was significantly more rapid in fentanyl group than in nalbuphine group. The duration of post-operative analgesia was more prolonged in nalbuphine group(166 $^{+}$/- 14.2min) as compared with fentanyl group (155 $^{+}$/- 20.12 min) but the difference was insignificant.There was nosignificant difference between both groups as regards the duration of sensory block, motor block, visual analogue scale score, hemodynamic parameters and oxygen saturation. Adverse effects were less common in nalbuphine group.[14]

In a similar study by Padma T et al, comparing effect of nalbuphine with bupivacaine and bupivacaine alone for lower limb surgeries, 50 patients of ASA grade I and II were randomly allocated in 2 equal groups of 25 each. One group received inj. hyperbaric bupivacaine 0.5% (3ml) and 400 mcg inj nalbuphine and other group received inj. hyperbaric bupivacaine 0.5% (3ml) and 0.4ml normal saline. The study concluded that the mean onset of sensory blockade was comparable in both the groups (1.2 +/-0.2min), the 2 segment regression time of sensory blockade was prolonged in nalbuphine group (115.32+/-9.12min) compared with control group (103.32+/-16.65min). Duration of post operative analgesia was significantly prolonged in nalbuphine group (464+/-20.02 min) compared with control group (158.5+/- 19.03 min). The incidence of hemodynamic changes and adverse effects like nausea vomiting were comparable in both the groups.[15]

In another similar study conducted by Xavier Culebras et al, compared intrathecal nalbuphine with intrathecal morphine, for elective cesarean delivery with spinal anaesthesia. Patients received 10 mg of hyperbaric bupivacaine 0.5% with eithermorphine 0.2 mg (Group 1), nalbuphine 0.2 mg (Group 2), nalbuphine 0.8 mg(Group 3), or nalbuphine 1.6 mg (Group 4). They observed that only patients in Groups 1 and 2 reported pain during surgery. Postoperative analgesia lasted significantly longer in the morphine group (275^{+}/- 28 min), compared with the nalbuphine groups. Among the nalbuphine groups, postoperative analgesia lasted longest with the 0.8-mg dose(176^{+}/-14min). The additional increase to 1.6 mg did not increase efficacy. The incidence of complication like postoperative nausea, vomiting, pruritiswas higher in the morphine group as compared to nalbuphine group. There was no maternal or new born respiratory depression. Neonatal conditions (Apgar scores and umbilical vein and artery blood gas values) were similar among all groups.[16]

In a similar study by Devendra verma et al, on postoperative analgesic efficacy of intrathecal tramadol versus nalbuphine added to bupivacaine in spinal anaesthesia, 90 adult patients of ASA grade I-II scheduled for lower limb orthopaedic surgeries under spinal anaesthesia were randomised to three groups of 30 each destined to receive 2.5ml (12.5mg) hyperbaric bupivacaine (0.5%) along with 1 ml of either normal saline (Group C), 50mg tramadol (Group T) or 2mg nalbuphine (Group N), making intrathecal drug volume to 3.5ml in each group. They observed that duration of postoperative analgesia was much longer in nalbuphine group (375^{+}/-25 min) as compared with control group (235^{+}/- 14.2min) and tramadol group(260^{+}/-16.3min). There was no significant difference in HR, SBP, DBP and Spo2 during intraoperative

period among three groups. The incidence of complications like postoperative nausea, vomiting, hypotension, bradycardia was comparable in all the three groups.[17]

In a study by Thomas et a, comparing the analgesic and respiratory depressant activity of nalbuphine and morphine, 60 healthy male patients received first single dose of 0.15mg/kg and then four successive dose of 0.15mg/kg of neither nalbuphine or morphine. They observed that multiple doses of morphine progressively increases pain tolerance from 30+/- 13% above control group with fist dose of 0.15mg/kg to 107+/- 13% above control group with last dose of 0.15mg/kg. In nalbuphine groupwith initial 0.15mg/kg dose there was 40+/- 13% increase in pain threshold but successive dose of nalbuphinedid not result in greater analgesia. Also, with increasing doses patients in morphine group had more respiratory depression than in nalbuphine group. Thus, authors'concluded that nalbuphine in contrast with morphine with increase dose exhibits ceiling effect for respiratory depression paralleled to its limited analgesic effect[18]

In a similar study conducted by Fournier R1, Van Gessel E, Macksay M, Gamulin Z. on onset and offset of intrathecal morphine(160mcg) versus nalbuphine (400mcg) for postoperative pain relief after total hip replacement with 4 ml normal saline administered intrathecally observed that duration of analgesia in morphine group(1040+/-440 min) was prolonged than nalbuphine group (218+/- 256 min). Also the onset of sensory blockade was faster in nalbuphine group (8+/-6 min) than morphine group (31+/- 32min).Thus, the study concluded that, administration of intrathecal nalbuphine resulted in a significantly faster onset of pain relief and shorter duration of analgesia than intrathecal morphine.[19]

In a study by mai Li et al, on the analgesic effect of subarachnoid administration of tetracaine combined with low dose morphine or nalbuphine for spinal anaesthesia, 60 ASA physical status class I or II patients were divided into two groups one received 0.4mg of morphine and other received 0.4mg of nalbuphine. In study, they observed that effective analgesia in postoperative period was more in morphine group (250 +/- 16min) compared with nalbuphine group(230 +/- 22 min). However, postoperative complication like nausea vomiting, pruritic was higher in morphine group compared with nalbuphine group.[20]

BASIC SCIENCES

Subarachnoid block can be used as the sole anaesthetic procedure when surgery is to be performed on the lower extremities, lower abdominal wall, and perineum. Spinal anaesthesia produces intense sensory and motor blockade as well as sympathetic blockade.

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

Strong contraindications include patient refusal, lack of patient co-operation, difficulties with positioning and increased intracranial pressure. Relative contraindications include situations that require some risk-benefit analysis include hypovolemia, coagulation disturbances, stenotic valvular disease, bacteraemia, and infection at the site of needle insertion.

Anatomy

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

Vertebral column

The vertebral column consists of 33 vertebrae which includes[21]

- Cervical – 7
- Thoracic – 12
- Lumbar – 5
- Sacrum – 5
- Coccyx – 4

Main function of vertebral column is to protect spinal cord.

Curves of spine:

In adults, vertebral column has four curvatures[22]

- Cervical and lumbar curve - convex anterior
- Thoracic and sacral curve - concave anterior

When in supine position the highest point of cervical and lumbar curvature is at C5 and L5;lowest points of thoracic and sacral are at T5 and S2 respectively

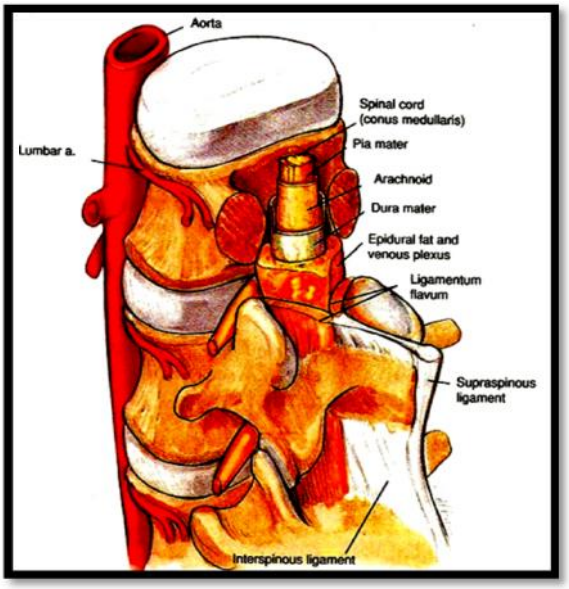


Figure 1: vertebral column

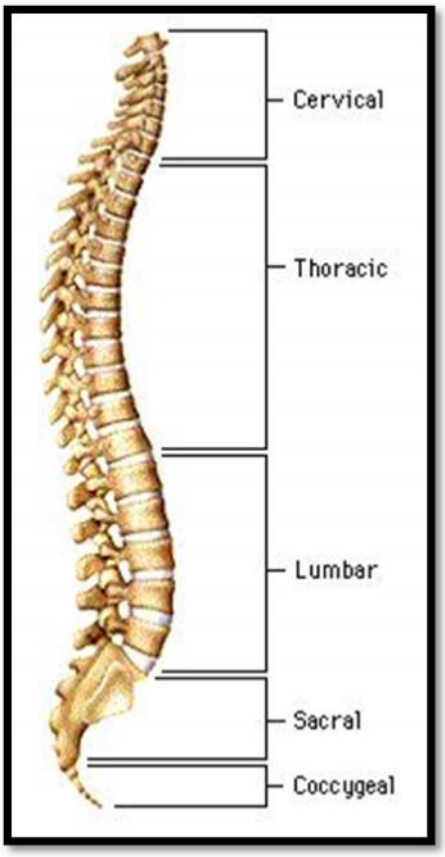


Figure 2: Curves of the spine

Vertebral ligaments

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

Supraspinous ligament: This is a strong fibrous cord which connects spinous processes from sacrum to C7 vertebra above which it continues as ligamentum nuchae.

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

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

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

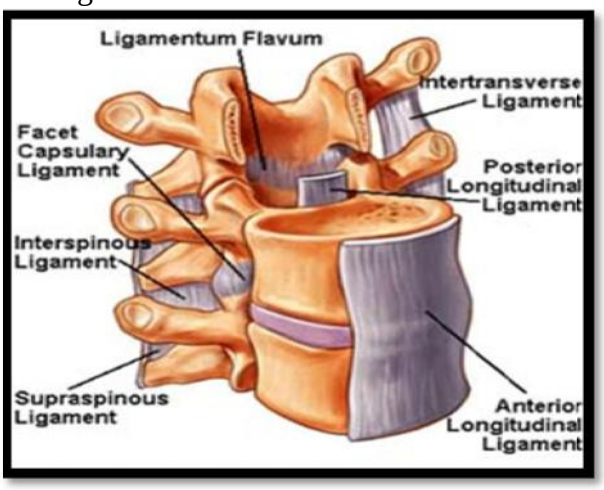


Figure 3: Spinal ligaments

Lumbar vertebrae

A typical lumbar vertebra consists of

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

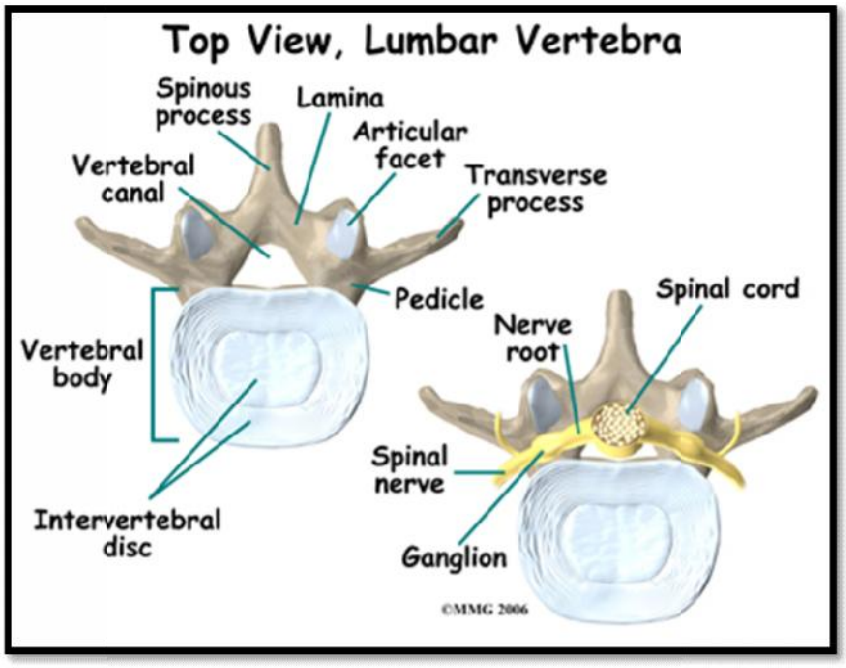


Figure 4: Typical Lumbar Vertebra

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 vertebrae in the upright position. In a patient lying in the lateral position it may also pass through L4 and L5 interspaces. The superior iliac crest is used to identify the L4 and L5 interspaces during spinal anaesthesia.

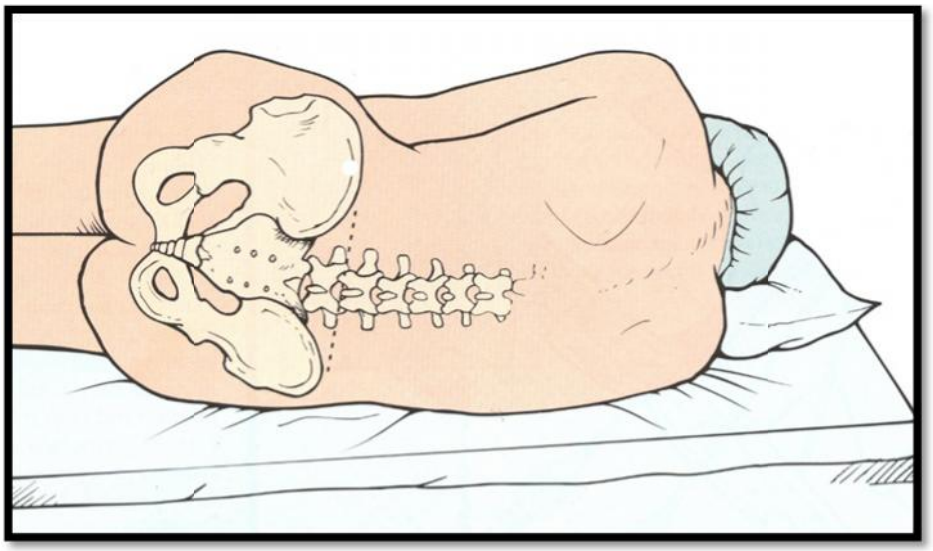


Figure 5: Line of Tuffier

Vertebral canal [6]

Vertebral canal is bound posteriorly by spinous processes and interspinous ligaments, laterally by the pedicles and postero- laterally by the laminae and ligamentum flavum. Superiorly it terminates into foramina magnum and inferiorly in the sacral hiatus. The vertebral canal contains spinal cord, roots of spinal nerves, spinal membranes, CSF, blood vessels and adipose tissues.

Spinal cord [21]

The spinal cord extends from the foramen magnum where it is continuous with the medulla and it tapers off into a conical extremity known as conus medullaris. The spinal cord is 40 - 50 cm long and 1 cm to 1.5 cm in diameter. Spinal cord ends at the level of L3 vertebra at birth but rises as the age progresses and reaches to L1 vertebra in adults.

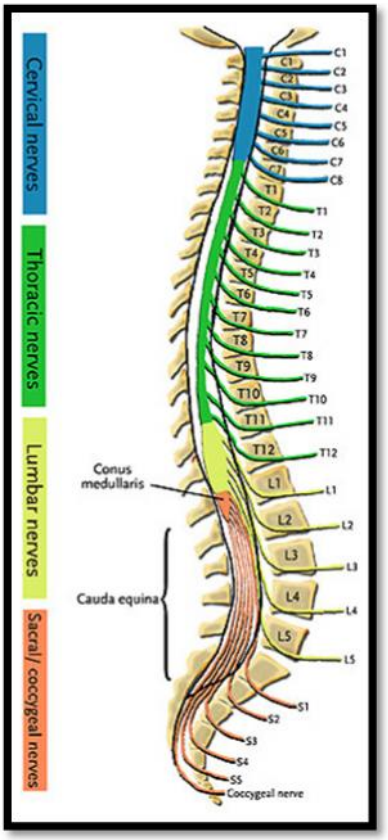


figure 6: spinal nerve roots

Blood supply of spinal cord [21]

The arterial blood supply to the spinal cord in the upper cervical regions is derived from two branches of the vertebral arteries, the anterior spinal artery and the posterior spinal arteries. The anterior spiral arteries are paired arteries which join to form a single artery that lies in the anterior median fissure of the spinal cord at the level of medulla. Paired posterior arteries form an anastomotic chain over the posterior aspect of the spinal cord. A plexus of small arteries, the arterial vasocorona, on the surface of the cord constitutes an anastomotic connection between the anterior and posterior spinal arteries. This arrangement provides uninterrupted blood supplies along the entire length of the spinal cord.

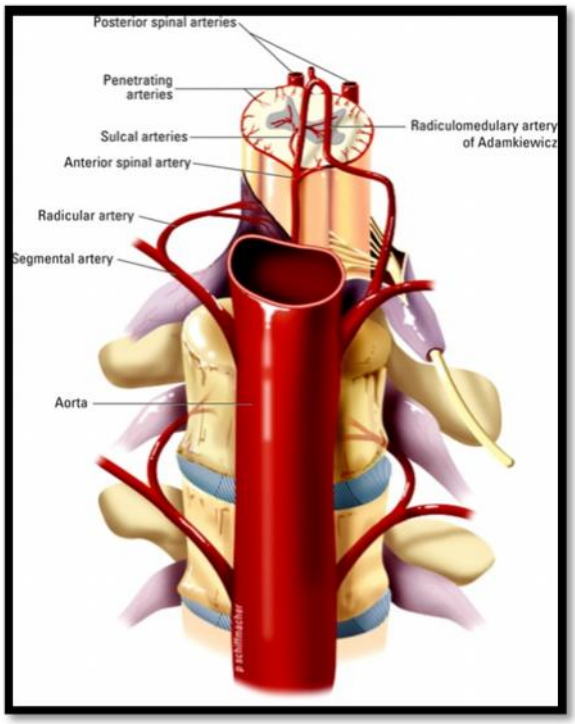


Figure 7: Blood Supply of Spinal Cord

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 fibres are split and not cut. Dural sac ends at lower border of S2, where it is pierced by filum terminale.

Arachnoid mater [24]

It is a delicate, non-vascular, middle covering and it is closely attached to the duramater. There is 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 avascular 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 is called subarachnoid space and is filled with cerebrospinal fluid and contains numerous arachnoid trabeculae which forms delicate sponge like mass. This space has three divisions which are free communications 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 subpial 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 ad 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 lateral ventricles into the third ventricle through the foramina of monro into the forth ventricle through the Aqueduct of Sylvius into the cerebro-medullary cisterna (cisterna magna) through foramen of Magendie and foramina of Lushka. 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 (25ml to 35 ml in spinal space).
- CSF pressure: 60 to 80 mm Hg in lumbar space.
- Ph: 7.27 to 7.37
- Pco_2 :48 mmHg
- HCO_3: 23mEq/L
- Sodium: 135 to 145 mEq/L
- Calcium: 2 to 3 meq/L
- Phosphorous: 1.6 mg/dl
- Magnesium: 2 to 2.5meq/L
- Chloride: 15 to 20 meq/L
- Proteins: 23 to 38 mg/dl

Physiology of subarachnoid block

Factors which controls the different effects of spinal anaesthesia are[25]

- Type of drug
- Amount of drug
- Injection site
- Rate of injection
- Density and baricity of solution
- Barbotage

Factors influencing distribution of Local Anaesthetic solution in Cerebrospinal Fluid.[24 25]

1. Patient characteristics

- Age
- Height
- Weight
- Gender
- Intra-abdominal pressure

2. Techniques

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

Physiologic response to subarachnoid blockade results from autonomic blockade with its effects on cardiac action and vascular bed from addition of somatic pain and the reflex responses associated with it and from the effects of blockade of motor fibers.

Sequence of subarachnoid blockade[28]

1. Autonomic preganglionic B fibers
2. Temperature fibers: first cold then warm
3. Pain:pin prick fibers first
4. Loss of tactile sensation
5. Motor paralysis
6. Deep pressure
7. Proprioception and vibratory sensation

During recovery return of sensation occurs in reverse order. The sympathetic fibers are affected first and are last to recover, while motor nerve fibers are affected last are first to recover.[29]

In subarachnoid block sympathetic fibers are blocked two segments higher than sensory fibers and sensory block is two segments higher than motor fibers.[29]

Cardiovascular effects of spinal anaesthesia[27]

Neuraxial blockade can impact the cardiovascular system by causing the following changes:

- Decrease in blood pressure
- Decrease in heart rate
- Decrease in cardiac contractility

Risk factors for bradycardia during spinal anaesthesia include patients with a baseline heart rate of less than 60, ASA I (healthy patients), prolonged P-R interval, beta blocker administration, and a block > than T5 level. Risk factors for hypotension include a block> T5 level, > 40 years of age, a baseline SBP < 120 mmHg, and a lumbar puncture at or above L2-L3.

Theories of causation of fall in BP

- Diminished cardiac output due to reduction of venous return to heart.
- Dilatation of post arteriolar capillaries and small venules
- Paralysis of sympathetic nerve supply to heart
- Paralysis of sympathetic nerve supply to adrenal gland with consequent catacholamines depletion.

Cerebral blood flow

In humans the cerebral blood flow is maintained at constant levels by cerebrovascular autoregulatory mechanism

Effects of SAB on respiratory system:

Due to motor blockade as well as differentiation with reduction of sensory input to respiratory centre breathing becomes quite during subarachnoid block. Intercostal paralysis is compensated by descent of diaphragm which is made easier by lax abdomen. Pulmonary gas exchange is preserved.

Effects of SAB on gastrointestinal system:

Due to neuraxial blockade upto T5 level results in sympathectomy with predomination of parasympathetic nervous system effects. This results in small and contracted bowel, increased peristalsis and relaxation of sphincters. Due to decrease

in mean arterial pressure there is nausea and vomiting and decrease in hepatic blood flow.

Effects of SAB on Neuroendocrine system:

Surgery produces host of neuroendocrine responses related to inflammatory response and activation of somatic and visceral afferent nerve fibers. This response results in release of ACTH, cortisol, epinephrine, norepinephrine, and vasopressin. Sufficiently high and prolonged neuraxial blockade can prevent these responses.

Effects of SAB on genitourinary system:

Auto regulation maintains renal blood flow as long as perfusion pressure is maintained within normal limits. Urinary retention occurs due to loss of autonomic bladder control. Detrusor function of the bladder is blocked by the local anaesthetics. Prolonged blockade of detrusor muscle leads to bladder over distention and urinary retention. Normal function does not return until sensory function returns till S3.

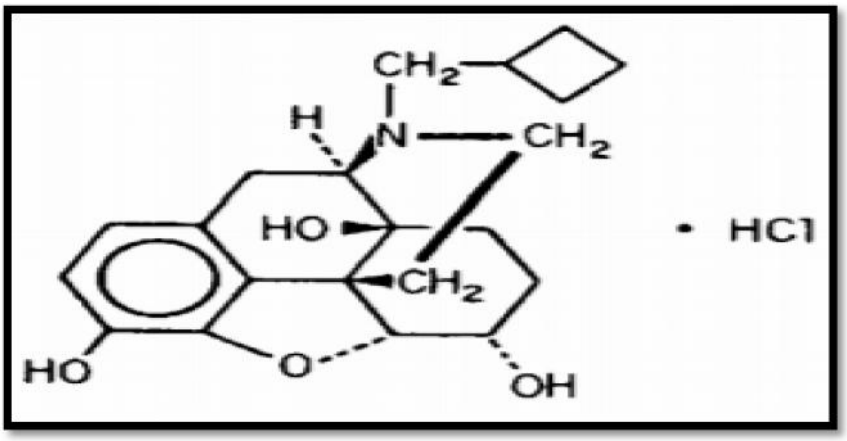
The engorgement of flaccid penis due to paralysis of nervigentis is the first sign of successful block. Tone of uterus is usually maintained after neuraxial block in pregnancy.

PHARMACOLOGY

NALBUPHINE:

Nalbuphine is a synthetic opioid agonist-antagonist. It is chemically related to antagonist naloxone and a potent agonist oxymorphone. Chemically nalbuphine hydrochloride is 17(cyclobutylmethyl)-4, 4,5o-epoxymorphinan-3,6o, 14-triol hydrochloride. molecular formula $C_{21}H_{27}NO_4$.

- Molecular weight -393.91.
- Melting point -230^{o}C
- PH: 8.71



Structural formula of nalbuphine

Pharmacological action

Nalbuphine belongs to mixed agonist– antagonist opioid analgesic group. It is agonist at kappa opioid receptors and a weak antagonist at mu opioid receptors. Nalbuphine is a potent analgesic and its analgesic potency is equivalent to that of the morphine.

Nalbuphine by its action on kappa opioid receptors inhibit release of neurotransmitter substance P that mediates pain. In addition it acts as post synaptic inhibitor on the interneuron and output neuron of the spinothalamic tract which transports nociceptive information.

Thus, when nalbuphine administered along with bupivacaine will have synergetic effect, thus prolonging the duration of sensory blockade without affecting sympathetic blockade and motor blockade.

Effects on various systems:

Respiratory system:

Nalbuphine may produce similar degree of respiratory depression as that of morphine. However, nalbuphine exhibits ceiling effect such that increase does more than 30mg does not produce any further respiratory depression. Nalbuphine hydrochloride has potent opioid antagonist activity at doses equal to or lower than its analgesic does. Hence, when administered with mu agonist opioids such as morphine, oxymorphone, fentanyl it may reverse or block opioid induced respiratory depression from the mu agonist analgesic.

Cardiovascular system:

Nalbuphine does not produce any significant cardiovascular effects in patients with ischemic heart disease.

Central nervous system:

The opioid antagonist activity of nalbuphine is 10 times that of pentazocine and therefore is less likely to produce psychomotor effects such as hallucination.

Autonomic System:

Nalbuphine causes less inhibition of gastrointestinal activity than other opioids.

Pharmacokinetics:[30]

Nalbuphine hydrochloride undergoes extensive first pass metabolism when administered parentally. Following intravenous administration of the drug, onset of action occurs within 2-3 min and its peak effect reaches within 30 min. Following IM administration of nalbuphine hydrochloride onset of action occurs within 15 min. The half-life of the drug is 3- 6 hrs. Nalbuphine exhibit low protein binding and it crosses the placenta.

The major metabolite of nalbuphine is N-hydroxycetocyclobutyl-methylnornalbuphine, and other metabolites correspond to hydroxylated ones. The urinary excretion of unchanged nonconjugated nalbuphine was limited to 4%of the amount of drug that reached systemic circulation. Nalbuphine can be characterized as perfusion limiting drug and its hepatic clearance depends on hepatic blood flow.[31 32 33 34 35].The elimination rate of nalbuphine decreases with age. Excretion of the drug and its metabolites occur through urine, bile and faeces.[36 37]

USES:

1. Pain relief in moderate to severe pain.
2. Pre anaesthetic sedation
3. Adjuvant in general anaesthesia induction and maintenance
4. Adjuvant along with local anaesthetic in spinal anaesthesia

Nalbuphine is available in 1ml ampule as a clear solution. Each ml contains 10mg or 20mg of nalbuphine hydrochloride.

DOSES [5]

Intravenous loading dose: 0.3 – 3 mg/kg IV over 15 min.

Maintenance: 0.25 -0.5 mg/kg.

Doses need modification in conditions with hepatic and renal impairment.

Epidural dose: 0.04mg/ml of local anaesthetic injected into the epidural space.

Spinal dose: 0.2mg – 1.6mg

ADVERSE DRUG REACTIONS:

The most common adverse effect of nalbuphine hydrochloride

1. Drowsiness
2. Nausea/ vomiting
3. Headaches
4. Diaphoresis
5. Dizziness/ vertigo

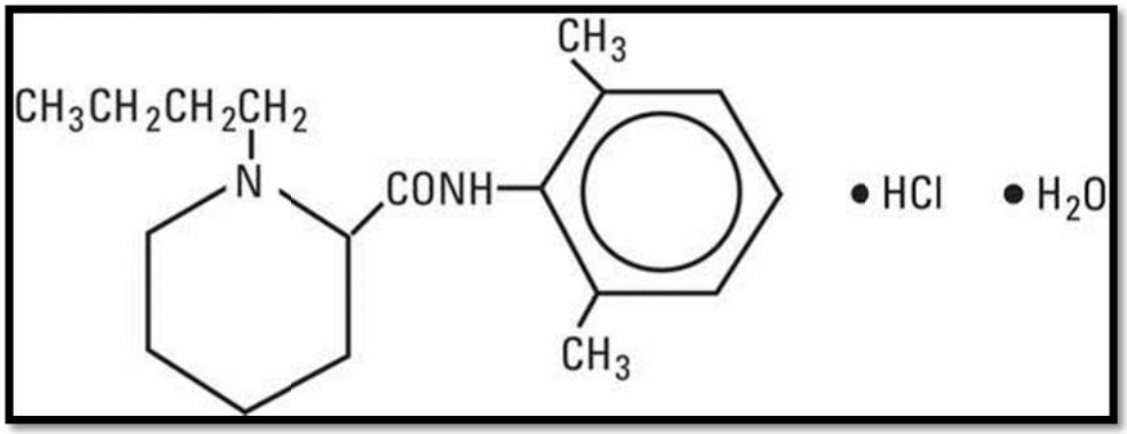
BUPIVACAINE

Introduction

- It is a local anaesthetic which belongs to amide group.
- It was first synthesized by Swedish investigator BoafEkenstan and colleagues in 1957.
- It is chemically known as 1- butyl 2 – piperidyl formo – 2’6’ – xylidine hydrochloride.

CHEMICAL STRUCTURE:

BUPIVACAINE [38 39 40 41]



PHYSICAL AND CHEMICAL PROPERTIES

- Molecular weight-325
- PH: 5.2
- Specific gravity: 1,025 at 37^{o}C
- Melting point : 247 to 258 ^{o}C
- Chemically its amide 2,6 methyl amide.

MECHANISM OF ACTION

Bupivacaine action is similar to any other local anaesthetics. The local anaesthetic primarily acts on the cell membrane of the axon on which it produces electrical stabilization. To prevent propagation of impulse large transient increase in permeability to sodium ion is necessary. Therefore, the resting membrane potential is maintained and depolarization in response to stimulation is inhibited.

The mechanism by which local anaesthetic blocks sodium conductance is as follow:

- The cationic form of local anaesthetics acts on the receptors within the sodium channels, on the cell membrane and block it. The two pathways by which local anaesthetics reach the sodium channels is as follows:

  1) Lipophilic pathway directly across the lipid membrane,

  2) Via exoplasmic opening.
- The second mechanism is by membrane expansion.

Dosages and preparations:

Dosages of bupivacaine depends on:

- Area to be anesthetized.
- Vascularity of the tissue.
- The number of neuronal segments to be blocked.

Available concentration of bupivacaine;

- 0,25%, 0.5%, 0.75%
- 0.25% and 0.5% solution in isotonic saline
- 0.5% solution in 8%dextrose.

Table: concentration, volume and dose of bupivacaine for various blocks

Types of block	concentration	Volume (ml)	Doses (mg)
Local infiltration	0.25%, 0.5%	5 - 20	125 - 175
SAB	0.5%, 0.75%	2 - 4	10 - 20
Epidural block	0.25%, 0.5%	15 - 30	50 - 200
Caudal block	0.25%, 0.5%	15 - 30	75 - 150
Brachial block	0.25%, 0.5%	15 - 30	75 - 225
Intercostal block	0.25%, 0.5%	3 - 5	15 - 20

The maximum allowable dose of bupivacaine is 400mg in 24hr. Addition of vasoconstrictors like epinephrine to bupivacaine produces slight increase in the duration of action. However, the peak blood concentration is lowered significantly, thereby reducing the systemic toxicity.

PHARMACOLOGICAL ACTION:

Cardiovascular system:

Due to decrease in the availability of sodium channels the primary electro physiological effect of local anaesthetic is a decrease in maximum rate of depolarization in purkinjefibersand ventricular muscles. There is also decrease in duration of action potential and effective refractory period. Bupivacaine also blocks calcium conductance therefore reducing cardiac contractibility and arrhythmogenic effects.

Low concentration of bupivacaine produces vasoconstriction and high doses produces vasodilation.

Respiratory system:

Excessive plasma levels of bupivacaine results in depression of medullary respiratory centre which intern causes respiratory depression.

Also high spinal or total spinal anaesthesia can cause respiratory muscle paralysis.

Central nervous system:

Due to blockade of inhibitory neural pathways in cerebral cortex initial doses of bupivacaine cases excitatory effects producing light headedness and dizziness followed by visual and auditory disturbances such as tinnitus. With further increase in doses depression of both fascilitatory and inhibitory pathways occur which leads to drowsiness disorientation and finally coma. Further increase in doses leads to respiratory arrest. Due to high potency of bupivacaine even smaller doses causes rapid onset of toxic symptoms.

Autonomic nervous system:

Due to faster conduction time of myelinated preganglionic beta fibers are more sensitive to action of local anaesthetics including bupivacaine. Therefore, blockade of these myelinated preganglionic sympathetic fibers leads towidespread vasodilatation and hypotension. bupivacaine doesn't inhibit noradrenaline uptake, therefore has no sympathetic potentiating effect.

PHARMACOKINETICS OF BUPIVACAINE

Rate of systemic Absorption of local anaesthetic is determined by

- Site of injection.
- Dosage and concentration of drug administered.
- And addition of a vasoconstrictors like epinephrine.
- Vascularity of tissue.

More the vascularity of tissue faster is the absorption of the drug eg: absorption of the drug is faster after intercostal block than after brachial plexus block. Higher the dose greater is the absorption of the drug.

DISTRIBUTION

T ½ of alpha, beta and gamma bupivacaine is 2-7min, 28 min and 3-5 hrs respectively.

Bupivacaine is distributed throughout the body. Higher concentration of bupivacaine is observed in highly perfused organs. Bupivacaine is rapidly metabolized in pulmonary vasculature; therefore concentration of the drug decreases as it passes through pulmonary vasculature.

BIOTRANSFORMATION AND EXCRETION

In liver bupivacaine undergoes N- dealkylation and hydroxylation and then conjugation which lead to formation of water soluble compound. Pipecoloxylidine is the major metabolite of Bupivacaine Hydrochloride

Excretion of the drug occurs through kidney.

Onset of action: 2-15 min

Peak plasma concentration: 30 to 45 min.

Duration of action: 2-9hrs

TOXICITY

Bupivacaine is more potent than lignocaine which causes higher toxicity. Toxic plasma concentration of bupivacaine is set at 4-5 mg/ml.

Adverse effects:

Effects on central nervous system : depression or excitation, nervousness, dizziness, blurring of vision, tremors, drowsiness, convulsions, respiratory arrest

Effects on cardiovascular system:

Hypotension myocardial depression and cardiac arrest.

Allergic reaction like bronchospasm, urticaria, hypotension .

Treatment of adverse effects:

- Maintain adequate circulation with IV fluid and vasopressors.
- Supportive treatment with oxygen.
- Controlled ventilation if required.
- Treatment of convulsions with diazepam or muscle relaxants.
- Treatment of allergic reaction with corticosteroids.

MATERIALS AND METHODS

The present study titled "COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH NALBUPHINE FOR SUBARACHNOID BLOCK IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES, A ONE YEAR RANDOMISED CONTROLLED TRIAL." was conducted in Department of Anaesthesiology KLE'S Dr. Prabhakar Kore Hospital and MRC between January 2016 to December 2016.

The study was conducted on 60 ASA grade I and II patients undergoing lower abdominal surgeries, after Institutional review board and ethical committee clearance was obtained and written informed consent taken from all the patients.

The inclusion and exclusion criteria were as follows.

Inclusion Criteria:

1. ASA physical status I and II.
2. Age between 18 to 40 years
3. Patients undergoing lower abdominal surgeries under spinal anaesthesia with a minimum duration of 1 hour.

Exclusion Criteria:

- Patients refusal to give consent
- Allergic to the study drugs-bupivacaine and nalbuphine
- Patients on chronic opioid usage.
- Patients with diabetes, liver disease, cardiac and neurological disorders.
- Patients with coagulation abnormalities
- Patients with spine defects or infection at the site.

Sample size calculation:

The sample size was calculated by using results of previous study taking onset of sensory blockade as the parameter.

With type I error rate $\alpha = 0.05$ and

Type II error rate $\beta = 0.1$

With a power of 90% and using all the values in the below mentioned formula-

$$n = \frac{(Z\alpha+Z\beta)^2 \ (S1^2 +S2^2)}{(X1^2 -X2^2)}$$

n = sample size in each group.

$Z\alpha = 1.96$

$Z\beta = 1.28$

S1 = S.D Of group A= 0.5

S2 = S.D Of group B =0.6

X1 = Is group A using 400 mcg of nalbuphine=5.9

X2 = Is Group B using normal saline = 5.7

$$N = \frac{(1.962 +1.282) (0.52 +0.62)}{(5.92 – 5.72)}$$

= 5

As the sample size obtained was very small therefore by taking the thumb rule sample size of 30 patients in each group was taken for the study.

DESIGN

Randomised control trial. Randomization was done into two groups by computer generated method.

Group A: Inj. bupivacaine hyperbaric 0.5% 3 ml + inj.Nalbupine 400mcg diluted with Normal saline to 3.5ml.

Group B: Inj. bupivacaine hyperbaric 0.5% 3 ml + Normal saline 0.5ml.

All the routine investigations namely CBC, RFT, LFT, coagulation profile, ECG, Chest X-Ray were done and NBM status was confirmed.

An IV line was secured with 18G IV cannula. All patients were preloaded with 10 ml/kg of Ringer's lactate solution. Standard monitors were attached namely pulse oximetry, ECG, NIBP and baseline values noted before performing the procedure. The study medication was prepared by the person who was not involved in the study to ensure blinding of the anaesthesiologist. Under all aseptic conditions, subarachnoid block was performed using 23G Quinke's spinal needle at L3 –L4 level in sitting position. Respective agents were injected according to the group. Hemodynamic parameters namely heart rate, systolic blood pressure, diastolic blood pressure and oxygen saturation were monitored throughout the surgical procedure.

Following parameters were observed and noted:

T0 – Time of spinal anaesthesia.

T1 – Time of onset of sensory blockade.

T2 – Time of onset of motor blockade.

T3 – Maximum Height of sensory blockade.

T4 – duration of sensory blockade.

T5 – duration of motor blockade.

T6 – duration of post operative analgesia

Sensory block: Sensory block was assessed by loss of sensation to cold swab in mid-clavicular line, on either side every 30 sec. The **onset of sensory blockade** was taken as the time taken from the injection of the drug to sensory block up to$T_{10.}$ **Duration of sensory blockade** was defined as two dermatome regression of anaesthesia from the highest level achieved. The **maximum height of sensory block** was considered as height of sensory block achieved at the end of 20 min

Motor block was assessed Using modified bromage scale.

MODIFIED BROMAGE SCALE:

0-able to move hip, knee, ankle and toes (0%)

1-Inability to raise extended leg but able to move knee and feet (33%) (Partial)

2-Inability to raise extended leg and move knee but able to move feet (66%)

3- Unable to move hip, knee and ankle (100%) (Complete block)

The **onset of motor blockade** was taken as the time taken from injection of the drug to time taken to reach modified Bromage score of 3. **Duration of motor blockade** was taken as the time for return to modified Bromage score 0.

Motor block was measured at 0,10,20,30 minutes post injection until patient returned to score of 0 in both lower limbs

Vital parameters were monitored every 5 mins for the first 30 mins then every 10 mins till end of surgery. Perioperatively patients were observed carefully for the side effects like respiratory depression, nausea, vomiting, itching etc.

In the postoperative period VAS score was calculated on a 10-cm long scale with ‘0’ on one end, meaning ‘no pain at all’, while ‘10’ on the other end representing ‘worst

pain imaginable'. Patients rated the degree of pain by making a mark on the scale. Thus, the pain score was obtained by measuring the distance from the '0' end to the indicated mark.

Postoperative rescue analgesic drug was given when patient's VAS score reached >3 (this time was taken as duration of postoperative analgesia). Inj. diclofenac 75 mg in 100ml saline was given as rescue analgesia.

All the parameters studied were observed and noted. The Students unpaired't' test was used to compare quantitative variables in both groups and the qualitative variables was compared using students paired 't' test for each group. The categorical data were compared using Chi square test. Data are mean (standard deviation) unless otherwise specified. Significance is taken as p value < 0.05.

RESULTS

The study was conducted in Department of Anaesthesiology KLE'S Dr.Prabhakar Kore Hospital and MRC between January 2016 to December 2016.

The study was conducted on 60 ASA grade I and II patients undergoing lower abdominal surgeries.

Randomization was done into two groups by computer generated method.

Group A: Inj. Bupivacaine hyperbaric 0.5% 3 ml + inj. Nalbuphine 400mcg diluted with Normal saline to 3.5ml.

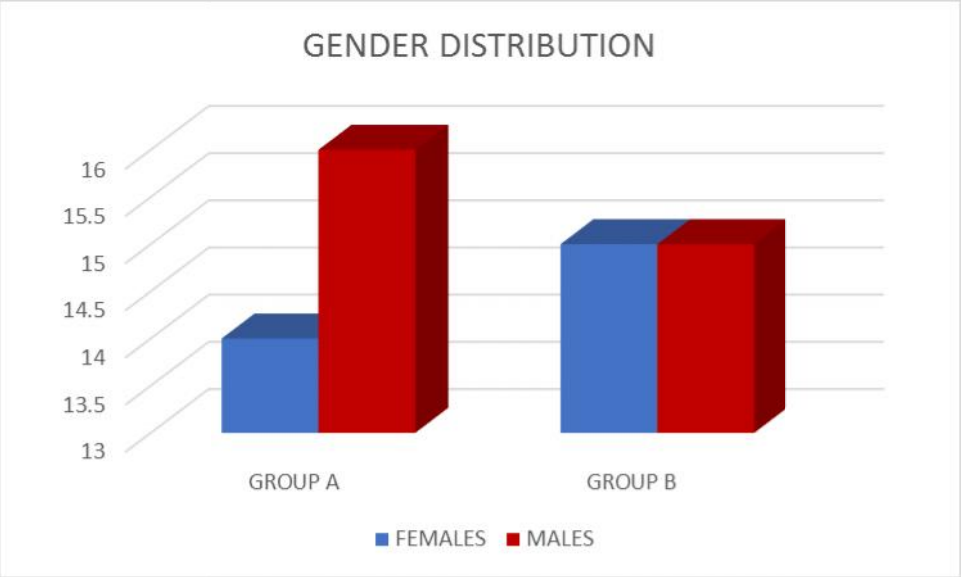
Group B: Inj. Bupivacaine hyperbaric 0.5% 3 ml + Normal saline 0.5ml.

The results obtained were tabulated and analysed

Table 1. Gender distribution

	GROUP A	GROUP B	TOTAL
FEMALES	14	15	29
MALES	16	15	31
TOTAL	30	30	60

Graph 1: gender distribution

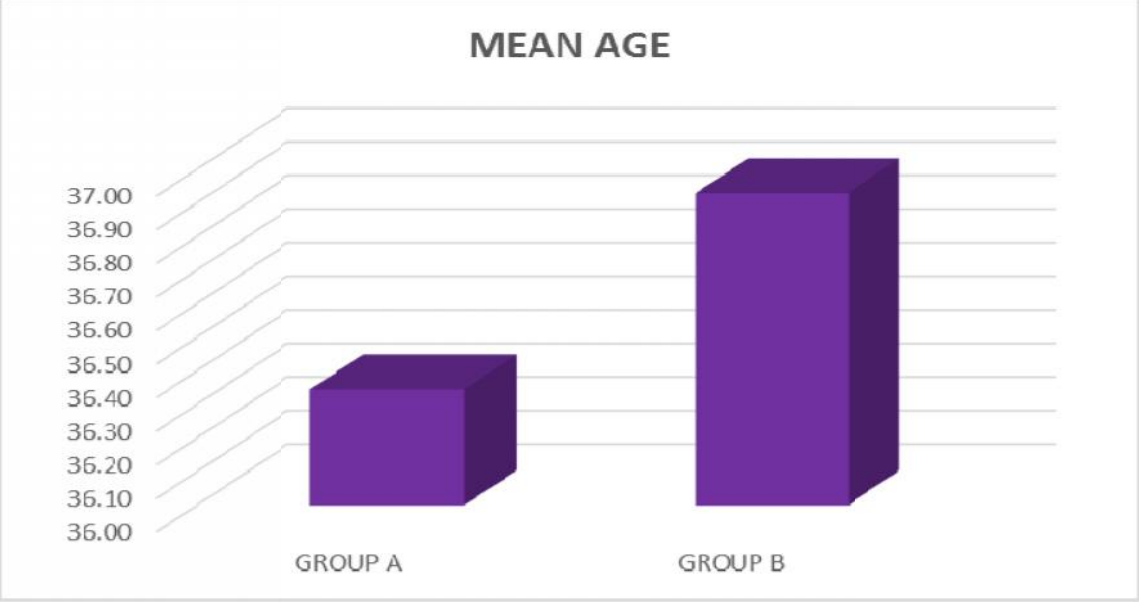


This is a table showing gender distribution in both group A and group B. Data was comparable in both groups

Table 2: mean age

MEAN AGE					
GROUP A		**GROUP B**		**p VALUE**	**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
36.34	5.66	36.93	6.43	0.7171	NS

Graph 2: mean age

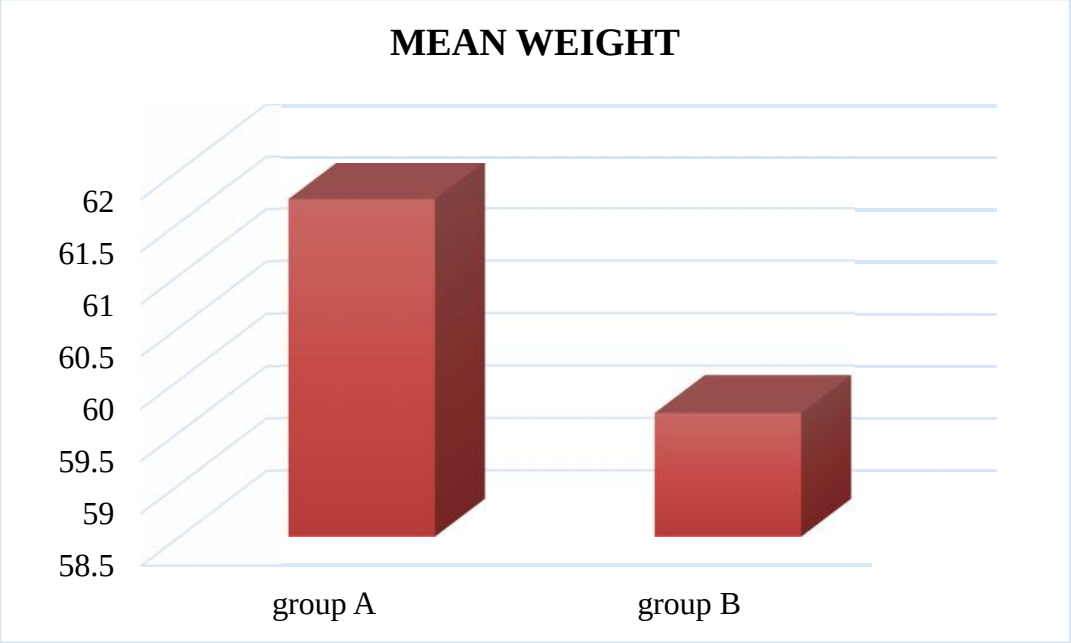


The mean and standard deviations of age in the two groups are shown in the above table. Using the student's unpaired t test, the p value obtained is 0.7171. This indicates that there is no significant difference in the mean age of the two groups.

Table 3: mean weight

MEAN WEIGHT					
GROUP A	**GROUP B**		**p VALUE**		**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
61.72	7.65	59.68	7.28	0.0558	NS

Graph 3; mean weight

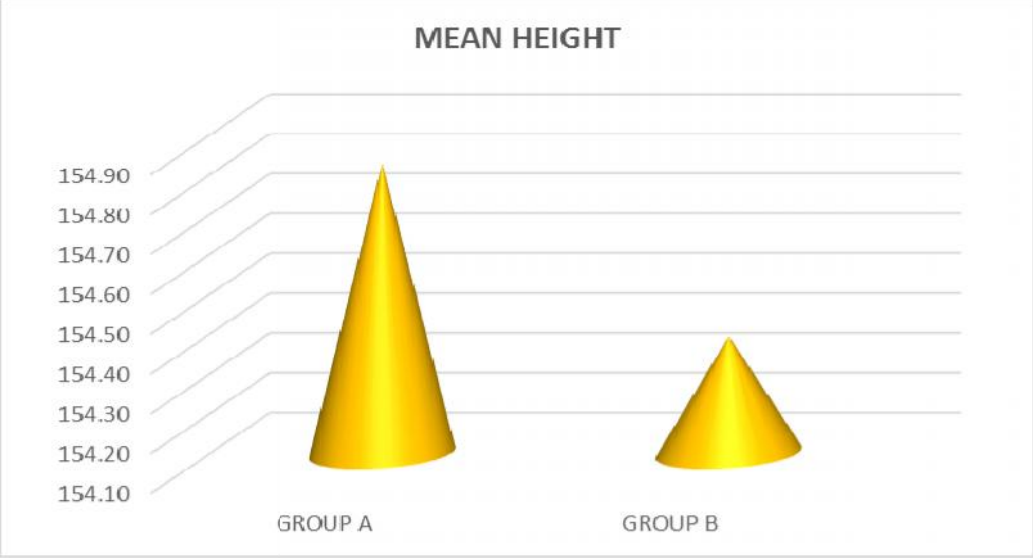


The mean and standard deviations of weight in the two groups are shown in the above table. P value obtained is 0.0558. This indicates that there is no significant difference in the mean weight of the two groups.

Table 4: mean height

MEAN HEIGHT					
GROUP A		**GROUP B**		**p VALUE**	**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
154.83	3.26	154.39	2.94	0.5995	NS

Graph 4: mean height

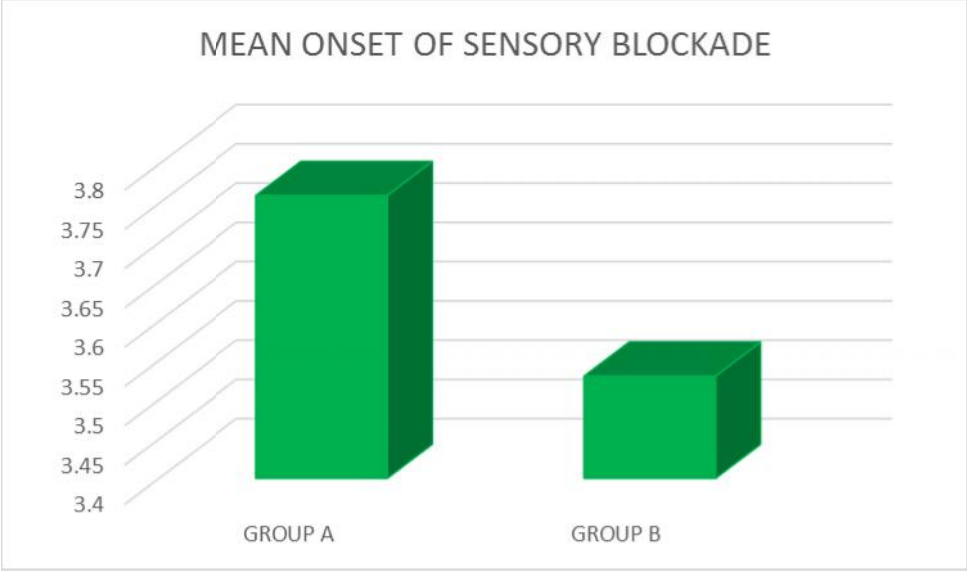


The mean and standard deviations of height in the two groups are shown in the above table. P value obtained is 0.5995.This indicates that there is no significant difference in the mean height of the two groups.

Table 5: mean onset of sensory blockade

MEAN ONSET OF SENSORY BLOCKADE					
GROUP A		**GROUP B**		**p VALUE**	**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
3.76	0.86	3.53	0.74	0.2768	NS

Graph 5:mean onset of sensory blockade

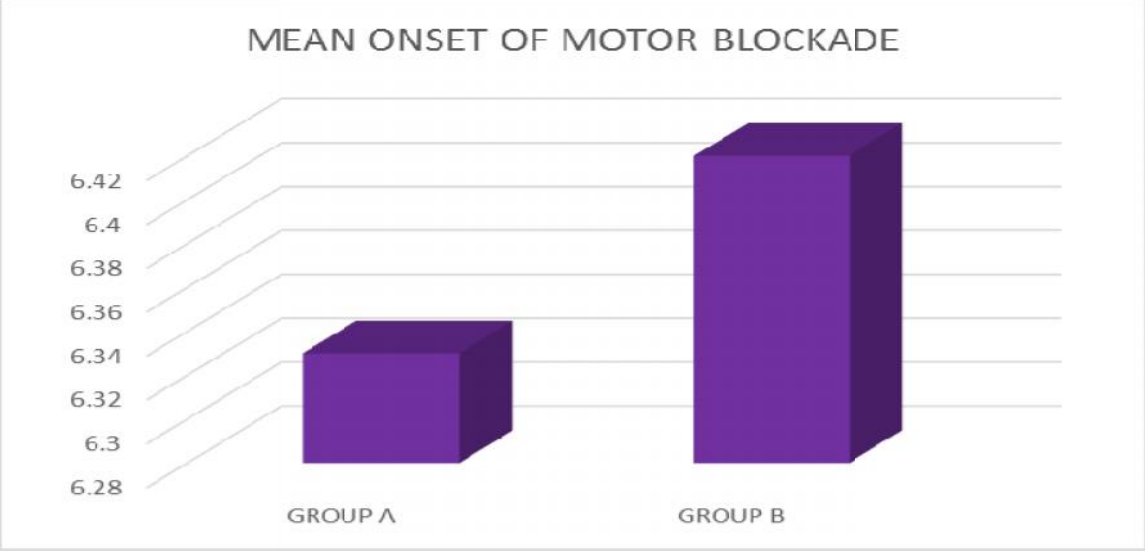


In the present study onset of sensory block was comparable in both group A and group B. P value obtained is 0.2768. This indicates that there is no significant difference in the mean onset of sensory block in the two groups.

Table 6: mean onset of motor blockade

MEAN ONSET OF MOTOR BLOCKADE					
GROUP A		**GROUP B**		**p VALUE**	**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
6.33	1.27	6.42	0.86	0.0525	NS

Graph 6: mean onset of motor blockade

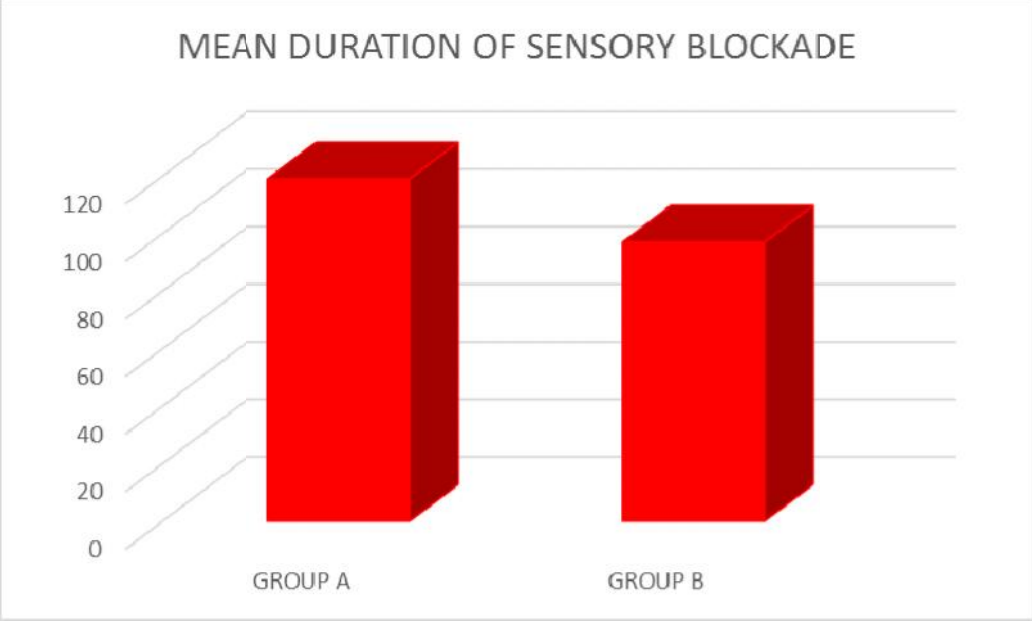


In the present study, the mean onset of motor block was comparable in both group A and group B and the p value obtained is 0.0525. This indicates that there is no significant difference in the mean onset of motor block in the two groups.

Table 7: mean duration of sensory blockade

MEAN DURATION OF SENSORY BLOCKADE					
GROUP A		**GROUP B**		**p VALUE**	**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
118.93	8.37	96.93	7.10	<0.0001	HS

Graph 7: mean duration of sensory blockade

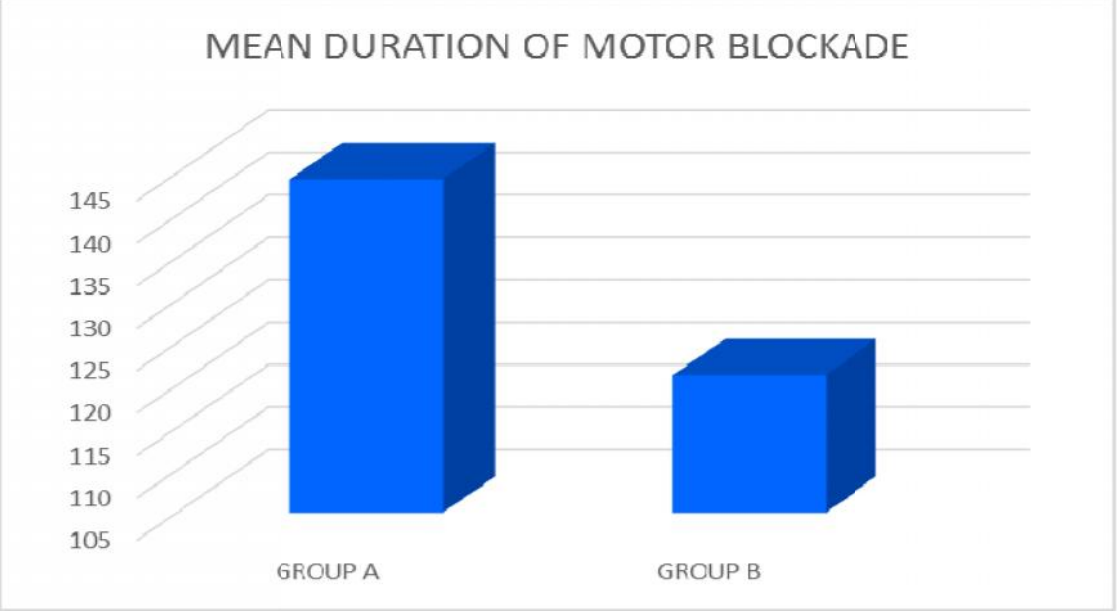


In the present study mean duration of sensory blockade was higher in group A (118.93+/-8.37) than group B (96.93+/- 7.10) and difference was statistically significant (p value <0.0001)

Table 8: mean duration of motor blockade

MEAN DURATION OF MOTOR BLOCKADE					
GROUP A		**GROUP B**		**p VALUE**	**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
144.28	8.94	121.21	5.19	<0.0001	HS

Graph 8: mean duration of motor blockade



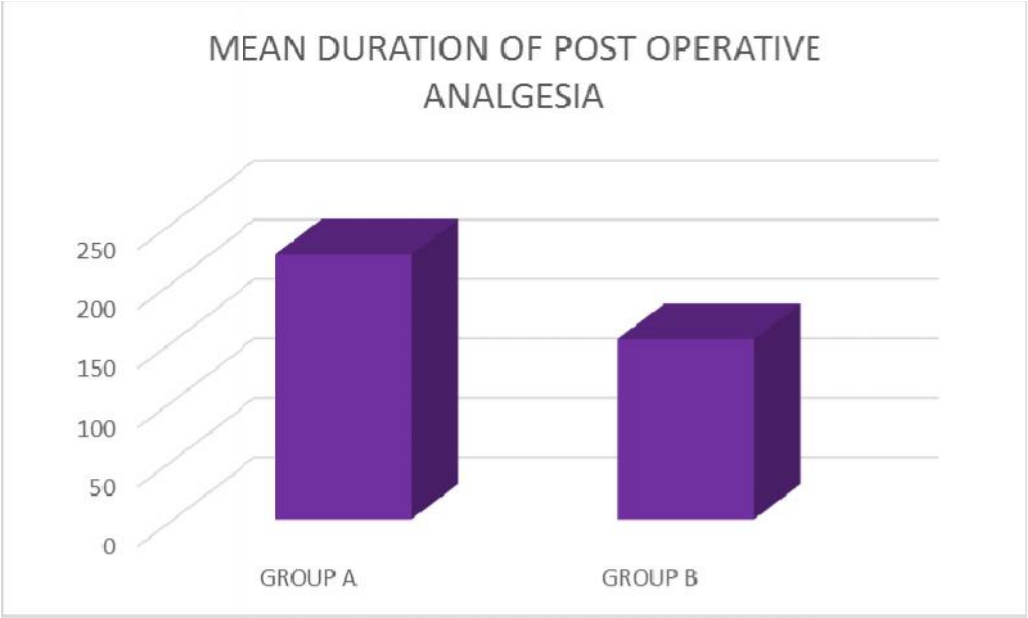
In the present study, mean duration of motor blockade was higher in group A (144.28+/-8.94) than group B, and the difference was statistically significant

(p value <0.0001).

Table 9: mean duration of post operative analgesia

MEAN DURATION OF POST OPERATIVE ANALGESIA					
GROUP A		**GROUP B**		**p VALUE**	**INFERENCE**
MEAN	**S.D.**	**MEAN**	**S.D.**		
222.93	19.75	151.64	10.61	<0.0001	HS

Graph 9: mean duration of post operative analgesia

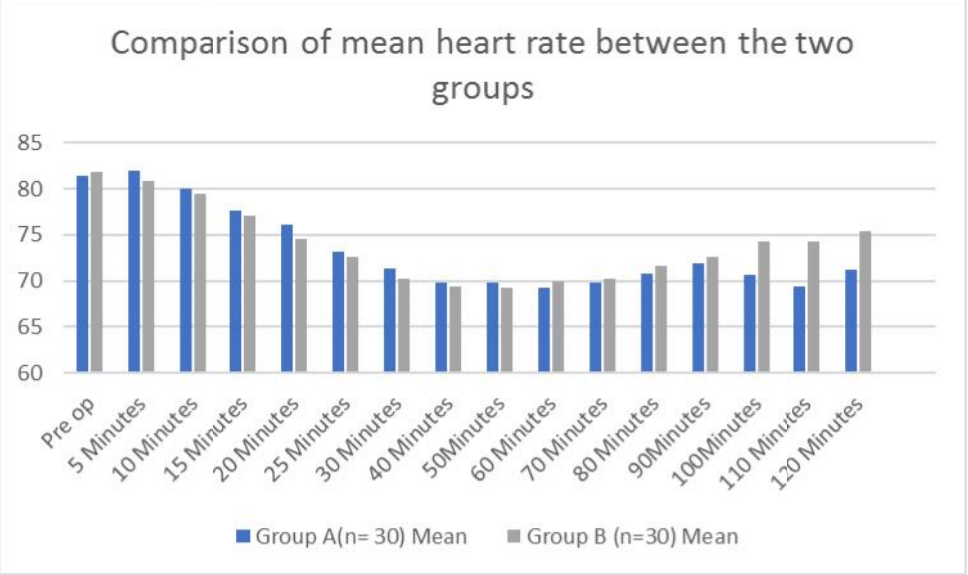


In the present study, mean duration of postoperative analgesia was higher in group A (222.93+/- 19.75) as compared with group B (151.64+/-10.61) and was statistically significant (p value <0.0001)

Table 10: Comparison of mean heart rate between two groups

Intervals	Group A(n= 30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Pre op	81.43	8.18	81.85	8.78	0.82
5 Minutes	81.95	9.00	80.85	9.08	0.59
10 Minutes	80.05	9.53	79.45	8.87	0.77
15 Minutes	77.70	9.38	77.03	9.17	0.75
20 Minutes	76.03	9.00	74.53	8.89	0.46
25 Minutes	73.15	8.76	72.58	8.27	0.76
30 Minutes	71.38	8.95	70.28	7.98	0.56
40 Minutes	69.80	8.47	69.33	7.53	0.79
50Minutes	69.78	8.31	69.25	7.71	0.77
60 Minutes	69.30	7.62	70.02	7.09	0.89
70 Minutes	69.83	7.28	70.27	6.62	0.98
80 Minutes	70.75	8.38	71.67	6.88	0.60
90Minutes	71.90	10.83	72.6	6.91	0.52
100Minutes	70.70	9.56	74.25	6.69	0.25
110 Minutes	69.35	8.76	74.27	7.20	0.89
120 Minutes	71.28	7.45	75.4	6.55	0.98

Graph 10: Comparison of mean heart rate between two groups

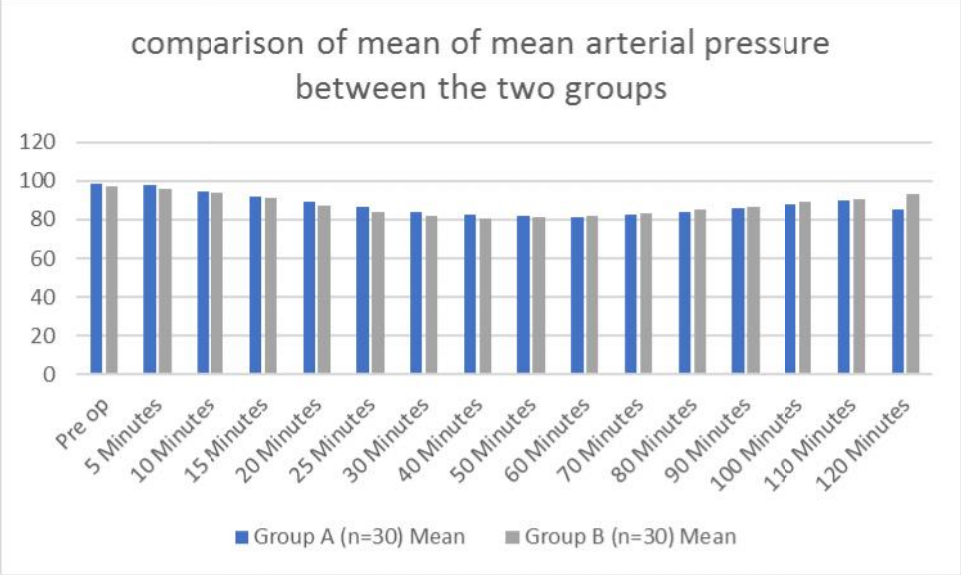


In the present study the mean heart rate at all time intervals were comparable between the groups (p> 0.05 was statistically not significant)

Table 11: Comparison of mean of Mean Arterial Pressure (MAP) between two groups

Intervals	Group A (n=30)		Group B (n=30)		p value
	Mean	SD	Mean	SD	
Pre op	98.4	6.71	97.42	8.42	0.57
5 Minutes	97.71	6.61	96.19	8	0.36
10 Minutes	94.33	6.43	94.06	8.07	0.87
15 Minutes	91.88	6.46	91	7.7	0.58
20 Minutes	88.95	6.58	87.43	7.21	0.33
25 Minutes	86.84	6.03	84.18	6.88	0.06
30 Minutes	83.74	5.41	82	6.35	0.19
40 Minutes	82.4	5.3	80.7	6.36	0.2
50 Minutes	81.9	5.75	80.99	5.86	0.53
60 Minutes	81.17	6.43	81.67	5.83	0.69
70 Minutes	82.41	4.88	83.06	5.56	0.57
80 Minutes	83.93	4.73	85.2	4.98	0.24
90 Minutes	85.76	4.63	86.62	4.61	0.41
100 Minutes	87.91	5.17	89.06	4.34	0.28
110 Minutes	89.84	4.31	90.7	4.82	0.46
120 Minutes	85.22	4.08	93.23	5.84	0.15

Graph 11: Comparison of mean of Mean Arterial Pressure (MAP) between two groups



In the present study, the mean of Mean Arterial Pressure (MAP) in group A and B at different time intervals was almost similar and hence statistically not significant

DISCUSSION

Spinal anaesthesia is one of the most preferred anaesthetic technique, because of its simplicity, rapid onset of action, adequate sensory and motor blockade and fewer complications.

The addition of opioids to local anaesthetics is the most common method to prolong the duration of sub arachnoid block.

Adequate analgesia in postoperative period not only prevents adverse effects associated with pain, but also maintains normal respiratory function preventing infection and atelectasis and provides better wound healing.

Intrathecal opioids causes segmental analgesia by binding to opioid receptors in dorsal horn of the spinal cord. They prolong duration of analgesia without affecting motor or autonomic nervous system function. Their combination with intrathecal local anaesthetics limits regression of sensory blockade which is seen with local anaesthetics alone. Therefore, opioids reduce the dose requirement for local anaesthetics and also provide significantly extended postoperative analgesia without prolonging the recovery.

Nalbuphine is an opioid structurally related to oxy- morphine. It is a highly lipid soluble opioid with agonist action at kappa opioid receptors and antagonist action on mu opioid receptors. They have short duration of action consistent with their lipid solubility and rapid clearance compared with other opioids like morphine.

The present study was conducted in the Department of Anaesthesiology at KLEs Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period of January 2016 to December 2016. In the study 60 patients of ASA grade I

and II undergoing lower abdominal surgeries were randomly divided into two groups. In group A patients received 3 ml of 0.5% Inj. Hyperbaric Bupivacaine with 400mcg of inj. Nalbuphine. and in group B patients received 3ml of 0.5% inj. Hyperbaric bupivacaine with 0.5ml normal saline intrathecally. The demographic data in both the study group and control group was comparable with respect to height, weight, age, sex, mean duration of the surgery and type of surgery.

In our study onset of sensory blockade was taken as the time taken from injection of the drug to sensory block up to T10 level.

In our study, the mean onset of sensory block was 3.76+/- 0.86 min in nalbuphine group and 3.53+/-0.75 min in control group. The difference was statistically insignificant. The findings of our study are in accordance with the results in a study by Jyothi B et al., with the mean onset of sensory block of 3.5+/-0.7min in nalbuphine group and 3.6+/-0.8min in control group.

In a similar study, Mukharjee et al., compared three different doses of nalbuphine namely 0.2mg (B), 0.4mg (C), 0.8mg (D) with 0.5ml of normal saline and observed that the mean onset of sensory blockade was comparable in all the 4 groups with 1.75+/-0.27min in control group and1.69+/-0.2min, 1.63+/-0.24min,1.59+/-0.18min in B, C, D groups respectively.

In our study, the mean onset of motor blockade was defined as time taken from injection of the drug to the time taken to reach modified bromage scale of 3.

In our study, we observed that the mean onset of motor blockade was comparable in both nalbuphine group (6.33+/-12min) and control group (6.42+/-0.86min). The difference was statistically not significant. The findings of our study are in accordance with the results in the study by Rahmi Dubey et al., who observed similar mean onset

of motor block in both nalbuphine group and control group was similar (1.54+/-0.5 min).

In a similar study by Mukharjee et al., the mean onset of motor block was comparable in all the 4 groups namely A(5.9+/-0.5min), B(5.8+/- 0.75min), C(5.7+/- 0.62min), D(5.6+/- 0.53min) administered normal saline, 0.2mg, 0.4mg, 0.8mg of nalbuphine respectively.

The mean duration of sensory blockade in our study in nalbuphine group was 118.93+/- 8.37 min and 96.93+/- 7.10min in control group, the difference was statistically significant. The findings of our study are in accordance with results of the study by Jyothi B et al.,who observed that the mean duration of sensory blockade was comparatively more in nalbuphine group (122.2+/- 5.5 min) than in control group (86.0+/- 4.4min).

In a similar study, by Padma T et al., comparing effect of bupivacaine with nalbuphine and bupivacaine alone for lower limb surgeries under spinal anaesthesia observed that duration of sensory blockade was prolonged in nalbuphine (115.32±9.12min) group compared with control group (103.32±16.65 min).

In our study, we observed that the mean duration of motor blockade in nalbuphine group was 144.28+/- 8.94 min and in control group was 121.21+/- 5.19 min the difference was statistically significant. Finding of our study are in accordance with results of the study by Devendra v. et al., who observed that duration of motor block was significantly prolonged in nalbuphine group (150±10.4min) compared with control group (129+/- 7.4 min).

In our study, duration of postoperative analgesia was defined as the time at which patients VAS score reached more than 3 from the time of injection of the drug in subarachnoid space.

In our study duration of postoperative of analgesia was significantly prolonged in nalbuphine group (222.93+/- 19.75 min) than in control group (151.64+/- 18.42 min). In a similar study, Rashmi Dubey et al., observed the mean duration of analgesia was 366+/- 15.5 min in nalbuphine group and 159.5+/-18.42 min in control group.

In a similar study, mostafa H et al., observed that duration of analgesia was more in nalbuphine group (166.33+/- 14min) compared with fentanyl group (150.83+/- 13 min).

Nalbuphine by its action on kappa opioid receptors inhibit release of neurotransmitter substance P that mediates pain. In addition it acts as post synaptic inhibitor on the interneuron and output neuron of the spinothalamic tract which transports nociceptive information.

Local anaesthetics acts by inhibiting voltage gated sodium channels thus interrupting sodium influx, which lead to inhibition of action potential and therefore inhibition of signal conduction. The principle site of action of local anaesthetics placed in lumbar subarachnoid space is preganglionic fibers as they leave spinal cord in the anterior rami.

Thus, when nalbuphine administered along with bupivacaine will have synergetic effect, thus prolonging the duration of sensory blockade without affecting sympathetic blockade and motor blockade.

In our study, patients in both the groups had similar haemodynamic results withot any adverse effects similar to results observed in studies by culebras et al and mostafa H et al.

According to study by Thomas et al., to compare respiratory depression and analgesic effect between equipotent doses of morphine and nalbuphine, observed that nalbuphine exhibit ceiling effect of analgesia and any further increase in the dose had similar intensity of analgesia.

Thus, our study addition of 0.4mg of nalbuphine to hyperbaric bupivacaine used intrathecally significantly prolonged duration of blockade as compared with hyperbaric bupivacaine alone.

Limitations and further scope of the study

1. The dose used in our study was chosen according to the physical characteristics of patients in our institute. However, comparative study with different doses could be studied.
2. To identify the ideal adjuvant, comparative study with different type of drugs can be carried out

CONCLUSION

In conclusion, addition of inj. Nalbuphine (400mcg) to 3 ml of 0.5% hyperbaric bupivacaine has similar onset of sensory and motor blockade, significantly prolongs duration of sensory and motor blockade and duration of postoperative analgesia compared to plain 3ml of 0.5% hyperbaric bupivacaine without any significant adverse effects.

SUMMARY

The present study titled “Comparison Of Bupivacaine and Bupivacaine With Nalbuphine For Subarachnoid Block In Patients Undergoing Lower Abdominal Surgeries was a randomized controlled trial conducted in the Department of Anaesthesiology, KLE’S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period January 2016 to December 2016.

After obtaining institutional ethical clearance and written informed consent from the patients and having met inclusion and exclusion criteria, 60 ASA grade I and II patients undergoing lower abdominal surgeries were randomly allocated into two groups. Group A received 3ml of 0.5% hyperbaric bupivacaine with 400 mcg inj. Nalbuphine. Group B received 3ml of 0.5% hyperbaric bupivacaine with 0.5 ml of normal saline

In our study, demographic data was comparable in both the groups. In our study, the mean onset of sensory block in nalbuphine group was 3.76+/- 0.86 min and in control group was 3.53+/-0.75 min. The mean onset of motor blockade in nalbuphine group was 6.33+/-12 min and 6.42+/-0.86 min in control group. The results were comparable and statistically not significant.

The mean duration of sensory blockade in nalbuphine group was 118.93+/- 8.37 min and 96.93+/- 7.10min in control group, the difference was statistically significant. In our study, we observed that the mean duration of motor blockade in nalbuphine group was 144.28+/- 8.94 min and in control group was 121.21+/- 5.19 min, the difference was statistically significant.

The duration of postoperative analgesia was significantly prolonged in nalbuphine group (222.93+/- 19.75 min) than in control group (151.64+/- 18.42 min) which was statistically significant. Hemodynamic parameters were comparable between the two groups with no major side effects / complications observed.

Based on the results of the study it can be concluded that nalbuphine added intrathecally along with 0.5% hyperbaric bupivacaine significantly prolongs sensory and motor blockade and duration of postoperative analgesia without any significant heamodynamic changes and adverse effects.

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ANNEXURES- I - ETHICAL CLEARANCE CERTIFICATE

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

Website: http//www.jnmc.edu
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Phone: (+ 91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 371 **Date: 17/11/2015**

To,

Dr.
PG student in Anaesthesiology,
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 BUPIVACAINE AND BUPIVACAINE WITH NALBUPHINE FOR SUBARACHNOID BLOCK IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES, A RANDOMIZED CONTROLLED TRIAL OVER ONE YEAR",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

Athi Darshan

(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.

ANNEXURES- II - CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____ we are requesting you to enrol yourself in study titled "COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH NALBUPHINE FOR SUBARACHNOID BLOCK IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES, A ONE YEAR RANDOMISED CONTROL TRIAL" ducted by Dr. _____, Post Graduate in M.D. Anaesthesiology under the guidance of Dr. _____Department of Anaesthesiology, J.N. Medical College, Belgaum under KLE university, Belgaum.

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 to participate you are free to withdraw at any time.

The purpose of research is to know the effect of NALBUPHINE in patients undergoing spinal anaesthesia

Purpose of the study:

Nalbuphine have a moderate duration of action consistent with their lipid solubility and rapid clearance compared with other opioids like morphine

There are very few studies in literature for nalbuphine use during subarachnoid block. Therefore, attempt is being made to study effect of nalbuphine adding to hyperbaric bupivacaine in patients undergoing lower abdominal surgeries under subarachnoid block.

Procedure Involved:

If you agree to enrol yourself in my study, I will ask your present past and family history. Then you will be clinically examined in detail and routine investigations like Hb, TC, DC, Platelet Count, RBS, Blood Urea, Serum Creatinine, Blood Grouping, Chest X-ray, ECG, will be done accordingly. You will be allotted into one of the two groups randomly using computer-generated software. One group will receive Inj.nalbuphine and bupivacaine and the other group will receive a normal saline and buvivacaine which have no effect on analgesia. This will be a double blinded procedure, where neither you nor I will know as to which group you have been allotted to.

Risks:

There is almost no risk involved with use of intrathecal nalbuphine. It may cause nausea, vomiting. Rarely may it cause allergic skin reactions,

Benefits:

It is an effective and safe for analgesia which can be used during spinal anaesthesia

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, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Dr. _____ at Department of Anaesthesiology, KLES Hospital& MRC.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr. _____, Department of Anaesthesiology, KLES Hospital and MRC, Belgaum, or Dr. _____, Dept Of Anaesthesiology, KLES Hospital and MRC, Belgaum.

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-9448863866, or extension 4052 at J.N. Medical College, Belgaum.

Consent for participation in research 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 of Subject : _____

Date:

Witness Name : _____ Signature:_____

Date:

Investigators Name: _____ Signature:_____

Date:

Place : _____

ANNEXURES- III - PROFORMA

"COMPARISON OF BUPIVACAINE AND BUPIVACAINE WITH NALBUPHINE FOR SUBARACHNOID BLOCK IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES,A ONE YEAR RANDOMISED CONTROL TRIAL

Name & Address of the patient:

_____

_____

Age of the Patient:_____ IP. No. _____

Weight of Patient: _____ Sex.

Anaesthesiologist: _____ Surgeon: _____

PREANAESTHETIC EVALUATION:

Chief Complaints:

Past History:

- History of Diabetes Mellitus/Hypertension/Asthma/Tuberculosis
- Drug Therapy:
- Previous Anaesthetic procedure/Previous surgeries:
- History of renal disease, hepatic disease and neurological diseases.

Family History

General Physical Examination:

Weight: Temperature: Pallor: Height

Cyanosis: Pedal Oedema: Clubbing:

Pulse: B.P: RR:

Airway Assessment:

Mouth Opening: Teeth:

Jaw Movements: MP Grading:

SYSTEMIC EXAMINATION:

Cardiovascular System:

Respiratory System:

Per Abdomen:

Central Nervous system:

Spine assessment:

INVESTIGATIONS:

Hb%: Urine Routine:

Any Other:

ASA STATUS: Grade 1 / 2

Diagnosis:

Proposed Surgery:

Inclusion Criteria:

- 1. ASA physical status I and II.
- 2. Age between 18 to 40 years.
- 3. Infraumbilical surgeries done under Spinal anaesthesia

Exclusion Criteria:

- Patients not willing to give consent
- Allergic to the study drugs-bupivacaine and nalbuphine
- A Pre-Operative baseline temperature of more than 37.5 degree Celsius
- Patients on long standing opioids
- Patients suffering from thyroid disorders
- Patients who are known case of liver disease
- Patients with coagulation abnormalities.
- Patients with spine defects or infection at the site.

Methodology:

After obtaining the approval of the Ethical committee and written informed consent, a total of 60 patients undergoing lower abdominal surgeries under spinal anaesthesia was be included in the study.

Patients were kept nil per orum for 6-8 hours. Randomization was done into two groups by computer generated method.

Group (A group): Inj. bupivacaine hyperbaric 0.5% 3 ml + inj. Nalbupine 0.5 ml diluted with Normal saline to 3.5ml intrathecally

Group (B group): Inj. bupivacaine hyperbaric 0.5% 3 ml + Normal saline 0.5ml intrathecally. An IV line was secured with 18G IV cannula. All patients were

preloaded with 10 ml/kg of Ringer's lactate solution. Monitors were attached before performing the procedure (pulse oxymeter, NIBP and ECG). The study medication was prepared by the person who was not involved in the study to ensure blinding of the anaesthesiologist. Under all aseptic conditions, SAB was given using 23G Quinke's spinal needle in sitting position. Respective agents were injected according to the group. The assessments of the hemodynamic parameters were noted. Onset of sensory block was judged by pin prick method and motor blockade was judged with Bromage scale.

Following observations were made:

T0 – Time of spinal anaesthesia.

T1 – Time of onset of sensory block.

T2 – Time of onset of motor block.

T3 – Max Height Of sensory block.

T4 – duration of sensory block.

T5 – duration of motor block.

T6 – Time to first dose of post-operative rescue analgesia.

Vital parameters were monitored every 5 min for 30 mins then every 10 mins till end of surgery. Perioperatively, patients were observed carefully for the side effects like respiratory depression, nausea, vomiting, itching etc.

VAS score was calculated on a 10cm long scale with '0' on one end, meaning 'no pain at all', while '10' on the other end representing 'worst pain imaginable'. Patient

rated the degree of pain by making a mark on the scale. Thus, the pain score was obtained by measuring the distance from the '0' end to the indicated mark.

Postoperative analgesic drugs were given when patient's VAS score reached >3 (this time was taken as the time of wear off of analgesia). Inj. diclofenac 75 mg was given intramuscularly as rescue analgesia.

Observations:

Readings were recorded in the following manner:

DRUG Administered: _____.

Group: _____

Variable

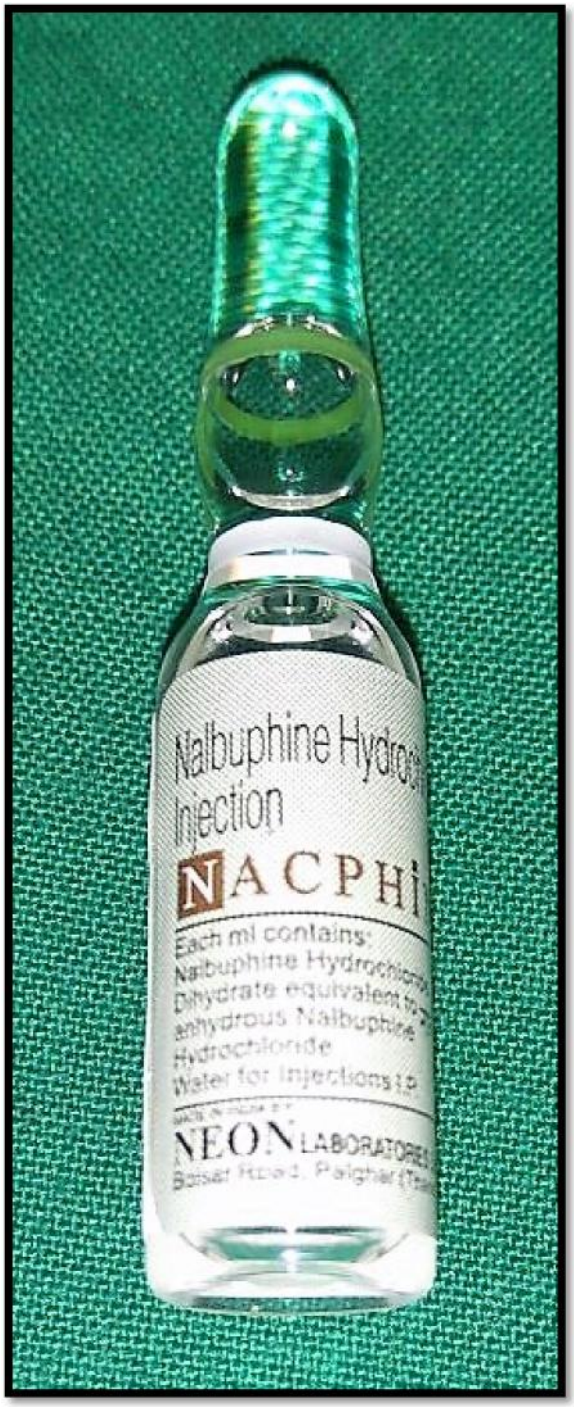
PARAMETER	**TIME**
Time of spinal anaesthesia	
Time of onset of sensory block.	
Time of onset of motor block.	
Duration of sensory block.	
Duration of motor block	
Duration of postoperative analgesia	

Side Effects –

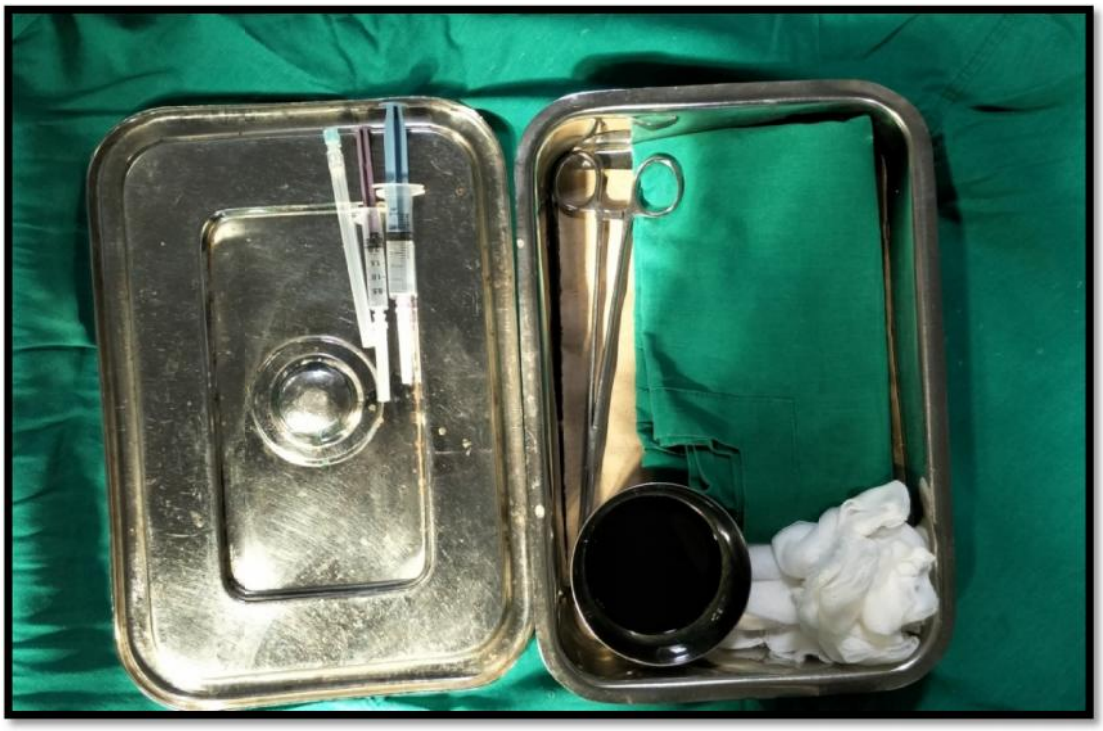
Signature of staff in charge:

ANNEXURES- IV – PHOTOGRAPHS

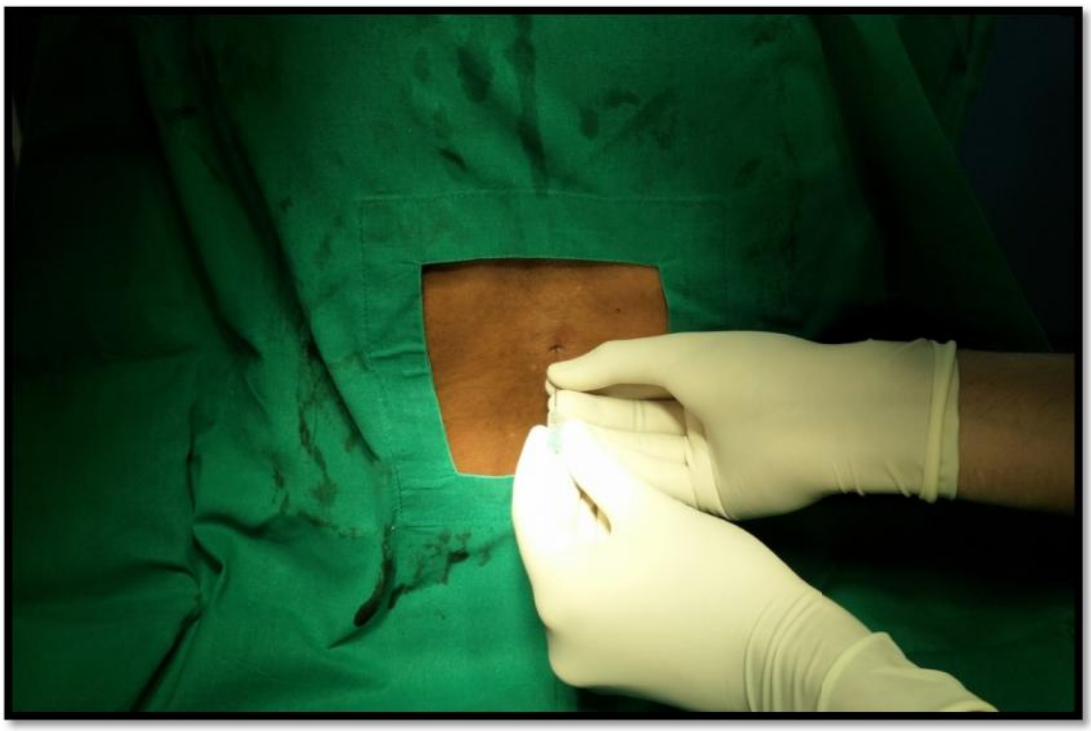
Bupivacaine ampule



Nalbuphine ampule



Spinal tray



Procedure of spinal anaesthesia

GROUP A										
age	**sex**	**IP NO**	**weight**	**height**	**Surgery**	**Max duration of analgesia**	**sensory block**		**motor blcok**	
							onset	**duration**	**onset**	**duration**
38	F	764011	50	155	TAH WITH BSO	200	2.8	121	4.2	141
39	M	760112	70	159	Hernioplasty	210	2.5	115	4.4	144
40	M	737924	56	156	Cystolithotripsy	225	3.6	112	4.6	133
40	F	759220	50	154	TAH WITH BSO	200	3.4	125	5.1	156
28	M	717539	67	158	Appendectomy	250	4.5	121	4.3	138
40	F	755567	59	153	TAH WITH BSO	210	2.9	114	5.5	144
38	M	743717	70	155	Hernioplasty	240	3.6	103	4.6	131
38	M	757767	72	158	Hernioplasty	200	4.5	112	5.5	126
40	M	758148	66	160	Hernioplasty	210	3.5	124	5.0	143
40	F	763715	60	155	Hernioplasty	200	3.3	130	5.4	152
24	F	757291	55	154	Appendectomy	210	2.8	128	6.5	156
40	M	766041	68	158	Hernioplasty	235	3	115	7.1	135
39	F	763798	65	150	TAH WITH BSO	225	4.3	126	6.2	143
40	M	758373	65	155	Hernioplasty	210	5.2	132	7.3	156
40	M	738110	68	156	Hernioplasty	200	3.4	127	8.0	148
40	M	738543	70	158	Appendectomy	200	3.6	116	8.1	144
20	F	738495	55	150	Cystolithotripsy	210	5.5	113	6.1	134
39	F	748338	50	152	TAH WITH BSO	210	4.5	113	6.6	137
40	F	745212	45	150	TAH WITH BSO	245	3.2	125	5.8	148
40	M	753878	67	155	Hernioplasty	200	4.1	124	6.8	154
39	F	755376	59	152	TAH WITH BSO	255	5.1	110	8.2	156
37	M	756376	74	160	Hernioplasty	240	5.5	114	6.7	144
37	F	754220	66	149	LAPROTOMY	230	3.6	100	7.3	133
29	M	754124	65	155	Hernioplasty	250	4.1	116	7.5	151
26	F	754708	57	156	LAPROTOMY	260	2.8	121	8.0	148
38	F	735467	62	150	TAH WITH BSO	245	2.6	110	6.7	133
29	F	732618	55	152	LAPROTOMY	235	3.8	127	6.5	154
38	M	753384	56	155	Hernioplasty	240	4.2	121	7.5	145
38	M	705425	68	160	Hernioplasty	220	3.1	134	8.0	157
39	M	4	60	156	Hernioplasty	255	3.1	115	6.5	146
36.34	14		61.72	154.83		222.93	3.76	118.93	6.33	144.28
5.66	16		7.65	3.26		19.75	0.86	8.37	1.27	8.94

GROUP B										
							Sensory block		Motor block	
age	sex	IP NO	weight	height	surgery	Max duration of analgesia	onset	duration	onset	duration
26	F	766216	50	154	Appendicities	125	2.5	100	6.1	115
40	F	767126	52	152	vaginal hysterectomy	156	2.2	90	5.3	121
40	M	762621	76	158	incisional hernia	148	2.8	95	5.6	115
40	F	737052	52	150	TAH with BSO	165	3.1	99	5.4	125
42	M	735532	60	160	hernioplasty	143	3.8	85	5.9	130
45	M	757413	58	155	hernioplasty	149	4.1	99	8	122
39	F	759527	60	154	TAH with BSO	161	4.4	100	5.9	124
41	M	733506	66	156	cystolithotripsy	155	3.2	90	6.1	118
48	M	738477	49	152	TAH with BSO	147	4.5	100	5.6	124
32	F	732974	55	150	TAH with BSO	148	4.3	110	6.7	115
30	F	735525	50	155	tubectomy	157	3.8	98	5.8	120
29	F	745378	58	151	tubectomy	144	4.4	85	5.1	115
38	M	737474	58	156	left urs	168	3.5	90	5.8	120
42	M	737477	66	158	hernioplasty	155	4.1	85	5.3	112
30	F	776911	50	150	tubectomy	149	3.2	100	5.9	128
39	M	762916	66	157	hernioplasty	141	5	90	6.9	116
38	M	762514	61	155	hernioplasty	155	2.4	95	5.2	125
34	M	765345	65	158	Appendicities	140	2.8	98	5.9	120
40	M	762196	68	160	hernioplasty	143	3.1	98	5.6	115
30	F	766112	53	150	tubectomy	133	4.1	100	6.2	125
39	F	766216	52	155	hernioplasty	156	2.5	102	6.6	125
40	M	762916	66	152	hernioplasty	170	3.5	105	5.9	130
36	F	768219	50	152	TAH with BSO	142	3.8	90	5.4	122
42	M	762169	62	154	hernioplasty	159	3.9	98	5.1	115
38	F	762621	58	155	TAH with BSO	162	2.5	95	5.5	120
40	M	762162	59	156	colostomy closure	150	3.6	102	5.3	125
39	M	755750	60	155	hernioplasty	163	3.5	100	5.6	122
17	F	755708	55	153	MYOMECTOMY	162	4.1	115	5.7	130
25	F	755628	54	150	Appendicities	155	3.8	102	5.1	125
23	F	755612	55	155	Appendicities	159	4.2	116	5.6	132
36.93	15		59.68	154.39		151.64	3.53	96.93	6.42	121.21
6.43	15		7.28	2.94		10.61	0.74	7.10	0.86	5.19
P value by students unpaired t test										
0.7171			0.0558	0.5995		0.0000	0.2768	0.0000	0.0525	0.0000
NS			NS	NS		HS	NS	HS	NS	HS