International Journal of Multidisciplinary Research and Growth Evaluation.

Comparison of intrathecal nalbuphine and fentanyl as an adjuvant to hyperbaric bupivacine for spinal anaesthesia in infraumbilical surgeries: A prospective randomized, double blind study

Dr. Anzil AR
Senior Consultant, Department of Anaesthesiology, Sahyadri Narayana Multispecialty Hospital, Shimoga, Karnataka, India

* Corresponding Author: **Dr. Anzil AR**

Article Info

ISSN (online): 2582-7138
Volume: 04
Issue: 01
January-February 2023
Received: 23-11-2022;
Accepted: 14-12-2022
Page No: 17-38

Abstract

Background and Aims: Central neuraxial blockade is the one of the most commonly performed technique in modern anaesthesia. The basics for the combination of local anesthestics and opioids is that these two groups of drugs provide analgesia by their action at two different sites. Nalbuphine {mixed μ antagonist and κ agonist} and Fentanyl {μ agonist} are two opioids. The aim of this study is to compare their onset of action and duration of sensory and motor blockade,post operative analgesia and to see whether any side effects.

Materials and methods: Fiftyfour patients belonging to ASA I and ASA II scheduled for infraumbilical surgery were divided into two groups of twentyseven each. Group A received 0.5% hyperbaric Bupivacaine 3 ml (15 mg) plus Nalbuphine 1 mg in 0.5 ml normal saline. Group B received 0.5% hyperbaric 3 ml (15 mg) plus fentanyl 25 mcg. Onset of actions of sensory and motor blockade, post-operative analgesia, hemodynamics and side effects were assessed.

Results: Onset, duration of sensory and motor blockade and duration of effective analgesia were comparable between both groups. mean onset time of sensory blockade of group A was 250.22±17.542 seconds and group B was 189.48±16.960 seconds .mean onset time of motor blockade in group A was 357.48±10.420 and group B was 343.56±8.317 . Mean duration of sensory blockade(149.63±3.702 mins) and motor blockade (199.52±7.778 mins) of group A was highest compared to Group B in sensory blockade(133.48±5.072 mins) and motor blockade (184.81±7.000 mins) which was statistically significant($P < 0.001$).

Conclusion: Nalbuphine had slower onset of sensory and motor blockade, while duration of motor blockade was prolonged in Nalbuphine group compared to fentanyl group

Keywords: Spinal anesthesia, Nalbuphine, Fentanyl, Sensory blockade, motor blockade, post operative analgesia, hemodynamics, infraumbilical surgeries

Introduction

Central neuraxial blockade is one of the most commonly performed technique in modern anaesthesia. In 1898, August Bier first described "cocainisation of the spinal cord". Over the years, the technique has been refined and has evolved into the modern concept of intrathecal, spinal or subarachnoid block. Spinal effects are produced by slow injection of a small volume of local anaesthetic solution containing dextrose (to make it hyperbaric).

Among the regional techniques available, spinal anaesthesia is an attractive option when the surgical site is below umbilicus1. It produces dense sensory, motor and sympathetic blockade. It has the advantages of low cost, better postoperative pain relief, decreased PONV, low incidence of thromboembolism when compared to general anaesthesia. In spite of the above benefits, the major limitation of subarachnoid block is short lived duration of anaesthesia. Normally, spinal anaesthesia with bupivacaine heavy (H) lasts for 2 to 2.5 hours2.

Adjuvants are added to improve the quality, to accelerate the onset of action and also to overcome the problems which occur during spinal analgesia. Adrenaline was the first spinal adjuvant used. Adrenaline reduces its toxicity but does not greatly prolong its effect. Adjuvants are administered by various routes like epidural, intrathecal and intravenous. Various adjuvants like morphine, fentanyl, nalbuphine, sufentanil, clonidine, midazolam, ketamine, neostigmine, sodabicarbonate are added to local anesthetics.

In 1979, Wang and his colleagues3 first used intrathecal opioids for acute pain treatment. The technique of intrathecal opioid administration along with local anaesthetics is to improve the quality of analgesia and decrease the requirement of postoperative analgesics4.

The basis for the combination of local anesthetics and opioids is that these two groups of drugs provide analgesia by their action at two different sites. Local anesthetics have their action at the spinal nerve axon and opioids act at the receptor site in the spinal cord5. Various opioids have been used intrathecally like morphine, fentanyl, buprenorphine and nalbuphine to fasten the onset and prolong the duration of sensory and motor blockade.

Nalbuphine is an opioid, synthetically prepared with mixed μ antagonist and κ agonist properties6. Nalbuphine when administered intrathecally binds to kappa receptors in the spinal cord and brain producing analgesia and sedation without μ adverse effects. It has minimal respiratory depressant effect and low abuse potential compared to other centrally acting opioid analgesics. Side effects like shivering, nausea, vomiting and urinary retention are infrequent with nalbuphine hydrochloride. Increased drug dosage is not required, Since nalbuphine reaches ceiling effect at lower intrathecal dosage. This also explains the safety margin of the drug.

Fentanyl, a potent synthetic μ agonist has been used extensively in intrathecal route .It is a potent synthetic μ receptor agonist. Fentanyl has structural similarities to local anesthetics. It has local anesthetic action on the primary afferent sensory C nerve fibers causing analgesia.

In my study I used nalbuphine hydrochloride and fentanyl as an adjuvants to hyperbaric bupivacaine in order to compare the onset and duration of sensory and motor blockade, postoperative analgesia and to see whether any side effects.

Anatomy of subarachnoid space

The vertebral canal extends from the foramen magnum to the sacral hiatus. The average length of the spinal cord in males is 45 cm & females it is 42cm. The average weight is approximately 30 gm.

The vertebral column consists of 33 Vertebrae:

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

With the exception of C1 the cervical, thoracic and lumbar vertebrae consist of a body anteriorly, two pedicles that project posteriorly from the body and two laminae that connect the pedicles. These structures from the vertebral canal which contains a spinal cord, spinal nerves and epidural space. The laminae give rise to the transverse processes that project laterally and the spinous process that projects posteriorly. These bony projections serve as sites for muscle and ligament attachments. The pedicles contain a superior and inferior vertebral notch through which the spinal nerves exit the vertebral canal.

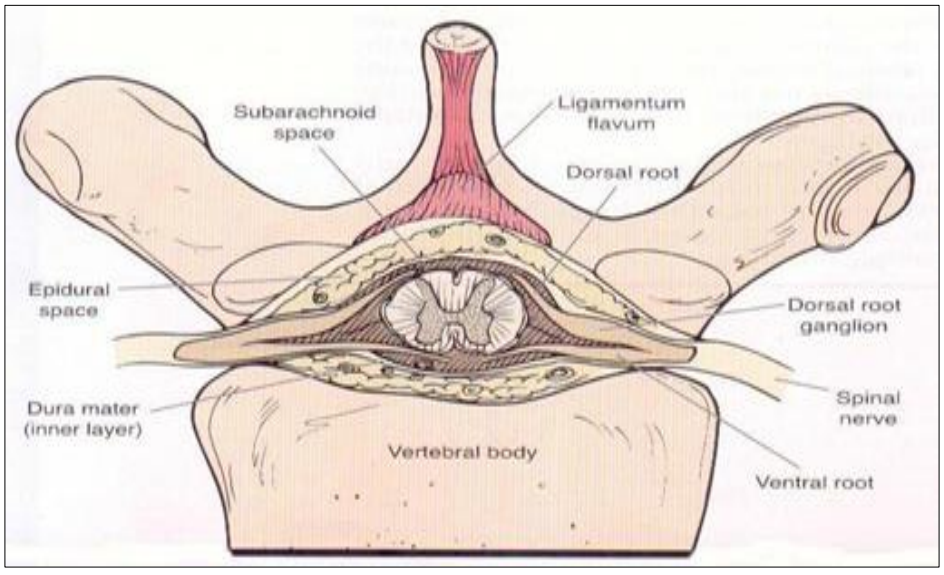


Fig 1: Cross section of Vertebra

Ligaments

The accurate knowledge of the ligaments in the vertebral column through which spinal needle passes is essential for anaesthesiologists in practicing spinal anaesthesia. The different sensations of resistance that these ligaments impart to the advancing needle can be appreciated with practice by the operator.

- **Supraspinous ligament**

The fibers of this ligament run longitudinally over the tips of the spinous processes from C7 to sacrum and continue above as the ligamentum nuchae.

- **Interspinous ligament**

This is a thin ligament joining the spinous processes together, uniting the lower border of one with the upper border of its caudal neighbour.

- **Ligamentum flavum**

This ligament is made of yellow elastic fibers. It runs from the anterior and inferior aspect of one lamina to the posterior and superior aspect of the lamina below. Laterally, it blends with the capsule of the joint between the articular processes and medially to meet its opposite number in the median plane, to become continuous with the deep fibers of the interspinous ligament[7]**.** They are thickest and strongest in the lumbar region where powerful stresses and strains have to be countered.

- **Posterior longitudinal ligament**

Runs along the posterior surface of bodies of the vertebrae.

- **Anterior longitudinal ligament**

Runs along the front of the vertebral bodies.

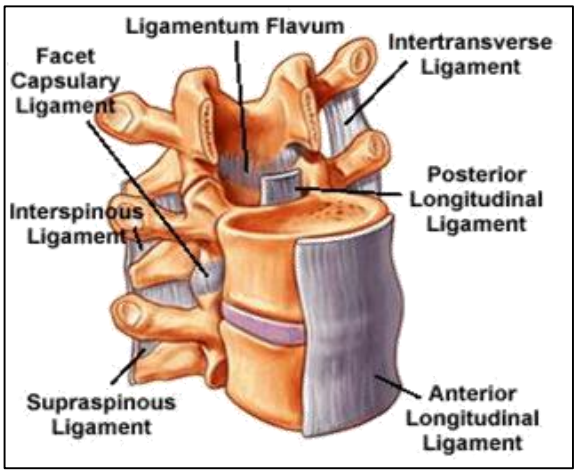


Fig 2: Vertebral Ligaments

Spinal Meninges

These spinal meninges consist of three protective membranes (duramater, arachnoid mater and piamater) which are continuous with the cranial meninges.

Dura Mater

The duramater is the outermost and the thickest meningeal tissue. The spinal duramater begins at the foramen magnum where it fuses with periosteum of the skull, forming the cephalad border of the epidural space. Caudally, the duramater ends at approximately S2 where it fuses with the filum terminale. It is composed of collagen fibers and elastin fibers arranged longitudinally. There is a potential space between these two membranes called the subdural space. The incidence of subdural injection during intended subarachnoid injection may be as high as ten percentage as per radiological literature7.

Arachnoid Mater

The arachnoid is the middle of the three coverings of the brain and spinal cord. It is a delicate avascular membrane separated from the pia mater by subarachnoid space, which is filled with CSF, and is closely applied to the dura mater and ends at the lower border of the second sacral vertebra.

PIA Mater

The pia mater is a delicate, highly vascular membrane closely investing and clinging to the surface of the cord and brain. It becomes continuous with the perineurium of the nerve, and consists of two layers. Caudally, the pia mater continues beyond the conus medullaris as the filum terinale.

Spinal Cord

It is an elongated portion of the central nervous system, which occupies upper two thirds of the vertebral canal, 42 – 45 cms in length and weighs around 30 gms. It extends from the upper border of the atlas vertebra to that of the lower border of first lumbar vertebra or upper border of the second lumbar vertebra. Above it continues with medulla oblongata, and below it tapers off into a conical conus medullaris. A delicate fibrous filament descends to the back of 1st segment of coccyx from apex of conus medullaris, known as the filum terminale. The cord has two enlargements cervical and lumbar corresponding to the nerve supply of the upper and lower limbs. The cervical enlargement extends from C3 to L2 and lumbar enlargement from T9 to T12.

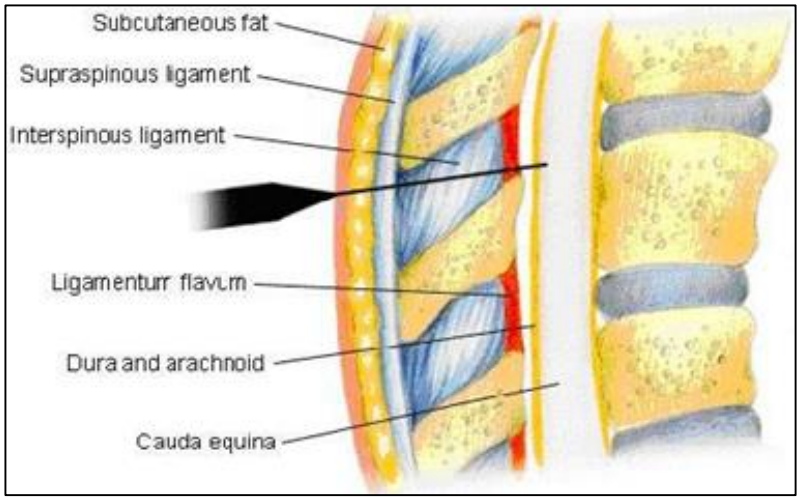


Fig 3: Structures encountered during Spinal Anaesthesia

Physiolgy of Sub Arachnoid Block

The cerebrospinal fluid is an ultrafiltrate of the blood plasma, it is a colourless, clear fluid, present in spinal and cranial sub arachnoid space and in the ventricles of the brain. Average volume of CSF in adults is 120-150ml, among this 35 ml seen in the ventricles and 25 ml in the cerebral sub arachnoid space and 75 ml in the spinal sub arachnoid space. CSF is secreted by choroid plexus at a rate of about 0.3-0.4 ml/minute.

Physical Characteristics of CSF

The PH is 7.4. The specific gravity is 1.007 and density is 1.0003, baricity is 1.000and the CSF pressure varies between 8-12mmHg, cell count is 3-5 cu mm and the protein content is 20 mg/dl and glucose content varies between 40-80mg/dl. Spread of the drug in subarachnoid space is determined by the specific gravity of the injected drug when compared with that of CSF.

Mechanism of Spinal Anesthesia

Local anesthetics for spinal anesthesia is usually injected into the sub arachnoid space between the spinous process of the third and fourth lumbar vertebra, the needle will enter the dura in the area of the caudaequina. Local anaesthetics penetrate the smaller roots more rapidly because of the larger surface area[8]. Local anaesthetics cause sodium channel blockade within the dorsal and ventral horns, thus inhibits the generation and propagation of electrical activity.

The block and recovery of sensory fibres occurs in this order. The most sensitive sensory fibres (sensation to cold)-are blocked first and remain blocked longest; delta fibres (pin-prick) are the second to be blocked and recover; A fibres (touch) are last to block and first to recover.The preganglionic sympathetic(B-fibres) are most sensitive to local anaesthetics. The motor fibres (Aα, the largest fibers) are less sensitive to local anaesthetics comparing to sensory fibers and there is a difference between sensory and motors block, motors function is better preserved sine more local anaesthetic is neeed to anesthetize the thick motor fibers.

Uptake and Elimnation of local Anesthetics from cerebrospinal fluid

Factors affecting uptake of local anaesthetic (LA) into neural tissue

- Concentration of LA in cerebrospinal fluid (CSF)
- Surface area of tissue exposed to CSF
- Lipid content of nerve
- Blood flow of nerve

Elimination of LA from CSF

- Through the arachnoid and dura to epidural space
- Vascular absorption via sub arachnoid and epidural blood vessels

The various factors that affect the spread of local anaesthetics include[9,10]

- **Patient factors**

1. Age
2. Height
3. Position
4. Spinal column configuration
5. CSF volume

- **Technical factors**

1. Site of injection
2. Spread of injection
3. Direction of needle
4. Local anesthetic dose
5. Local anesthetic baricity
6. Local anesthetic volume

Factors not affecting the spread of local anesthetic in the sub arachnoid space

1. Weight of patient
2. Local anesthetic concentration
3. CSF composition
4. CSF circulation
5. Vasoconstrictors

The sequence of nerve modality block:

1. Preganglionic sympathetic B fibers
2. Temperature (Cold > Warm)
3. Pinprick
4. Pain
5. Touch
6. Pressure
7. Proprioception
8. Somatic motor fibers

Indication

Infra umbilical surgeries, lower limb surgeries and urological surgeries, obstetric and gynaecological surgeries and surgeries around the perineum. Spinal anesthesia can be combined with epidural anesthesia in obstetrics, vascular and orthopedic surgeries.

Contraindications

Absolute Contraindications

- Patients refusal despite adequate information.
- Infection at the site of injection.
- Dermatologic conditions.
- Septicemia or Bacteremia.
- Shock or severe hypovolemia.
- Abnormality in blood clotting mechanism.
- Increased intracranial pressure.
- Lack of skill in spinal anesthesia.
- Allergy to local anesthesia.

Relative contraindications

- Deformities of the spinal column.
- Pre-existing disease of the spinal cord.
- Chronic headache or backache.
- Cardiac diseases-marked aortic stenosis.

Spinal Anesthesia Technique

Position of the Patient

Lateral decubitus position is the most popular position because of comfort. The vertebral column is then flexed to widen the interlaminar spaces, by drawing the knees upto the chest and putting the chin down on the chest, the head supported by a pillow.

Needles for Spinal Anesthesia

Needles either small bore or with a rounded, non-cutting bevel are used.

The Quincke-Babcock spinal needle (needle with sharp point with a medium length cutting bevel), the Whitacre needle and the sprotte needle (needles of completely rounded, non-cutting bevels with solid tips, openings are on the side, 2 to 4 mm proximal to the tip) are used.

Aseptic Technique

Before the spinal anesthesia, the anesthesiologist must perform a through surgical scrub using alcohol-based antiseptic solutions.

The patient's back is prepared with Betadine-based antiseptic and sterile drapes are applied. The insertion site for lumbar puncture should be identified by the line between the upper border of the iliac crests, which passes through either the spinous process of L4 or the interspace between L4 and L5. Spinal needle is introduced through Midline approach either in sitting /right lateral decubitus position. 26 gauge spinal needle is used and the needle is introduced through middle of the interspace and after piercing the skin and subcutaneous tissue, it is advanced in a perpendicular direction with the long axis of the vertebral column. Stylet is gently removed, appearance of CSF through the hub of the needle confirms correct position of needle.The hub of the needle is held between thumb and index finger of the anesthesiologists non dominant hand and syringe is attached to the needle, gentle aspiration done to confirm free flow of spinal fluid and the drug is injected. Then the patient is placed in supine position continuous monitoring of vital parameters done and level of analgesia confirmed by loss of sensation to pinprick. Motor block is assessed by modified Bromage score.

Physiologic Responses

Effects on Cardiovascular System[11]

The response are due to combined effects of autonomic denervation, with higher levels of blockade, the added effects of vagal nerve innervations. Spinal anesthesia causes some degree of hypotension and reflex bradycardia because of reduction in cardiac output and systemic vascular resistance. The level of sympathetic denervation determines the magnitude of cardiovascular responses to spinal anaesthesia, the higher the level of neuronal blockade,the greater the change in haemodynamic parameters. The bradycadia is mediated by significant decreases in right atrial pressure and pressure in the great veins as they enter the right atrium.The direct relationship between right atrial pressure and heart rate during spinal anaesthesia is mediated by intrinsic chronotropic stretch receptors located in the right atrium and adjacent great veins, the mechanism for these changes is described as **Bezold-Jarisch reflex**

The bradycardia seen during spinal anesthesia is due to blockade of preganglionic cardiac accelerator fibres arising from T1 to T4 during high levels of anesthesia[12]**.**

Effects on respiratory system

It reduces minute ventilation but maintain ventilatory response to CO2.It's Hyperbaric arousal phenomenon is like natural sleep. High spinal anesthesia cause intercostal paralysis, Arterial blood gas tension, decrease resting tidal volume, maximum inspiratory volume remain unaltered because diaphragmatic activity is unimpaired.

Gastro Intestinal Effect:

Preganglionic fibres from T5-L1 are inhibitory to gut. So in sympathetic blockade the small intestine contracts with relaxed sphincters and peristalsis remains normal. Handling of viscera causes discomfort and bradycardia since vagus is not blocked.

Hepatic and Renal effects

The hepatic blood flow decreases and is directly proportional to the decrease in blood pressure. There may be normal hepatic oxygen extraction. Renal blood flow is maintained by autoregulation and doesnot decrease till mean arterial pressure goes below 50 mm Hg.

Genito Urinary system

Sphincters of bladders are not relaxed, and the ureteric tone are greatly altered. Urinary retention occurs. Penis is often engorged. Uterine tone is unchanged in Pregnancy. In absence of hypotension, spinal anaesthesia has got no effect on the pregnancy, progress of labour and uterine blood flow.

Metabolic and Hormonal effect

Spinal anaesthesia blocks the hormonal and metabolic responses to nociceptive stimuli arising from the operative site. It minimizes the rise in blood sugar, cortisol, catecholamines, renin and aldosterone release associated with stress. Post-operative negative nitrogen balance and secretion of antidiuretic hormone are inhibited.

Thermo Regulation

Extensive spinal blockade impairs central thermo regulatory control[13]. The main cause of hypothermia during spinal anesthesia is the redistribution of blood flow and heat to the periphery because of vasodilation.

Complication of Sub Arachnoid Block

- Immediate
- Hypotension
- Bradycardia
- Toxicity due to intravascular injection
- Anaphylactic reactions
- Hypotension (brainstem hypoxia)

Late

- Post dural puncture headache
- Retention of urine
- Hematoma formation
- Backache
- Meningitis
- Transient lesions of cauda equina
- Sixth nerve palsy
- Anterior Spinal artery syndrome

Pharmacology of Drugs

Pharmacology of Bupivacaine [14,15]

Bupivacaine belongs to amide group of local anaesthetics. This long acting local anaesthetic was first synthesized by A.F. Ekenstam in 1957.

Commercial bupivacaine is a racemic mixture of R(dextro) and S(levo) stereoisomers. It is available as hydrochloride salt for anaesthesia.

Chemical Name [16]

1-Butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide

Chemical Structure

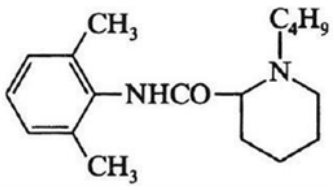


Fig 4: Bupivacaine structure

Physio- chemical properties
Pka - 8.2
Molecular Formula - C18H28N2O
Molecular Weight - 290 gm/mol
Plasma protein binding - 95%
Lipid solubility - 28 mg/L
Solubility in water - 1 in 25
Solubility in alcohol - 1 in 8
Elimination half-life – 210 minutes
Toxic plasma concentration ->1.5µg/ml
Approximate duration of action -175 minutes

The drug is very stable to acids, alkalis and repeated autoclaving. Bupivacaine 0.5% is the preferred strength. Higher concentration result in greater variability of spread[10]. Bupivacaine is four times as potent as lignocaine, hence 0.5% solution is approximately equivalent to 2% lignocine. It is more cardiotoxic than lignocaine and which is aggravated by hypoxia, hypercapnia and by pregnancy. It causes more sensory than motor block. It is not recommended for intravenous regional analgesia. Duration of effect is between 5 and 16 hours and is one of the longest acting local analgesics, which is related to binding to nerve tissue. Small percentage of a given dose of drugs is excreted unchanged in the urine and the remainder is metabolized in the liver.

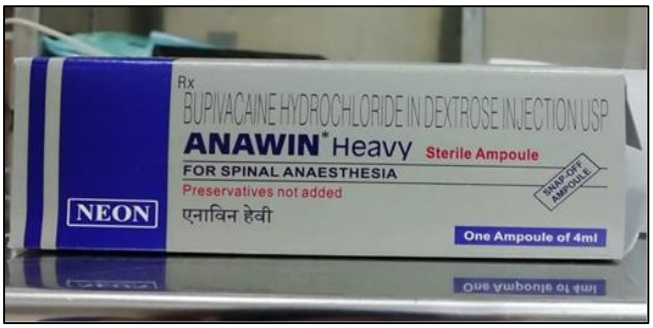


Fig 5: Bupivacaine Ampoule

Uses
- Spinal anesthesia
- Epidural anesthesia
- Caudal anesthesia
- Continuous epidural anesthesia
- Peripheral nerve block
- Infiltration anesthesia

Onset time and duration of action

Site of action	Onset(minutes)	Duration(minutes)
Intrathecal	5	90 -120
Epidural	15- 20	165
Brachial plexus	10- 20	600

Pharmacokinetics
Once injected intrathecally, it gets absorbed by the nerve rootlets and it rapidly absorbed from the site of injection, but the rate of absorption depends on the vascularity and the presence of vasoconstrictors.
Because of high lipid solubility it easily penetrates nerve and vascular tissue, 80-95% of absorbed bupivacaine binds to the plasma proteins.

Distribution
Rapid distribution phase: (α)
Slow disappearance phase:(β)

Biotransformation
Possible pathways of metabolism of bupivacaine include aromatic hydroxylation and conjugation. Only the N-dealkylated metabolite, N-desbutyl bupivacaine has been measured in blood (or) urine after epidural (or) spinal anesthesia. Alpha acid glycoprotein is the most important plasma protein binding site of bupivacaine and its concentration is increased by many clinical situations including post-operative trauma.

Excretion
It is through the kidney, 4-10% of the drug is excreted unchanged.

Mode of Action

a. Site of action
1. The spinal nerve rootlet fine nerve filaments having a large surface area are exposed to the local anaesthetics
2. Posterior and lateral aspects of the spinal cord.

b. Sodium Channel blockade
They impede sodium ion access to the axon interior by occluding the transmembrane Sodium channels thus delaying the process of depolarization and axon remains polarized.

Pharmacodynamics
It has got a longer duration of action but a slower onset.

Cardiovascular system
It reduces cardiac output by reducing the sympathetic tone, by slowing the heart rate and by reducing the venous return, it produces a fall in arterial blood pressure but it is relatively slow and is seldom very profound. It produces a fall in central venous pressure. It causes an increase in lower limb blood flow. It causes a reduction in incidence of deep vein thrombosis.

Respiratory system
It relaxes bronchial smooth muscle. It causes apnea due to phrenic and intercostal nerve paralysis or depression of the medullary respiratory center following direct exposure to drug.

Gastro intestinal tract
There is an increased in gastro intestinal motility and emptying of the gastric contents are better.

Toxicity[17]
Toxicity is related to plasma level of unbound drug and more likely due to an inadvertant intravenous injection. Systemic

toxicity reactions primarily involve central nervous system and cardio vascular system. The blood level required to produce central nervous system toxicity is less than that required to produce circulatory collapse.

Central Nervous System Toxicity
Early symptoms are circumoral numbness, tongue paresthesia and dizziness. Sensory complaints include tinnitus and blurred vision. Excitatory signs (restlessness, agitation, nervousness, paranoia) often precede central nervous system depression (slurred speech, drowsiness, unconciousness). Muscle twitching heralds the onset of tonic clonic seizures. Respiratory arrest often follows. The excitatory reactions are the result of selective blockade of inhibitory pathways.

Cardiovascular System Toxicity
The rate of depolarization in fast conducting tissue of purkinje fibres and ventricular muscle is decreased. The rate of recovery of bupivacaine induced block is slower than that of lignocaine. Extremely high concentration of the drug causes sinus bradycardia, hypotension, atrioventricular heart block, idioventricular rhythms, and life threatening arrhythmias such as ventricular tachycardia, ventricular fibrillation and cardiac arrest.

Pharmacology of Nalbuphine
Narcotic analgesics are associated with significant abuse potential. To overcome the abuse potential, various synthetic opioids were developed. Those substances are referred to as mixed agonist-antagonist analgesics. Nalbuphine is one among them.

Chemistry
Nalbuphine hydrochloride, a synthetic narcotic agonist-antagonist analgesic of the phenanthrene series. Chemically, it is related to the opioid antagonist naloxone and opioid agonist oxymorphone. Nalbuphine is soluble in water at 25oC, ethanol 0.8% and available only as an injectable solution.

Chemical name
17-(cyclobutylmethyl)-4,5-epoxy-,morphinan-3,6,14-triol, hydrochloride

Chemical structure

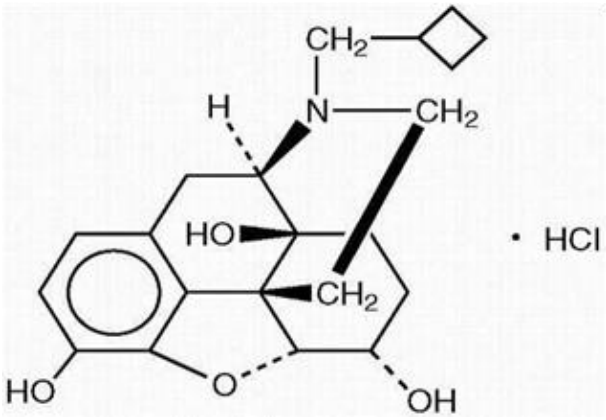


Fig 6: Nalbuphine structure

Physio – chemical properties

- pKa - 8.71
- Molecular formula - C21 H27 NO 4 .HCl
- Molecular Mass - 393.91 g/mol

Preparations and storage
- Available as 10mg, 20mg solutions in 1ml ampoule.
- Should be stored at room temperature (15°c to 30°c).
- Protect from excessive light.

Fig 7: Nalbuphine Ampoule

Uses of Nalbuphine
- As an adjuvant to general anesthesia
- As an adjuvant to neuraxial anesthesia
- Obstetric analgesia during labor and delivery
- As an adjuvant to peripheral nerve blocks.
- In the management of postoperative pain.

Off label uses
- Opioid induced pruritus.
- Opioid induced respiratory depression[18]
- Post anesthesia shivering
- Sickle cell anemia with crisis

Pharmacokinetics
Nalbuphine is inactive orally and intravenous route is the conventional route of administration. It can also be administered by intramuscular, subcutaneous, neuraxial routes.

Bio-availability is around 80%.
Volume of distribution is 3.8 litres/kg.

Onset of action → Intravenous administration is within 2-3 mins
Onset of action → Subcutaneous, intramuscular < 15

Mins Plasma half-life - 5 hr
Duration of analgesia - 3 to 6 hours

Mechanism of action [19]
By its agonist action, nalbuphine stimulates κ receptors there by inhibiting the release of neurotransmitters like substance P that mediate pain. It acts as a post-synaptic inhibitor on the "inter neurons & output neurons" of the Spino-thalamic tract which transport nociceptive information.

Adverse effects
The most common side effects of nalbuphine are sedation,

sweating, nausea, vomiting, dizziness, vertigo, dry mouth, headache. Other effects are bradycardia, hypotension, urinary urgency. Because of the ceiling effect,[20] nalbuphine causes less respiratory depression compared to other opioids. It is classified as category _B' (animal studies have failed to demonstrate fetal risk and there are no controlled studies in pregnant women) drug in pregnancy. It should be avoided in patients who are hypersensitive to the drug or its components.

Pharmacology of Fentanyl

Fentanyl is a synthectic, lipophilic phenylpiderine opioid agonist with analgesic and anesthetic properties. First synthesized by Paul Janssen in 1960 by assaying analogues of the structurally related drug pethidine[21].

Chemical name

—N‖-phenyl-—N‖-(1-phenethyl-4-piperidinyl) propanamide

Chemical sturucture

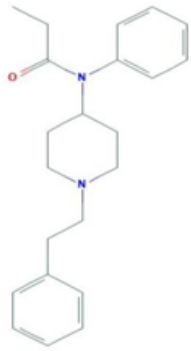


Fig 8: Fentanyl structure Physio- chemical properties

Pka – 8.99
Molecular formula –C22H28N2O
Molecular weight -336.5 g/ml
Protein binding -80 %

Uses

Pain management
Premedication
Adjuvant to regional anaesthesia
Patient controlled analgesia

Preparations and storage

Available as 100mcg/2ml and 500mcg/10 ml ampoules
Transdermal patches
Lozenges for children

Fig 9: Fentanyl Ampoule

Fentanyl is potent agonist at μ opioid receptors. Approximately 100 times more potent than morphine and is widely used in anaesthetic practice. In small doses (1 mcg/Kg, intravenously) it has a rapid onset and a short duration of action (20-30min), and produces mild sedation. By contrast, in high doses (50-150mcg/Kg) profound sedation and unconsciousness occur, and Fentanyl has been used as the sole anaesthetic agent, although awareness has been reported during surgery. When given in high doses muscular rigidity of the chest wall may occur.

Fentanyl like other opioid analgesics, depresses respiration in a dose-dependent manner. Cardiovascular stability is present even when the drug is administered in high dosage although bradycardia can occur and may require treatment with atropine. High dose Fentanyl anaesthesia also reduces or eliminates the stress response to surgery.

Duration of action: Since Fentanyl is highly lipid-soluble it rapidly crosses the blood-brain barrier, and concentrations inj the CNS usually reflects those in plasma (with a time delay of approximately 5 min). in small doses (1-2 mcg/Kg) its duration of action is short, since plasma and CNS concentrations Fall below an effective level during the distribution the distribution phase. Consequently, there is rapid recovery from its effects. In contrast, after large or multiple doses of Fentanyl, the distribution phase is completed while the plasma concentration of Fentanyl is still higher than the minimum effective level. Recovery from the effects of the drug then depends on its relatively slow elimination from the body, and its duration of action is significantly prolonged. In these circumstances, profound respiratory depression may be present for several hours during the postoperative period

Pharmacokinetics

There is considerable inter-individual variation in the pharmacokinetics of Fentanyl. After and intravenous bolus dose, plasma concentrations decline rapidly (distribution half-life approximately 13 min). its terminal half life is 3-4 hours in normal subjects, but may be as long as 7-8 hours in some patients. The volume of distribution is relatively large (approximately 4 L/Kg) due to its high lipid solubility and extensive uptake by tissues and clearance is slightly less than hepatic blood flow. Fentanyl is predominantly metabolized by N-dealkylation and hydroxylation in the liver, and metabolites can be detected in blood within 1-2 minutes. Approximately 70% of the drug is excreted in urine as inactive metabolites over several days[22].

Adverse effects

- Nausea and vomiting
- Dry mouth
- Itching
- Respiratory depression
- Constipation
- Dry mouth
- Retension of urine

Aims and Objectives

- **AIM**

Comparison of intrathecal nalbuphine and fentanyl as an adjuvant to hyperbaric bupivacine in infraumbilical surgeries.

- **Objectives of Study Primary**

1. Onset of sensory blockade and motor blockade
2. Duration of sensory blockade and motor blockade
3. Post-operative analgesia

1. Haemodynamic parameters
2. Incidence of side effects

Review of Literature

1. Umesh N Prabhakaraiah et al.[23] Conducted a study in 2016 titled ―Comparison of nalbuphine hydrochloride and fentanyl as an adjuvant to bupivacaine for spinal anesthesia in lower abdominal surgeries‖.It was a prospective randomized double-blind study.60 patients belonging to the ASA I and II were randomly allocated into two groups of thirty each. Patients in bupivacaine nalbuphine group (Group BN) received 0.8 mg (0.3 ml) of nalbuphine with 12.5 mg (2.5 ml) of 0.5% hyperbaric bupivacaine diluted to 3 ml and bupivacaine-fentanyl group (Group BF) received 25 µg (0.5 ml) of fentanyl with 12.5 mg (2.5 ml) of 0.5% hyperbaric bupivacaine.Results: Postoperative visual analog scale score was 4.8 ± 1.12 in Group BN, and in Group BF, it was 3.86 ± 1.04 which was statistically highly significant (P = 0.0007). The number of patients demanding rescue analgesia in early postoperative period was 18 (60.0%) in Group BN and 7 (23.33%) in Group BF which was statistically significant (P = 0.004).It was concluded that Fentanyl was more efficient than nalbuphine in providing early postoperative analgesia when used as an adjuvant to hyperbaric bupivacaine.

2. Bisht S et al.[24] conducted a study on titled ―Comparison of intrathecal fentanyl and nalbuphine: A prospective randomized controlled study in patients undergoing total abdominal hysterectomy‘‘ One hundred ASA 1-3 patients, aged 30-65 years posted for elective total abdominal hysterectomy (TAH) were randomly divided into two groups of fifty each. Group FB received 15 mg of 0.5% bupivacaine (3 ml) plus 25 µg of fentanyl (0.5 ml) and Group NB received 15 mg 0.5% bupivacaine (3 ml) plus 1 mg nalbuphine (0.5 ml).The onset of sensory blockade, time to attain peak sensory block and complete motor block was significantly faster in Group FB ($p < 0.001$). The duration of motor block was comparable in both the groups. The time for sensory block to regress by two segments was significantly longer in Group NB, 97.72 ± 9.50 min, than in Group FB, 88.88 ± 9.48 min. The time to first analgesic requirement in Group NB was 460.78 ± 77.98 min compared to 283.44 ± 78.97 min in Group FB ($p < 0.001$). No statistical difference was seen in terms of adverse effects. Two patients in both groups complained of nausea. Hypotension and pruritus were seen in two and one patient respectively in Group FB.It was concluded Although the time to onset and peak sensory level is longer with nalbuphine as intrathecal adjuvant than fentanyl, time for sensory level to regress by two segments and the postoperative analgesia time is longer with nalbuphine.

3. Bhavana B et al[25] conducted a study on titled-Postoperative Analgesic Efficacy of Intrathecal Fentanyl Compared to Nalbuphine with Bupivacaine in Spinal Anesthesia for Lower Abdominal Surgeries‖ .This was a prospective, randomized double-blind study.124 patients aged 18–55 years with ASA I and II were randomly divided into two groups – Group N: hyperbaric bupivacaine with nalbuphine (300 µg); Group C: hyperbaric bupivacaine with fentanyl (25 µg). Results: Duration of onset of sensory blockade was 3.9 ± 0.35 min in Group C and 3.1 ± 0.18 min in Group F. Two-segment sensory regression time was prolonged in Group C (193.16 ± 39.55) compared to Group F (167.41 ± 30.17 min).it was concluded that Intrathecal nalbuphine at a dose of 300 µg in 3 ml 0.5% heavy bupivacaine in patients undergoing elective lower abdominal surgeries showed delay in onset time for sensory blockade and produced prolonged postoperative analgesia, prolonged sensory blockade, and minimal bradycardia which could be easily managed.

4. Dr. Rajkumar N Jaisinghani et al[26] conducted a study titled A prospective randomized double blind comparative study of 0.8 mg nalbuphine hydrochloride and 25 mcg fentanyl as adjuvant to 0.5% hyperbaric bupivacaine in sub arachnoid block in lower limb surgeries. Sixty patients of either sex, ASA class I and II were included in this study. Patients received
0.5% hyperbaric bupivacaine 15 mg along with either 25mcg fentanyl or 0.8mg nalbuphine hydrochloride. Results: Duration of postoperative analgesia was significantly longer with nalbuphine (318±13.88 min)as compared to fentanyl (296.26±13.31min). Side effects like nausea vomiting, hypotension and bradycardia and shivering was more with fentanyl while sedation was minimal with both the drugs. Conclusion: Nalbuphine hydrochloride is a better alternative as an adjuvant for postoperative analgesia and less side effects than fentanyl for lower limb surgeries.

5. **Jaideep Singh et al[27]** Conducted a study on titled ―Intrathecal Nalbuphine an Effective Adjuvant for Post Operative Analgesia (A Comparitive Study with Fentanil)‖ it was a prospective, randomized, comparative study.60 patients of ASA grades I and II of either sex in the age group of 20-60 years will be randomly allocated to one of the two groups. Group A (n = 30) received 3 ml of 0.5% hyperbaric bupivacaine intrathecally with 25 mcg fentanyl ; group B (n = 30) received 3 ml of 0.5% hyperbaric bupivacaine .8 mg nalbuphine intrathecally. The onset of sensory and motor blockade, The onset of complete motor block was more rapid with fentanyl than nalbuphine and this was statistically significant ($p<0.05$).In the study they conclude that both Nalbuphine or Fentanyl in combination with low dose hyperbaric bupivacaine (15mg) are equally efficacious and haemodynamically stable in patients undergoing lower limb surgeries. However, Nalbuphine with comparatively prolonged post operative analgesia and effective analgesia time and lesser side effects is a better adjuvant than Fentanyl for intrathecal injections of Bupivacaine 0.5%(H) in surgeries undergoing spinal anaesthesia. with no statistically significant difference.

6. Shagufta Naaz et al[28] conducted a study titled ―A Comparative Study of Analgesic
Effect of Intrathecal Nalbuphine and Fentanyl as Adjuvant in Lower Limb Orthopaedic Surgery‖ .A randomised, double blinded, prospective study on 90 patients of ASA I and II undergoing lower limb orthopaedic surgery under subarachnoid block was done. Patients were randomly allocated into three groups (n=30). Each group received 12.5 mg of 0.5% of injection bupivacaine heavy along with either 25 µg of 0.5 ml fentanyl (Group F) or 0.8 mg of 0.5 ml nalbuphine (Group NL) or 1.6 mg of 0.5 ml nalbuphine (Group NH).The duration of analgesia (in minute) was 441±119.69 in NL Group, 450±103.38 in NH Group and 300.0±88.53 in Group F ($p=0.05$). There was no significant

difference regarding block characteristics and haemodynamic parameters. Total 24 hours analgesic requirement was titrated by analgesic score which was 2.25±0.7 (NH Group), 1.875±0.83 (NL Group) and 3.375±1.77 (F Group) p=0.0186 by ANOVA. The adverse effects of NL Group were least.There was no significant advantage of intrathecal fentanyl or 1.6 mg nalbuphine over low dose 0.8 mg nalbuphine.

7. Dr. Neelam Singh et al[29] conducted a study on titled—A Clinical Comparative Study of Intrathecal Nalbuphine Versus Intrathecal Fentanyl Added to 0.5% Hyperbaric Bupivacaine For Perioperative Anaesthesia And Analgesia in Lower Abdominal Surgeries.‖ 60 Adult male and female patients belonging to (ASA) physical status I – II, age group 18-60 yrs posted for Elective Lower abdominal surgeries were included in the study. Group I: Patients received 2.8 ml of 0.5% hyperbaric bupivacaine with 600 mcg (0.6 ml) of nalbuphine.(total vol 3.4 ml) Group II: patients received 2.8ml of 0.5% hyperbaric bupivacaine along with 30 mcg 0.6 ml) of fentanyl (total vol 3.4 ml) group iii: patients received 2.8ml of 0.5% hyperbaric bupivacaine along with 0.6 ml of normal saline (total vol 3.4 ml). group I & II: were study groups and group iii was control. it reveals that duration of analgesia was longer in both- group I (nalbuphine (404.5±22.82 mins) and group ii (fentanyl(295.5±21.82 mins) in comparison to control group iii (265±23.5). but group i had longer duration of analgesia than group ii(404.5±22.82 minsvs 295.5±21.82 mins).total number of rescue analgesics required in 24 hours was lesser in both group I (nalbuphine (1.85±0.74 mins) and group ii (fentanyl (2.05±0.75) in comparison to control group (3.5±0.60). but group i had lesser number of rescue analgesics required in 24 hours than group II and group iii.it was concluded that addition of nalbuphine to intrathecal bupivacaine causes prolongation of duration of sensory block and duration of analgesia and less requirement of analgesics in post-operative period without increasing the side effects or complication.

8**. Tiwari AK et al**[30] conducted a study on titled —Intrathecal bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block: a randomized prospective double-blind clinical study. 75 patients of ASA grades 1 and 2 of either sex in the age group of 20-60 years were randomly allocated to 1 of 3 groups. Group A (n = 25) received 2.5 mL of 0.5% hyperbaric bupivacaine + 1 mL sterile water intrathecally; group B (n = 25) received 2.5 mL of 0.5% hyperbaric bupivacaine + 1 mL (200 µg) nalbuphine intrathecally; group C (n = 25) received 2.5 mL of 0.5% hyperbaric bupivacaine + 1 mL (400 µg) nalbuphine intrathecally. Onsets of sensory and motor blockade and duration of motor blockade were not affected. Two segment regression time of sensory blockade and duration of analgesia were maximally prolonged in group C ($P < 0.05$). The visual analogue scale scores were in the following order: group A > group B > group C at 90, 120, and 150 minutes after induction ($P < 0.05$). Hemodynamic and respiratory complications were absent except in 2 patients in groups A and C each, and 1 patient in group B developed bradycardia ($P > 0.05$). One patient in group A had nausea and vomiting, 2 patients in each group developed shivering . Nalbuphine hydrochloride (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.

9. Kumkum Gupta et al[31] conducted a study on 2015 titled —Intrathecal nalbuphine versus intrathecal fentanyl as adjuvant to 0.5% hyperbaric bupivacaine for orthopedic surgery of lower limbs under subarachnoid block:A comparative evaluation‖ It was a prospective randomized double-blind study.68 adult patients of ASA physical status I and II of both gender aged 25–65 years were randomized into two groups of 34 each to receive either fentanyl 25 µg (Group I) or nalbuphine 2 mg (Group II) with 3.5 mL 0.5% hyperbaric bupivacaine, making intrathecal drug volume to 4 mL in each group. The time to two dermatome regressions and time for complete motor recovery were significantly prolonged in patients of Group II with statistical significant difference ($P < 0.05$). Duration of analgesia was also extended in patients of Group II (378.0 ± 35.72 min) as compared to Group I (234.0
24.10 min) with highly significant difference ($P < 0.001$). No drug related side effects were observed in either group and was concluded that Intrathecal nalbuphine 2 mg as adjuvant to 0.5% bupivacaine was clinically more efficient than fentanyl for enhancing the postoperative analgesia.

10. Hala Mostafa Gomaa et al[32] did a study on —Comparison between post-operative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine for cesarean section‖ 60 female patients of ASA grades I and II presented for elective cesarean were divided into 2 equal groups; Group F: 30 patients received intrathecal injection of 2 ml of 0.5% hyperbaric bupivacaine plus 0.5 ml fentanyl (25 lg); Group N: 30 patients received intrathecal injection of 2 ml of 0.5% hyperbaric bupivacaine plus 0.5 ml nalbuphine (0.8 mg). Results: 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 but the difference was insignificant. No significant difference was found between both groups as regards the duration of sensory block, motor block, duration of analgesia, visual analog scale score, hemodynamic parameters and oxygen saturation. Adverse effects were less common in nalbuphine group but the difference was insignificant.

11. Sandip Roy Basunia et al[33] conducted a study titled —A Prospective, Double-blind Dose-ranging Study of Intrathecal Nalbuphine in the Lower Abdominal and Lower Limb Surgeries‖.This was a prospective, randomized, double-blind study. Eighty ASA I and II patients undergoing elective lower abdominal and lower limb surgeries under subarachnoid block were randomly allocated to four groups (A, B, C, and D of twenty patients each) to receive 0.5 ml normal saline or 0.8, 1.2, and 1.6 mg nalbuphine added to 0.5% hyperbaric bupivacaine 15 mg. Results: Two-segment regression time of sensory blockade and duration of effective analgesia were prolonged in both Group C (1.2 mg nalbuphine) and Group D (1.6 mg nalbuphine) compared to Groups A and B ($P < 0.05$), but the incidence of side effects was significantly higher in Group D ($P < 0.05$). finally concluded Nalbuphine 1.2 mg is the optimum intrathecal dose which prolongs postoperative analgesia without increased side effects.

12. Diwash Rajbhandari et al[34] conducted a study titled as —The Comparison of Effectiveness of Different Doses of Fentanyl added to Hyperbaric Bupivacaine for Spinal Anaesthesia in Emergency Appendectomy‖. 120 patients were enrolled for the study and randomly divided into 4 groups. Group A (3ml of 0.5% hyperbaric bupivacaine + 0.6ml of normal saline), Group B (3ml of 0.5% hyperbaric

bupivacaine + 10µg of fentanyl (0.2ml) + 0.4ml of normal saline), Group C (3ml of 0.5% hyperbaric bupivacaine + 20µg of fentanyl (0.4ml) + 0.2ml of normal saline) and Group D (3ml of 0.5% hyperbaric bupivacaine + 30µg of fentanyl (0.6ml)). Results: There was no significant difference in ASA and nausea/vomiting except in shivering, rescue analgesia and pain free period. The duration of pain free period was longer in Group D. Group A had the highest incidence of Nausea/vomiting. The Group C (2.22±2.11hrs) patients required longer duration for sensory regression of two dermatomes whereas Group A (1.49±0.01hrs) had shorter duration for sensory regression of two dermatomes.

13. Tripat kaur bindra et al[35] conducted a study on 2018 titled as ―Post operative Analgesia with Intrathecal Nalbuphine versus Intrathecal Fentanyl in caesarean section: A double –blind randomized comparative study.150 parturients of (ASA) physical status I and II of age group 20–45 years with normal coagulation profile undergoing cesarean section under spinal anesthesia. These patients were randomized into three groups with fifty patients in each group. Group I received 2 ml of 0.5% hyperbaric bupivacaine (10 mg) plus 0.4 ml nalbuphine (0.8 mg), Group II received 2 ml of 0.5% hyperbaric bupivacaine (10 mg) plus 0.4 ml fentanyl (20 µg), and Group III received 2 ml of 0.5% hyperbaric bupivacaine (10 mg) plus 0.4 ml of normal saline.Results: The mean duration of effective analgesia was 259.20 ± 23.23 min in Group I, 232.70 ± 13.15 min in Group II, and 168.28 ± 7.55 min in Group III. The mean number of rescue analgesics required was significantly lower (P < 0.001) in Group I as compared to Group II and III.Conclusion: Both intrathecal nalbuphine 0.8 mg and fentanyl 20 µg are effective adjuvants to 0.5% hyperbaric bupivacaine in subarachnoid block. However, intrathecal nalbuphine prolongs postoperative analgesia maximally and may be used as an alternative to intrathecal fentanyl in cesarean section.

14. **Farahat I. Ahmed**[36] conducted a study on 2017 titled Intrathecal nalbuphine versus fentanyl as an adjuvant to bupivacaine in spinal anesthesia for elective cesarean section:a randomized double-blind study.80 full-term parturients scheduled for elective cesarean section were randomly allocated into two groups. Nalbuphine group (BN group) received 12.5mg of 0.5% hyperbaric bupivacaine with 800 µg nalbuphine intrathecally. Fentanyl group (BF group)12.5 mg hyperbaric bupivacaine with 25 µg fentanyl intrathecally.Results

Onset of sensory and complete motor block, maximum height of sensory block, and time to two-segment sensory regression were significantly faster in BF group than in BNgroup. Maximum dermatomal block level was significantly higher in BF group than in BN group. Durations of postoperative complete and effective analgesia were highly significantly longer in BN group than the corresponding durations in BF group. There was no pruritus in BN group (0%), but it occurred in five (12.5%) parturient in BF group, which was mild. Conclusion As an adjunct to hyperbaric bupivacaine in spinal block, fentanyl was superior to nalbuphine in enhancing the onset of both sensory and motor block. Nalbuphine is superior to fentanyl in increasing the duration of postoperative complete and effective analgesia.

15. **Dr. Avinash Bapurao Pawar**[37] et all conducted a study on titled ―A Comparative Study of Intrathecal Bupivacaine with Nalbuphine and Bupivacaine with Fentanyl for Intra and Post-Operative Analgesia in Gynaecological Surgeries . 60 patients of ASA grade I and II in the age group of 40-60 years were randomly allocated into two groups GROUP A: [n =30] received 0.5% hyperbaric Bupivacaine 15 mg with Nalbuphine 0.8 mg GROUP B: [n =30] received 0.5% hyperbaric Bupivacaine 15 mg with Fentanyl 25 mcg. The onset ofsensory block was more rapid with Fentanyl than Nalbuphine and this was statistically significant but the duration of post-operative analgesia(sensory and motor) and the effective analgesic time were more prolonged in Nalbuphine group than in Fentanyl group with no statistically significant difference. There was no significant difference found in various hemodynamic, vital parameters intra operatively or any side effects between the two groups. Addition of Nalbuphine to intrathecal Bupivacaine improved the quality of intraoperative and postoperative analgesia with minimal side effects.

Lacunae in Literature

In most of studies has been done in the age group of 18-20 years; Studies in extremes of age is needed to be done to see the effect of the study drugs.

Post-operative sedation need to be evaluated thoroughly

The effect of the study drugs in people with other comorbidities like diabetes and hypertension is not known and needs further studies.

Materials and Methods

Study site

This study was conducted in the Department of Anesthesiology and Critical care, **Sahyadri Narayana Multispeciality Hospital, Shiomga, Karnataka.**

Study design: Randomized controlled trial, Double blinded.

Sample size: Two groups of 27 subjects each.

Duration of study: June 2019 to October 2020

Sampling method: Random sampling

Statistical Analysis: Student's t-test, chi-square test

Sample Size

Sample size calculation using the formulae

$$N=\frac{\{z_{1-\alpha/2}\sqrt{2p(1-p)}+z_{1-\beta}\sqrt{p_1(1-P_1)+p_2(1-P_2)}\}^2}{(p_1-p_2)^2}$$

Where, p =

P1 : Proportion in the first group

P2 : Proportion in the second group

α : Significance level

1-β : Power

According to the similar study

-Comparison of Nalbuphine Hydchloride and Fentanyl as an Adjuvant to Bupivacaine for spinal Anesthesiain lower abdominal surgeries-Umesh N Prabhakaraiah,

Post-operative analgesia in Group BN= 60%

Post-operative analgesia in Group BF = 23.33%

P1 : 60%

P2 : 23.33%

α : Significance level = 5%

1-β : Power = 80%

N= 27 in each group

Accordingly, **54** patients should be included in the study.

Inclusion Criteria
1. 18 - 60 years of age of either sex
2. ASA physical status 1 or 2
3. Patients who gave valid informed written consent
4. Patients undergoing elective infraumbilical surgeries

Exclusion Criteria
1. Lack of valid informed written consent
2. Infection at the subarachnoid block injection site
3. Patients with neurological and musculoskeletal disease
4. Patients with bleeding disorders
5. Patients on anticoagulants
6. Pregnancy
7. History of allergy to local anaesthetic
8. Patient with alcohol/drug abuse
9. Hypovolemic shock

Methodology

The study population was consist of 54 patients aged between 18-60 years of either sex with ASA physical status 1 and 2, posted for elective infraumblical surgeries lasting more than 30 mintues to 180 minutes. After obtaining institutional ethical and scientific committee clearance(IREC) and written informed consent, 54 adult patients were allocated randomly into group A and group B based on simple sealed envelope method with 27 patients in each group. (n=27).

Detailed pre anaesthetic evaluation was done on the previous day of surgery. All patients were adviced to be nill per orally 6 hours for solids and 2 hours for clear liquids prior to surgery. Anaesthesia machine was checked and all the drugs and equipments necessary for emergency resuscitation were kept ready. On receiving the patient to operating room, an intravenous line was secured with 18 gauge (G) cannula. All patients were connected to multi parameter monitor and monitored for heart rate(HR), non invasive blood prssure(NIBP), electrocardiography (ECG) and arterial pulse saturation (SpO2).

The study drug was prepared by an assistant not involved in the study. The patient and anesthesiologist performing and collecting the data were blinded to the study drug.The patient placed in the right lateral decubitus position.Under strict aseptic precautions, lumbar puncture was performed at L3-L4 intervertebral space with 26 G quincke needle using the median approach. After free flow of clear cerebrospinal fluid(CSF), drug injected at 0.2ml/sec.

- **Group A received 15mg (3 ml) of 0.5% Bupivacaine(H) and Nalbuphine 1 mg (diluted with isotonic normal saline) - Total volume 3.5 ml**
- **Group B received 15mg (3 ml) of 0.5% Bupivacaine (H) and Fentanyl 25 mcg (0.5ml) - Total volume 3.5ml.**

Oxygen at 4l/min was administered through face mask. Hemodynamic parameters like peripheral oxygen saturation, non invasive blood pressure, pulse rate were recorded at regular intervals intraoperatively and postoperatively up to 24 hours.In the post-operative period, patients were assessed for pain by VAS score at 2, 4, 6, 8, 12, 18 and 24 hours. After giving spinal block the study assessment as follows .

Assessment of sensory blockade

Sensory block was assessed by pinprick method in the midclavicular line using 27G hypodermic needle, every minute until the block reached T10 dermatome. After that, level was checked every 2 mins until maximal sensory block was attained .The time of onset, highest level of sensory blockade, time for 2 segment regression of sensory level, duration of sensory block was noted.

Assessment of motor blockade by **Modified Bromage scale**
Modified Bromage Scale

Grade 1- Complete block (unable to move feet or knees)
Grade 2-Almost complete block(able to move feet only)
Grade 3- Partial block (just able to move knees)
Grade 4- Detectable weakness of hip flexion while supine (full flexion of knees)
Garde 5- No detectable weakness of hip flexion while supine
Grade 6- Able to perform partial knee bend

This was assessed at 1 minute interval until complete motor block occurred.Onset of motor block was defined as the time taken from the injection of drug to the development of complete motor block i.e Bromage score-1.Complete recovery from motor block was defined as attaining Bromage Score-6 and the duration of motor block means that the time taken from the onset of complete motor blockade to complete recovery of motor block.

Assessment of Pain

Pain was assessed using Visual analogue Scale at intervals in post-operative period at 2,3,4,8 and 12 hr.

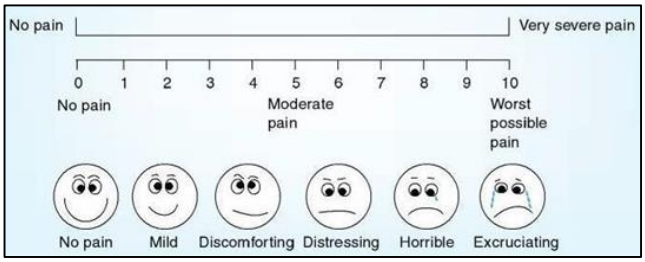


Fig 10: Visual Analogue Scale

Table

Score 0 – 1	No pain
Score 2 – 4	Mild pain
Score 5 – 6	Moderate pain
Score 7 – 8	Severe pain
Score 9 – 10	Unbearable pain

Inj.Tramadol 2mg/kg slow IV was administered as a rescue analgesic when score crossed a score of 4.

Duration of Analgesia

It is the period from the time of subarachnoid block to the time when the patient needs the first dose of rescue analgesic drug.

Assessment of Sedation by Ramsay Sedation Score
Ramsay Sedation Scale
1. Patient anxious, agitated or restless.

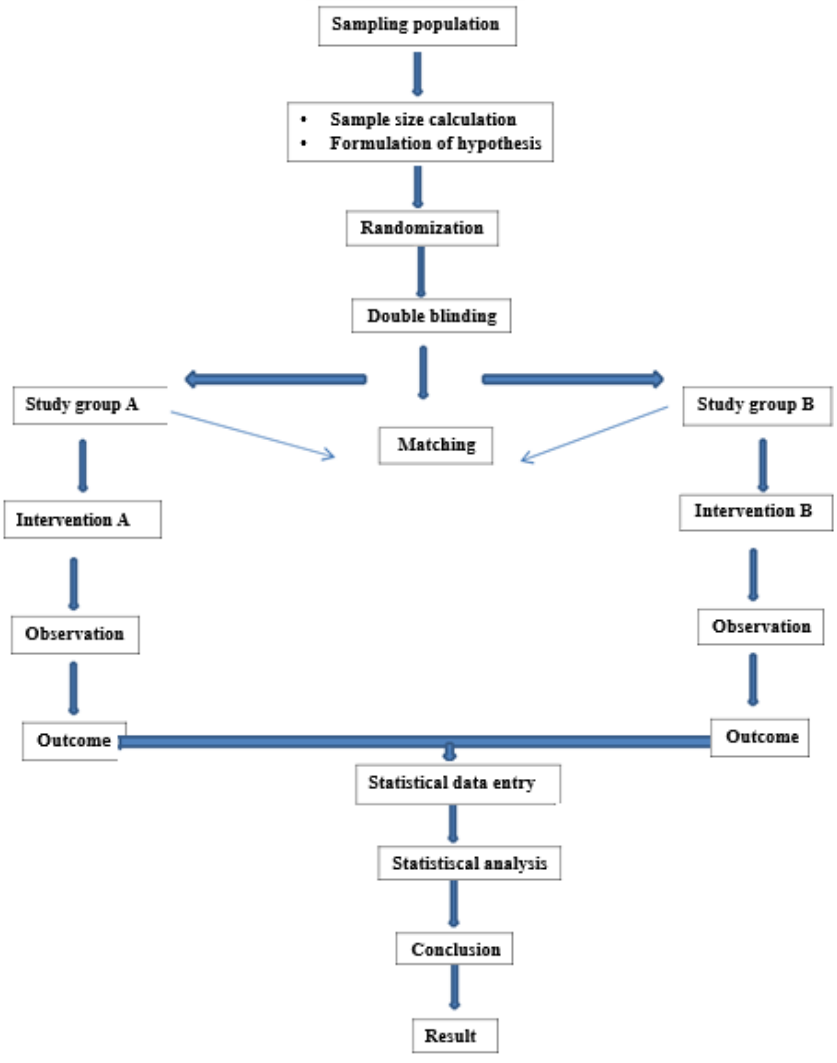
2. Patient cooperative, oriented, and tranquil alert.
3. Patient responds to commands.
4. Asleep, but with brisk response to light glabellar tap or loud auditory stimulus.
5. Asleep, sluggish response to light glabellar tap or loud auditory stimulus.
6. Asleep, no response.

Sedation was assessed with Ramsay sedation scale and recorded. Score of 4 and above is considered as sedated and was monitored up to 12hrs in postoperative period.
Post operatively the patients were followed for upto nausea, vomiting, pruritus, respiratory depression, urinary retention. 24 hours for any adverse effects like any neurological complications and.

Definitions

- **Onset of sensory blockade:** It is the time taken from deposition of study drug till the patient does not feel the pin prick at T10 level.
- **Duration of Sensory blockade:** defined as the time interval elapsed between onset of sensory block at T10 to regression of sensory block to S1.
- **Maximum height of sensory blockade:** Is defined as the time from deposition of the study drug to time to reach the T6 level.
- **Time for two segment regression of sensory blockade:** It is the time in minutes taken to regress the level of loss of pin prick sensation achieved to two lower sensory dermatomal level.
- **Onset of motor blockade:** Is defined as time taken from deposition of the study drug till the patient develops modified Bromage scale Grade 1 motor blockade.
- **Duration of motor block:** Is defined as the time taken from onset of motor block till the patient attains complete motor recovery (modified Bromage 6).
- **Hypotension:** Is defined as fall in the mean arterial pressure to less than 20% from baseline.
- **Bradycardia:** Is defined as decrease in the heart rate to less than 60 beats/min.

Study Flow Chart



Observations and Results

Statistical Analysis

The statistical procedures were performed by the statistical package IBM SPSS statistics 20. The p-value less than 0.05 ($p<0.05$) was treated as significant in two tail condition.

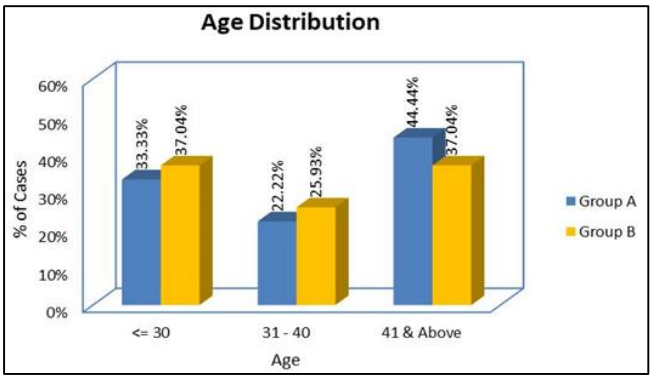
The randomization of two groups was done by matching their Ages, BMI, demographic factors and hemodynamic factors such as Pulse rate, SBP, MAP by Unpaired t-test. Similarly, the onset time for sensory block, and motor blocks were compared between groups by Chi-Square test. The intra and post-operative pulse rates, SBP, MAP at different intervals were compared between groups by Unpaired t-test. The sensory level and sedation score between two groups were analysed and interpreted by chi–square test. The duration of analgesia between the groups were analysed and interpreted by Kaplan – Mayer survival Function.

Results

Randomization by group matching

Table 1: Matching of two groups according to their age

	Group A		Group B		
Parameter	Mean	SD	Mean	SD	P value (chi-square test)
Age(years)	38.89	12.192	37.19	12.351	0.612



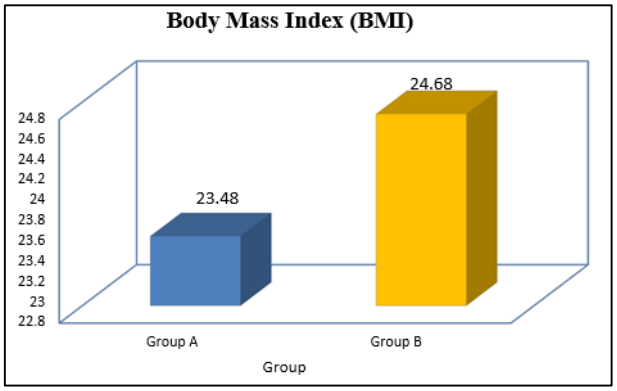
Graph 1: Mean age distribution between two groups

The two groups were matched according to their age for randomization and found that there was no difference(p value > 0.612) between the mean ages between them (38.89±12.192) and (37.19±12.351)

Table 2: Matching two groups according to their BMI (Body Mass Index)

Parameter	Group A		Group B		
	Mean	SD	Mean	SD	P value
BMI(kg/m^2)	23.48	1.896	24.68	1.787	0.243

The Group A had a mean BMI of 23.48±1.896 and Group B had a mean BMI of 24.68±1.787.There were no statistically significant differences between the two groups in terms of BMI(P value =0.243).

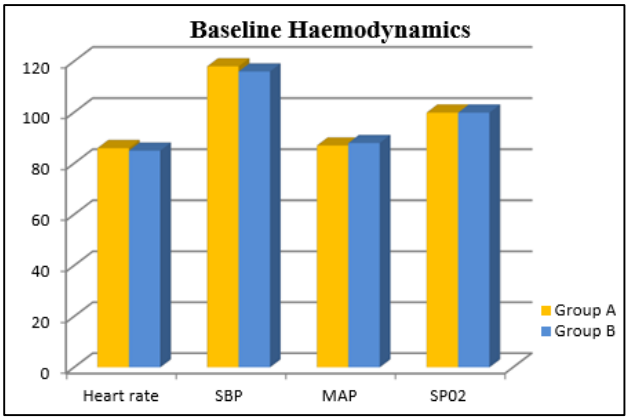


Graph 2: Comparison of two groups according to their mean BMI

Table 3: Matching of two groups according to their Baseline hemodynamic characteristics

Baseline	Group A		Group B		
Parameter	Mean	SD	Mean	SD	P value
Heart rate (bpm)	86.8	9.56	85.47	10.65	0.712
SBP (mm Hg)	118.65	11.48	116.48	10.54	0.658
MAP (mm Hg)	87.6	7.65	88.68	7.52	0.89
SPO2 (%)	99.9	0.20	99.9	0.20	1

The mean pre-op Heart rate, SBP, MAP and SPO2 of Group A and Group B were matched and found that no significant differences were observed between the two groups (p>0.05).

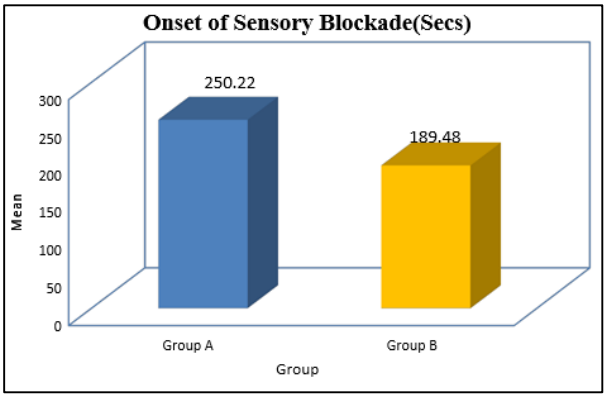


Graph 3: Matching of two groups according to their mean baseline hemodynamic characteristics

Table 4: Comparison of onset of sensory blockade between two groups

Parameter	Group A		Group B		
	Mean	SD	Mean	SD	P value
Onset of sensory blockade (seconds)	250.22	17.542	189.48	16.960	<0.001

The mean time of onset of sensory block in Group A was 250.22 ± 17.542 and Group B was 189.48 ± 16.960 with a p value of < 0.001 which is statistically significant.

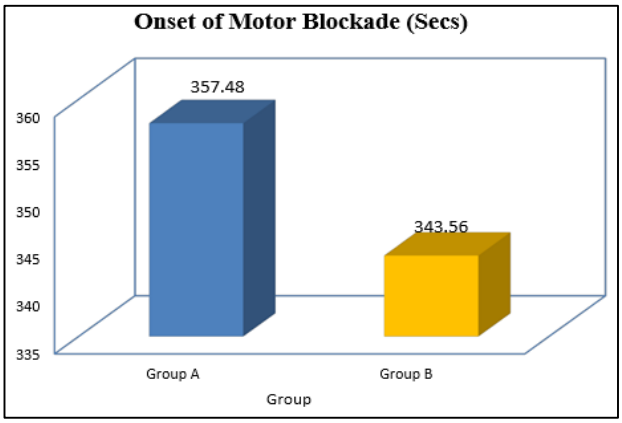


Graph 4: Comparison of two groups according to onset of sensory blockade

Table 5: Comparison of onset of motor blockade between the two groups

Parameter	Group A		Group B		
	Mean	SD	Mean	SD	P value
Onset of motor blockade (seconds)	357.48	10.420	343.56	8.317	< 0.001

The mean time of onset of motor blockade in Group A was 357.48 ± 10.420 and Group B was 343.56 ± 8.317 with a p value of < 0.001 which is statistically significant.

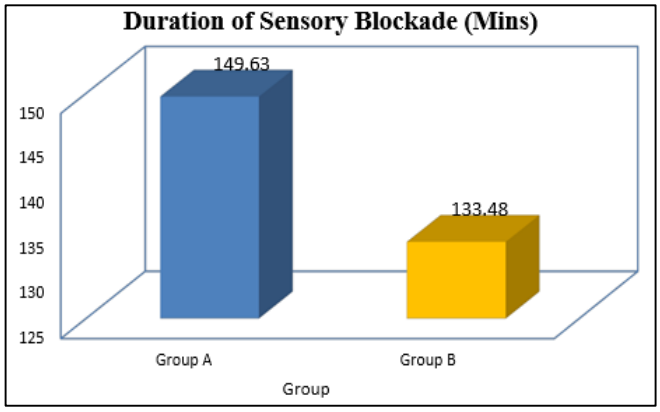


Graph 5: Comparison of two groups according to onset of motor blockade

Table 6: Comparison of duration of sensory blockade between two groups

Parameter	Group A		Group B		
	Mean	SD	Mean	SD	P value
Duration of sensory blockade (minutes)	149.63	3.702	133.48	5.072	<0.001

The mean time of duration of sensory blockade in Group A was 149.63 ± 3.702 and Group B was 133.48 ± 5.072 with a p value of < 0.001 which is statistically significant.

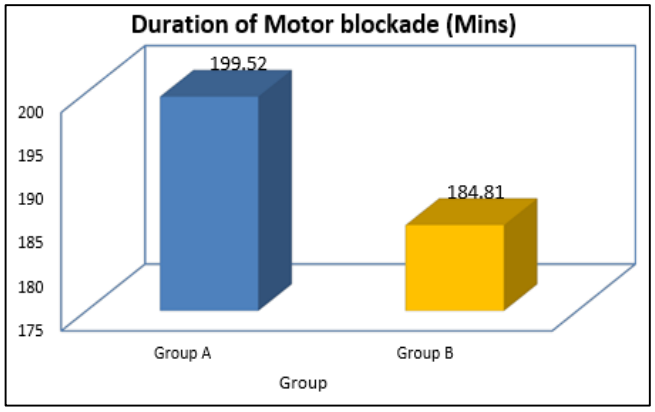


Graph 6: Comparison of two groups according to duration of sensory blockade

Table 7: Comparison of mean duration of motor blockade between two groups

Parameter	Group A		Group B		
	Mean	SD	Mean	SD	P value
Duration of motor Blockade (minutes)	199.52	7.778	184.81	7.000	<0.001

The mean time of duration of motor block in Group A was 199.52 ± 7.778 and Group B was 184.81 ± 7.000 with a p value of < 0.001 which is statistically significant.

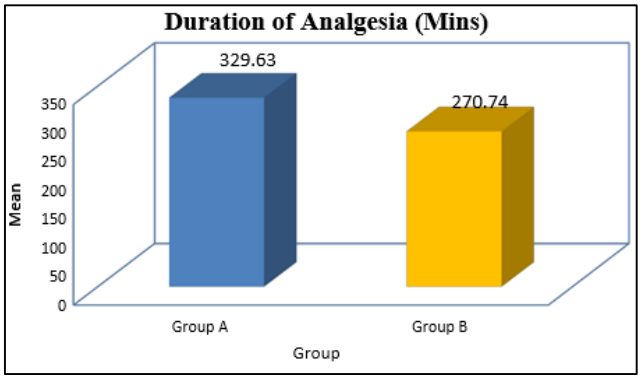


Graph 7: Comparison of two groups according to their mean duration of motor blockade

Table 8: Comparison of duration of analgesia between two groups

Parameter	Group A		Group B		
	Mean	SD	Mean	SD	P value
Duration of Analgesia (minutes)	329.63	37.157	270.74	24.207	<0.001

The mean time of rescue analgesia in Group A was 329.63 ± 37.157 and Group B was 270.74. ± 24.207 with a p value of < 0.001 which is statistically significant.

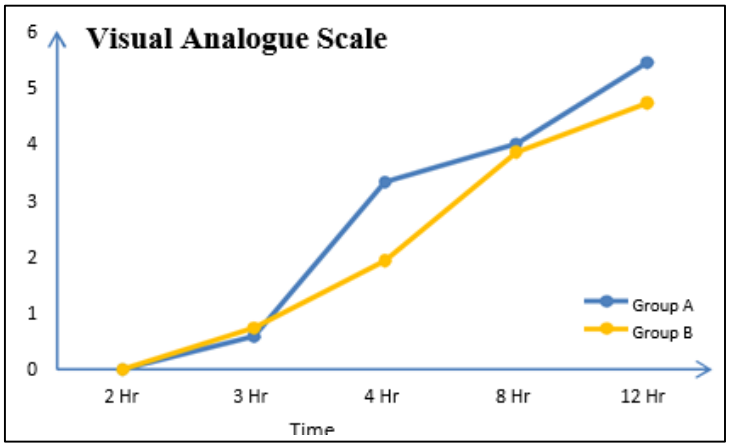


Graph 8: Comparison of two groups based on mean duration of analgesia

Table 9: Comparison of VAS score between two groups

VAS	Group A	Group B	P value
2 Hr	0 ± 0	0± 0	NA
3 Hr	0.62 ± 0.723	0.71 ± 0.631	<0.001
4 Hr	3.33± 0.961	1.93± 1.29	<0.001
8 Hr	4 ± 0.00	3.45± 1.35	0.746
12 Hr	5.44 ± 0.726	4.73± 1.00	0.091

Patents were assessed for pain in the post-operative period using visual Analogue Scale. Pain assessment was done at 2,3,4,8 and 12 hours. Significant difference were noted until 3 to 4 hours. Rescue analgesia was given to Group B earlier than Group A.

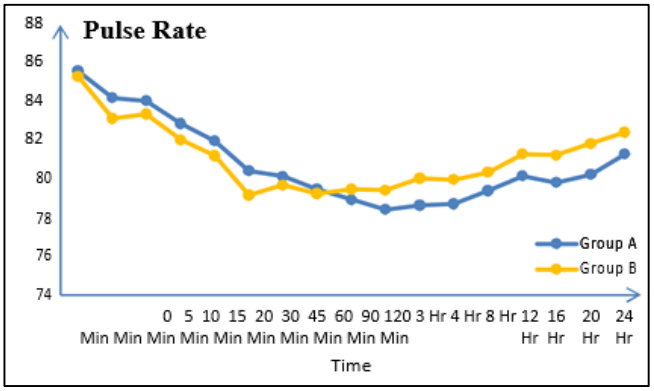


Graph 9: Comparison of mean VAS score between two groups

Table 10: *Comparison* of Pulse Rate between groups at different intervals

Pulse Rate (Bpm)	Group A		Group B		
	Mean	SD	Mean	SD	P value
5 Min	84.22	9.772	83.15	11.076	0.707
10 Min	84.07	10.561	83.37	11.063	0.363
15 Min	84.07	9.693	82.04	12.027	0342
30 Min	80.44	9.188	79.19	9.977	0.632
1 Hr	79.48	8.781	79.26	9.151	0.928
2 Hr	78.44	7.387	79.44	8.868	0.654
3 Hr	78.67	8.449	80.07	7.676	0.525
8 Hr	79.41	8.536	80.37	8.21	0.199
12 Hr	80.19	9.418	81.33	7.483	0.079
16 Hr	79.85	8.787	81.26	7.689	0.135
24 Hr	81.32	8.697	82.44	7.428	0.126

Pulse rate was measured at different intervals such as 5,10,15,30 minutes and 1,2,3,8,12,16 and 24 hours. Mean pulse rates at the above different times between the two groups are not significantly significant(p values >0.05)

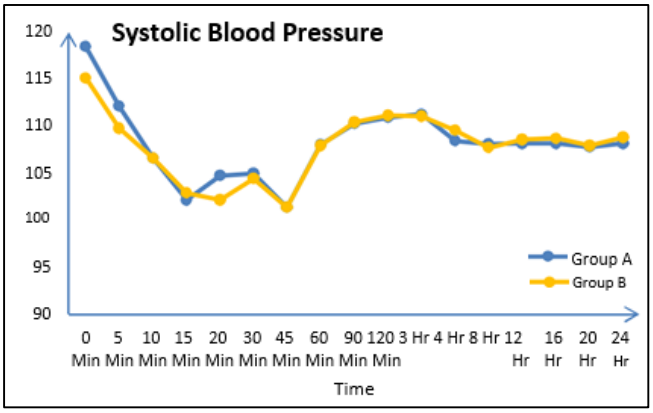


Graph 10: Comparison of mean pulse rate between two groups at different time intervals

Table 11: Comparison of Systolic blood pressure (SBP) between at different time intervals

SB P(mm Hg)	Group A		Group B		
	Mean	SD	Mean	SD	P value
5 Minutes	112.22	9.74	109.85	8.787	0.352
10 Minutes	106.67	8.771	106.67	6.794	1
15 Minutes	102.22	9.337	102.96	8.234	0.758
30 Minutes	105.04	11.319	104.52	8.368	0.849
1 Hour	108.07	15.674	108.00	13.989	0.985
2 Hour	110.96	15.406	111.19	12.677	0.954
3 Hour	111.33	15.252	111.11	13.107	0.954
8 Hour	108.15	8.338	107.78	7.511	0.864
12 Hour	108.22	6.641	108.59	8.924	0.863
16 Hour	108.22	7.197	108.74	8.93	0.815
24 Hour	108.85	7.197	108.89	9.74	0.776

The mean systolic blood pressure at different intervals such as at 5,10,15, 30 minutes and 1,2,3,8,12,16 and 24 hours are shown in the above table 10.There were no significant difference of mean SBP between the two groups.(p value > 0.05).

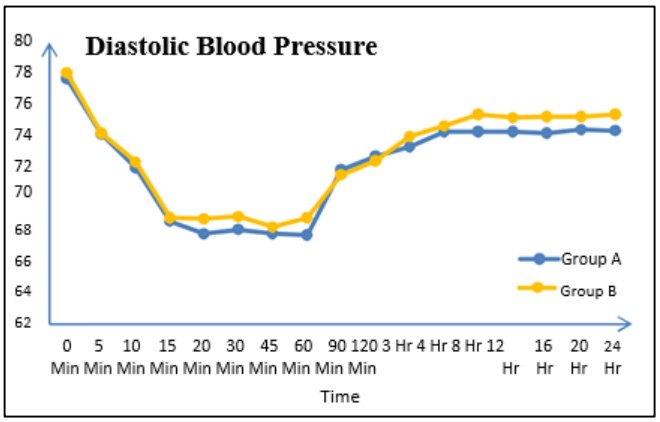


Graph 11: Comparison of mean SBP between two groups at different time intervals

Table 12: Comparison of Diastolic Blood Pressure between two groups at different time intervals.

DBP (mm Hg)	Group A		Group B		
	Mean	SD	Mean	SD	P value
5 Minutes	74.15	6.175	74.22	5.473	0.963
10 Minutes	72	7.338	72.37	7.767	0.858
15 Minutes	68.59	6.512	68.81	7.131	0.905
30 Minutes	68.07	6.263	68.89	6.009	0.628
1 Hour	67.7	7.01	68.81	5.955	0.533
2 Hour	72.74	6.472	72.44	6.381	0.866
3 Hour	73.33	6.102	74.00	4.532	0.65
8 Hour	74.3	5.539	75.41	5.010	0.443
12 Hour	74.3	5.967	75.19	5.144	0.56
16 Hour	74.22	6.135	75.26	4.904	0.496
24 Hour	74.37	5.845	75.41	4.766	0.478

The mean Diastolic blood pressure at different intervals such as at 5,10,15, 30 minutes and 1,2,3,8,12,16 and 24 hours are shown in the above table 10.There were no significant difference of mean DBP between the two groups.(p value > 0.05).

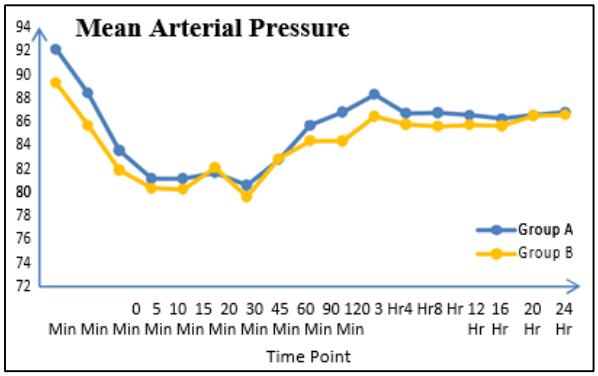


Graph 12: Comparison of Mean DBP between two groups at different time intervals

Table 13: Comparison of MAP (Mean Arterial Pressure) between two groups at different time intervals

MAP (mm Hg)	Group A		Group B		
	Mean	SD	Mean	SD	P value
5 Minutes	88.44	8.546	85.7	6.827	0.199
10 Minutes	83.56	9.345	81.93	6.725	0.465
15 Minutes	81.19	9.568	80.37	8.015	0.736
30 Minutes	81.67	10.385	82.11	7.361	0.857
1 Hour	82.78	11.298	82.85	10.053	0.980
2 Hour	86.85	11.162	84.37	8.554	0.363
3 Hour	88.33	11.014	86.44	8.030	0.475
8 Hour	86.78	9.287	85.63	7.581	0.621
12 Hour	86.56	8.963	85.74	8.254	0.730
16 Hour	86.26	8.869	85.67	7.590	0.793
24 Hour	86.81	8.691	86.59	7.677	0.921

The Mean arterial blood pressure at different intervals such as at 5,10,15, 30 minutes and 1,2,3,8,12,16 and 24 hours are shown in the above table 10.There were no significant difference of MAP between the two groups.(p value > 0.05)

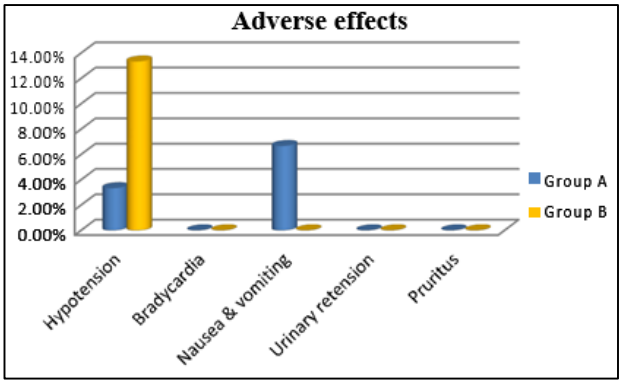


Graph 13: Comparison of Mean MAP between two groups at different time intervals

Table 14: Comparison of adverse effects occurred in two groups

Adverse effects	Group A	Group B	P value
Hypotension	1	2	0.299
Bradycardia	0	0	NA
Nausea & vomiting	2	0	0.150
Urinary retension	0	0	NA
Pruritus	0	0	NA

Hypotension was noted in both groups. Nausea and Vomiting was noted in group B only. No other adverse effects were seen.There were no significant association between two groups

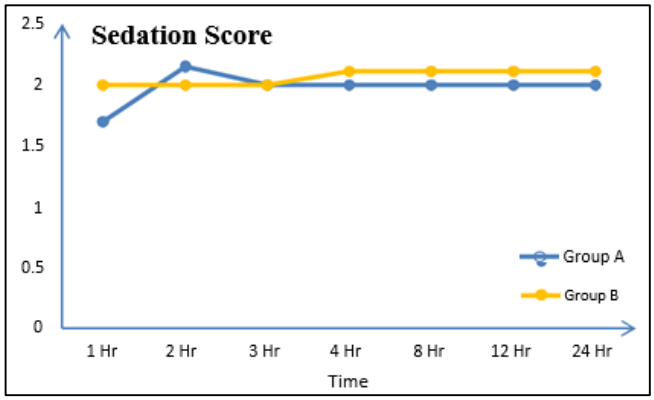


Graph 14: Comparison of mean adverse effects between two groups

Table 15: Comparison of sedation score between two groups

Sedation Score	Group A(Mean±SD)	Group B (Mean±SD)	P value
1 Hour	1.7 ± 0.465	2 ± 0	0.002
2nd Hour	2.15 ± 0.362	2± 0	0.038
3rd Hour	2 ± 0	2± 0	NA
4th Hour	2 ± 0	2.11± 0.32	0.077
8th Hour	2 ± 0	2.11± 0.32	0.077
12th Hour	2 ± 0	2.11± 0.32	0.077
24th Hour	2 ± 0	2.11± 0.32	0.077

Based on Ramsay Sedation Score both groups had mean grade 2 score. There were no significant difference of sedation between two groups



Graph 15: Comparison of Mean sedation score between two groups

Discussion

Over the years, extensive research have been done to improve the quality of spinal anaesthesia by varying drug regimens and technical methods. Normally adjuvants are added to hyperbaric bupivacaine 0.5% and administered intrathecally to prolong the anaesthetic effects. They produce antinociceptive effect by acting perineurally or at different receptor sites in the spinal cord.

Intrathecal opioids when used as adjuvants are capable of producing early onset of sensory, motor blockade and prolonged postoperative analgesia. They also allow early ambulation of patients due to their sympathetic and motor sparing activities.

Nalbuphine hydrochloride is a mixed μ antagonist and κ agonist opioid. It has been found to cause prolongation of the effects of local anaesthetics in intrathecal, epidural and peripheral nerve blocks with the advantages of minimal respiratory depression and better hemodynamic stability.

Fentanyl is potent agonist at μ opioid receptors. Fentanyl, like other opioid analgesics, depresses respiration in a dose-dependent manner. High dose Fentanyl anaesthesia also reduces or eliminates the stress response to surgery.

This prospective randomised controlled study performed in 54 patients who underwent infraumbilical surgeries under spinal anaesthesia. The demographic parameters like age and BMI were comparable. The mean age of the patients in the Group A (Nalbuphine) was 38.89±12.192 years. The mean age of the patients in the group B (Fentanyl) was 37.19±12.351 years. The mean BMI of the patients in the Group A (Nalbuphine) was 23.48±1.896 kg/m2 and the mean BMI of the patients in the Group B (Fentanyl) group was 24.68±1.787 kg/m2. The baseline vital parameters like heart rate(HR),Systolic blood pressure(SBP),Mean arterial Pressure(MAP) and peripheral oxygen saturation (SpO2) were recorded before the initiation of spinal Anaesthesia. These parameters were compared between the groups and found out that there were no significant difference.

In the present study, it was observed that the mean onset time of sensory blockade of Group A was 250.22±17.542 seconds and group B was 189.48±16.960 seconds.it was significantly differed (P < 0.001) in respect of their sensory onset with significant delay seen in group A. The mean onset time of

motor block was also delayed in group A. The onset time of motor block with Group A was 357.48±10.420 seconds and with group B was 343.56±8.317 seconds.it was significantly differed(P <0.001).

The sensory and motor block were checked after performance of subarachnoid block using pinprick and modified Bromage scale respectively. The mean duration of sensory and motor blocks between the two groups was significantly (p<0.001) differed from each other. The mean duration of sensory blockade (149.63±3.702 minutes) and motor blockade (199.52±7.778 minutes) of Group A was highest compared to group B in Sensory blockade (133.48±5.072 minutes) and Motor blockade (184.81±7.000 minutes).

The patients were followed in the postoperative period for the presence of pain by the Visual Analogue Scale. The VAS score of 4 is considered as the termination of analgesia. When the patients had a VAS score of 4, rescue analgesic (Tramadol 2 mg/kg) was given. The mean duration of analgesia in the group A (Nalbuphine) was found to be (329.63±37.157) minutes and in the group B (fentanyl) was found to be (270.74±24.207) minutes. Statistical analysis revealed significant p value (<0.001) and noted more duration of analgesia in Group A.

Hypotension occurred in 3 out of 54 patients, with group B>A(1 and 2),but were not statistically significant. Correction of hypotension required less than 10-15mg of ephedrine in incremental boluses. Otherwise the patients remained hemodynamically stable throughout perioperative period. The statistical analysis of the pre,intra and post-op hemodynamic variables such as PR, SBP, MAP and SPO2 between the two groups showed no statistically significant hemodynamic fluctuation. Nausea and Vomiting noted in two patients in group A. There were no other adverse effects noted in both groups .The post-operative sedation (Table-10 in group A and Group B exhibiting mean score of two. None of the patient showed signs of respiratory depression. So in post operative period patient is with adequate sedation which will reduce anxiety and pain.

Bisht S et al24. conducted a study by comparing intrathecal fentanyl 25 mcg and nalbuphine 1 mg added to 0.5 % Bupivacaine (3 ml) in 100 patients undergoing total abdominal hysterectomy. They observed the onset of sensory blockade in Nalbuphine group was 4.20±0.52 mins and in fentanyl group was 3.09±0.47 mins. They got onset of motor blockade in Nalbuphine group was 7.93±0.67 and in fentanyl group was 6.85±0.66. The duration of motor block was comparable in both the groups. The time to first analgesic requirement in nalbuphine Group was 460.78 ± 77.98 min compared to 283.44 78.97 min in fentanyl group. (p < 0.001). No statistical difference was seen in terms of adverse effects.It was concluded Although the time to onset and peak sensory level is longer with nalbuphine as intrathecal adjuvant than fentanyl, time for sensory level to regress by two segments and the postoperative analgesia time is longer with nalbuphine.

Dr. Rajkumar N Jaisinghani et al26 in his study compared 0.8 mg nalbuphine hydrochloride and 25 mcg fentanyl as adjuvant to 0.5% hyperbaric bupivacaine(3 ml) for 60 patients undergoing sub arachnoid block in lower limb surgeries. They observed that duration of postoperative analgesia was significantly longer with nalbuphine (318±13.88 min)as compared to fentanyl (296.26±13.31min). Total duration of motor block was significantly prolonged with nalbuphine (197.83±11.29min) as compared to fentanyl (186.80±11.49min). Onset of motor block was faster with fentanyl (354.23±33.36sec) than nalbuphine (374.20±27.62sec) This can be attributed to high lipid solubility of fentanyl. Total duration of sensory block was higher with nalbuphine (152.9±9.65min) as compared to fentanyl (145.87±6.02min) and this was statistically significant Nalbuphine hydrochloride is a better alternative as an adjuvant for postoperative analgesia and less side effects than fentanyl for lower limb surgeries.

Bhavana B et al25. conducted a study on Intrathecal Fentanyl (25 mcg) Compared to Nalbuphine (300 mg) with Bupivacaine in Spinal Anesthesia for Lower Abdominal Surgeries‖ they observed the onset of sensory blockade was 3.9 ± 0.35 min in nalbuphine Group and 3.1 ± 0.18 min in fentanyl Group . Two-segment sensory regression time was prolonged in Nalbuphine group(193.16 ± 39.55) compared to Fentanyl group (167.41 ± 30.17 min). There is a significant difference in the onset of sensory blockade in both groups . Rescue analgesia was given at 268.33 ± 44.44 min in nalbuphine group which was significantly prolonged as compared to fentanyl group in which rescue analgesia was given at 220.91 ± 24.36 min.it was concluded that Intrathecal nalbuphine at a dose of 300 µg in 3 ml 0.5% heavy bupivacaine in patients undergoing elective lower abdominal surgeries showed delay in onset time for sensory blockade and produced prolonged postoperative analgesia, prolonged sensory blockade, and minimal bradycardia which could be easily managed.

Jaideep Singh et al27. compared between Intrathecal Nalbuphine (0.8mg) and Fentanyl (25 mcg) in 60 patients.The onset of complete sensory and motor block was more rapid with fentanyl than nalbuphine and this was statistically significant (p<0.05).In the study they concluded that both Nalbuphine or Fentanyl in combination with low dose hyperbaric bupivacaine (15mg) are equally efficacious and haemodynamically stable in patients undergoing lower limb surgeries. However, Nalbuphine with comparatively prolonged post operative analgesia and effective analgesia time and lesser side effects is a better adjuvant than Fentanyl for intrathecal injections of Bupivacaine 0.5%(H) in surgeries undergoing spinal anaesthesia.

The results of the present study, when compared to the studies of the authors discussed above, have similar outcome with respect to the onset and duration of sensory and motor block, the duration of analgesia and better postoperative sedation with stable hemodynamic profile.

Table 13: Present study Results

	Group A	Group B	P value
OSB(seconds)	250.22±17.542	189.48±16.960	<0.001
OMB(seconds)	357.48±10.420	343.56±8.317	<0.001
DSB(minutes)	149.63±3.702	133.48±5.072	<0.001
DMB(minutes)	199.52±7778	184.81±7.000	<0.001
Duration of Analgesia (minutes)	329.63±37.157	270.74±24.207	<0.001

OSB - Onset of sensory blockade, OMB – Onset of motor blockade, DSB - Duration of sensory blockade,DMB – Duration of motor blockade

Table 14: Study results of Bisht S et al [24]

	Group A	Group B	P value
OSB(seconds)	4.20±0.86	3.09±0.47	<0.001
OMB(seconds)	7.93±0.67	6.85±0.66	<0.001
DSB(minutes)	97.72±9.50	88.88±9.48	<0.001
Duration of Analgesia (minutes)	460.78±77.98	283.44±78.97	<0.001
OSB - Onset of sensory blockade, OMB – Onset of motor blockade,			
DSB - Duration of sensory blockade			

Table 15: Study results of Dr. Rajkumar N Jaisinghani et al [26]

	Group A	Group B	P value
OMB(seconds)	374.20±27.62	354.23±33.36	<0.001
DSB(minutes)	152.9±9.65	145.87±6.02	<0.001
Duration of Analgesia (minutes)	318±13.88	296.26±13.33	<0.001

Table 16: Study results of Bhavana B et al [25]

	Group A	Group B	P value
OSB(minutes)	3.9±0.35	3.1±0.18	<0.001
DSB(minutes)	193.16±39.55	167.41±30.17	<0.001
Duration of Analgesia(minutes)	268.33±44.44	220.91±24.36	<0.001

OSB - Onset of sensory blockade, OMB – Onset of motor blockade, DSB - Duration of sensory blockade, DMB – Duration of motor blockade.

Conclusion

Nalbuphine hydrochloride 1 mg compared to Fentanyl 25 mcg when added as an adjuvant to hyperbaric bupivacaine 0.5% in subarachnoid block for infraumblical surgeries had a slower onset of sensory and motor blockade. The two segment dermatome regression time and duration of motor blockade was prolonged in Nalbuphine group. The duration of postoperative analgesia was also significantly increased in nalbuphine group. There was no increase in the risk of side effects like pruritus, hypotension, bradycardia and urinary retention.

Limitations of the Study

This Study is conducted among ASA I and II patients only. The effects of Nalbuphine and Fentanyl on high risk patients is not evaluated.

This Study is conducted among patients between 18 to 60 years of age only. The effects in extremes of ages is not evaluated.

Any failed Subarachnoid blocks during study to be excluded from study (Conversion to General anesthesia or other alternatives). But fortunately we did not faced any such cases.

Further studies are required to study efficacy of higher doses to know the benefits or complications.

Future of the study

Studies may be done to find out whether a higher dose of fentanyl in Subarachnoid block will further improve the duration of sensory and motor block with better post operative pain management and if it is associated with any side effects. Further studies are required to study the analgesic efficacy of different modalities in combination with Subarachnoid block, and ideal treatment regimen to control postoperative pain following infra umbilical surgeries.

Summary

Comparison of efficacy and hemodynamic stability of intathrecal Nalbuphine and Fentanyl as an adjuvant to hyperbaric bupivacaine for infraumbilical surgeries under subarachnoid block was evaluated using a prospective, double-blinded, randomized controlled trial. After institutional ethical and scientific committee clearance, fiftyfour patients belonging to ASA physical status I and II, scheduled for infra umbilical surgery was selected for the study. Patients were divided into two groups of twentyseven each. Randomization was done by computer generated random number. After getting a written informed consent, all patients were pre-medicated with T.Alprazolam on the previous day of surgery and kept nil per oral for over 6 hours. On day of surgery all basic monitors were connected, and the patents were pre-hydrated with 15ml/Kg Ringer's Lactate. After taking a baseline reading of vitals, patients belonging to Group A received - 0.5% hyperbaric bupivacine 3 ml (15mg) + Nalbuphine 1 mg in 0.5 ml normal saline. And patients belonging to Group B received 0.5% hyperbaric bupivacine 3 ml (15mg) + Fentanyl 25 µg .

During the intra operative period vitals (SBP, DBP, HR,SPO2) were recorded every for 1 minute for first 5 minutes, every 5 minutes till half an hour and every 15 min till the end of the procedure.

The onset of actions sensory and motor blocks were accessed by pin prick and modified bromage scale respectively. The total duration of sensory and motor blocks were also accessed by 2 segment regression of sensory blockade and by modified bromage scale respectively.

Observed values were systematically documented. Demographic profile, basal vitals, total duration of surgery were normally distributed and hence were analyzed using unpaired t test. Onset of action of sensory and motor blocks, duration of actions of sensory and motor blockade and hemodynamic parameters like heart rate, Systolic blood pressure and Diastolic blood pressure at different intervals were not normally distributed and hence, were analyzed using Repeated measures ANOVA.

It was found that demographic profile, duration of surgery and basal vital parameters were comparable in both groups. There was a statistically significant difference between the two groups in terms of onset of actions of sensory and motor blocks with group A having a longer duration for onset of actions of both sensory and motor blocks. There was also a statistically significant difference noted between two groups in terms of durations of action of sensory and motor blocks with group A having a significantly prolonged duration of actions of both sensory and motor blockade.

Hemodynamics as seen with Heart rate, Systolic blood pressure and Diastolic blood pressure is significantly stable with both groups, Nausea and vomiting and hypotension are reported but were not statistically significant. These observations suggest that, the addition of intrathecal Fentanyl had significantly faster onset of sensory and motor blockade and intrathecal Nalbuphine has prolonged duration of sensory and motor blockade with appropriate level of sedation.

In the study concluded that Nalbuphine hydrochloride 1 mg compared to Fentanyl 25 mcg when added as an adjuvant to hyperbaric bupivacaine 0.5% in subarachnoid block for infraumblical surgeries had a slower onset of sensory and motor blockade. The two segment dermatome regression

time and duration of motor blockade was prolonged in Nalbuphine group. The duration of postoperative analgesia was also significantly increased in nalbuphine group.

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