"EFFICACY OF INTRATHECAL FENTANYL-BUPIVACAINE(H) AND BUPRENORPHINE-BUPIVACAINE(H) ON THE ONSET AND DURATION OF BLOCKADE AND LEVELS OF SEDATION IN LOWER ABDOMINAL SURGERIES – A ONE YEAR HOSPITAL BASED RANDOMIZED CONTROL TRAIL

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ENDORSEMENT

This is to certify that the dissertation entitled **"EFFICACY OF INTRATHECAL FENTANYL-BUPIVACAINE(H) AND BUPRENORPHINE-BUPIVACAINE(H) ON THE ONSET AND DURATION OF BLOCKADE AND LEVELS OF SEDATION IN LOWER ABDOMINAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMIZED CONTROL TRAIL"** is a bonafide research work done by **(REG NO.BA0119012)** Department of Anaesthesiology, Jawaharlal Nehru Medical College, Nehru Nagar, Belagavi – 590 010.

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LIST OF ABBREVIATIONS USED

SAB	-	Subarachnoid block
ASA	-	American society of Anaesthesiologists
CNS	-	Central nervous system
$O_{2\backslash}$	-	Oxygen
CVS	-	Cardiovascular system
RS	-	Respiratory system
DBP	-	Diastolic blood pressure
ECG	-	Electrocardiogram
GIT	-	Gastrointestinal tract
Hb	-	Haemoglobin
HR	-	Heart rate
PR	-	Pulse rate
Inj.	-	Injection
IV	-	Intravenous
Kgs	-	Kilograms
L	-	Liters
Mg	-	Milligrams
Mins	-	Minutes
Ml	-	Milliliters
µg	-	Micrograms
MPG	-	Mallampati Grading
RBS	-	Randombloodsugar
RR	-	Respiratory rate

SBP	-	Systolic blood pressure
SPO_2	-	Saturation percentage of oxygen
Temp	-	Temperature
TLC	-	Total Leucocyte count
α	-	Alpha
β	-	Beta
NSAIDs	-	Non steroidal anti-inflammatory drugs
MAP	-	Mean Arterial Pressure
DBP	-	Diastolic Blood Pressure
SBP	-	Systolic Blood Pressure
T	-	Thoracic vertebral level

ABSTRACT

Background : Opioids are been used as adjuncts to Subarachnoid Block since 1979. Neuraxial opioids when added to local anaesthetics hasten the onset of action,prolong the duration of motor and sensory block and improves quality of perioperative analgesia. But adding these opioids has some adverse effects too - most common among them being sedation.The present prospective randomized study was under taken to compare two opioids –fentanyl and buprenorphine with bupivacaine(hyperbaric) 0.5% in lower abdominal surgeries.

Methods : After obtaining ethical committee clearance, eighty four patients belonging to ASA I&II ,aged 18-65years were allocated into two groups.All patients were given SAB with 3.0ml of 0.5%Bupivacaine(H) and the first group received Fentanyl 12.5mcg(0.25ml) as an additive while the second group received Buprenorphine 75mcg(0.25ml)as an additive. The onset, duration of sensory and motor blockade ,sedation and hemodynamic parameters were monitored.

Results: Onset of sensory and motor block was faster in fentanyl group (i.e.1 and 3minutes respectively)as compared buprenorphine group(i.e 3 and 5minutes respectively). Duration of analgesia was significantly prolonged in buprenorphine group.It was 285.71±16.25minutes and 238.1±24.32 minutes respectively for buprenorphine and fentanyl groups.Levels of sedation was higher in buprenorphine group when compared to fentanyl group(Wilson's sedation score 2 and 1 respectively).

Conclusion : Based on this study, it may be concluded that – intrathecal admistration of Bupivacaine-Fentanyl requires lesser time for onset of sensory and motor block, but lesser duration of motor block and total duration of block, with faster requirement of rescue analgesia when compared to intrathecal Bupivacaine-Buprenorphine group. However more extensive studies are needed to comfirm the diagnosis.

Keywords : Subarachnoid block,adjunct, opioids, fentanyl,buprenorphine

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INTRODUCTION

The most commonly used anaesthetic technique in lower abdominal surgeries is Subarachnoid Block (SAB). The first SAB was performed in 1889 by Augustus Bier- he used cocaine as the anaesthetic agent and with the beginning of 1940- SAB was regularly used. Hence its been decades since regional anaesthesia especially SAB has gained extensive popularity in developing and developed countries on account of its good outcome. SAB is a form of regional anaesthesia where conduction block of nerve roots is achieved by injecting 10-20mg of local anaesthetic solution into subarachnoid fluid using lumbar puncture. [1]

The most commonly used regional anaesthesia is the neuraxial blockade. The endocrine-metabolic response to surgeries seem to blunted with SAB (or even epidural anaesthesia) as compared to general anaesthesia, thus making it the most accepted mode of anaesthesia in surgeries.

Prolonging the duration of sensory and motor blockade is becoming more important for certain procedures. Prolonging the duration of sensory blockade helps in relieving post-operative pain. [2]

Since the development of neuraxial anaesthesia technique numerous local anaesthetics such as cocaine, procaine, tetracaine, etidocaine, lignocaine, bupivacaine were studied for their effects.

Previously hyperbaric lignocaine5% was used for SAB , but its use declined due to risks of cauda equina syndrome and transient neurological symptoms. Hence the preferred drugs for SAB include bupivacaine and ropivacaine.

Bupivacaine an aminoamide local anaesthetic is a highly potent hydropobic drug. The conduction blockade is dependent on concentration or dosage of local anaesthetic. But it has many disadvantages as a result of sympathetic and motor blockage resulting in hypotension, bradycardia and immobility.(2)

Thus, the duration of action and the hemodynamic instability can be improved by using adjuvants like opioids, ketamine, midazolam , alpha-2 agonists and few other drugs like magnesium sulphate has also been tried - opioids being most popular. (1)

Opioid analogues have been used as additives in SAB to hasten the onset of action , prolong the block duration and to improve the quality of perioperative analgesia. The frequently used opioids include fentanyl and buprenorphine.

But adding these opioids has some adverse effects too - most common among them being SEDATION. Thus, it is important to know the level/grade of sedation caused by this type of regional anaesthesia.(3)

Thus, the present study was underataken to compare two opioids –fentanyl and buprenorphine with bupivacaine(hyperbaric) 0.5% in lower abdominal surgeries.

OBJECTIVES

Primary objective:

1. To compare the onset and duration of sensory and motor blockage between 0.5% Bupivacaine (H) with Fentanyl (12.5mcg) and buprenorphine (75mcg) respectively.

2. To compare the level of sedation caused by intrathecal opioids- fentanyl and buprenorphine (using "Modified Wilson Scale")

Secondary objective :

To evaluate the hemodynamic changes and evaluate other associated complication.

REVIEW OF LITERATURE

SAB became the most well-established mode of anaesthesia by mid-1940. SAB is a form of regional anaesthesia where conduction block of nerve roots is achieved by injecting local anaesthetic solution into subarachnoid fluid using lumbar puncture. It causes complete analgesia with muscle relaxation(profound) and small contracted bowel. When SAB was found to be safe in expert hands- it became one of the most sorted technique for lower abdominal procedures- like hernia repairs, gynaecological, urological, perineum or genital procedures. (1)

Dr August bier was the first scientist to perform a planned subarachnoid block 1989 - 16th August , by injecting 3 milliliters of *0.5% Cocaine* in a man posted for surgery. He further tested the efficacy in six other patients, posted for lower limb surgeries. He further decided to experiment (PDPH) on himself and his assistant Dr Otto Hildebrandt. Dr Bier experienced post dural puncture headache, following which he experimented on Dr Hildebrandt. He used cocaine for the spinal anesthesia on his assistant, studied the effects on his lower extremities. Dr A Bier studies the response to needle pricks, cuts on thigh, avulsion of pubic hair, torsion of testicles on his assistant, for which he reported to have minimal to no pain sensation. He experienced nausea, vomiting, PDPH, bruising and agony in the leg subsequently, which was further described by Bier to be caused by the loss of CSF. He further analysed that using small – gauge needles might decrease the incidents of PDPH. (2)

SAB has many advantages – ease of administration and rapid onset of action. The main disadvantage are its limited duration of action and hence lack of post-operative analgesia without the use of adjuncts.

Local anaesthetics are either isobaric , hyperbaric or hypobaric. Isobaric solution can be converted to hyperbaric adding dextrose to the solution. Arthur Barker, was a lecturer of

surgery at London University, who described the progression of spinal anesthesia procedures in 1907, comprising the usage of a hyperbaric local anesthetic, importance of the sterile techniques, and the comfort of using midline techniques over the paramedian approach for spinal anesthesia.

Barker's needle was sharp, average length bevel with a stylet, it lacked the inner cannula and was made up of nickel. Labat manufactured a sturdy nickel needle with sharp and short bevel, with stylet to reduce the tissue damage during the procedure. Spinal anesthesia has advanced significantly since 1885 and is now being used most frequently and effectively. Nevertheless, the anatomy of the spinal cord, the type of local anesthetic used, physiologic properties of the drug and the spinal anesthesia along with patient factors like the positioning and the approach also affects the spinal anesthesia considerably.

Sergio D Belzarena in 1992 evaluated the efficacy of intrathecal Fentanyl in patients undergoing caesarean section with variable doses. He stated that adding low dose of Fentanyl (25 mcg) to Bupivacaine provides excellent anesthesia with increased postoperative analgesia and minimal side effects.[4]

Reuben SS, Dunn SM et al in 1994 December performed a dose response study in 60 patients undergoing elective lower limb extremity revascularisation under spinal anesthesia. Patients were divided randomly into six groups each receiving either 0/5/10/20/40/50 microgram of fentanyl diluted with normal saline to make the final volume up to 1ml, through the spinal catheter postoperatively. In their study they did not use any local anesthetic. It was a combined spinal technique using a Teflon catheter. They observed that the dose of analgesia started with 20 micrograms and higher concentration of fentanyl, patients experienced the onset of satisfactory analgesia. They also observed that the duration of analgesia followed dose dependent increase up to 40

mcg of Inj.fentanyl and increasing the dose to 50-micrograms group provided no better analgesia. Increasing the dose of the fentanyl was associated with pruritis which was seen in five of ten patients. [5]

Yet another study done in 2006 by Fauzia Bano et al. J Coll Physician Surg. Pak. studied the effect of adding Fentanyl to intrathecal Bupivacaine 0.5%. 60 female patients belonging to ASA I & II undergoing elective LSCS under SAB was randomly selected and were divided into 2 groups receiving Bupivacaine 0.5% with either 0.25ml of NS or 0.25ml of Fentanyl. The duration and quality of SAB and its effects on the patient were observed. The conclusion drawn was that addition of Fentanyl to intrathecal Bupivacaine results in faster onset with improved peri-operative analgesia without increasing the side effects. [6]

Seewal,Shende et al in 2007 started a dose response study with addition of various doses of fentanyl intrathecally to 0.5% bupivacaine on patients posted for lower abdominal surgery belonging to ASA II and I. They included 60 patients and randomly allocated them in 5 groups and were administered 2.2 ml of hyperbaric Bupivacaine with saline as control and variable doses of Fentanyl 10,20,30,40 mcg in other groups. The volume of the drugs was kept constant by adding saline. They observed that Inj Fentanyl at a dose of 10 mcg intrathecally, was appropriate for non-obstetric cases. It significantly improved the post op analgesia. They also observed that on increasing the dose to 40mcg of Fentanyl had no further advantage. [7]

A different study done by Nemethy in 2010, Maria assessed the sedation caused by regional analgesia using a scale called as Modified Wilson Sedation Scale. [8] This scale will be used in assessing the level sedation in the patients assessed in this study

In a study done by Arvinder Paul Singh, Kaur R, Kumari A in 2016 compares Fentanyl (0.2ml) and Buprenorphine (0.2ml) used as adjunct to Ropivacaine 0.75% as the

combination drug used in SAB in lower limb surgeries. The trail was done on 90 ASA I and ASA II patients aged between 18-60yrs. They were randomly divided into 3 groups I- receiving Ropivacaine 0.75% with 0.2ml of NS, II- receiving Ropivacaine 0.75% with 0.2ml of Fentanyl and III- receiving Ropivacaine 0.75% with 0.2ml Buprenorphine. The onset and duration of sensory and motor blockade & haemodyanamic parameters were monitored. They concluded that both Fentanyl and Buprenorphine prolong the duration of motor and sensory blockade compared to Ropivacaine alone and that Buprenorphine is better than Fentanyl in prolonging the duration of blockade. [(9)]

In a study done by Kamal, Sonya, Davies C V in January 2017 compares intrathecal 0.5% Bupivacaine(H) with 25mcg of Fentanyl and intrathecal 0.5% Bupivacaine with 75mcg of Buprenorphine in caesarean section.60 patients belonging for ASA I and II , between 18-35 years of age , posted for elective LSCS were chosen and divided into two groups Group F receiving Fentanyl as adjunct to SAB and group B receiving Buprenorphine as adjunct to SAB. The onset, maximum level and duration of sensory and motor blockade and haemodynamic parameters were monitored. They concluded that although fentanyl produces faster sensory block, duration of anaesthesia is longer with buprenorphine. [(10)]

Another study done in 2017 by Binu Sajid, Konnanath Ramadas &Indu Susheela compares the various doses of Buprenorphine for analgesia in caesarean section. 90 patients belonging to either ASA II & I undergoing elective LSCS, aged between 20-35yrs and weight of 45-75kgs were selected and divided into 3 groups A- receiving 45mcg of Buprenorphine, B- receiving 60mcg of Buprenorphine & C- control. The onset of sensory block level up to T4, peak of sensory level and intra-operative haemodynamic status was all monitored. The duration after which post-operative

analgesia was required was also observed. Levels of sedation in each group was recorded as it was one the most common side effects of Buprenorphine. They concluded that maximum duration of analgesia and decreased analgesia requirement without significant increase in adverse drug reactions was seen with 60mcg of Buprenorphine. (11)

Yet another study done in 2019 by Abate SM , Belihu AE in Saudi compared the addition of fentanyl to bupivacaine against plain bupivacaine in 552 patients undergoing LSCS. They observed that there was lower incidence of hypotension with addition of fentanyl rather than using plain bupivacaine intrathecally.(12)

In another study done by Sandhya A Bakshi, Anuradha Digambar Kulkarni, Dipak Kumar Hiralal in 2020 compared use of intrathecal adjuncts buprenorphine and clonidine against plain bupivacaine in 108 patients undergoing Abdominal Hysterectomy. They concluded that buprenorphine is preferred over clonidine as an adjuvant as there was better intraoperative haemodynamic stability (despite the bradycardia that was seen) and prolonged period of postoperative analgesia. (13)

Basic Sciences

Applied anatomy

Knowledge about the vertebral column's anatomy and its contents remains vital for all anaesthesiologists for safe and efficacious administration of SAB- in terms of spread of the drug and the level of the blockage achieved.

Vertebral Column

Foremost function of vertebral column is to shield the Spinal cord. There are about 33 vertebrae which includes:

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

Curvature of vertebral column

Curves of spine have a momentous effect on the spread of drugs in subarachnoid space and these curves include:

- Cervical curve - anterior convexity
- Thoracic curve- anterior concavity
- Lumbar curve - anterior convexity

Highest point of curves – C5 and L5

Lowest point of curves –T5 and S2

Vertebral ligaments

- Supraspinous ligament : strong fibrous band connecting apies of spinous processes from scarum to cervical five where it continues as ligamentum nuchae
- Interspinous ligament: thin membranous ligament which connects spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament
- Ligamentum flavum: this ligament comprises yellow elastic fibres and connects adjacent lamina. Laterally this ligament begins at the root of articular processes and extends posteriorly and medially to the point where laminae join to form spinous process
- Longitudinal ligaments: there are two longitudinal ligaments (anterior and posterior) that bind vertebral bodies together

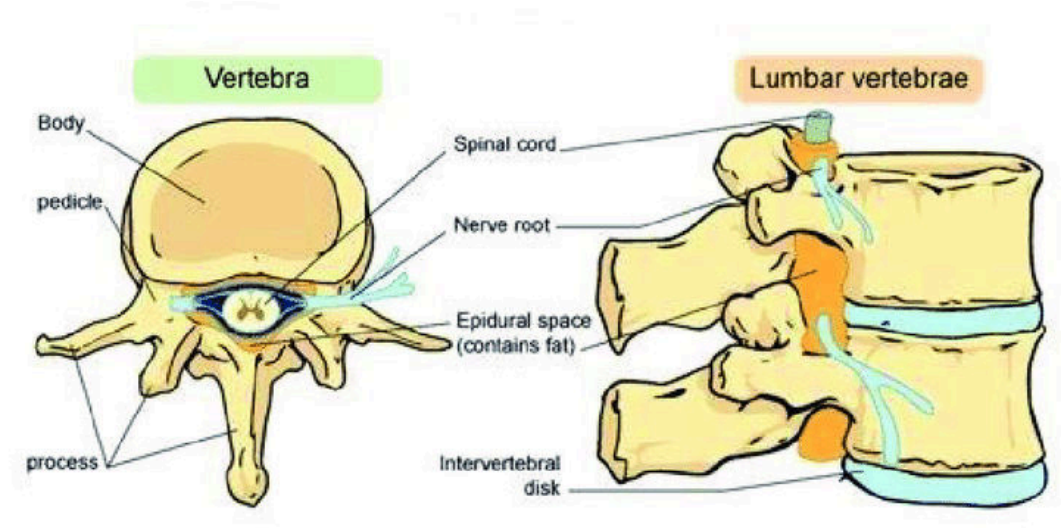


Figure 1: Vertebral column

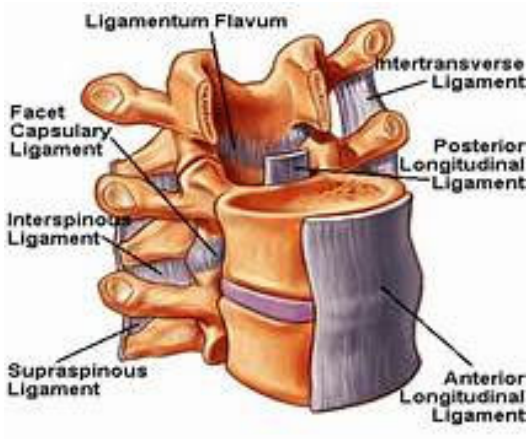


Figure 2: Spinal Ligaments

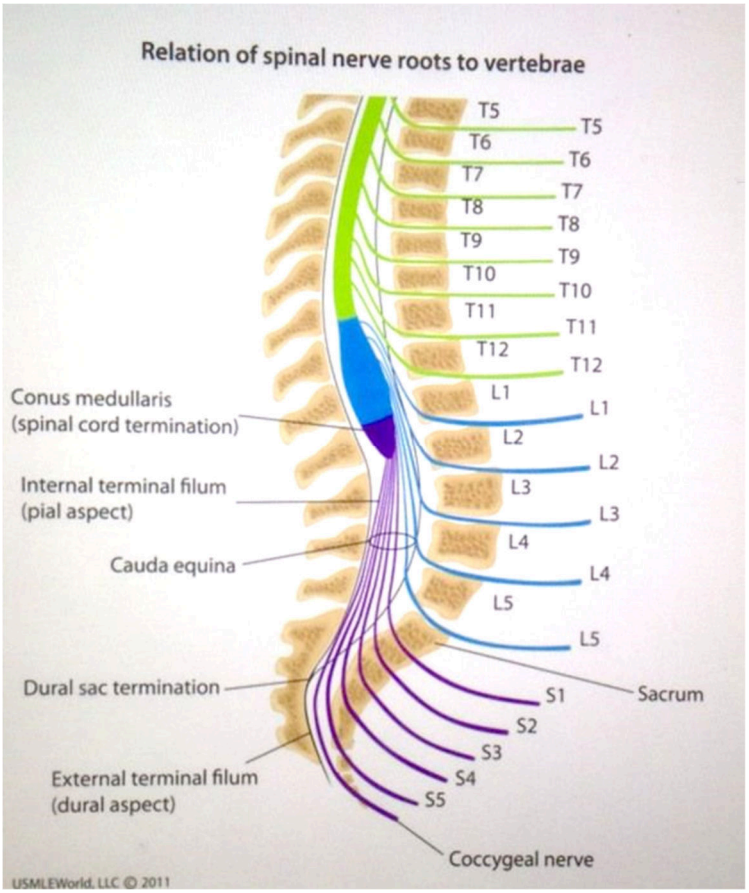


Figure 3: Spinal nerve roots

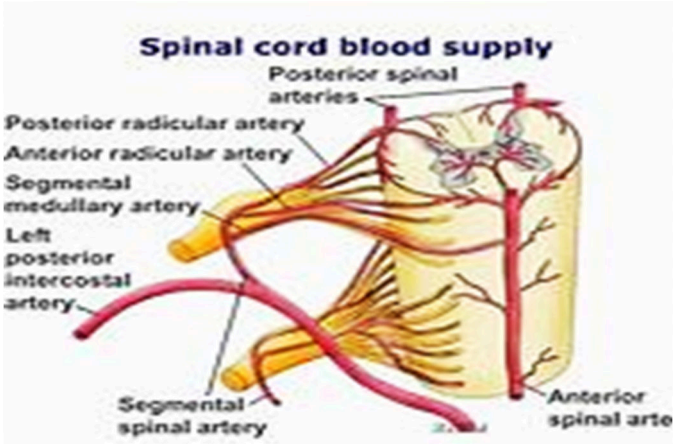


Figure 4: Blood supply

Intervertebral discs

These discs connects vertebral bodies. They forms about 25% of the length of the spine. They have two parts. The outer fibrous part called the annulus fibrosus is made up fibrous tissue, while the nucleus pulposus is the softer core.

Topographical line of Tauffier

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

Lumbar vertebrae

- A kidney shaped body
- Two pedicles directed backwards from the upper part of the body
- Two transverse processes
- Two laminae meeting posteriorly and enclosing the triangular vertebral foramen
- Spinous processes which are thick, broad and quadrilateral in shape
- Two upper and lower articular processes which prevents rotation but allow limited flexion and extensive between contiguous vertebrae [(1)]

Vertebral canal

Spinal cord – spinal nerve roots – meninges – cerebrospinal fluid – vessels – fat – loose areolar tissue

Spinal cord

Length of spinal cord : male-45cm ; female- 42cm

Weight of cord- 30g

It is the continuation from medulla oblongata below the level of foramen magnum and tapers off into a conical extremity known as conus medullaris.

Filum terminale descends to the back of first segment of coccyx from apex of conus medullaris [(1)]

At birth,spinal cord ends at the level of lower border of lumbar (L)three vertebra

In adults-1. 50% cases at lower border of Lumbar (L)1

2. 40% cases at upper border of Lumbar (L)2

3. 3 % cases at upper border of lumbar (L)3

31 pairs of spinal nerves arises from the spinal cord- ventral and dorsal root. The anterior and posterior roots after crossing the SAS, passes through the dura and extradural space independently and unite at the level intervertebral foramen forming spinal nerve trunk, which then divides into posterior and anterior primary divisions. White matter amount decreases from cervical down to lumbar region. Grey matter on the other hand is increased in both lumbar and cervical enlargement. [(2)]

Blood supply of spinal cord

Arterial supply- anterior and posterior spinal arteries. The anterior spinal artery lies in the anterior median fissure. Anterior spinal artery is formed by 2 arteries- one given off each vertebral artery at the level of foramen magnum. It receives

small communications from the intercostal and lumbar arteries provide the extra blood supply needed in the cervical, thoracic and lumbar enlargements.

2 posterior spinal arteies- 1 on each side. They are derived from vertebral artery or more often from a primary branch of each vertebral artery. They supply the posterior one-third of the spinal cord.

Venous drainage- is through a plexus. Plexus consists of anterior and posterior veins in the neck, azygous veins in the thorax, lumbar veins in the abdomen and lateral sacral veins in the pelvis.

Longest feeder artery – radicularis magna that supplies anterior spinal artery in the area of lumbar enlargement of the cord. (1)

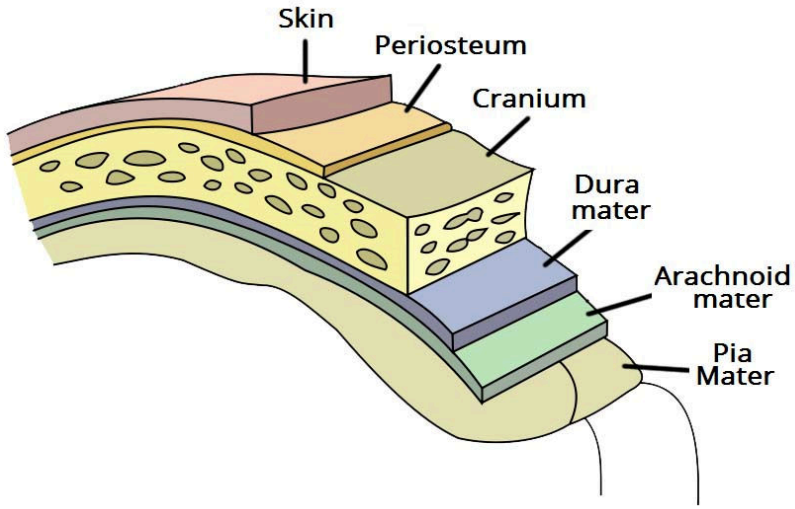


Figure 5: Meninges

Meninges

The meninges refer to the **membranous** coverings of the brain and spinal cord. There are three layers of meninges,known as the **dura** mater, **arachnoid** mater and **pia** mater.

These coverings have two major functions:

- Provide a **supportive framework** for the cerebral and cranial vasculature.
- Acting with cerebrospinal fluid to **protect** the CNS from mechanical damage. (11)

Dura mater

The dura mater – outermost layer of the meninges.Lies just below the bones of skull and Vertebral column. It is thick, tough and inextensible.

Within cranial cavity, dura has 2 connective tissue sheets:

- Periosteal layer: lines the inner surface of the bones of the cranium
- Meningeal layer: deep to periosteal layer inside the cranial cavity.It is the only layer present in the vertebral column.

Between these 2 layers, dural venous sinuses are located. They are responsible for the venous vasculature of the cranium, draining into the internal jugular veins.

It receives blood supply – Primarily from the middle meningeal artery and vein. It is innervated by Trigeminal nerve(V1,V2 & V3). (1)

Arachnoid Mater

The arachnoid mater is the middle layer of the meninges, lying directly underneath the dura mater It consists of layers of connective tissue, is **avascular**, and does not receive any innervation.

Underneath the arachnoid is a space known as the **sub-arachnoid space**. It contains cerebrospinal fluid, which acts to cushion the brain. Small projections of arachnoid mater into the dura (known as **arachnoid granulations**) allow CSF to re-enter the circulation via the dural venous sinuses (1)

Pia mater

The pia mater is located underneath the sub-arachnoid space. It is very thin, tightly adhered to the surface of the brain and spinal cord. It is the only covering to follow the contours of the brain (the gyri and fissures)

It is also highly vascular like dura . [3]

Cerebrospinal Fluid

Cerebrospinal fluid (CSF), clear, colourless liquid that fills and surrounds the brain and the spinal cord and provides a mechanical barrier against shock.

Formed primarily in the ventricles of the brain, the cerebrospinal fluid supports the brain and provides lubrication between surrounding bones and the brain and spinal cord. When an individual suffers a head injury, the fluid acts as a cushion, dulling the force by distributing its impact. The fluid helps to maintain pressure within the cranium at a constant level. An increase in the volume of blood or brain tissue results in a corresponding decrease in the fluid. Conversely, if there is a decrease in the volume of matter within the cranium, as occurs in atrophy of the brain, the CSF compensates with an increase in volume. The fluid also transports metabolic waste products, antibodies, chemicals, and pathological products of disease away from the brain and spinal-cord tissue into the bloodstream. CSF is slightly alkaline and is about 99 percent water. There are about 100 to 150 ml of CSF in the normal adult human body

Composition :

Volume : 120 – 150ml (25-35ml in spinal space)

Specific gravity : 1.003 – 1.009 (37 degree Celsius)

CSF pressure: 60-80 mm Hg in lumbar space

pH :7.27-7.37

PCO2:48mmHg

HCO3: 23mEq/L

Sodium :135-145 mEq/L

Magnesium : 2-2.5mEq/L

Chloride : 15-20 mEq/L

Calcium : 2-3mEq/L

Phosphorous : 1.6mg/dl

Proteins : 23-38mg/dl

Physiology of Subarachnoid Block

Spread ,duration ,density and dose are the two most important factors that determine the spread and duration of subarachnoid anesthesia. Density is the ratio of the mass of a substance to its volume. Baricity is the ratio of two densities; here, the density of CSF and that of the injected local anesthetic. Currently used local anesthetics are made hyperbaric by mixing with dextrose. Plain local anesthetic solutions are isobaric or slightly hypobaric.

Hyperbaric local anesthetics are denser than CSF and will flow with gravity to the dependent areas of the spine, usually the upper thoracic region in supine patients. Positioning patients upright or lateral can limit the initial spread of hyperbaric local anesthetic. But, when the patient returns to the supine position, even after 20 to 30 minutes, the sensory level reaches the usual mid-thoracic dermatomes. Bulk displacement determines the initial spread of isobaric drug. Subsequently, movement of CSF by either transmission of cardiac pulsations or gross patient movements (i.e., turning from lateral to supine position)will determine the ultimate spread of block. In nonpregnant patients, hyperbaric local anesthetics produce more consistent levels of

sensory block than isobaric drug . When used for subarachnoid anesthesia for cesarean section, there is little difference between equal doses of isobaric or hyperbaric bupivacaine. (1)

CENTRAL NERVOUS SYSTEM

The exact site of action of subarachnoid remains unknown. Local anesthetic can be detected throughout the spinal nerve rootlets and spinal cord after intrathecal injection. Intrathecal local anesthetics reduce, but do not routinely eliminate, somatosensory evoked potentials (SSEPs). Cortical evoked potentials from direct spinal cord stimulation diminish but persist. These results suggest that some block of spinal cord conduction occurs but that subarachnoid anesthesia occurs mostly within the spinal nerve roots. (2)

Differential Nerve Block- Neuraxial local anesthetics have different potencies on motor, sensory, and sympathetic nerves. This differential block is largely related to the size of different nerves. Large motor nerves (and larger lumbar and sacral nerve roots) are most resistant to local anesthetic block. Analgesia (loss of sensation of sharpness to pinprick) extends two or more segments more cephalad than anesthesia (loss of sensation to touch). Sympathetic block (as measured by increase skin temperature) may extend as many as six spinal segments higher than the upper limit of sensory block. (11)

CARDIOVASCULAR SYSTEM

Intrathecal injection of local anesthetics produces extensive sympathetic block. Cardiac output increases after induction of subarachnoid anesthesia and that a fall in systemic vascular resistance leads to lower blood pressures. The degree of hypotension varies widely among patients. Risk factors include pregnancy, hypovolemia, advanced age, obesity, concurrent general anesthesia, and sensory level above T6. Heart rate may increase, decrease, or remain unchanged. Thoracic levels of anesthesia can produce

cardiac sympathetic block (T1–T4). The resultant vagal predominance can decrease heart rate.

GARTROINTESTINAL SYSTEM

Neuraxial anesthesia-induced sympathetic block leads to unopposed vagal stimulation of the gastrointestinal system. Secretions increase, sphincters relax and the bowel constricts. Many patients experience nausea and vomiting. Risk factors for nausea and vomiting include: female gender, opioid premedication and high level of block. (1)

SPLEEN

Enlarges 2-3 times in high blocks when its sympathetic efferent fibres are paralysed. Colonic blood supply and oxygen availability are increased in animals following spinal anaesthesia, an important factor in preventing anastomotic breakdown following gut resection.

LIVER

No effects of major significance

ENDOCRINE SYSTEM

SAB delays adrenal response to injury and trauma, so the is no change in 17-hydroxy corticosteroids

SAB depresses the hyperglycaemic response to surgery and stress and so is useful in diabetic patients. The response to insulin is augmented-hypoglycaemia.

GENITOURINARY SYSTEM

Sympathetic supply to kidney is from T11 to L1 via lower splanchnic nerve. Any changes in renal blood flow is due to hypotension

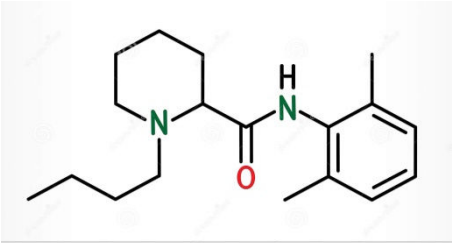
Postspinal retension of urine may be prolonged as S2 to S3 contain small autonomic fibres and their paralysis lasts longer than that of larger sensory and motor fibres.

UTERUS

No effect on tone of uterus. Small dose of LA required because of decreased extradural space in prgnancy.

BODY TEMPERATURE-Vasodilatation favours heat loss.

BUPIVACAINE



Bupivacaine

Bupivacaine hydrochloride, chemically known as [1-butyl-N-(2, 6-dimethylphenyl) piperidine-2-carboxamide] belong to the amide group of local anesthetics. It was first synthesized in 1957.

Properties of Bupivacaine:

• Racemic mixture

• Crystalline white amorphous powder soluble in water

• Amide

• Molecular weight – 325

• pka - 8.2

• Plasma protein binding - 96%

• pH of saturated solution - 5.2

• Specific gravity - 1.021 at 37°C

MECHANISM OF ACTION

Similar to other local anesthetics, Bupivacaine binds to the specific receptors' sites on the voltage gated sodium channels. It blocks the Na+ current and reduces the

excitability of the nerve cells. It causes blockade of the nerve conduction by inhibiting the passage of sodium ions through the channels in the neuronal membranes. This decreases the permeability of the sodium channel which in turn decreases the rate of depolarization. As the threshold potential is not reached, action potential fails to develop. Local anesthetics has no effect on the resting transmembrane potential or threshold potential.

The mechanisms explaining the blockade of the sodium channels are:

a) As the drug is deposited near the nerve terminals, the local anesthetics in its ionised forms attaches to the receptors on cell membrane and block the channels. By selectively binding to the sodium channels in its inactivated - closed states, it makes the channel impermeable to the sodium. It hinders the conduction of nerve impulses as the action potential fails to generate.

b) The second mechanism includes the membrane expansion which include nonspecific drug and receptor interaction.

Pharmaco- kinetics:

Absorption:

The absorption of the local anesthetic drugs depends on various factors which includes site and vascularity of the area, dose, and additives. The addition of a vasoconstrictor to the local anesthetic delays the absorption of the Bupivacaine and thereby prolongs the duration of action. There is faster rate of absorption in the vessel rich areas then less vascular areas.

Distribution:

- It is readily distributed throughout the body with a volume of distribution of 72 litres. The clearance is 0.47 lit / min.
- T ½ α (uptake is done by rapid equilibrium in the tissues): 2- 7 mins.

- T ½ β (distribution to the slow perfused tissue) : 28 mins
- T ½ γ (Due to metabolism and elimination) : 3-5 hrs

Metabolism & Excretion:

Bupivacaine undergoes N-dealkylation and hydroxylation in the liver which is further conjugated to form and metabolized in the liver. Here it undergoes N-dealkylation, aromatic hydroxylation amide hydrolysis and then conjugated to form a water-soluble compound. The N-dealkylated metabolite N-desbutylbupivacaine has been measured in blood or urine after being administered under spinal anesthesia. Excretion is done through the kidneys.

Bupivacaine is available in various concentrations:

1. 0.25%, 0.5% and 1% 2. 0.5% solution in 8% dextrose – heavy

The recommended dose of Bupivacaine is 2mg/kg, maximum up to 150 mg in 4 hrs.

Duration of action (without adrenaline) – 120 to 200 mins.

Effects on various organ system:

CENTRAL NERVOUS SYSTEM

At higher doses, it causes CNS depression as it readily crosses the blood brain barrier. Overdose of the drug might lead to dizziness, visual and auditory problems for e.g. tinnitus, inability to concentrate. As Bupivacaine is highly lipophilic, smaller doses of the drug if accidently administered intravascular might lead to toxic effects.

AUTONOMIC NERVOUS SYSTEM

Bupivacaine does not have sympathetic accentuating activity as it does not inhibit the noradrenaline uptake. Myelinated preganglionic β fibres are more sensitive to the effects of Bupivacaine and have faster rate of conduction. The sensory fibres are blocked more effectively than the motor fibres.

CARDIOVASCULAR SYSTEM

Bupivacaine cause decrease in the rate of depolarization of the neurons in the purkinje fibre and the ventricles. There is slower rate of recovery with Bupivacaine which in turns leads to incomplete restoration of V-max between the action potentials. This explains the arrhythmogenic potential of Bupivacaine. Bupivacaine blocks the calcium channels and interrupts the calcium transport. This results in decrease in cardiac contractility. Higher doses of Bupivacaine produce vasodilatation while vasoconstriction is seen at lower doses.

Respiratory system:

Respiratory depression any be seen with higher level of drug. There is respiratory paralysis associated with paralysis of the respiratory muscles and the diaphragm in cases of high spinal or total spinal anesthesia. CC/CNS dose ratio for Bupivacaine is 3.7 ± 0.5 μg which accounts for higher incidence of Irreversible cardiovascular collapse. [1]

OPIOIDS

The term opioid is related to all the compounds derived from the opium, whereas Opium is derived from the term Opos, which is Greek word for juice. Opium is derived from the plant Papaver somniferum. It was first described in the literature by Theophrastus during the 3rd century. The plant is used to derive more than 20 different kind of alkaloids. Serturner in the year 1806, isolated a pure alkaloid and named Morphine after the Greek god Morpheus. By mid-19th century, pure alkaloids were readily used in the medical fraternity.

OPIOID RECEPTORS

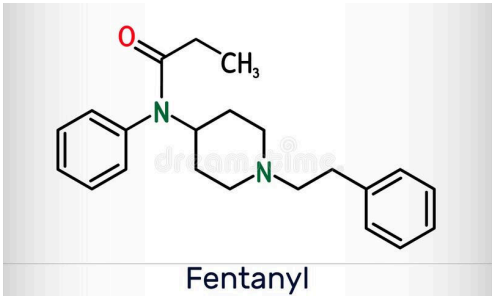
Opioid receptors were classified into three groups, according to the radioligand binding assays in 1973 and were termed μ for the morphine group, κ for the ketocyclazocine group, and σ for the SKF10047 (N-allylnormetazocine) group. δ-receptor were the group of high affinity receptors for enkephalins and was discovered in vas deferens of mouse. Another ε-receptor was thought to be the binding site for β-endorphin which was also found to be present in the vas deferens of the mouse.

MECHANISM OF ACTION OF OPIOIDS

The opioids exert its action at both spinal and supra spinal levels. The majority of the receptors are present at the substantia gelatinosa in the dorsal horn of the spinal cord. The supra spinal actions are mediated through the descending inhibitory pathways. In substantia gelatinosa, the receptors are present mainly on the presynaptic terminals of the primary afferent sensory neurons. Some of the receptors are also present on the post synaptic dendrites of the inter neurons. These neurons regulate the spinothalamic transmissions. The presynaptic neurons hinder the release of various neurotransmitters including substance P, glutamate etc, whereas the post synaptic receptors inhibit the

evoked excitatory post synaptic potential also known as EPSP. The μ and Δ receptors act on the potassium channels and facilitates the opening of the receptors, which further leads to the hyperpolarisation. It also leads to the reduced neuronal firing. It reduces the action potential plateau and thereby reducing the calcium influx and the neurotransmitter release. Contrary to the above-mentioned receptors, κ receptors, shuts the calcium channels

FENTANYL



Fentanyl citrate is a synthetic opioid belonging to the group phenylpiperidine. The IUPAC nomenclature is [N-(1-(2-Phenylethyl)-4-piperidinyl)-N-phenyl propenamide]. It was first synthesized by Dr Paul Jennsen, a Belgian chemist in 1960. Structurally it is related to pethidine and it is 75 to 125 times more potent than Morphine.

Routes of administration

1. Oral as syrup or lozenges
2. Intravenous route – most commonly used mode of administration.
3. Epidural route
4. Intrathecal route
5. Intranasal route
6. Dermal Patches

The onset of action is 1-2min after intravenous administration, with a duration of action of approximately 60 mins. The onset is immediate after epidural administration, while it is up to 5 mins after intrathecal administration. The duration of action after intrathecal administration may last up to 3- 5 hours. Due to its highly lipid soluble property, it has greater potency and rapid onset of action. It has rapid redistribution to the inactive tissues, making the duration of action shorter. The effective analgesic concentration of Fentanyl is between 1-3mcg/kg- higher doses are associated with decrease in the ventilatory response to the carbon dioxide.

MECHANISM OF ACTION OF FENTANYL:

Fentanyl is a highly selective synthetic μ receptor agonist. It has greater analgesic properties than Morphine, Pethidine and Alfentanil. The interaction of Fentanyl with μ receptors at the supraspinal site is mainly responsible for the analgesia. Interaction with κ receptors produces spinal analgesia, sedation, and anaesthesia. Metabolism: Fentanyl is metabolised in liver to form inactive metabolites by N-dealkylation. It produces nor-Fentanyl and after further hydroxylation, it is degraded to hydroxypropionyl derivatives. It strongly binds to alpha-1-acid glycoprotein and albumin.

Absorption and distribution:

Fentanyl has a bioavailability of 33% through oral route. It is 80-94% bound to the plasma proteins.

The volume of distribution is 0.88-4.4 L/kg.

Excretion:

The clearance of Fentanyl is 0.4-1.5 L/min and the elimination half-life is around 1.5- 6 hrs. 10% of the drug is excreted in the urine. The clearance is affected and decreased in patients with hepatic insufficiency.

Analgesic efficacy: The minimal analgesic dose of Fentanyl is 0.011 mg/kg, with therapeutic index of 323 and pka of 8.4.

The onset of action and the duration of action of the drug depends upon the route of drug administration.

Effects on various organ system:

CARDIOVASCULAR SYSTEM:

Fentanyl causes stimulation of the central nucleus, thereby causing bradycardia. The decrease in the heart rate is primarily dose- dependent and also depends on the speed of injection. It causes reduction in systemic vascular resistance, which further causes decrease in the blood pressure. It is often associated with decrease in heart rate. Fentanyl causes decrease in speed of A.V conduction and it prolongs the R-R interval. There is decrease in A-V node refractory period and the duration of purkinje fibre action potential. It is rarely associated with histamine release. The bradycardia associated with fentanyl is of vagal origin.

RESPIRATORY SYSTEM:

Fentanyl at doses 1-2 mcg/kg decreases the respiratory rate and increase the tidal volume. At higher doses, greater than 3 mcg/kg, Fentanyl decreases both the respiratory rate and the tidal volume. The ventilatory drive to the hypoxia and the hypercarbia is decreased. Fentanyl has antitussive property. Chest wall Rigidity, also known as "Wooden chest" phenomenon, primarily seen after rapid intravenous administration of large doses of Fentanyl. It is due to the effect of the drug on the μ receptors, which are located on the GABA interneurons. Intrathecal administration has not shown such side effects. It can be controlled with early use of the muscle relaxant during the induction of anesthesia.

CENTRAL NERVOUS SYSTEM

Fentanyl depresses the central nervous system. At lower doses of 1-2 mcg/kg Fentanyl is devoid of any hypnotic and sedative effects. The effects are more on intravenous administration of the drug than the intrathecal administration. There is miosis due to the stimulation of the Edinger Westphal nucleus. Fentanyl, in higher doses above 30 μg/kg

IV, causes change in the somatosensory evoked potentials. It causes slight rise in the intracranial pressures with decrease in the mean arterial pressure and the cerebral perfusion pressures.

GASTROINTESTINAL SYSTEM:

It causes decrease in the intestinal motility and may result in constipation. There is increase in the tone of sphincter of Oddi and biliary ducts.

ENDOCRINE EFFECTS:

It is more effective than morphine in blunting the stress response. It modulates the nociception at various levels of the neural axis, also it influences the centrally mediated neuroendocrine response.

RENAL EFFECTS:

It has minimal effects on the renal function.

ADVERSE EFFECTS:

Fentanyl causes bradycardia, hypotension, and respiratory depression at dose dependent manner. There are incidences of pruritis, urinary retention, post-operative shivering, nausea, and vomiting. Delirium and seizures might be seen at higher doses. Pruritus is one of the commonest complications. It can be generalized, preferably on face, neck, and thorax. The drug moves into the cerebrospinal fluid with further cephalad migration and it interacts with the trigeminal nucleus. The “itch-reflex” is initiated due to the interaction of the opioid with the substantia gelatinosa through its indirect action on the trigeminal nucleus located in the medulla. The complaints of PONV is around 30% more in women than in men. Urinary retention is usually seen in young males, with incidence 0-80% depending on the dose administered. It occurs primarily due to the interaction of the drug with the opioid receptors. It inhibits the sacral parasympathetic nerves leading

to the detrusor muscle relaxation and further causing retention of urine. Respiratory depression seen with Fentanyl is rare following intrathecal administration.

There might be incidences of delayed respiratory depression after 2 hours following the drug administration in dose dependent manner.

Indications:

• During induction of anesthesia, to blunt the intubation stress response.

During SAB for hastening onset & prolonging duration of block

• During cardiovascular surgeries.

• For postoperative analgesia

• In labor analgesia

• Used for sedation for patients on mechanical ventilators.

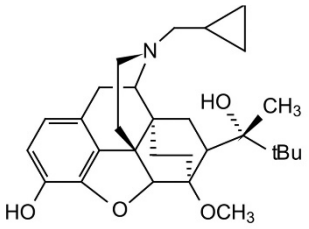
Contraindications:

Patients with bronchial asthma and neuromuscular disorders like Myasthenia gravis, patients who are receiving MAO inhibitor within 14 days, patients with known case of Bronchial asthma

Antagonist:

Naloxone is the drug of choice for opioid toxicity, along with mechanical ventilation to support respiratory depression. Symptomatic treatment is done for pruritis and nausea vomiting. Patients are catheterised in view of opioid induced urinary retention.

BUPRENORPHINE



buprenorphine

Buprenorphine is a derivative of thebaine, an alkaloid found in opium poppies (Papaver somniferum).

Buprenorphine also has the following characteristics:

• Classified as a partial mu agonist, kappa antagonist, nociceptin agonist. As a partial agonist, its effects increase only to a certain point with increased dose, and level off at moderate doses, thus contributing to its being abused less than full agonists.

• A potent analgesic, used in low doses to avoid side effects. Formulations include intravenous or intramuscular (Buprenex) and transdermal (Butrans®).

• Mildly reinforcing, which improves treatment adherence and, therefore, clinical effectiveness compared with antagonist treatment

• Limit on the maximum effect that can be achieved. However, the ceiling effect may not apply to the analgesic effect .

BIO-AVAILABILITY, METABOLISM, EXCRETION

Bio-availability The bio-availability of buprenorphine varies depending on the route of administration .

- Oral (Swallowed) → Very rapidly metabolized and poor bio-availability
- Sublingual (Absorbed Transmucosally) → Skips first pass metabolism, so significantly better bioavailability
- Intrathecal at a dose of 60mcg or 75mcg has been found to be effective

- Dermal patches- are also found to be very effective
- IV and IM not so commonly used routes

METABOLISM AND EXCRETION

Buprenorphine is primarily metabolized in the gastrointestinal tract and the liver, using the CYP 3A4 system. Most buprenorphine metabolites are excreted fecally rather than through renal excretion. As a result, buprenorphine is relatively safe for patients with renal insufficiency.

MATERIALS & METHODS

SOURCE OF DATA- Patients in the age group of 18-65years belonging to ASA Grade I and II scheduled for elective infraumbilical surgeries at KLE's Dr.Prabhakar Kore Hospital and Medical Research Centre & KLE's Dr.Prabhakar Kore Charitable hospital

TYPE OF STUDY: Randomised control study.

DURATION OF STUDY AND STUDY POPULATION: Patients of both sexes between age group of 18 year to 65 years belonging to ASAI and ASAII between January 2020 to December 2020 undergoing elective surgeries at KLE'S Dr. Prabhakar Kore charitable hospital and Medical Research Center, Nehru Nagar, Belagavi- 590010 will be recruited as per inclusion and exclusion criteria.

INCLUSION CRITERIA:

- Patients undergoing elective infraumbilical surgeries lasting 45 - 90minutes
- Age : 18-65 years
- ASA Grade I and II patients
- Patients giving consent
- Weight ----> 50-75Kg
- Height -----> 150-175cm

EXCLUSION CRITERIA:

- Hypovolemic patients
- Uncooperative patients
- Patients with spinal deformity
- Contraindication to spinal anaesthesia
- Pregnant patients.

- Pre-existing neurological deficits in the lower extremities and CVS, RS, CNS, psychological ,

  hepatic/ renal disease.

After obtaining the approval of ethical committee and written informed consent, a total of **84** patients undergoing elective infraumbilical surgeries under SAB will be included in the study.

SAMPLE SIZE CALCULATION

Sample size formula:

The minimum sample size formula based on mean and standard deviation is

$$n = \frac{(z_\alpha + z_\beta)^2 (s_1^2 + s_2^2)}{(\bar{X}_1 - \bar{X}_2)^2}$$

where z_α is linked with the level of significance and z_β is linked with the power of the test. For 5% level of the significance $z_\alpha = 1.96$ and $z_\beta = 0.84$ for 80% power of the test.

Ref:

$\bar{X}_1$ is the mean of the first group (249) and $\bar{X}_2$ is the mean of the second group (296).

s_1 is the standard deviation of the firstgroup (72) and s_2 is the standard deviation of the second group (81).

With these values the sample size obtained is 42.

There will be two groups having 42 cases in each sample.

Randomization in 2 steps

0.5% Bupivacaine (H) with 25mcg Fentanyl group →**42**

0.5% Bupivacaine (H) with 75mcg Buprenorphine group →**42** [10]

Randomization achieved by Computer based/generated randomized chart After considering inclusion and exclusion criteria and having obtained informed consent,

patients will be randomly divided with the help of computer generated randomization table into one of the two groups.

- Group A
- Group B

A through *Pre-anaesthetic evaluation* will be done. Detailed medical and personal history will be obtained. A detailed physical examination will be done. Routine investigations- CBC, RBS, S.Creatinine, Blood grouping and typing, CXR, ECG to be done. Patients will be asked to be fasting overnight. Advise patient to take T.Alprazolam 0.25mg and T.Pantoprozole 40mg on the day before surgery.

In preoperative holding area, a IV access will be secured and patients will be preloaded with RL 10ml/Kg half an hour before induction of anaesthesia.

Inside operation theatre - standard non-invasive monitors will be attached such as as pulse oximeter , ECG , non-invasive BP and baseline HR, BP and spO_2 will be recorded. Patients will be then put in either sitting or lateral position and under strict aspectic precautions , L_2-L_3 is space identified.Skin infiltrated with 2ml of 2% Lignocaine. Using 23G/25G Quincke's spinal needle SAB given after confirming free flow of clear CSF.

Group A - 3ml of 0.5% hyperbaric Bupivacaine with 0.25ml (12.5mcg) of Fentanyl making a total volume of 3.25ml of drug is injected in L_2-L_3 SAS.

Group B - 3ml of 0.5% hyperbaric Bupivacaine with 0.25ml (75mcg)of buprenorphine making a total volume of 3.25ml of drug is injected in L_2-L_3 SAS.

Patient should immediately be put in supine position.

Intraoperative& Postoperative assessments are performed.

The following parameters are measured :

Sensory Blockade

Assessed by using a needle or spirit swab along the mid-axillary line every minute till the T10 level is reached- this is noted as the time taken for the onset of action. The highest level reached is also noted. Surgery is allowed to start after the T10 dermatome is blocked . The sensory blockade assessed once in every 15mins .

If the SAB does not act (waited for 30 min) and GA or any other type of anaesthesia is given the case is excluded from the study.

Motor Blockade

Assessed using Modified Bromage Scale

Bromage 3(complete)- Unable to move feet or knees

Bromage 2(almost complete)- Able to move feet only

Bromage 1(partial)-just able to move knees

Bromage 0 (none)-Full flexion of knees and feet

Motor blockage onset-Time taken to reach Bromage grade3

Total duration of motor blockade is the time taken to return back to Bromage grade 3 to 0. [1]

If the Bromage 3 is not attained then the highest grade reached is noted

Sedation

Following onset during the time under anesthesia level of sedation in patient is graded using Modified Wilson Sedation Scale. [8]

1 – Oriented, eyes may be closed but can respond

2 –Drowsy , eyes closed , arousable only to command

3-Arousable to mild physical stimulation (earlobe tug)

4- Unarousable to mild physical stimulation

Post-operative Analgesia

After surgery the time when the first rescue analgesia given is noted. (Inj.Diclofenac 75mg in 100ml NS is given)

Vitals

HR, BP , SpO_2 will be noted throughout the surgery every 15 mins

Hypotension is defined as a decrease in the systolic BP by 20% from the baseline values/systolic BP less than 90mm Hg . It is treated with bolus fluid administration , if still low, then mephentermine 6-12 mg is used to treat.

Bradycardia –decrease in HR less than 50bpm & is treated with IV atropine 0.6mg.

Supplemental Oxygen will be given through face mask.

Other Side effects :Any other side effects observed is documented

STATISTICAL ANALYSIS

The study is focused on comparison of two groups. For the continuous quantitative variables mean and standard deviation will be calculated. The inter group continuous variables will be compared using suitable tools of statistics like unpaired student's t test. Two quantitative variables, within a group, will be compared using student's paired t test.

Discrete variables will be represented by median. Suitable graphs will be used to depict the comparison.

The categorical data will be expressed in terms of rates, ratios and percentages. The association between the outcome, clinical and demographic characteristics will be tested using Chi-square test or Fisher's exact test.

For all the tests the value of p less than 5% (0.05) will be considered significant.

RESULTS

One year hospital based study, conducted in KLES Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi between January 2020 to December 2020 .

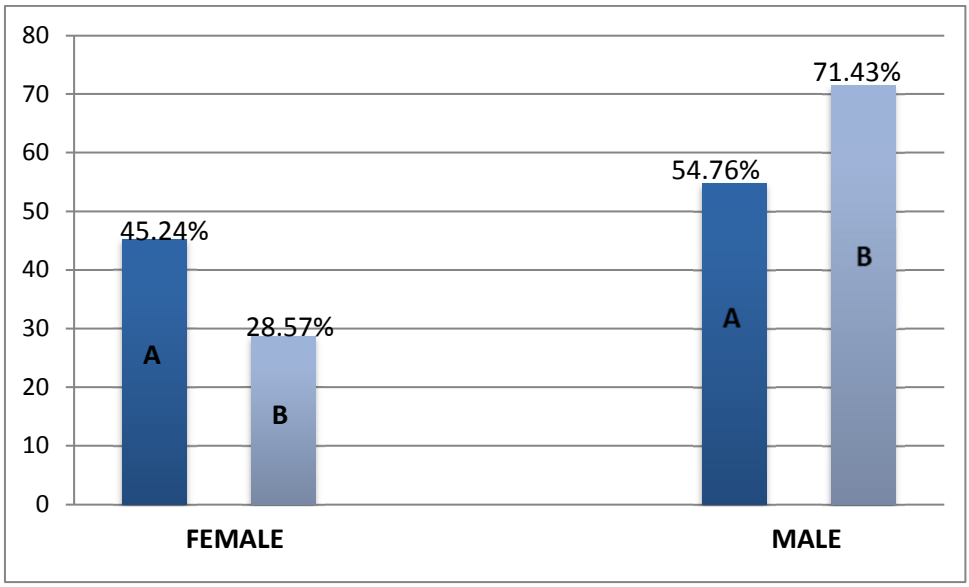
Totally 84 patients of ASA Grade I & II, aged between 18 to 65 year of either gender were distributed into two groups of 42 each. Group A receiving Fentanyl 0.25cc(12.5mcg) plus Bupivacaine 0.5% (H) 3.0cc and Group B receiving Buprenorphine 0.25cc(75mcg) plus Bupivacaine 0.5%(H) 3.0cc.

The study results are tabulated, analyzed and the observations and results are discussed below.

Table 1.Sex distribution

GENDER	GROUP A	Percentage	GROUP B	Percentage
FEMALE	19	45.24	12	28.57
MALE	23	54.76	30	71.43
TOTAL	42	100.00	42	100.00

GRAPH 1: SEX DISTRIBUTION

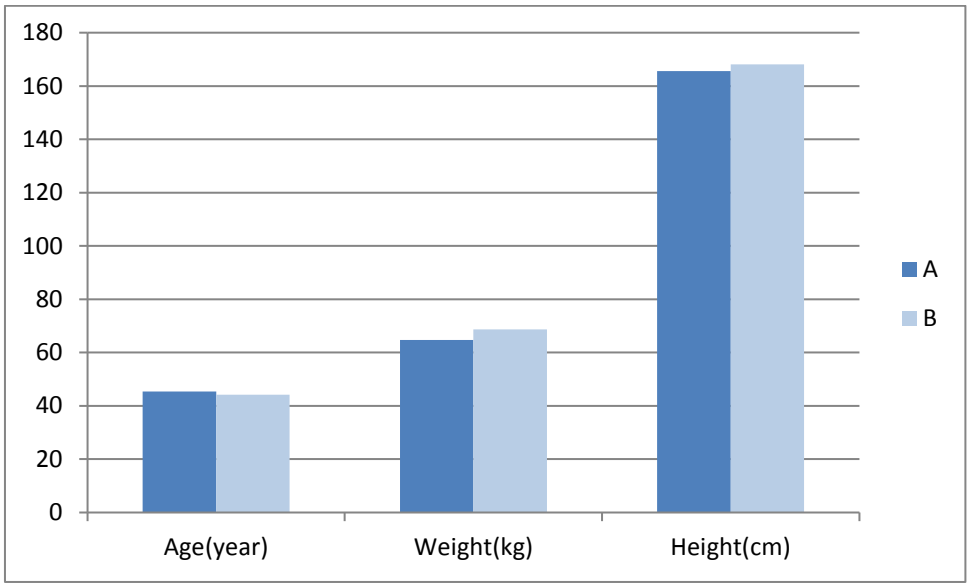


In this study, 45.24% of patients are females in Group A compared to 28.57% in Group B, 54.76% of patients are males in Group A compared to 71.43% in Group B. The male to female ratio was 1:0.83 in Group A and 1:0.4 in Group B. However the sex distribution in group A and B was comparable(p=0.81).

TABLE 2. MEAN AGE & ANTHROPOMETRY DISTRIBUTION

VARIABLES	GROUP-A		GROUP-B		p value
	MEAN	SD	MEAN	SD	
AGE (year)	45.33	15.16	44.21	15.12	0.7357
WEIGHT (kg)	64.74	11.32	68.67	8.18	0.0720
HEIGHT (cm)	165.62	4.65	168.12	3.54	0.069

GRAPH 2: MEAN AGE AND ANTHROPOMETRY

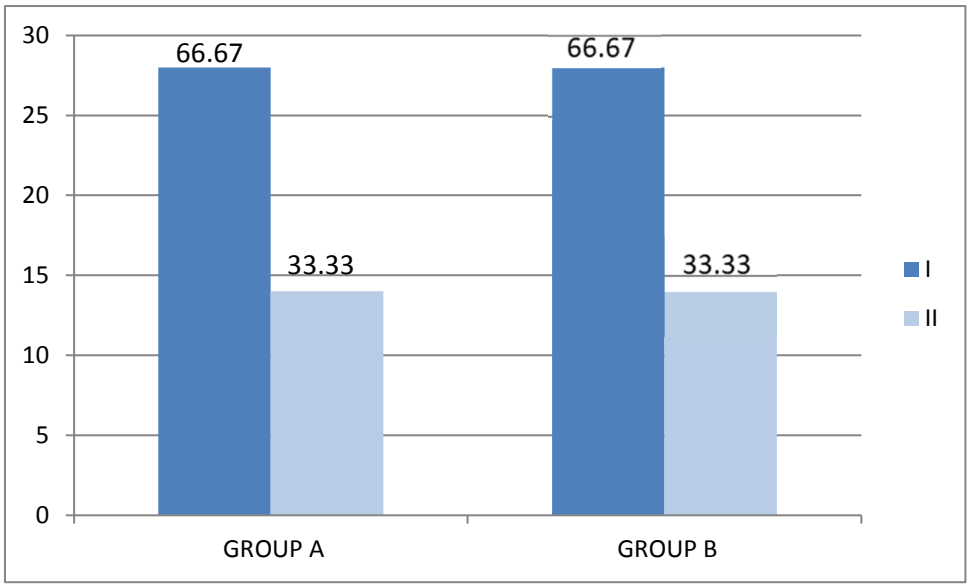


In this study, Group A and B with regards to mean age (45.33±15.16 and 44.21 ± 15.12 year respectively; p= 0.7357) , mean weight (64.74±11.32 and 68.67±8.18 kg respectively; p= 0.0720)and mean height(162.62±4.65 and 168.12±3.54 cm respectively; p=0.069), no statistical difference was observed with regards to age, weight and height.

TABLE 3. ASA GRADE

ASA	GROUP A		GROUP B	
	Number	Percentage	Number	Percentage
I	28	66.67	28	66.67
II	14	33.33	14	33.33
TOTAL	42	100.00	42	100.00

GRAPH 3: ASA GRADE

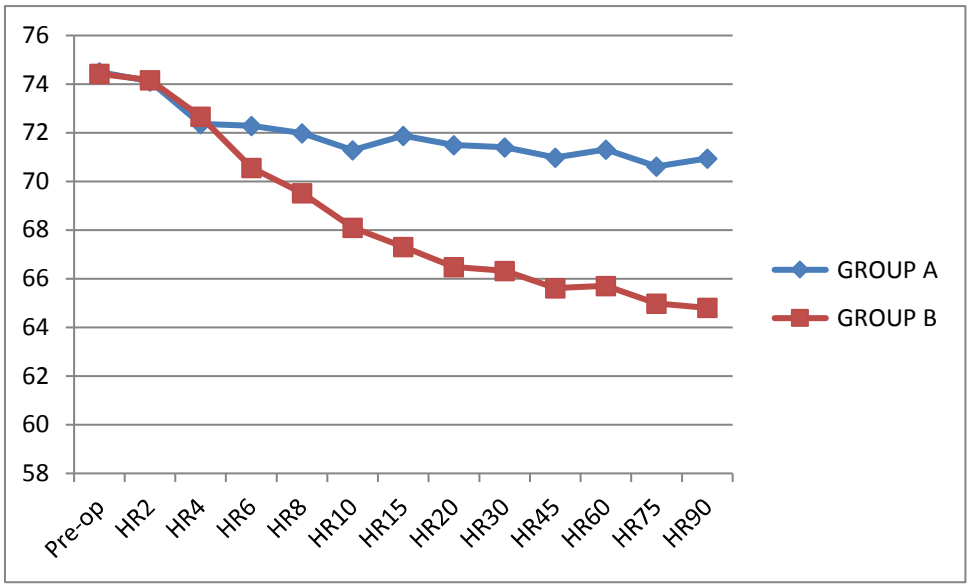


In this study, group A have 66.67% of participants belonging to ASA I and 33.33% to ASA II and group B have 66.67% of participants belonging to ASA I and 33.33% to ASA II, therefore there is no statistical difference between the two groups.

TABLE4: COMPARISON OF MEAN HEART RATE (bpm)AT DIFFERENT INTERVAL(min) BETWEEN GROUP A AND GROUP B

	GROUP A		GROUP B		
Bpm/min	**MEAN**	**S.D.**	**MEAN**	**S.D.**	**p VALUE**
Pre-op	74.50	9.67	74.43	7.58	0.9700
HR2	74.12	8.26	74.17	6.90	0.9772
HR4	72.36	8.16	72.67	6.41	0.8472
HR6	72.29	7.91	70.57	6.52	0.2817
HR8	71.98	8.03	69.52	6.42	0.1258
HR10	71.29	7.49	68.10	5.90	0.0330
HR15	71.88	10.16	67.31	5.99	0.0140
HR20	71.50	9.18	66.48	5.85	0.0037
HR30	71.40	8.72	66.33	5.72	0.0023
HR45	70.98	7.22	65.62	5.98	0.0004
HR60	71.31	6.71	65.71	5.79	0.0001
HR75	70.62	7.20	64.98	5.87	0.0002
HR90	70.95	7.21	64.81	5.64	0.0000

GRAPH 4: MEAN HEART RATE

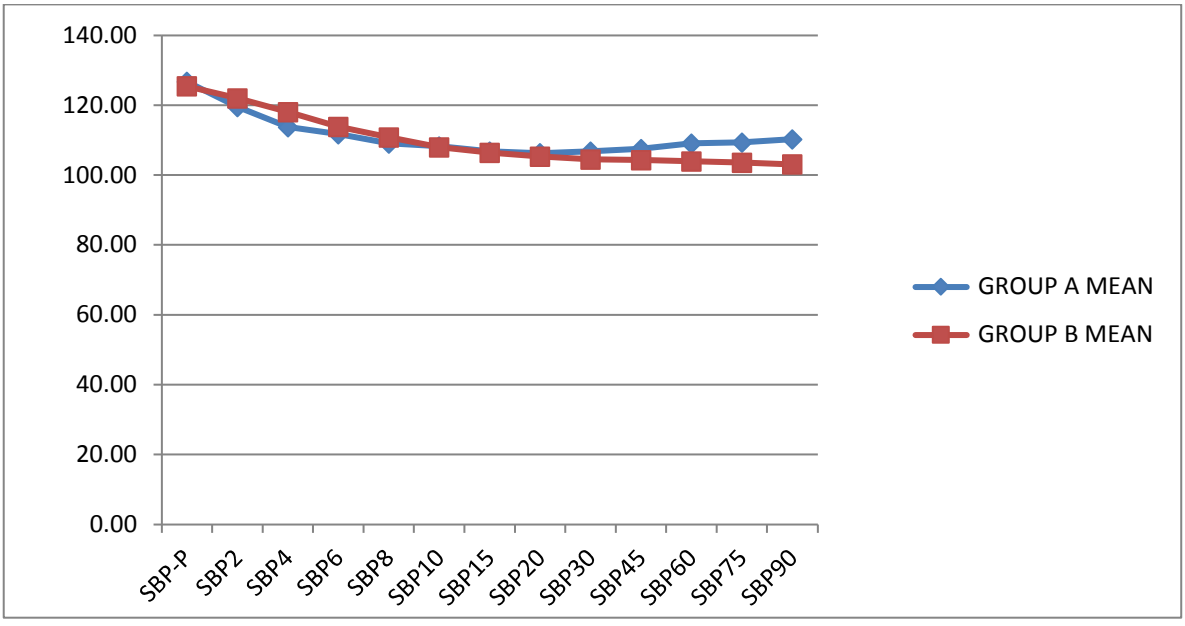


In this study the mean heart rate at preoperative period in Group A was noted as 74.50 ± 9.67 bpm and in Group B 74.43 ±7.58 bpm, which was statistically insignificant. At 10minutes the mean heart rate in Group B was 66.48± 5.85 bpm and in Group A was 71.50± 9.18bpm with a significant difference (p=0.0037). At 90 minutes the mean heart rate in Group B was 64.81± 5.64bpm and in Group A was 70.95± 7.21 bpm with a significant difference (p=0.0000).

TABLE 5: COMPARISON OF MEAN SYSTOLIC BLOOD PRESSURE(mm Hg) AT DIFFERENT INTERVALS (min) BETWEEN GROUP A AND GROUP B

	GROUP A		GROUP B	
SBP(mmHg/min)	**MEAN**	**S.D.**	**MEAN**	**S.D.**
Pre-Op	126.74	13.20	125.48	10.33
SBP2	119.50	12.07	122.05	8.32
SBP4	113.74	10.26	118.07	7.83
SBP6	111.74	10.06	113.81	8.20
SBP8	109.12	9.76	110.79	8.20
SBP10	108.29	10.27	108.02	8.26
SBP15	106.79	11.99	106.40	7.89
SBP20	106.31	11.06	105.29	7.82
SBP30	106.81	11.09	104.50	6.91
SBP45	107.50	8.80	104.36	6.86
SBP60	109.05	8.82	103.93	6.52
SBP75	109.36	8.26	103.62	6.34
SBP90	110.31	8.01	103.12	6.06

GRAPH 5: MEAN SYSTOLIC BLOOD PRESSURE(SPB)

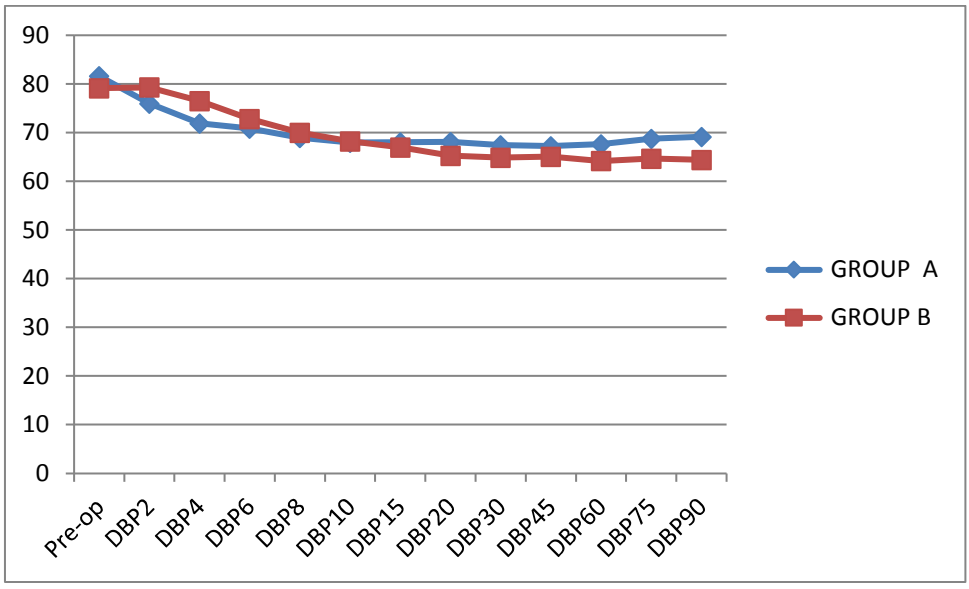


In this study, the mean systolic blood pressure in group A & B at frequent interval was noted. There was a slight fall in SBP as the duration of block progressed from 2min to 6min and further fall observed at about 15min after which the change in SBP was almost the comparable between the two groups. At 20 min mean SBP in Group A was 106.31± 11.06 and that in Group B was 105.29±7.82. At 30min mean SBP in Group A was 106.81± 11.09 and that in Group B was 104.90±6.91. At 90 min mean SBP in Group A was 110.31± 8.01 and that in Group B was 108±6.06. However the mean SBP at all intervals in Group A & B were comparable (p>0.05).

TABLE 6: COMPARISON OF MEAN DIASTOLIC BLOOD PRESSURE(mm Hg) AT DIFFERENT INTERVALS(min) BETWEEN GROUP A AND GROUP B

	GROUP-A		GROUP-B		
mmHg/min	MEAN	SD	MEAN	SD	P-VALUE
Pre-Op	81.64	8.17	79.14	8.00	0.1603
DBP2	76.02	10.02	79.31	8.05	0.1015
DBP4	71.93	8.92	76.52	7.57	0.0128
DBP6	70.88	9.50	72.83	7.92	0.3094
DBP8	68.93	7.59	70.00	7.19	0.5087
DBP10	67.98	7.76	68.21	6.89	0.8822
DBP15	68.02	9.26	66.95	6.64	0.5440
DBP20	68.10	8.88	65.26	5.37	0.0804
DBP30	67.45	7.36	64.90	5.67	0.0794
DBP45	67.24	8.70	65.05	5.29	0.1671
DBP60	67.64	7.31	64.19	5.58	0.0172
DBP75	68.76	8.36	64.67	5.03	0.0080
DBP90	69.12	6.46	64.40	5.14	0.0004

GRAPH 6: MEAN DIASTOLIC BLOOD PRESSURE(DBP)

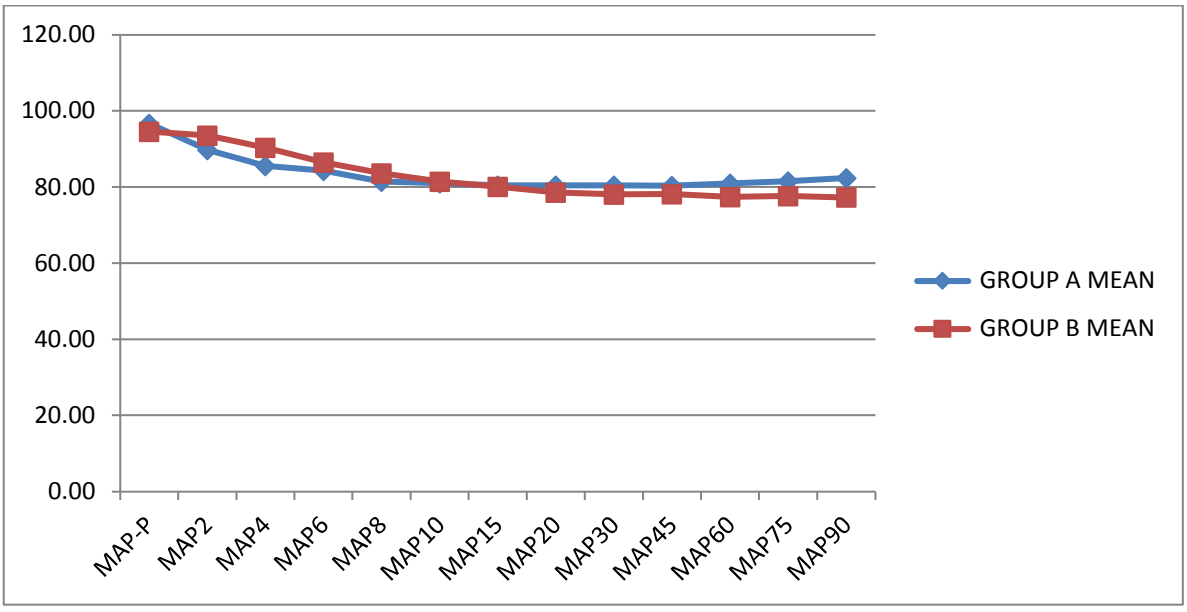


In this study, the mean diastolic blood pressure in group A & B at frequent interval was noted. There was a slight fall in DBP as the duration of block progressed from 2min to 6min and further fall observed at about 15min after which the change in DBP was comparable between the two groups. At 20 min mean DBP in Group A was 68.10± 8.88 and that in Group B was 65.26±5.37. At 30min mean DBP in Group A was 67.45± 7.36 and that in Group B was 64.90±5.67. At 90 min mean DBP in Group A was 69.12± 6.46 and that in Group B was 64.40±5.14. However the mean DBP at all intervals in Group A & B were comparable (p>0.05).

TABLE 7: COMPARISON OF MEAN ARTERIAL PRESSURE(mmHg) AT DIFFERENT INTERVALS (min) BETWEEN GROUP A AND GROUP B

	GROUP-A		GROUP-B		
mmHg/min	MEAN	SD	MEAN	SD	P-VALUE
Pre-Op	96.67	9.18	94.59	7.74	0.2632
MAP2	89.82	10.28	93.56	7.28	0.0579
MAP4	85.58	9.07	90.37	6.84	0.0077
MAP6	84.28	9.39	86.49	7.53	0.2366
MAP8	81.46	7.79	83.60	6.66	0.1808
MAP10	81.04	7.86	81.48	6.80	0.7823
MAP15	80.44	8.38	80.10	6.59	0.8361
MAP20	80.41	9.02	78.60	5.70	0.2748
MAP30	80.42	7.44	78.10	5.60	0.1105
MAP45	80.37	8.43	78.15	5.35	0.1547
MAP60	80.98	7.25	77.44	5.48	0.0133
MAP75	81.55	7.97	77.65	4.96	0.0864
MAP90	82.41	6.51	77.31	4.97	0.0122

GRAPH 7: MEAN ARTERIAL PRESSURE(MAP)

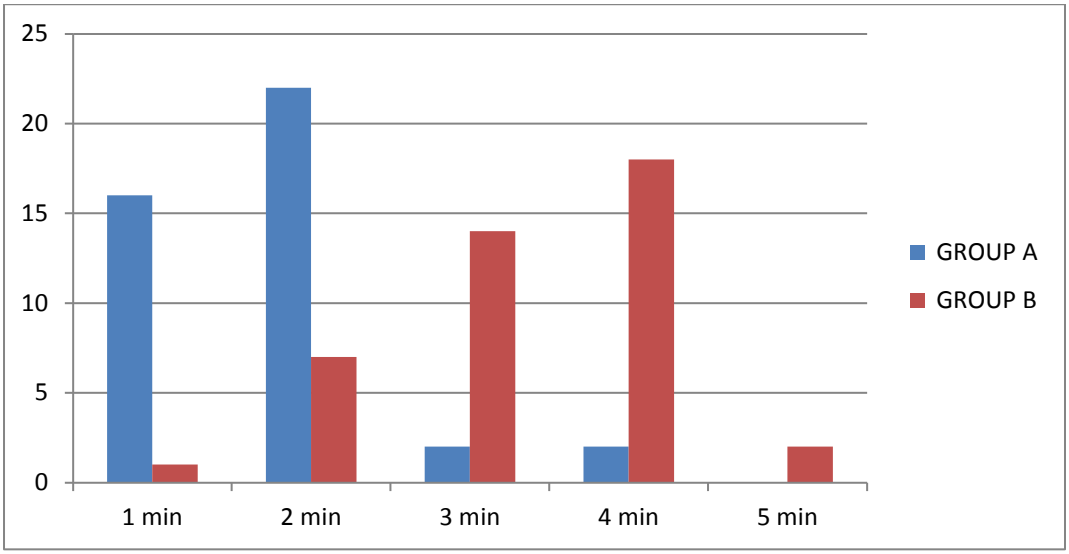


In this study, the mean arterial pressure in group A & B at frequent interval was noted. There was a slight fall in MAP as the duration of block progressed from 2min to 6min and further fall observed at about 15min after which the change in MAP was comparable between the two groups. At 20 min mean MAP in Group A was 80.41± 9.02 and that in Group B was 78.60±5.70. At 30min mean MAP in Group A was 80.42± 7.44 and that in Group B was 78.10±5.60. At 90 min mean MAP in Group A was 82.41± 6.51 and that in Group B was 77.31±4.97. However the mean MAP at all intervals in Group A & B were comparable (p>0.05).

TABLE 8: COMPARISON OF MEAN ONSET OF SENSORY BLOCK (SB)

SB ONSET-(min)	GROUP-A	GROUP-B	P-VALUE
1	16	1	< 0.0001
2	22	7	<0.0001
3	2	14	<0.0001
4	2	18	<0.0001
5	0	2	<0.0001
TOTAL	42	42	

GRAPH 8: ONSET OF SENSORY BLOCK

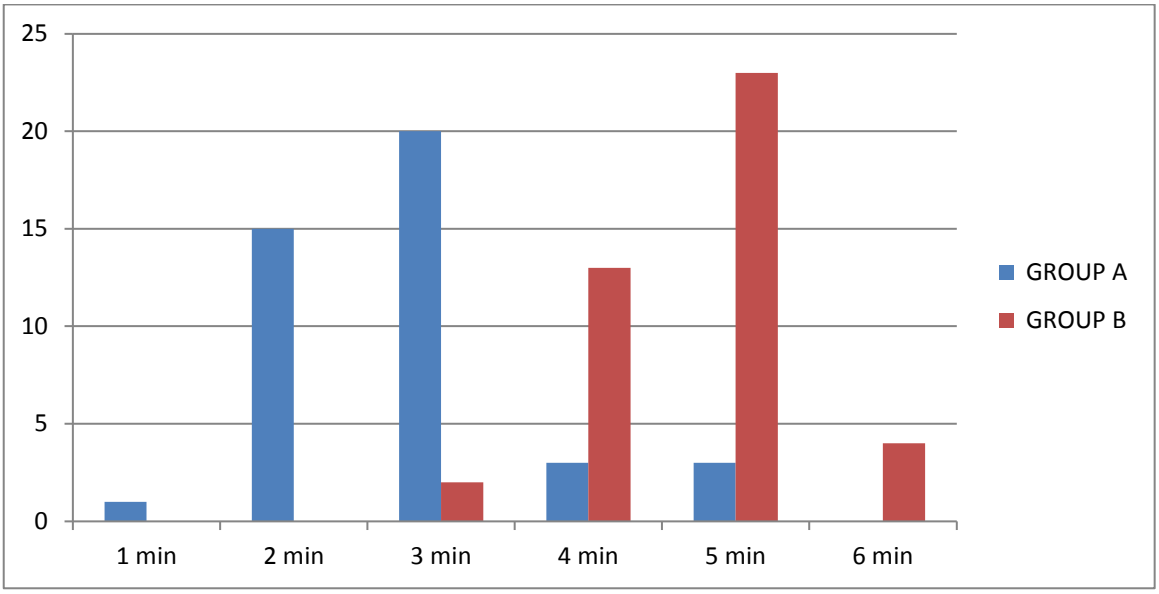


In this study a significant delay in the mean onset time of sensory block in Group B compared to Group A . Most of the participants of Group A had a fast onset as early as 1min from administration of the SAB while most participants of Group B had a delayed onset after atleast 3 min after the SAB. This difference was found to be statistically significant (p=0.0001).

TABLE 9: COMPARISON OF MEAN ONSET OF MOTOR BLOCK

MB ONSET	GROUP A	GROUP B	p VALUE
1	1	0	< 0.0001
2	15	0	<0.0001
3	20	2	<0.0001
4	3	13	<0.0001
5	3	23	<0.0001
6	0	4	<0.0001
TOTAL	42	42	

GRAPH 9: ONSET OF MOTOR BLOCK

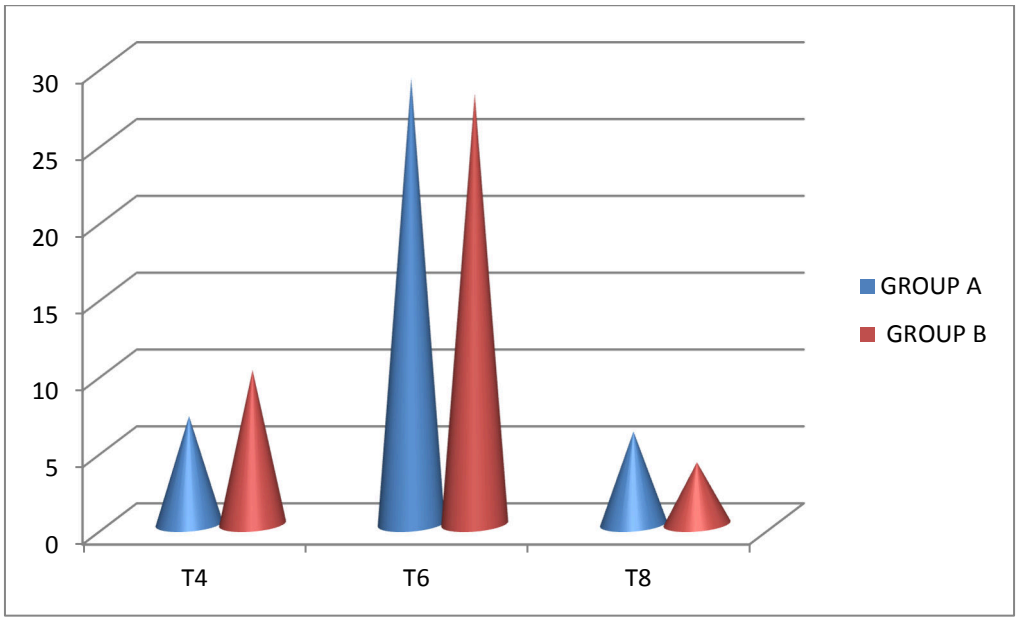


In this study a significant delay in the mean onset time of motor block in Group B compared to Group A . Most of the participants of Group A had a fast onset as early as 3min from administration of the SAB while most participants of Group B had a delayed onset of motor block by about 5min after the SAB. This difference was found to be statistically significant (p=0.0001).

TABLE10: HIGHEST LEVEL OF SENSORY BLOCK

HIGHEST LEVEL	GROUP-A	GROUP-B	p VALUE	INFERENCE
T4	7	10	0.6228	NS
T6	29	28	0.522	NS
T8	6	4	0.468	NS
TOTAL	42	42	0.694	NS

GRAPH 10: HIGHEST LEVEL OF SENSORY BLOCK

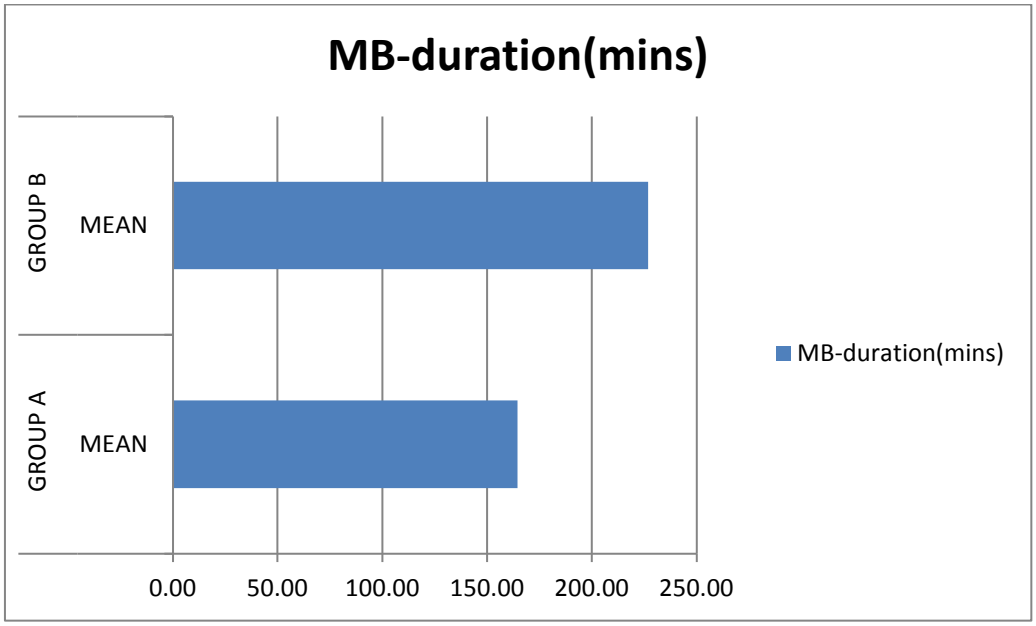


In the present study, Group A and Group B has maximum patients with the block level of T6. The highest levels achieved by both groups appears comparable(p=0.6228)

TABLE 11: COMPARISON OF DURATION OF MOTOR BLOCK

	GROUP A		GROUP B		p VALUE
	MEAN	SD	MEAN	SD	
MB-duration(mins)	164.52	18.24	226.90	16.15	< 0.0001

GRAPH 11 : DURATION OF MOTOR BLOCK (BROMAGE 3)

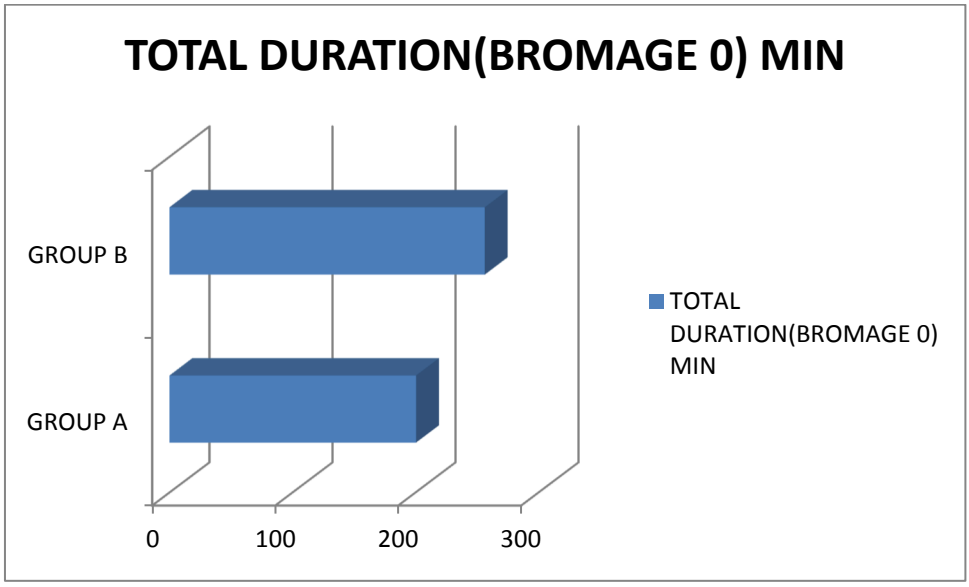


In this study the mean duration of block(block at Modified Bromage Grade 3) - in Group A the duration of motor blockade was 164.52± 18.24min while most participants of Group B the duration of motor blockade was 226.90± 16.15min after the SAB. This difference was found to be statistically significant (p=0.0001).

TABLE 12: COMPARISON OF TOTAL DURATION OF MOTOR BLOCKADE(mod. Bromage 0)

TOTAL DURATION	GROUP-A(min)		GROUP-B(min)		
	Mean	SD	Mean	SD	p Value
	200.48	24.49	256.43	15.27	<0.0001

GRAPH 12: TOTAL DURATION OF MOTOR BLOCK (BROMAGE 0)

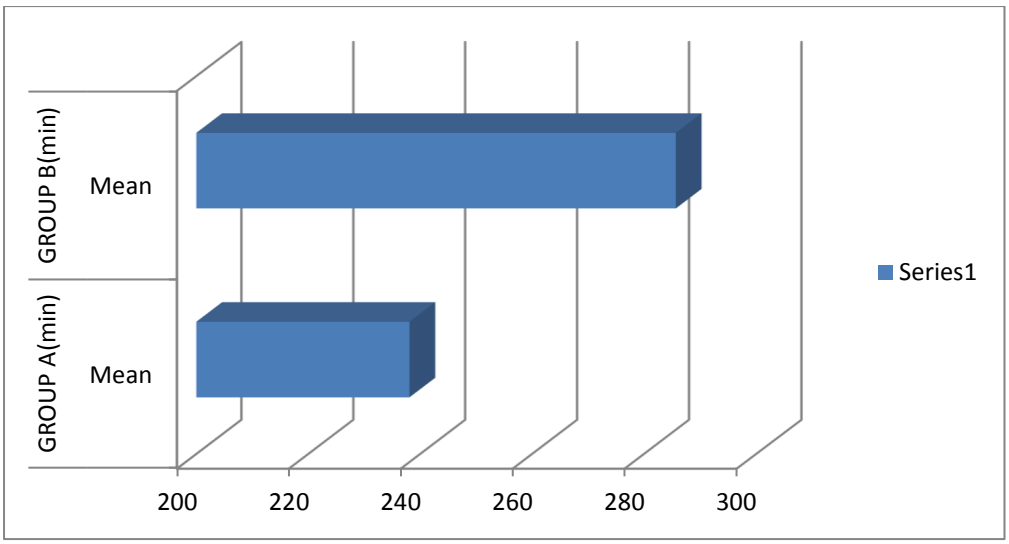


Its been observed in this study that the total duration of SAB in Group B is much longer than in Group A. The total duration of blockade in Group A is 200.48 ± 24.49min while that of Group B is 256.43±15.27. This is also seen that this difference is highly significant($p<0.0001$).

TABLE 13: COMPARISON OF TIME REQUEST FOR POST-OPERATIVE RESCUE ANALGESIA

Rescue analgesia(min)	Group A(min)		Group B(min)		
	Mean	SD	Mean	SD	p VALUE
	238.1	24.32	285.71	16.25	<0.0001

GRAPH 13: TIME FOR FIRST RESCUE ANALGESIA

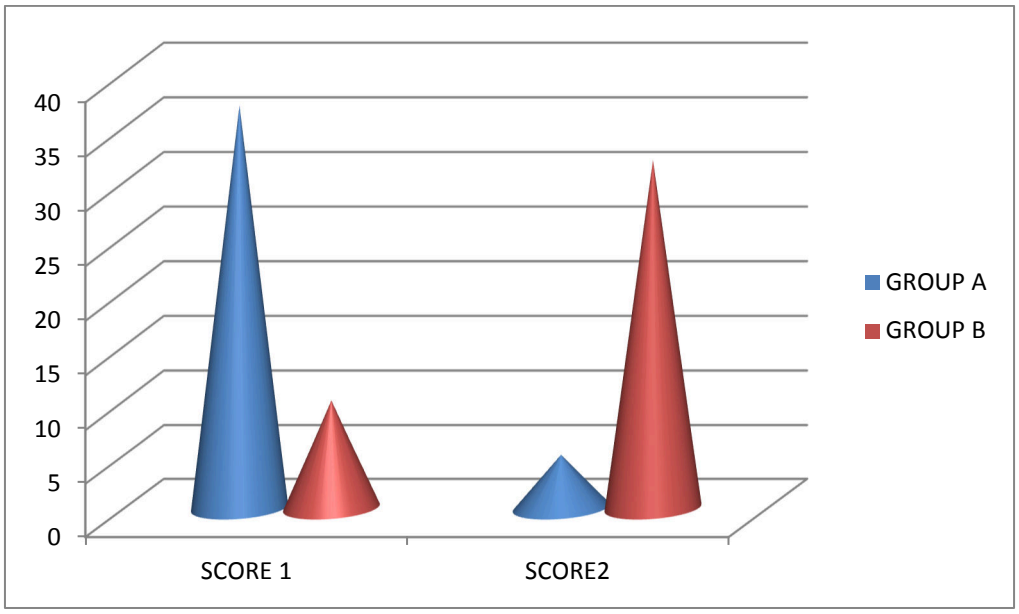


Its been observed in this study that the time required for rescue analgesia in GroupB is much longer than in Group A. The time required for rescue analgesia in Group A is 238.1 ± 24.32min while that of Group B is 285.71±16.25. This is also seen that this difference is highly significant ($p<0.0001$).

TABLE 14:SEDATION SCORE COMPARISON BETWEEN THE TWO GROUPS

	GROUP A		GROUP B	
Sedation Score	**1**	**2**	**1**	**2**
	37	5	10	32

GRAPH 14: SEDATION SCORES



The sedation scores of the two groups are- higher sedation is observed with buprenorphine Group B when compared to Fentanyl Group A. this difference is significant.($p<0.005$)

DISCUSSION

SAB is the most accepted technique for lower abdominal surgeries. It has various advantages over general anaesthesia which includes lesser stress response, avoidance of tracheal intubation and better post-operative compliance and analgesia. Addition of opioids along with the local anaesthetics further increases the efficacy of the drug acting synergistically The local anaesthetic and the opioids act on different receptors. The opioids act on the opioids receptors in the substantia gelatinosa while the local anaesthetic blocks the impulse transmission at the root of the neurons. The combined effect results in the synergic action and prolonged post-operative pain relief. In our study design, we had two groups with two different doses of drugs used. The Group A received 3 ml of 0.5% Bupivacaine with 12.5 mcg of Inj Fentanyl while Group B received 3 ml of 0.5% bupivacaine with 75 mcg of Inj Buprenorphine. The drug was injected subarachnoid space for Spinal anaesthesia for patients posted for lower abdominal surgeries. There have been numerous studies showing the efficacy of adding an opioid to the local anesthetic for regional anesthesia. [1]

The present study is a one year hospital based randomized clinical trial conducted during the period of January 2020 to December 2020. A total of 84 patients, who were distributed into 2 groups of 42 each undergoing lower abdominal surgeries, aged between 18-65year of either gender, belonging to ASA I or II, posted in KLES Dr.Prabhakar Kore Hospital and Medical Research Centre, Belgaum were studied.

In this study there was no statistical difference observed between Group A and B with regards to distribution of sex($p>0.05$), mean age(45.33 ± 15.16 and 44.21 ± 15.12 year respectively;$p>0.05$), mean weight($64.74\pm$ 11.21 and $68.67\pm$ 8.18 kg respectively;$p>0.05$) and mean height (165.62 ± 4.65 and 166.12 ± 3.54cm

respectively;p>0.05). These findings suggests that the demographic and pre anaesthetic characteristics between group A and B are comparable.

In this study,the baseline hemodynamic parameters i.e; mean systolic blood pressure, mean diastolic pressure and mean arterial pressure were comparable between the two groups throughout the period of SAB block. . At 20 min mean SBP in Group A was 106.31± 11.06 and that in Group B was 105.29±7.82. At 30min mean SBP in Group A was 106.81± 11.09 and that in Group B was 104.90±6.91. At 90 min mean SBP in Group A was 110.31± 8.01 and that in Group B was 108±6.06. At 20 min mean DBP in Group A was 68.10± 8.88 and that in Group B was 65.26±5.37. At 30min mean DBP in Group A was 67.45± 7.36 and that in Group B was 64.90±5.67. At 90 min mean DBP in Group A was 69.12± 6.46 and that in Group B was 64.40±5.14mmHg. At 20 min mean MAP in Group A was 80.41± 9.02 and that in Group B was 78.60±5.70 mmHg. At 30min mean MAP in Group A was 80.42± 7.44 and that in Group B was 78.10±5.60. At 90 min mean MAP in Group A was 82.41± 6.51 and that in Group B was 77.31±4.97. Hence, the mean SBP,DBP & MAP at all intervals in Group A & B were comparable (p>0.05).

Similar observation was made Kamal et where there was no significant difference between fentanyl and buprenorphine group in terms of SBP,DBP and MAP. But the study observed that there was significant fall in BP within the first 10min of SAB. [10]

The mean heart rate between the two groups was initially comparable(p>0.05) but after 10 min the mean heart rate in Group A was 71.50± 9.18bpm and that in Group B was 66.48 5.85 with a significant difference (p=0.0037). At 90 minutes the mean heart rate in Group B was 70.95± 7.21 bpm and that in Group A was 64.81± 5.64bpm with a

significant difference (p=0.0000). It was observed that there was a decrease in HR by about 10.2 - 15.8% in this study.

In the study by Arvinder Paul Singh et al, the group with Buprenorphine as an adjunct to Ropivacaine showed significant decrease in heart rate-initially average heart rate was 82±15.12bpm and at 20mins average heart rate was 68±10.12bpm. [9]

Sandhya A Bakshi et al, studied using intrathecal Buprenorphine and Clonidine and found that significant bradycardia was observed with clonidine-16.68% against buprenorphine with 2.78%with p<0.016(significant).[13]

Similar observation was made Kamal et where the mean heart rate showed comparable difference from about 15min(p<0.05),there was about 5-10%decrease in mean heart rate in the Buprenorphine group. [10]

In this study, a significant delay in the mean onset time of sensory and motor block in Group B (3min and 5min respectively) compared to Group A (1min and 3min respectively) .This difference was found to be statistically significant (p=0.0001). While there was significant difference between the two groups in terms of time of sensory and motor onset there is no significant difference the highest levels of SAB blockade(T6 in both groups).

In this study, since a fixed volume of drug was injected in the subarachnoid space, the total height of blockade reached was T6 level.

Fauzia Bano et al, in their study used 25mcg of Fentanyl with bupivacaine and plain bupivacaine showed faster onset with Fentanyl-bupivacine group (1±0.51min; p<0.05). The highest level reached was comparable between the two groups showing that the level reached depends on total volume of drug given and not on the additives . [2]

The mean duration of motor block(block at Modified Bromage Grade 3) and total duration of motor blockade in Group B(226.90± 16.15min and 256.43±15.27min

respectively) is longer when compared to Group A(164.52± 18.24min and 200.48 ± 24.49min respectively) .This difference was found to be statistically significant (p=0.0001). The time required for rescue analgesia in Group A is 238.1 ± 24.32min while that of Group B is 285.71±16.25. This is also seen that this difference is significant (p<0.0001).

Similar observations were made by Kamal et al, the total duration of analgesia was 214±35min and 317±54min with Fentanyl-Bupivacaine and Buprenorphine-Bupivacaine respectively, this difference being significant(p=0.000005). [10]

Arvider Paul Singh et al, studied difference between Buprenorphine-ropivacaine and Fentanyl-ropivacine combinations and found that, time for motor block onset was 3.30 ±1.03min and 2.75±1.02min respectively.Duration of motor blockade was 387.0±39.4min and 305.4±35.8min respectively and these difference were found to be significant (p<0.005). [9]

The sedation scores of the two groups are- higher sedation is observed with buprenorphine Group B when compared to Fentanyl Group A. this difference is significant. (p<0.005). Nemethy et al, used this Modified Wilson Scale for sedation levels in intrathecal anaesthesia and found that opioids like buprenorphine in higher doses (60/75mcg) caused significant sedation. [8]

CONCLUSION

Based on this study, it may be concluded that – intrathecal admistration of Bupivacaine-Fentanyl requires lesser time for onset of sensory and motor block, but lesser duration of motor block and total duration of block, with faster requirement of rescue analgesia when compared to intrathecal Bupivacaine-Buprenorphine group. However more extensive studies are needed to comfirm the diagnosis.

SUMMARY

SAB is the most prevalent mode of anaesthesia in lower abdominal surgeries. In our study titled "**Efficacy of intrathecal Fentanyl-Bupivacaine(H) and Buprenorphine-Bupivacaine(H) on the onset and duration of blockade and levels of sedation in lower abdominal surgeries - a one year hospital based randomized control trail**", we conducted our study on patients of age group 18-65 years belonging to ASA I-II posted for lower abdominal surgeries. Written informed consent were taken from the patients and ethical committee clearance was acquired. Patients were randomly allocated into two groups with 42 patients each in two groups.

Group A - 3ml of 0.5% Hyperbaric Bupivacaine with 0.25ml (12.5mcg) of Fentanyl making a total volume of 3.25mlof drug is injected in L_2-L_3 SAS.

Group B - 3ml of 0.5% hyperbaric Bupivacaine with 0.25ml (75mcg) of buprenorphine making a total volume of 3.25ml of drug is injected in L_2-L_3 SAS .

In both the groups, the demographic variables were comparable and were statistically insignificant. In the study, the gender distribution was comparable and there was no significant difference. In Group A, there were 19 females and 23 males whereas in Group B, there were 12 females and 30 males who participated in the study. The ASA grading was and not significant,hence comparable .

Time taken for the onset of sensory block in the Group A is fast - as early as 1min from administration of the SAB while most participants of Group B had a delayed onset after atleast 3 min after the SAB. This difference was statistically significant (p=0.0001).

Time taken for the onset of motor block in Group B is about 5mins as compared to Group A with 3min after the SAB . This difference was found to be statistically significant (p=0.0001).

The highest level of sensory block achieved in both the groups ranged from T4-T8 maximum of them reaching a level of T6. The highest levels achieved by both groups appears comparable(p=0.6228)

The mean heart rate at the beginning in Group A and Group B was comparable with insignificant difference. At 20minute the mean heart rate in Group B was 71.50± 9.18bpm and that in Group A was 66.48± 5.85bpm with a significant difference (p=0.0037). At 90 minutes the mean heart rate in Group B was 70.95± 7.21 bpm and that in Group A was 64.81± 5.64bpm with a significant difference (p=0.0000).

The SBP, DBP and MAP all are comparable between the two groups since the beginning(p>0.05).

The mean duration of motor block (block at Modified Bromage Grade 3) in Group B , 226.90± 16.15min, is longer when compared to Group A, 164.52± 18.24min .This difference was found to be statistically significant (p=0.0001). The total duration of motor blockade similarly is longer in Group B , 256.43±15.27min, when compared to Group A, 200.48 ± 24.49min, and this difference is statistically significant(p=0.0001). Time required for first post-operative rescue analgesia was more delayed in Group B , 285.71±16.25min , when compared to Group A, 238.1 ± 24.32min , and this difference was again significant.(p<0.001).

The sedation scores of the two groups are- higher sedation is observed with buprenorphine Group B when compared to Fentanyl Group A. this difference is significant.($p<0.005$)

Overall, Intrathecal Buprenorphine-Bupivacaine required more time for onset of sensory and motor blockade and provided similar level of sensory block with longer duration of motor blockade and more delayed requirement of first post-operative rescue analgesia along with higher sedation scores when compared to Intrathecal Fentanyl-Bupivacaine.

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ANNEXURE I

INFORMED CONSENT

EFFICACY OF INTRATHECAL FENTANYL-BUPIVACAINE(H) AND BUPRENORPHINE-BUPIVACAINE(H) ON THE ONSET AND DURATION OF BLOCKADE AND LEVELS OF SEDATION IN LOWER ABDOMINAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMIZED CONTROL TRAIL

PRINCIPAL INVESTIGATOR:

CO- INVESTIGATOR :

INTRODUCTION AND PURPOSE:

The present study is conducted among adult patients scheduled for various elective surgeries under subarachnoid block in the Department of Anaesthesiology at KLE's Dr. Prabhakar Kore Charitable Hospital and Medical Research Centre, Belagavi. You are requested to participate in the study and your participation is completely voluntary.

The purpose of research is :

1. To compare the onset and duration of sensory and motor blockage between 0.5% Bupivacaine (H) with Fentanyl and buprenorphine respectively Fentanyl-12.5mcg Buprenorphine- 75mcg
2. To compare the level of sedation caused by intrathecal opoids- fentanyl and buprenorphine (using "Modified Wilson Scale")

PROCEDURE:

If you agree to enroll in my study, I will ask your present, past and family history. Then you will be clinically examined in detail. You will be allotted into one of the two groups randomly using computer generated software. Group F will be given Fentanyl as adjunct with SAB while Group B will be given Buprenorphine.

BENEFITS:

Prolonged anaesthesia and minimal heamodynamic change

Patient will not be eligible for any kind of monetary benefits or free services by virtue of your participation in the study.

RISKS:

Methods applied to do the study are safe.

COST OF PARTICIPATION:

The cost of the investigation will be done by the study subject. The other indirect expenses will be borne by the investigator.

PRIVACY AND CONFIDENTIALITY:

The results of the study may be published in journals for scientific purposes. However, your identity will not be revealed. All information collected will be coded so that no one other than the investigator will know your identity.

WITHDRAWAL FROM THE STUDY:

You can withdraw from the study at any time if you wish to do so.

ALTERNATIVES:

In case you opt out of the study, it will not affect your relationship with KLE's Dr. Prabhakar Kore Hospital.

AUTHORIZATION TO PUBLISH RESULTS:

The researcher may use the information gathered from this study for presentation in scientific meetings. However, your identity will not be revealed.

INSTITUTIONAL/ SPONSORS POLICY:

In the event of any injury related to this study , no reimbursement or compensation will be given by law. However , treatment will be made available at KLE's Hospital & MRC , Belgaum.

LEGAL RIGHTS:

By signing this consent form, you are not waiving any of your legal rights

CONSENT SUMMARY:

I have been explained all the contents of this consent form in my local language and having understood and clarified all my queries about the study to the best of my knowledge, I hereby give my voluntary consent for participation in the study. I do sign the informed consent form in front of an eye witness whom I recognize.

Name and Signature/ left thumb impression of the participant:

Name and Signature of the investigator:

Name and Signature/ left thumb impression of the eye witness(Relative):

Signature of the Guide: **Date:**

Informed Consent for Participation In Research Trial

EFFICACY OF INTRATHECAL FENTANYL-BUPIVACAINE(H) AND BUPRENORPHINE-BUPIVACAINE(H) ON THE ONSET AND DURATION OF BLOCKADE AND LEVELS OF SEDATION IN LOWER ABDOMINAL SURGERIES - A ONE YEAR HOSPITAL BASED RANDOMIZED CONTROL TRAIL

I,Mr/Mrs _____voluntarily agree for the participation of my child as a subject for the study, by signing this consent form I am not giving up any of my legal rights, I may withdraw from the study any time. I am signing the consent form after having read or been read to me in the vernacular language ,including the risk and the benefits and having all my queries cleared.

Signature or the left thumb impression of parent/guardian:

Name of study patient:

Name and signature of witness:_____

Name and signature of investigator:_____

Date: Place:

ANNEXURE II

PROFORMA

Patients Name : I.P No. :

Age : Weight:

Height : Gender :

Date of operation : Occupation :

Address : Anaesthesiologist:

Preanaesthetic evaluation

Chief complaints

Past History

- HTN / DM/ IHD / Arrhythmia / LVH / Valvular heart disease
- H/o uncontrolled hypertension/diabetes mellitus
- H/o previous surgery.
- Drug therapy

Family History

General physical examination

Weight (Kg) : Temperature (^{0}F) : Pallor :

Icterus : Cyanosis : Pedal oedema

: Clubbing: PR : BP: RR:

Systemic examination:

RS: CNS:

CVS: GIT:

Musculoskeletal disorders:

Jaw movements : Teeth:

Airway assessment : Spine:

Investigations

Hb%: TLC: Platelet Count : INR: FBS:

Diagnosis

Pre-operative physical state: ASA I / II / III / IV / V

Proposed surgery

Pre-operative baseline values

HR : BP: SpO2:

Following monitoring was done throughout the procedure

Pulse oxymetry: NIBP:

ECG:

Group: A B

Sensory Block:

a)	Onset at T10(min)	
b)	Duration at T10(min)	
c)	Highest level of sensory block	

Motor Block:

a)	Onset (min) Grade 3 motor blockade	
b)	Total duration of Motor blockade (min)	

Sedation Score: 1 / 2 / 3 / 4

Vital Parameters:

Time	HR	SBP	DBP	MAP	SpO2
2min					
4min					
6min					
8min					
10min					
15min					
20min					
25min					
30min					
45min					
60min					
75min					
90min					
105min					
120min					

Post-operative Analgesia:

Time to request for first post-operative rescue analgesia either diclofenac/paracetamol (min):

- SIGNATURE OF THE ANAESTHESIOLOGIST: _____
- SIGNATURE OF THE WITTNESS - _____

SIGNATURE OF THE PRINCIPAL INVESTIGATOR - _____

ANNEXURE III

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 182. **Date: 24/12/2019**

To,

BA0119012
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 **"EFFICACY OF INTRATHECAL FENTANYL-BUPIVACAINE(H) AND BUPRENORPHINE-BUPIVACAINE(H) ON THE ONSET AND DURATION OF BLOCKADE AND LEVELS OF SEDATION IN LOWER ABDOMINAL SURGERIES- A ONE YEAR HOSPITAL BASED RANDOMIZED CONTROL TRAIL ",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE IV

PHOTOS

Photo 1: Bupivacaine(heavy)

Photo 2:Lignocaine 2%)

Photo 3: Buprenorphine.

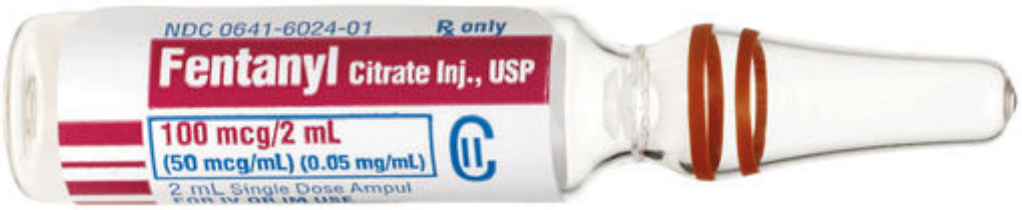

Photo 4:Fentanyl

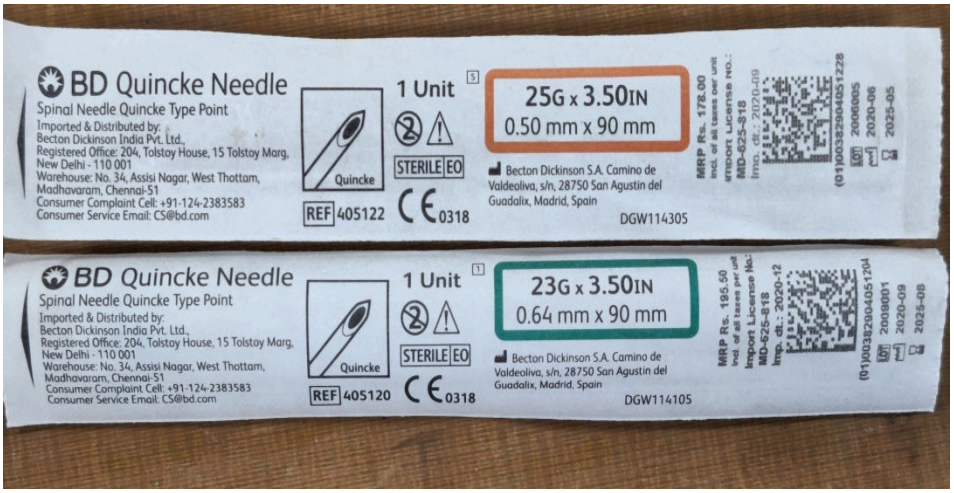

Photo 5: Spinal Needles

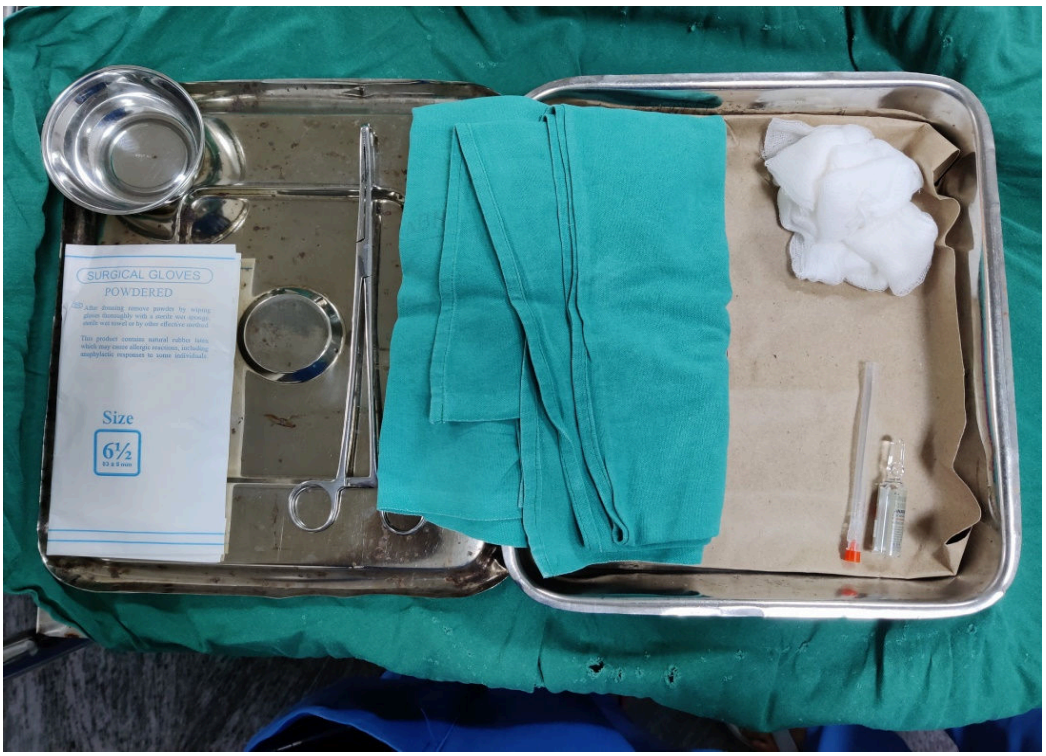

Photo 6: Spinal set

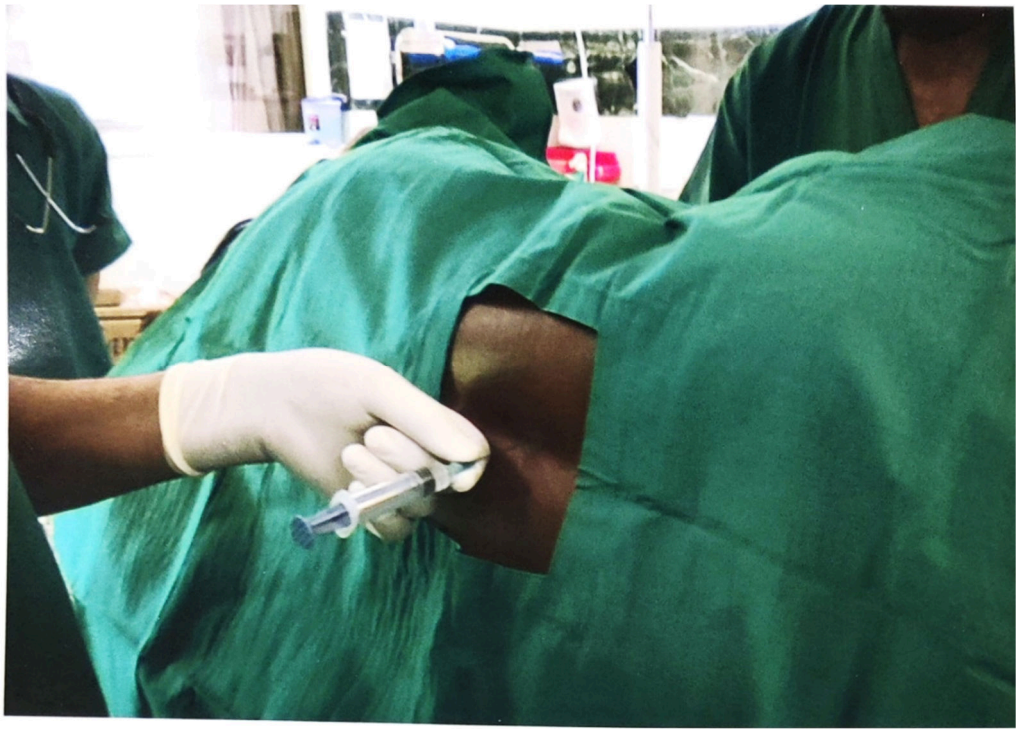

Photo 7: Administering SAB

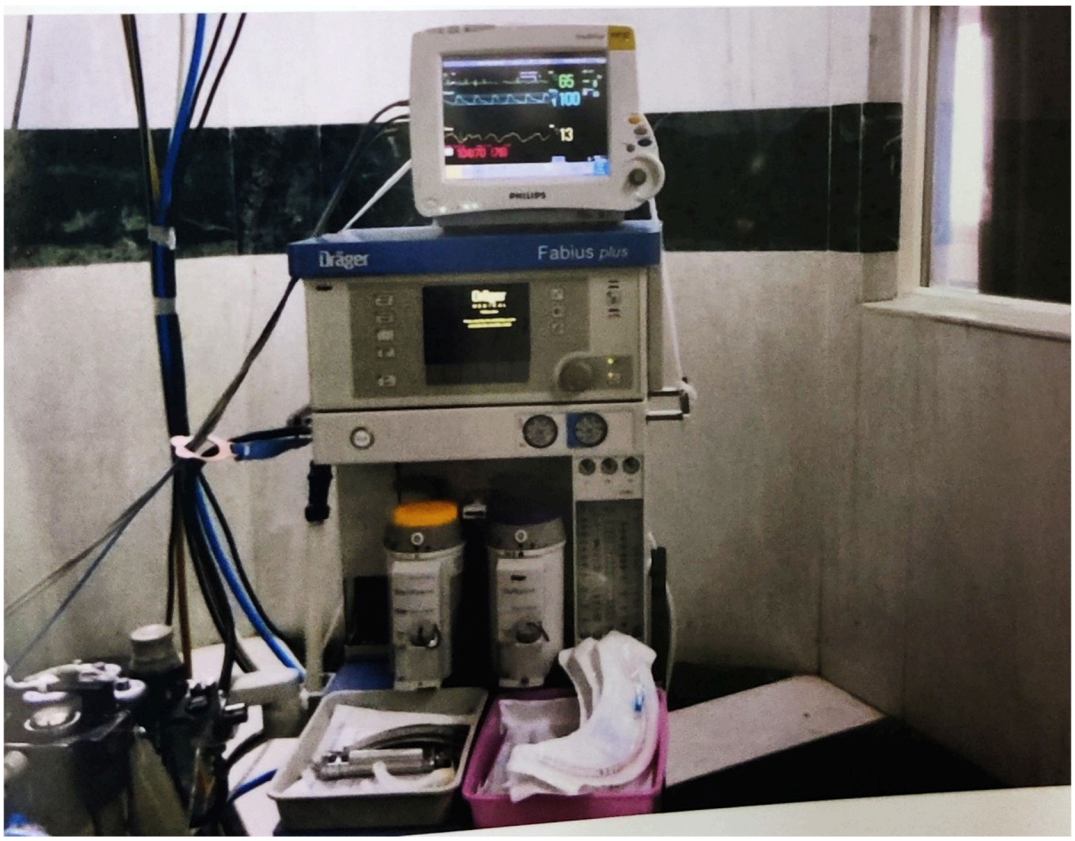

Photo 8: Anaesthesia Work Station and Monitor

KEY TO MASTER CHART

HR	-	Heart rate
SBP	-	Systolic Blood Pressure
DBP	-	Diastolic Blood Pressure
MAP	-	Mean Arterial Pressure
spO2	-	Saturation
SB	-	Sensory Block
MB	-	Motor Block

ANNEXURE VI- MASTER CHART

FENTANYL

Serial No.	I.P no.	Sex	Age(yrs)	weight(kg)	height(cm)	ASA	proposed surgery	HR(bpm)-P	SBP-P	DBP-P	MAP-P	SpO2-P	HR2	SBP2	DBP2	MAP2	HR4	SBP4	DBP4	MAP4	HR6	SBP6	DBP6	MAP6	HR8	SBP8	DBP8	MAP8	HR10	SBP10	DBP10	MAP10
1	995438	F	63	60	165	II	HR	89	115	80	91.67	100	86	124	73	90	82	114	66	82	78	112	69	83	78	104	64	77	78	100	60	75
2	997435	F	19	50	160	I	URS	72	130	80	96.67	100	74	130	80	86	72	110	70	76	70	110	70	76	74	108	70	75	72	110	70	76
3	999753	M	56	76	168	II	HR	60	150	90	110	100	65	124	90	101	65	120	67	87	67	120	66	84	68	123	73	90	66	121	73	89
4	1000787	M	55	68	162	I	HR	68	120	70	86.67	100	68	120	90	100	67	110	70	80	68	112	68	83	65	110	70	75	66	110	60	78
5	1001293	F	45	65	165	I	HR	70	120	80	93.33	100	72	120	66	84	72	120	73	90	71	121	73	89	70	118	69	85	69	118	70	86
6	1002095	M	40	72	170	I	HR	79	130	80	96.67	100	78	140	75	97	78	140	70	94	80	140	74	96	82	130	80	90	78	140	90	100
7	1002252	F	26	65	160	I	HR	60	100	70	80	100	57	89	49	55	54	97	51	62	59	92	44	56	61	99	59	67	64	93	54	63
8	1001399	M	31	75	168	I	DB	76	110	70	83.33	100	72	105	59	74	71	107	64	78	70	102	61	75	73	100	70	78	73	100	60	75
9	1002736	F	32	60	154	I	tRECTC	58	100	70	80	100	69	94	51	65	64	92	48	63	64	92	51	65	63	93	49	64	60	100	70	76
10	1003048	F	51	66	158	I	HR	76	136	90	105.3	100	74	130	79	96	72	132	79	97	74	127	76	93	72	126	77	93	72	128	80	97
11	1004102	F	36	68	154	II	PUTAT	88	130	80	96.67	100	88	131	79	96	80	124	77	93	81	123	76	92	82	123	73	84	80	113	67	82
12	1002300	M	58	100	168	II	pf varic	80	140	90	106.7	100	76	128	69	89	76	118	66	83	78	112	64	80	82	110	60	76	80	108	65	80
13	1001900	M	60	70	174	II	HR	70	140	90	106.7	100	78	130	86	101	76	126	83	97	75	123	88	100	78	125	78	94	74	121	77	92
14	1007104	F	33	68	164	I	URECT(	88	120	80	93.33	100	82	112	66	81	80	118	66	83	81	108	68	81	84	114	65	81	81	107	60	76
15	1001148	M	25	60	168	I	I&D	75	120	70	86.67	100	78	112	69	83	71	104	64	77	73	101	62	75	68	103	62	76	69	99	59	72
16	1013054	F	21	65	165	I	I&D	80	124	80	94.67	100	79	117	80	92	76	122	79	93	78	122	81	95	75	111	80	90	74	109	76	87
17	1013390	F	65	50	160	I	omy-cl	78	120	74	89.33	100	78	123	70	88	79	111	64	80	76	106	60	75	74	104	60	75	73	103	59	74
18	1013619	F	35	60	160	II	I&D	78	114	70	84.67	100	80	111	65	80	78	103	61	75	80	109	62	78	82	102	61	75	76	102	60	74
19	1013736	M	42	60	170	I	xcision	80	124	78	93.33	100	79	117	80	92	77	122	79	93	78	122	81	95	75	111	80	90	74	109	76	87
20	1013621	F	30	50	163	I	I&D	96	120	77	91.33	100	80	120	83	95	82	114	80	91	85	111	79	90	84	109	76	87	82	111	80	90
21	1014207	F	65	50	164	I	HR	80	130	90	103.3	100	80	130	90	94	78	120	90	100	78	120	90	100	76	120	80	93	78	120	80	93.3
22	1012786	F	25	45	160	I	URECT(	64	120	90	100	100	58	90	60	70	56	93	60	71	58	94	60	71	57	100	60	73	58	100	60	73.3
23	1014810	M	18	46	164	I	ndicec	85	120	80	93.33	100	80	120	80	93.3	76	110	70	83.3	76	110	70	83	75	100	60	73	75	100	70	80
24	1013930	M	48	100	170	I	grafting	60	140	80	100	100	60	130	80	96.7	61	120	80	93.3	58	118	90	99	59	114	70	85	58	112	72	85.3
25	1015819	M	25	75	170	I	HR	62	120	90	100	100	70	140	80	100	65	120	70	86.7	64	110	70	83	62	112	72	85	62	116	70	85.3
26	1015804	M	43	60	165	I	HR	70	110	70	83.33	100	74	110	72	84.7	72	100	70	80	71	100	68	79	70	96	57	70	70	100	60	73.3
27	1020377	M	48	70	170	II	DJ sten	90	160	90	113.3	100	90	140	90	107	89	130	90	103	85	120	70	87	86	118	72	87	85	120	68	85.3
28	1020496	M	49	60	168	II	S+DJ st	89	130	90	103.3	100	92	120	90	100	94	110	72	84.7	90	100	72	81	88	100	70	80	89	90	60	70
29	1021615	F	56	60	168	I	URS	80	120	80	93.33	100	78	112	80	90.7	76	110	76	87.3	78	110	74	86	75	108	68	81	76	110	66	80.7
30	1025319	F	35	70	165	I	rrhoid	70	120	90	100	100	70	110	80	90	68	108	70	82.7	66	106	66	79	66	106	66	79	65	104	68	80
31	1025290	F	60	50	164	I	RIF fem	86	120	70	86.67	100	82	110	70	83.3	80	100	70	80	80	100	68	79	78	90	60	70	78	92	57	68.7
32	1025425	M	65	65	168	II	h of cy	74	130	90	103.3	100	74	120	80	93.3	72	110	70	83.3	70	110	68	82	68	100	70	80	66	100	68	78.7
33	1025231	M	65	65	165	II	grafting	70	130	80	96.67	100	70	120	80	93.3	68	110	70	83.3	68	108	70	83	65	106	70	82	66	108	68	81.3
34	1021612	M	65	70	170	II	stosco	70	150	90	110	100	70	120	80	93.3	69	110	80	90	69	110	80	90	68	106	78	87	68	104	76	85.3
35	1021687	M	48	70	170	II	URS	76	160	100	120	100	76	140	90	107	75	130	90	103	74	130	90	103	72	120	80	93	70	120	76	90.7
36	1021479	F	24	55	165	I	grafting	68	120	80	93.33	100	68	110	70	83.3	66	108	70	82.7	66	106	70	82	66	104	68	80	66	104	70	81.3
37	1019814	F	51	60	165	II	grafting	76	140	90	106.7	100	76	120	80	93.3	74	118	80	92.7	74	116	78	91	75	116	76	89	75	114	66	82
38	1028307	M	65	70	175	II	HR	68	130	80	96.67	100	66	120	72	88	66	110	72	84.7	66	112	70	84	67	114	68	83	66	110	66	80.7
39	15377(canc	M	60	65	170	I	FJ	60	130	90	103.3	100	60	120	84	96	60	118	80	92.7	58	116	76	89	60	118	78	91	60	116	76	89.3
40	1023032	M	56	65	168	I	grafting	60	120	70	86.67	100	60	110	76	87.3	60	108	74	85.3	58	106	72	83	58	90	60	70	59	92	66	74.7
41	1025618	M	50	70	168	I	arthro	80	130	90	103.3	100	76	120	80	93.3	72	110	70	83.3	74	108	66	80	74	106	68	81	75	100	60	73.3
42	1028612	M	60	70	168	I	HR	70	130	80	96.67	100	70	130	70	90	70	120	70	86.7	69	118	66	83	68	116	68	84	68	114	66	82

Serial No.	HR15	SBP15	DBP15	MAP15	HR20	SBP20	DBP20	MAP20	HR30	SBP30	DBP30	MAP30	HR45	SBP45	DBP45	MAP45	HR60	SBP60	DBP60	MAP60	HR75	SBP75	DBP75	MAP75	HR90	SBP90	DBP90	MAP90	SpO2	SB-onset(mins)	highest level	MB-Onset(mins)	MB-duration(mir	total duration(mi	rescue analgesia(
1	74	100	60	76	74	100	60	75	74	100	60	72	70	100	64	74	70	100	65	75	70	100	70	80	70	110	60	80	100	1	T8	2	180	210	240
2	76	110	70	78	74	110	70	76	72	114	70	78	70	120	70	84	72	110	70	80	70	110	70	80	70	110	70	76	100	1	T6	1	180	210	270
3	65	118	69	85	66	110	70	86	67	110	73	85	64	114	69	84	66	120	70	86	65	120	83	87	64	120	76	89	100	2	T6	3	150	180	210
4	68	100	60	76	66	100	66	78	67	110	70	82	66	114	70	85	68	120	70	85	66	120	80	85	68	120	80	90	100	1	T6	2	180	200	240
5	69	120	70	85	68	118	73	88	68	116	64	81	70	116	70	86	68	118	75	89	70	118	69	85	70	117	68	84	100	1	T6	2	210	240	270
6	68	137	90	97	72	130	80	94	70	130	70	90	72	130	74	90	70	130	70	90	72	130	74	92	68	130	70	90	100	2	T6	3	160	200	240
7	63	100	50	65	62	103	48	61	59	107	58	69	60	99	57	66	68	98	59	69	58	97	51	59	58	100	60	70	100	3	T6	4	200	240	270
8	69	94	51	65	69	92	48	63	69	92	51	65	70	93	49	64	71	94	57	69	70	92	51	65	72	100	60	74	100	4	T6	5	150	180	240
9	64	93	58	69	63	100	64	70	63	100	60	70	64	94	51	64	64	100	50	65	64	94	50	64	65	100	70	80	100	2	T6	4	170	240	270
10	74	135	80	99	70	120	70	88	74	123	80	94	72	121	82	95	74	120	70	84	74	122	84	96	72	120	80	90	100	3	T6	5	170	230	270
11	118	73	88	82	107	60	76	85	105	60	74	82	85	102	61	75	84	110	62	78	84	104	61	75	84	108	62	76	100	4	T4	5	200	240	270
12	81	110	70	76	82	110	63	75	84	110	70	83	81	105	60	75	82	107	64	78	82	106	65	78	82	104	64	77	100	2	T6	4	180	240	250
13	73	118	79	92	78	118	79	92	78	118	74	89	75	112	70	84	74	108	72	84	73	114	74	87	72	111	73	86	100	2	T8	3	150	180	210
14	80	104	57	73	82	107	60	76	78	108	63	78	80	100	70	80	79	100	82	88	80	112	60	77	80	112	66	81	100	2	T6	3	170	210	240
15	70	92	57	69	71	94	64	74	68	96	64	75	69	96	59	71	70	100	70	76	70	104	64	77	72	102	66	78	100	1	T6	2	180	220	270
16	73	104	67	79	68	103	66	78	74	108	72	84	73	114	74	87	73	114	74	87	72	111	73	86	70	113	70	84	100	1	T6	2	150	180	200
17	70	101	62	75	68	100	60	60	70	92	52	65	69	94	54	67	68	93	55	68	66	98	60	73	67	97	55	69	100	2	T6	3	150	180	240
18	80	105	59	74	78	100	54	69	69	94	51	65	77	92	48	63	78	92	51	65	78	94	57	69	76	93	58	69	100	1	T6	3	150	180	240
19	73	104	67	79	70	103	66	78	72	98	67	77	74	96	66	76	72	104	67	79	70	105	68	80	68	104	67	79	100	2	T6	3	150	180	230
20	83	122	81	95	81	114	79	91	80	115	80	92	79	119	78	92	80	120	76	91	81	122	80	94	81	122	80	94	100	1	T6	2	150	190	230
21	76	120	90	100	76	120	94	103	76	120	70	87	75	118	90	99.3	76	130	90	103	76	118	90	99.3	75	120	86	97.33	100	2	T6	2	150	200	240
22	58	100	60	73.3	59	110	70	83.3	60	110	70	83	60	110	70	83.3	60	110	70	83.3	60	110	70	83.3	60	110	70	83.33	100	2	T8	3	180	240	270
23	72	110	70	83.3	74	110	70	83.3	75	110	70	83	74	110	60	76.7	75	110	70	83.3	74	112	70	84	74	116	70	85.33	100	1	T6	3	170	200	270
24	60	114	70	84.7	58	116	70	85.3	60	114	72	86	59	114	68	83.3	60	114	60	78	59	112	64	80	62	120	80	93.33	100	2	T6	2	150	180	210
25	60	114	70	84.7	60	114	72	86	59	112	70	84	59	116	80	92	60	118	70	86	61	120	70	86.7	60	120	70	86.67	100	1	T8	2	180	210	240
26	71	102	62	75.3	72	104	64	77.3	70	110	65	80	73	100	70	80	72	112	70	84	72	110	74	86	74	118	74	88.67	100	2	T8	3	180	240	270
27	84	120	70	86.7	86	120	84	96	85	118	84	95	86	116	80	92	85	118	70	86	84	120	80	93.3	88	124	80	94.67	100	2	T6	3	180	210	240
28	88	92	64	73.3	89	94	68	76.7	86	98	57	71	87	100	60	73.3	88	100	72	81.3	88	108	70	82.7	89	110	68	82	100	1	T4	2	180	240	270
29	77	112	70	84	76	110	70	83.3	78	108	72	84	78	110	68	82	76	110	70	83.3	78	112	70	84	76	110	68	82	100	2	T4	3	150	180	240
30	68	108	68	81.3	66	108	70	82.7	68	110	68	82	66	110	70	83.3	68	108	68	81.3	66	108	68	81.3	68	108	66	80	100	1	T6	2	150	180	210
31	78	90	70	76.7	75	97	60	72.3	78	96	62	73	78	100	60	73.3	76	100	62	74.7	75	100	64	76	74	102	66	78	100	2	T4	3	180	210	240
32	66	90	60	70	68	96	60	72	68	100	60	73	68	100	62	74.7	69	102	60	74	68	104	64	77.3	66	106	68	80.67	100	2	T4	3	150	180	210
33	68	108	66	80	67	106	68	80.7	68	108	70	83	68	106	72	83.3	70	108	70	82.7	68	106	68	80.7	68	100	66	77.33	100	2	T6	3	150	180	240
34	66	104	76	85.3	68	104	76	85.3	68	108	74	85	67	108	72	84	68	108	70	82.7	66	108	70	82.7	68	106	66	79.33	100	2	T6	3	160	180	210
35	70	110	78	88.7	72	110	80	90	70	110	76	87	70	110	74	86	70	110	70	83.3	69	110	70	83.3	70	110	70	83.33	100	1	T6	2	150	180	240
36	68	106	68	80.7	68	106	70	82	67	104	70	81	68	106	70	82	66	108	70	82.7	68	110	66	80.7	68	106	70	82	100	2	T6	2	150	180	210
37	74	110	70	83.3	74	108	68	81.3	74	109	70	83	75	110	70	83.3	74	108	68	81.3	72	106	66	79.3	75	108	70	82.67	100	1	T4	2	180	210	240
38	66	108	66	80	67	106	68	80.7	68	108	66	80	68	106	68	80.7	66	106	66	79.3	65	108	70	82.7	68	110	68	82	100	2	T6	3	150	180	210
39	58	114	74	87.3	58	112	74	86.7	59	110	70	83	60	110	70	83.3	60	110	72	84.7	60	110	74	86	60	110	70	83.33	100	1	T8	3	120	150	180
40	60	97	66	76.3	59	100	60	73.3	60	100	62	75	60	100	66	77.3	62	106	66	79.3	60	106	70	82	61	106	70	82	100	2	T6	3	150	180	210
41	74	102	60	74	74	104	60	74.7	75	108	66	80	74	110	60	76.7	73	112	62	78.7	72	110	68	82	75	110	66	80.67	100	1	T4	2	170	200	240
42	66	114	64	80.7	68	118	68	84.7	66	114	66	82	68	114	68	83.3	70	114	66	82	70	112	68	82.7	72	110	66	80.67	100	2	T6	3	150	180	210

BUPRENORPHINE

Serial No.	I.P no.	Sex	Age(yrs)	weight(kg)	height(cm)	ASA	proposed surg	HR(bpm)-P	SBP-P	DBP-P	MAP-P	SpO2-P	HR2	SBP2	DBP2	MAP2	HR4	SBP4	DBP4	MAP4	HR6	SBP6	DBP6	MAP6	HR8	SBP8	DBP8	MAP8	HR10	SBP10	DBP10	MAP10
1	997628	M	38	75	165	I	URS	76	130	80	96.67	100	72	120	80	93	68	118	70	86	68	110	70	83	66	108	66	80	65	106	66	79.33333333
2	997116	M	65	70	170	I	orchidec	68	130	70	90	100	68	130	70	90	65	120	80	93	64	118	70	86	64	114	66	82	62	110	66	80.66666667
3	995303	M	27	75	170	I	PCNL	76	126	86	99.33	100	74	126	86	99	72	118	84	95	63	116	80	92	65	114	70	84.67	64	114	68	83.33333333
4	995497	M	60	80	176	II	TURP	70	130	80	96.67	100	76	130	90	103	74	120	90	100	74	118	80	93	73	116	76	89.33	72	114	70	84.66666667
5	995551	F	42	68	165	I	DJ stent	70	116	82	93.33	100	70	120	80	93	68	116	66	83	65	110	66	81	66	112	66	81.33	66	114	68	83.33333333
6	995522	M	29	76	176	I	cystosco	78	120	80	93.33	100	76	120	90	100	75	118	90	99	74	112	80	91	72	110	80	90	72	110	76	87.33333333
7	992246	M	60	80	170	II	cystosco	70	130	90	103.3	100	72	130	90	103	72	128	88	101	70	124	86	99	68	122	84	96.67	66	120	76	90.66666667
8	994420	M	38	80	174	I	URS	80	120	90	100	100	80	120	80	93	80	120	76	91	78	116	70	85	75	112	70	84	74	110	70	83.33333333
9	993273	M	61	80	172	I	PCCL	80	140	90	106.7	100	78	130	90	103	78	130	88	102	76	126	88	101	74	110	80	90	74	112	76	88
10	993321	M	38	75	170	I	URS	80	130	80	96.67	100	76	120	90	100	76	120	88	99	75	120	86	97	74	116	80	92	72	110	80	90
11	990423	M	65	70	168	I	TURP	70	150	90	110	100	70	140	90	107	70	140	88	105	70	136	90	105	68	126	80	95.33	65	120	80	93.33333333
12	998430	F	46	85	168	II	TAH	80	120	70	86.67	100	80	120	90	100	79	118	70	86	75	112	70	84	75	110	80	90	74	112	82	92
13	999192	F	44	55	165	I	implant	70	120	80	93.33	100	78	130	90	103	75	120	90	100	74	118	86	97	72	112	82	92	70	110	80	90
14	949241	F	52	60	164	I	TAH wit	68	130	70	90	100	68	130	70	90	66	120	70	87	65	116	68	84	64	114	66	82	64	112	66	81.33333333
15	999893	M	20	65	170	I	HR	68	100	60	73.33	100	66	100	70	80	66	100	66	77	64	97	60	72	62	90	60	70	60	85	58	67
16	999205	F	55	70	165	II	hysterec	74	120	70	86.67	100	72	120	70	87	72	110	70	83	70	108	66	80	68	106	66	79.33	64	104	66	78.66666667
17	1001764	M	34	70	170	I	grafting	98	140	90	106.7	100	98	120	73	89	90	118	78	91	86	121	80	94	89	123	73	89.67	85	111	70	83.66666667
18	999415	M	23	65	168	I	bladder	67	110	70	83.33	100	72	110	70	83	68	110	68	82	66	100	70	80	66	110	70	83.33	66	100	68	78.66666667
19	999771	M	65	68	164	II	TURP	66	120	70	86.67	100	72	120	72	88	71	118	70	86	70	114	66	82	68	112	66	81.33	65	110	60	76.66666667
20	1000151	M	50	75	170	II	grafting	70	120	80	93.33	100	72	110	70	83	71	110	68	82	70	100	70	80	70	90	60	70	66	90	57	68
21	1008280	F	50	60	156	II	CRIF	68	148	76	100	100	68	140	84	103	66	136	80	99	65	134	80	98	66	130	70	90	65	104	64	77.33333333
22	1011245	M	32	70	168	I	URS	76	120	80	93.33	100	74	120	90	100	72	112	80	91	70	112	76	88	70	110	70	83.33	66	104	66	78.66666667
23	1011257	M	34	80	170	I	URS	76	130	80	96.67	100	72	130	80	97	70	120	80	93	65	110	76	87	64	108	76	86.67	65	106	74	84.66666667
24	1001352	F	58	65	166	II	Flap rep	70	130	90	103.3	100	70	120	90	100	70	116	80	92	66	112	74	87	66	110	72	84.67	65	108	72	84
25	1011730	M	65	66	170	I	HR	66	150	90	110	100	66	140	90	107	64	137	82	100	60	122	78	93	58	120	71	87.33	60	127	73	91
26	1012712	F	45	60	165	I	HR	80	120	70	86.67	100	80	110	70	83	80	110	76	87	76	100	55	70	68	100	50	66.67	66	90	50	63.33333333
27	1013424	M	43	70	168	II	debridm	76	130	70	90	100	74	120	70	87	74	120	72	88	72	110	70	83	70	110	70	83.33	68	108	70	82.66666667
28	1015066	M	54	65	168	I	HR	60	130	70	90	100	70	126	80	95	70	120	70	87	68	120	66	84	65	114	66	82	64	112	64	80
29	1015543	M	56	70	170	II	Excision	74	120	90	100	100	76	120	80	93	74	110	80	90	72	110	70	83	70	108	66	80	68	108	65	79.33333333
30	1015810	M	30	60	168	I	implant	72	120	80	93.33	100	70	120	76	91	68	118	76	90	66	116	74	88	67	114	70	84.67	66	112	68	82.66666667
31	1016268	M	29	55	170	I	ORIF	74	120	80	93.33	100	70	120	70	87	68	116	68	84	66	112	66	81	68	114	68	83.33	66	114	70	84.66666667
32	1015874	M	65	75	170	II	HR	65	130	80	96.67	100	65	120	80	93	64	112	76	88	64	112	76	88	66	114	74	87.33	65	112	72	85.33333333
33	1016035	M	57	70	168	I	HR	72	120	80	93.33	100	70	120	68	85	68	118	68	85	66	116	66	83	66	118	70	86	67	116	70	85.33333333
34	1016334	F	49	65	168	I	HR	62	110	70	83.33	100	60	110	70	83	60	108	70	83	56	100	60	73	55	100	56	70.67	55	96	56	69.33333333
35	1015195	M	18	50	164	I	ileostom	80	120	70	86.67	100	75	120	70	87	74	116	68	84	72	114	66	82	70	112	64	80	68	110	64	79.33333333
36	1018286	F	18	50	165	I	appendi	84	120	80	93.33	100	80	118	76	90	78	118	76	90	76	116	74	88	75	114	72	86	74	112	70	84
37	1020415	M	59	70	170	II	cystosco	78	130	90	103.3	100	74	110	70	83	72	108	68	81	70	106	66	79	68	104	66	78.67	66	104	66	78.66666667
38	1020767	M	64	68	170	II	URS	90	130	90	103.3	100	90	130	80	97	88	126	80	95	85	120	76	91	84	118	74	88.67	82	116	70	85.33333333
39	1021891	F	30	68	164	I	URS	88	110	70	83.33	100	87	120	80	93	86	110	72	85	85	108	68	81	85	100	60	73.33	82	100	58	72
40	1016162	F	43	60	165	I	HR	76	130	80	96.67	100	74	120	80	93	74	118	80	93	72	110	70	83	70	100	70	80	70	96	60	72
41	1016546	M	22	75	170	I	ORIF tib	76	130	80	96.67	100	76	126	86	99	76	120	84	96	75	116	80	92	74	100	78	85.33	72	100	70	80
42	1022613	M	24	70	168	II	Arthros	84	120	80	93.33	100	84	120	80	93	80	118	70	86	80	112	70	84	76	108	66	80	74	108	70	82.66666667

Serial No.	HR15	SBP15	DBP15	MAP15	HR20	SBP20	DBP20	MAP20	HR30	SBP30	DBP30	MAP30	HR45	SBP45	DBP45	MAP45	HR60	SBP60	DBP60	MAP60	HR75	SBP75	DBP75	MAP75	HR90	SBP90	DBP90	MAP90	SpO2	SB-onset(mins)	highest level	MB-Onset(mins)	MB-duration(mins	total duration(min)	rescue analgesia(min)
1	64	104	60	74.66666667	64	102	62	75.3	64	102	60	74	62	104	70	81.3	62	106	68	80.7	64	108	66	80	62	106	68	81	100	3	T4	4	180	240	270
2	64	114	68	83.33333333	65	112	68	82.7	66	110	70	83.3	62	108	68	81.3	64	106	66	79.3	62	106	66	79	64	104	66	79	100	4	T6	5	240	270	300
3	62	112	66	81.33333333	60	110	60	76.7	58	108	60	76	58	108	60	76	58	108	62	77.3	58	108	64	79	60	106	64	78	100	4	T6	6	240	270	300
4	70	112	70	84	70	110	68	82	68	110	66	80.7	68	108	66	80	69	110	66	80.7	68	108	65	79	69	106	66	79	100	4	T6	5	210	240	270
5	65	112	66	81.33333333	64	112	64	80	65	110	66	80.7	64	112	64	80	62	110	60	76.7	62	112	62	79	62	110	64	79	100	5	T6	6	240	270	300
6	74	110	74	86	72	110	72	84.7	70	108	74	85.3	68	106	72	83.3	68	106	70	82	66	106	66	79	64	104	64	77	100	4	T6	6	240	270	300
7	66	114	74	87.33333333	65	112	70	84	64	110	70	83.3	64	112	68	82.7	65	112	70	84	65	110	70	83	65	110	70	83	100	3	T6	4	210	240	270
8	72	110	68	82	72	108	68	81.3	70	110	70	83.3	68	112	68	82.7	65	110	66	80.7	64	108	64	79	65	108	64	79	100	4	T4	5	240	270	300
9	72	112	76	88	72	110	70	83.3	70	110	70	83.3	70	108	74	85.3	68	108	74	85.3	66	106	74	85	68	108	74	85	100	4	T6	5	240	270	300
10	70	108	64	78.66666667	68	100	60	73.3	65	100	58	72	64	100	60	73.3	64	98	60	72.7	64	96	60	72	64	100	60	73	100	4	T6	5	210	240	270
11	65	110	80	90	65	120	70	86.7	66	110	70	83.3	66	110	70	83.3	68	100	60	73.3	66	100	60	73	65	100	58	72	100	4	T8	5	210	240	270
12	72	110	76	87.33333333	72	110	74	86	70	110	72	84.7	68	108	70	82.7	66	104	70	81.3	66	106	66	79	66	102	66	78	100	4	T6	5	240	270	300
13	68	106	76	86	68	106	74	84.7	66	104	72	82.7	66	104	70	81.3	66	104	68	80	68	106	68	81	66	104	70	81	100	5	T6	6	240	270	300
14	64	110	66	80.66666667	64	110	66	80.7	66	112	66	81.3	64	110	66	80.7	66	108	66	80	66	108	68	81	66	104	66	79	100	4	T4	5	220	240	270
15	58	88	58	68	57	90	58	68.7	57	90	60	70	55	90	58	68.7	54	88	56	66.7	54	90	54	66	56	92	54	67	100	4	T6	5	210	240	270
16	65	106	65	78.66666667	62	104	64	77.3	64	106	62	76.7	63	108	60	76	60	106	58	74	58	104	56	72	56	100	58	72	100	4	T4	5	210	240	270
17	86	115	74	87.66666667	84	112	66	81.3	85	111	70	83.7	86	111	70	83.7	85	108	60	76	84	106	62	77	82	104	60	75	100	2	T8	4	210	240	270
18	64	100	60	73.33333333	62	90	60	70	64	90	60	70	64	92	60	70.7	66	94	60	71.3	64	96	62	73	64	94	60	71	100	3	T6	5	240	270	300
19	64	104	60	74.66666667	64	100	58	72	64	96	60	72	64	100	60	73.3	63	100	62	74.7	62	100	66	77	62	100	64	76	100	2	T8	3	210	240	270
20	65	90	60	70	64	90	58	68.7	64	90	60	70	63	90	58	68.7	63	92	60	70.7	62	92	62	72	64	92	64	73	100	3	T6	4	240	270	300
21	64	102	64	76.66666667	62	100	60	73.3	60	102	66	78	56	102	70	80.7	60	106	58	74	58	102	68	79	56	110	60	77	100	4	T4	5	240	270	300
22	65	104	65	78	64	102	64	76.7	64	102	62	75.3	62	100	60	73.3	62	102	60	74	60	100	58	72	60	102	56	71	100	3	T6	4	220	240	270
23	65	104	70	81.33333333	64	100	70	80	64	97	57	70.3	64	100	60	73.3	64	100	58	72	63	100	60	73	64	100	64	76	100	3	T4	5	240	270	300
24	65	106	72	83.33333333	64	104	70	81.3	64	100	66	77.3	64	100	68	78.7	64	100	70	80	63	100	70	80	64	104	70	81	100	4	T4	5	240	270	300
25	58	124	78	93.33333333	58	124	76	92	56	120	74	89.3	56	120	76	90.7	57	120	78	92	56	118	76	90	56	120	80	93	100	3	T4	5	240	270	300
26	60	90	52	64.66666667	62	91	53	65.7	62	97	56	69.7	63	90	60	70	62	91	53	65.7	62	90	60	70	62	90	60	70	100	2	T6	5	240	270	300
27	68	104	70	81.33333333	66	104	66	78.7	65	102	65	77.3	65	100	60	73.3	65	100	64	76	65	100	66	77	64	100	60	73	100	2	T6	4	210	240	270
28	64	112	60	77.33333333	64	110	60	76.7	67	108	60	76	68	104	60	74.7	68	104	66	78.7	65	104	64	77	64	104	66	79	100	1	T6	3	240	270	300
29	68	106	64	78	66	108	64	78.7	68	106	64	78	66	104	60	74.7	68	104	68	80	66	106	68	81	66	104	68	80	100	3	T6	4	210	240	270
30	66	110	66	80.66666667	65	108	65	79.3	65	106	64	78	66	104	62	76	66	106	64	78	64	108	66	80	66	106	66	79	100	3	T6	4	240	270	300
31	68	112	70	84	66	110	68	82	68	112	68	82.7	66	110	66	80.7	68	108	68	81.3	66	104	66	79	65	102	66	78	100	4	T4	5	210	240	270
32	66	114	70	84.66666667	64	112	68	82.7	64	110	66	80.7	64	112	68	82.7	64	110	68	82	64	112	66	81	64	110	66	81	100	3	T6	4	210	240	270
33	66	116	70	85.33333333	66	114	68	83.3	68	112	66	81.3	66	110	68	82	66	112	68	82.7	64	112	68	83	66	112	66	81	100	2	T6	4	240	270	300
34	55	94	52	66	54	94	54	67.3	55	96	52	66.7	55	94	52	66	54	94	50	64.7	55	96	50	65	54	96	52	67	100	4	T6	5	240	270	300
35	66	110	64	79.33333333	67	108	64	78.7	66	106	64	78	65	106	64	78	68	106	66	79.3	68	108	66	80	66	104	66	79	100	3	T6	5	210	240	270
36	72	108	68	81.33333333	70	106	66	79.3	66	104	66	78.7	68	104	66	78.7	68	104	66	78.7	66	106	66	79	65	106	66	79	100	3	T6	5	240	270	300
37	68	102	66	78	66	100	66	77.3	68	102	66	78	66	100	68	78.7	66	102	66	78	68	100	66	77	66	100	64	76	100	4	T6	5	240	270	300
38	80	114	76	88.66666667	76	110	70	83.3	75	110	72	84.7	75	112	72	85.3	74	114	72	86	74	114	72	86	74	112	70	84	100	4	T6	5	240	270	300
39	82	96	58	70.66666667	82	97	57	70.3	82	94	50	64.7	81	96	58	70.7	80	96	60	72	82	96	58	71	82	95	60	72	100	2	T8	4	210	240	250
40	66	90	60	70	66	94	66	75.3	68	96	68	77.3	67	100	66	77.3	68	100	65	76.7	67	96	65	75	66	98	65	76	100	2	T6	4	210	230	260
41	70	100	66	77.33333333	70	102	70	80.7	70	102	72	82	71	104	70	81.3	72	100	60	73.3	72	100	68	79	71	96	68	77	100	3	T6	4	240	270	300
42	75	104	70	81.33333333	76	106	66	79.3	75	108	66	80	75	110	66	80.7	74	108	66	80	72	104	68	80	71	106	66	79	100	3	T4	5	240	250	270