‘A COMPARATIVE STUDY BETWEEN INTRATHECAL CLONIDINE AND NEOSTIGMINE WITH INTRATHECAL BUPIVACAINE IN LOWER ABDOMINAL SURGERIES’

Dissertation submitted in partial fulfilment of

M.D. DEGREE EXAMINATION

M.D ANAESTHESIOLOGY – BRANCH X

CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2016

DECLARATION

I hereby declare that the dissertation entitled "**A comparative study between intrathecal clonidine and neostigmine with intrathecal bupivacaine in lower abdominal surgeries**" was done by me in the Department of Anaesthesiology, Chengalpattu Medical College under the guidance and supervision of **Prof.Dr.Revathy, M.D**,**D.A**, Professor and Head, Department of Anaesthesiology, Chengalpattu Medical College.

This dissertation is submitted to the Tamilnadu Dr.MGR Medical University, Chennai towards the partial fulfilment of the requirement for the award of M.D.Degree in Anaesthesiology.

I have not submitted this dissertation on any previous occasion to any University for the award of any degree.

Place : Chengalpattu

Date : **Dr.Vaishnavi Devi.V**

CERTIFICATE

This is to certify that the dissertation entitled "**A comparative study between intrathecal clonidine and neostigmine with intrathecal bupivacaine in lower abdominal surgeries"** is a record of bonafide work done by **Dr.Vaishnavi Devi.V** in the Department of Anaesthesiology, Chengalpattu Medical College, Chengalpattu under the supervision of **Prof**.**Dr.Revathy M.D.D.A,** Professor and Head, Department of Anaesthesiology and submitted in partial fulfilment of the requirements for the award of M.D. Degree in Anaesthesiology by The Tamilnadu Dr. MGR Medical University, Chennai. This work has not previously formed the basis for the award of a degree or diploma.

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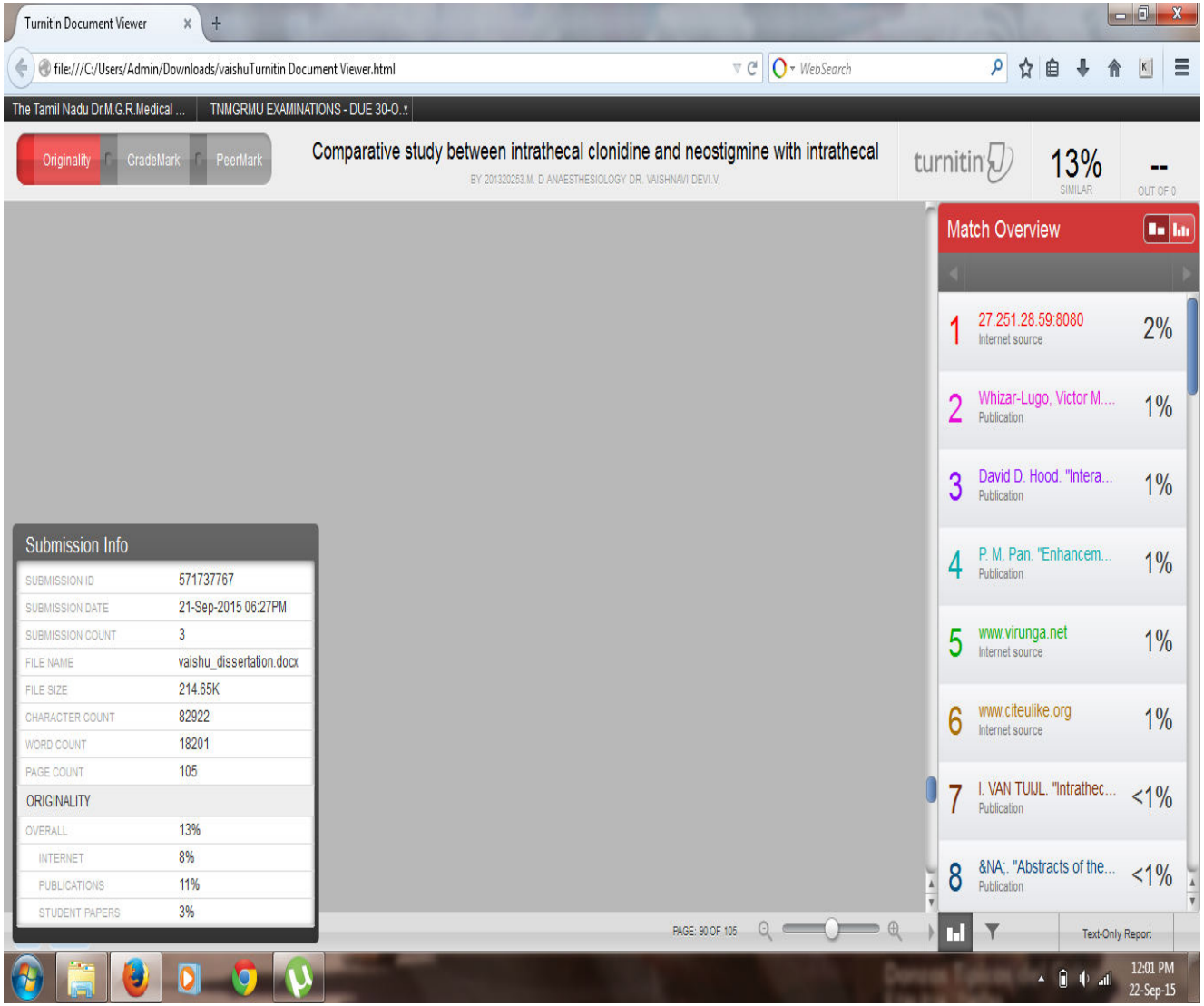
Dr.Vaishnavi Devi.V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ABSTRACT

BACKGROUND

Lower abdominal surgeries like hernioplasty, abdominal hysterectomy are commonly performed surgeries. Providing good analgesia with adequate muscle relaxation during intra operative period and managing pain in the post operative period is a good practice of anaesthesia. As pain influences the morbidity and mortality of the patients, it's important to ease pain due to surgery for better outcome of the patients.

Commonly, lower abdominal surgeries are performed under spinal anaesthesia, as it is easy to perform, single shot technique when compared to epidural anaesthesia and general anaesthesia. But the main problem of spinal anaesthesia is that postoperative analgesia lasts only for considerable period.

This study is conducted to analyse the effect of adding additives 50 µ of neostigmine and 50 µ of clonidine to 0.5% hyperbaric bupivacaine and evaluating the duration of postoperative analgesia with each drug and the intraoperative haemodynamic stability in patients undergoing lower abdominal surgeries.

AIM:

To study the better adjuvant for intrathecal bupivacaine to achieve better quality regional block with stable haemodynamic status and good postoperative pain relief.

OBJECTIVES:

The objective of the study is comparative evaluation of clonidine and neostigmine with 0.5% hyperbaric bupivacaine in spinal anaesthesia with respect to

Onset time for sensory block

Onset time for motor block

Level of sensory blockade

Quality of motor blockade

Intraoperative haemodynamics

Duration of postoperative analgesia

Quality of postoperative analgesia and Adverse effects

MATERIALS AND METHODS

Study involves adult patients aged between 18 – 60 years, ASA grade 1 and 2 posted for lower abdominal surgeries.Patients were randomly divided into two groups group A ,B,C ,group A received intrathecal neostigmine 50 micrograms with 2.5 ml of 0.5% hyperbaric bupivacaine and group B received 50 micrograms of clonidine with 2.5ml of 0.5% hyperbaric bupivacainegroup C received plain hyperbaric bupivacaine 0.5% 2.5 ml.On the day of surgery IV line secured with 18G cannula, IV midazolam 1mg given as premedication. Patients connected to multiparamonitor showing ECG, PR ,NIBP and SPO 2 and basal readings recorded. All patients are preloaded with IV fluids of 10 ml/kg .Under strict aseptic precautions lumbar puncture performed at L3-L4 space using 25 G spinal needle in right lateral position, the study drugs are injected into subarachnoid space at the rate of 1ml/3 sec. Patient turned supine immediately and supplemental oxygen given.

Following parameters are observed

Onset time for sensory block

Onset time for motor block

Level of sensory blockade

Quality of motor blockade

Intraoperative haemodynamics every 5^{th} minute

Duration of postoperative analgesia

Quality of postoperative analgesia and Adverse effects

RESULTS

This study was done to compare the use of neostigmine 50µ , clonidine 50µ along with 0.5% hyperbaric bupivacaine in spinal anaesthesia in patients undergoing lower abdominal surgeries in providing postoperative analgesia with stable haemodynamic status.

A total of 60 patients were randomly allocated into three groups, 20 patients in each group. Group A received 2.5 ml of 0.5% hyperbaric bupivacaine, Group B received 50µ of neostigmine with 2.5 ml of 0.5% hyperbaric bupivacaine, Group C received 50µ of clonidine with 2.5 ml of 0.5% hyperbaric bupivacaine. Various haemodynamic parameters complications if any were recorded at second minute after spinal and every 5 minutes till the end of surgery.

The observations were noted as follows

Sensory block mean onset time for Group A is 176.2 ± 6.948, Group B is 96.9 ± 19.472 and Group C is 113.95 ± 14.666.

Motor block mean onset time is Group A is 166.2 ± 7.824, Group B is 96.2 ± 29.243, Group C is 102.75 ± 29.993 seconds.

Duration of surgical anaesthesia in Group A is 176.2 ± 6.948, Group B is 96.9 ± 19.472 and Group C is 113.95 ± 14.666.

Haemodynamic changes were significant between three groups.

No significant changes were observed with VAS score.

Complications were seen in Group B nausea, vomiting, cough and chest pain and in Group C bradycardia and hypotension were seen.

CONCLUSION

The observations of this study regarding the sensory and motor block onset time, duration of sensory and motor block, postoperative analgesia show that spinal neostigmine has faster onset in both sensory and motor blockade, but spinal clonidine has longer duration of sensory and motor blockade, and has good post operative analgesia.

The findings suggest that the use of clonidine 50µ along with 2.5 ml of 0.5% hyperbaric bupivacaine in lower abdominal surgeries has an added advantage in comparison with hyperbaric bupivacaine, as it provides longer duration of sensory and motor blockade, faster onset time of sensory block and good post operative analgesia, promotes early ambulation, shorter duration of hospital stay and thus reducing postoperative morbidity. Also it avoids multidrug exposure and its side effects.

This study concluded that spinal clonidine 50µ along with 0.5% hyperbaric bupicaine is better than 0.5% hyperbaric bupivacaine alone as a effective adjuvant , providing good postoperative analgesia.

INTRODUCTION

Pain is subjective in nature and can only be perceived by the sufferer. *International association of the study of pain (IASP) defined 'pain as an unpleasant sensory or emotional experience which is associated with actual or potential tissue damage or described in terms of such damage'.* No two patients, even if they having the same operation , will experience same pain. Alleviation of pain during and after surgery plays important role in outcome of the patients.

As anaesthesiologist effective post operative pain management is an essential part in the care of surgical patients. As said by *Durate in 1997* 'post operative pain is acute form of pain resulting from surgical injury which causes inflammation and neuronal damage that resolves during the appropriate healing period'.

Effective control of postoperative pain can reduce morbidity and mortality by providing patient comfort and satisfaction , early mobilization thus less chances of deep venous thrombosis and faster recovery with less likelyhood of development of chronic neuropathic pain at lower cost and less hospital stay.

Different modalities of management of post operative pain are available which includes pharmacological and non pharmacological therapies. Pharmological methods include administration of drugs like opioids , non opioids and adjuvants (ketamine , clonidine , neostigmine).

As most lower abdominal surgeries are commonly performed under spinal ansesthesia , adding adjuvants which prolong the duration of analgesia and provide

post operative pain relief can be beneficial. As spinal anaesthesia is performed with single puncture and single shot technique with convention local anaesthetic agents which will not be able to alleviate postoperative pain,continuous research is going on to extend intraoperative analgesia to post operative period.

Addition of opioids to spinal anaesthesia improves analgesia but the period of post operative analgesia lasts only for considerable period. So newer adjuvants like clonidine , neostigmine , ketamine to local anaesthetic agents have been tried with varying success rates. Clonidine , alpha 2 agonist which is centrally acting and neostigmine , anticholinesterase has been tried for post operative analgesia with varying successful rates.

This study is designed to find the effect of adding clonidine and neostigmine with 0.5% hyperbaric bupivacaine for spinal anaesthesia in lower abdominal surgeries.

AIMS AND OBJECTIVES

AIM:

To study the better adjuvant for intrathecal bupivacaine to achieve better quality regional block with stable haemodynamic status and good postoperative pain relief.

OBJECTIVES:

The objective of the study is comparative evaluation of clonidine and neostigmine with 0.5% hyperbaric bupivacaine in spinal anaesthesia with respect to

Onset time for sensory block

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Duration of postoperative analgesia

Quality of postoperative analgesia and Adverse effects

ANATOMY

VERTEBRAL COLUMN:

The vertebral column forms the central pillar of the body. It consist of 33 vertebrae in total – 7 cervical vertebrae, 12 thoracic , 5 lumbar , 5 sacral and 4 coccyx. The adult spine has four curvatures – cervical and lumbar curvature with lordosis , thoracic and sacral curvature concave forwards (kyphosis). The thoracic and sacral curvatures are primary , present during embryonic period where as cervical and lumbar curvatures develope later. These curvatures are produced by posture and configuration of bones to themselves. The vertebral column encloses vertebral canal which consist of spinal cord and nerves.

VERTEBRAE:

A vertebra has following parts – body of vertebra , vertebral arch , processes – articular , transverse and spinous , vertebral foramina. The vertebral bodies are separated from each other by intervertebral discs. The vertebral arch consists of right and left pedicles and laminae. At the junction of pedicles and lamina arises the transverse process facing laterally. Spinous process of vertebra arises from the posterior side. The superior and inferior articular processess projects vertically from the vertebral arches and have articular facets.

LUMBAR VERTEBRA:

Lumbar vertebrae are 5 in number. The lumbar vertebrae has large vertebral body which is kidney shaped. It has a triangular vertebral foramen. It has thick and

short pedicles. The lamina is short , broader and stronger and does not overlap each other. The transverse process of lumbar vertebrae are slender , has articular facets. A mammillary process projects posteriorly from the superior articular process. The spinous process of lumbar vertebrae are thick , oblong and horizontal. The fifth lumbar vertebra is the largest , wedge shaped , deeper in front than back , so it produces lumbosacral angle.

SPINAL CORD:

The spinal canal has spinal cord which is the continuation of medulla oblongata and ends below as conus medullaris from which filum terminale descends till coccyx. In adults the spinal cord ends at the level of L1 , in children ends at the level of L3. The spinal cord contains a covering called meninges , which has three layers – pia mater , arachnoid mater and dura mater from inside out. The pia mater is very close to the spinal cord , the arachnoid mater is usually adherent to the dura mater. The Cerebrospinal fluid (CSF) is present between the pia mater and the arachnoid maters in the subarachnoid space. Spinal cord gives rise to 31 pairs of spinal nerves – eight cervical , twelve thoracic , five lumbar , five sacral and one coccygeal. Each spinal nerve consist of anterior and posterior spinal nerve roots . The lower spinal nerves form cauda equina (horse tail). The cauda equina consist of lumbar and sacral nerves bathed in CSF that descends to meet their respective foramina.

The blood supply to the spinal cord and spinal nerve roots is derived from single anterior spinal artery and two posterior spinal arteries. The anterior spinal

artery , branch from vertebral artery , supplies anterior two third of the spinal cord . The posterior spinal arteries , branch from posterior inferior cerebellar arteries , supplies posterior one third. The anterior and posterior spinal arteries receive extra blood flow from intercostals arteries in thoracic region and from lumbar arteries in lumbar region. The artery of Adamkiewicz , large radicular artery , usually unilateral , provides major blood supply to anterior and lower two third of spinal cord, arises from aorta.

ANATOMY OF SUBARACHNOID SPACE:

The subarachnoid space lies between pia mater and arachnoid mater. This space communicates with ventricular system of the brain.

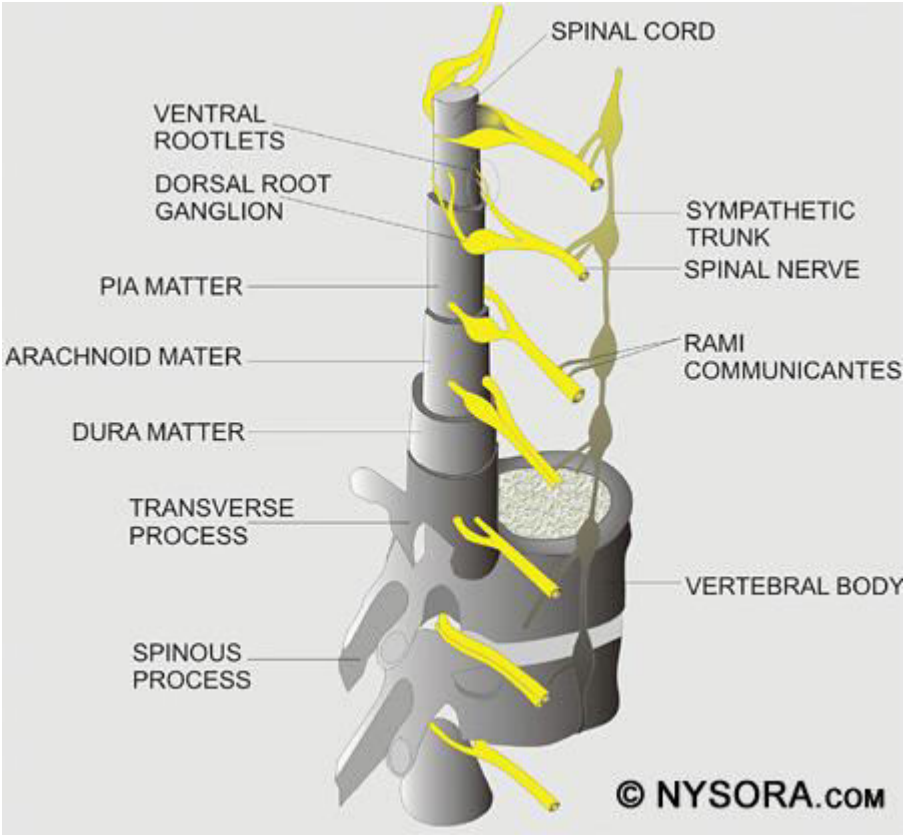
Contents :

Spinal nerve roots

Cerebrospinal fluid

Denticulate ligaments

Reticulum of fibers connecting pia mater and arachnoid mater.



SPINAL ANAESTHESIA:

Spinal anaesthesia is performed by injecting local anaesthetic agents into subarachnoid space by means of lumbar puncture. First spinal anaesthesia was performed by J.Leonard Corning ,a New York neurologist in the year 1885, in dogs. First spinal anaesthesia in human was performed by August Bier in 1898 using 0.5% cocaine.

TECHNIQUE:

Positioning the patient after getting informed consent plays impotant role in spinal anaesthesia. Three types of positioning have been described – lateral decubitus , sitting and prone position. Usually spinal anaesthesia is performed in lateral decubitus and sitting position. The patient should be asked to flex his or her

spine in order to widen the vertebral spaces. The lumbar puncture is usually performed at the level of L3 and L4 interspace or L4 and L5 interspace. The line that joins the highest point of iliac crests , the intercrestal line , also called line of Tuffier. This line usually corresponds to L4 vertebra or L4/L5 space. The introduction of spinal needle at this space is appropriate as the spinal cord ends at the level of L1 in adults. The entry of needle at the intervertebral space can be midline or paramedian approach.

After infiltration of the preferred intervertebral space with local anaesthetic agents , spinal needle is inserted and it passess through following structures before puncturing dura mater , where a “pop off ” is felt.

Skin

Subcutaneous tissue

Supraspinous ligament

Interspinous ligament

Ligamentum flavum

After puncturing the dura mater, the stylet of spinal needle is withdrawn to see the cerebrospinal fluid in the hub of the needle. The local anaesthetic agent is injected after aspirating the CSF.

MECHANISM OF ACTION OF SPINAL ANAESTHESIA:

The site of action of local anaesthetic agents in spinal anaesthesia is mainly on the nerve roots. The following are blocked after injecting the local anesthetic agents into CSF in subarachnoid space – sympathetic pre ganglionic b fibers , sensory fibers (Aβ , Aδ, C fibers) , motor fibers (Aα , Aγ)(differential blockade) .

PHYSIOLOGICAL EFFECTS OF SPINAL ANAESTHESIA:

EFFECTS ON CARDIOVASCULAR SYSTEM:

Spinal anaesthesia produces variable decrease in blood pressure along with decrease in heart rate. Usually this effect is due to block of sympathetic fibers which innervates arteries and veins. Due to sympathetic blockade, there is both venous and arteriolar dilatation causing venous pooling of blood and decreased systemic vascular resistance respectively. A high sympathetic block prevents the compensatory vasoconstriction and also block the sympathetic cardiac accelerator fibers that arises from T1-T4, leading to bradycardia and cardiac arrest due to unopposed vagal tone.

PULMONARY EFFECTS:

Effect of spinal anaesthesia on respiratory system is very less , as the nerve fibers that innervate diaphragm arise from C3-C5. Usually even in patients with high thoracic levels, tidal volume remains normal with very little decrease in vital capacity. Only in patients with severe respiratory disease, who rely on action of accessory muscles of respiration for breathing will have difficulty.

EFFECT ON GASTROINTESTINAL SYSTEM:

Spinal anaesthesia blocks sympathetic fibers that supplies the gut, thereby increasing the vagal tone, resulting in small contracted gut with active peristalsis. It also decreases hepatic blood flow by decreasing mean arterial pressure.

EFFECT ON GENITOURINARY SYSTEM:

Spinal anaesthesia has very little effect on renal function as the blood flow to the kidney is maintained due to autoregulatory mechanism. Urinary retention after subarachnoid block is common as both the sympathetic and parasympathetic supply to the bladder is blocked. So in long duration surgeries it is must to place a urinary catheter preoperatively.

EFFECT ON ENDOCRINE SYSTEM:

Surgical trauma causes significant neuroendocrine response by activation of somatic and visceral nerve fibers. It causes increased serum concentration of cortisol , epinephrine , norepinephrine , vasopressin , renin – angiotensin and also increase in oxygen consumption by tissues. Due to this neuroendocrine response there is intra operative tachycardia , hypertension , hyperglycemia and increased catabolism with decreased immunity. Spinal anaesthesia decreases this stress response to surgery thus decreasing intra operative and post operative complications.

FACTORS INFLUENCING SPINAL ANAESTHESIA:

- POSITION OF THE PATIENT DURING INJECTION OF DRUG:

  If hyperbaric solution is used , in sitting posture solution gets settled down , in lateral position , the side on which the patient lies the drug get fixed later in spreads to other side.

- INTERVERTEBRAL SPACE CHOSEN:

  The higher the intervertebral space chosen , higher will be the level of analgesia. It is better to chose L2-L3 space in upper abdominal surgeries , L3-L4 space in lower abdominal surgeries , L4-L5 space in perineal procedures.

- VOLUME OF DRUG INJECTED:

  Height of analgesia acquired in spinal anaesthesia is directly dependent on the volume of drug injected into the subarachnoid space.

- BARBOTAGE:

  It is a method of mixing the drug which is to be injected into subarachnoid space with volume of cerebrospinal fluid for the purpose of dispersion. By barbotage , the concentration and specific gravity of the drug injected is reduced thereby decreasing the effect of gravity after injection of drug.

- DOSE OF DRUG:

Greater the concentration and dose of drug , longer will be the duration of analgesia.

- FORCE AND RATE OF INJECTION OF DRUG:

Greater the force and rate of injection of the drug , higher will be the level of block achieved. A slow and gentle injection will have lower level of block .

- SPECIFIC GRAVITY OF THE DRUG INJECTED:

Specific gravity of the injected drug will have significant effect on spinal anaesthesia. The solution may be hyperbaric , hypobaric or isobaric in nature. In hyperbaric and hypobaric solution , the posture of the patient during and after the procedure will have great impact.

- POSTURE OF THE PATIENT AFTER INJECTION OF DRUG:

If the patient assumes lateral position after giving spinal anaesthesia and the curves of spine are without effect , the gravity of solution determines the side of analgesia.

If the patient lies supine after spinal , the baricity of the drug injected and the anatomy of the spine influences the level of spread.

If the patient is in lithotomy position , the lumbar curvature is obliterated. In this posture the hyperbaric solution moves cephalad and the hypobaric solution moves caudally.

- DURATION OF ANALGESIA:

  Depends on the drug used , bupivacaine addition of additives increases the duration of analgesia.

- FIXATION OF DRUG:

  Depends on the drug used , lignocaine takes 2-5 mins where as bupivacaine takes about 3- 15 mins.

- OTHER FACTORS:

  Age, curvature of spine , intrabdominal pressure , needle direction , patient height and pregnancy.

MECHANISM OF ACTION OF LOCAL ANAESTHETIC AGENTS IN SPINAL ANAESTHESIA:

- The site of action of local anaesthetic agents in spinal anaesthesia is mainly on the spinal nerve roots.

- Local anaesthetic agents acts on the sodium and potassium channels in the dorsal horns of nerves and inhibits the generation and propagation of nociceptive signals.

- Motor block is achieved by inhibiting ion channels in the ventral horns of the nerves.
- Centrally administered local anaesthetic agents acts by blocking calcium channels , which causes development of resistance to electrical stimulation from nociceptive afferent fibers.

ADDITIVES IN SPINAL ANAESTHESIA:

The aim of adding additives along with local naesthetic agents in spinal anaesthesia is to increase the quality of spinal anaesthesia and analgesia.

- Additives decrease the requirement of local anaesthetic agents.
- It intensifies and prolong the duration of analgesia
- Has synergistic action , thus decreasing the dose of drug and side effets of individual agents.

INDICATIONS OF SPINAL ANAESTHESIA:

- In lower abdominal surgeries – inguinal hernia , appendicectomy
- Urogenital surgeries
- Surgeries on lower extremities
- Gynaecological surgeries – abdominal and vaginal hysterectomy
- Obstetrical – caesarean section

CONTRAINDICATIONS FOR SPINAL ANAESTHESIA:

- **Absolute :**

  Patient refusal

  Infection at the puncture site

  Coagulopathy and bleeding diathesis

  Platelet less than 1,00,000

  Severe hypovolemia

  Increased intracranial pressure

  Severe Mitral and aortic stenosis

  Patients allergic to local anaesthetic agents

- **Relative**

  Patients with pre existing neurological deficit

  Patients with severe spine deformities

  Patients who are not cooperative for the the procedure

  Sepsis

  Stenotic valvular lesions

COMPLICATIONS OF SPINAL ANAESTHESIA:

- **Early :**

  Failure or incomplete block

  Total spinal anesthesia

  High spinal

  Hypotension

  Bradycardia

  Cardiac arrest

  Nausea and vomiting

  Shivering

- **Delayed :**

  Backache

  Urinary retension

  Post dural puncture headache

  Nerve root injury and Meningitis

PHARMACOLOGY

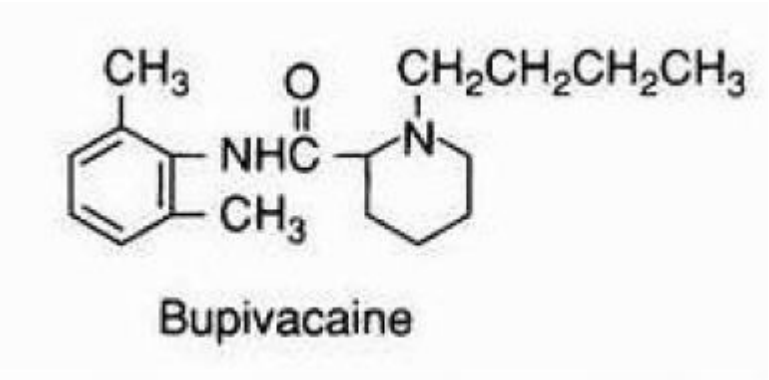
BUPIVACAINE:

It is the first amide local anaesthetic agent,long acting agent, synthesised by B.A.F Ekenstan in 1957. It was first used clinically by Talivuo and Widman in 1963.

CHEMICAL FORMULA:

2-piperidinecarboxamide, 1-butyl-N-(2, 6- di methyl phenyl)-, mono hydrochloride , mono hydrate.

STRUTURAL FORMULA:



Bupivacaine

PHYSICAL PROPERTIES:

pKa is 8.1

Protein Binding is 95%

Higher Lipid Solubility

Molecular weight is 288

Aqueous lipid solubility coefficient is 343

It is a white crystalline powder which is freely soluble in 95 % ethanol, also soluble in water, and shows little solubility in chloroform or acetone.

It has left(S) or right (R) configuration. The available bupivacaine in market is racemic mixtures of the enantiomers. The permeability of the drug through dura and the movement of bupivacaine through the sodium channel present in the nerve membrane are determined by the molecular weight.

As bupivacaine has high lipid solubility it enhances the speed of onset of action and also increases the potency and duration of effect, rapid entry into the lipid membrane of the cells and longer duration of action.

MECHANISM OF ACTION OF BUPIVACAINE:

Bupivacaine , is the drug that causes reversible interference in the entry of sodium into the nerve cell causing decreased membrane permeability and increases the threshold for electrical excitability. It inhibits the generation and conduction of nerve impulses by increasing the threshold of excitation in the nerve, also slows the propagation of the nerve impulse, and reduce the rate of rise of the action potential.

Binding affinity of local anaesthetics to sodium channels are stereo specific and depends on the state of the sodium channel.

Sodium channels exist in 3 states - activated (open), inactivated (closed) and resting (closed) states, during various phases of the action potential. Bupivacaine binds to sodium channels that exist in inactivated closed state, thus preventing

their change to rested closed and activated open states when nerve stimulus is initiated.

Bupivacine binds to the sites located on the inner side of the sodium channels and obstructs the external openings and maintains the channel in inactivated closed state, which is not permeable to sodium, the conduction of nerve impulses stops. The use of local anaesthetic agent alone is less common than the use of local anesthetic-opioid combination because of a significant failure rate (regression of sensory block and inadequate analgesia) and relatively high incidence of hypotension.

The quality of anaesthesia is related to the diameter, myelination of the nerve fibers and conduction velocity of affected nerve fibers. The order of anaesthesia of nerve fibers are as follows: pain , temperature, touch, proprioception, and skeletal muscle tone.

PHARMACOKINETICS:

- **ABSORPTION:**

The rate of absorption of the drug depends on the total dose and concentration of drug administered, the route by which it is administration, the vascularity of the site in which it is administered, and presence or absence of epinephrine in the anaesthetic solution.

The onset of action of bupivacaine is fast and long-lasting. The duration of action is longer. It is said that there is a period of analgesia that persists even after the return of sensation, thus delays the requirement of rescue analgesia.

- **DISTRIBUTION:**

Bupivacaine has high protein binding capacity of about 95% , so the plasma concentration of the drug administered will be less. Bupivacaine has a low foetal/maternal ratio (0.2-0.4). First pass pulmonary extraction is dose dependent.Lipid soluble, non-ionized form of drug enters the foetal blood from the mothers circulation.

Based on the route of administration, bupivacaine gets distributed to all tissues in the body, with high concentrations found in organs with high blood supply such as the liver, lungs, heart and brain.

Plasma profile of bupivacaine has been studied which shows that after direct intravenous injection of the drug , a three-compartment distribution is seen. The first compartment signifies the rapid intravascular distribution of the drug. The second compartment shows the equilibration of the drug in organs with rich blood supply such as the brain, myocardium, lungs, kidneys, and liver. The third compartment represents an equilibration of the drug in otissues with less blood supply, such as muscle and fat.

The elimination of drug from the tissues depends mainly on the ability of binding sites in the circulation to carry it to the liver where it gets metabolized.

After injection of bupivacaine , peak levels of bupivacaine in the blood are reached within 30 to 45 minutes, declines to insignificant levels from next 3 to 6 hours.

The effect of bupivacaine can be altered by the presence of hepatic or renal disease, addition of epinephrine , renal blood flow and the route of administration of drug.

The half-life $t^{1/2}$(hrs) :

Adults : 2.7 hours *Neonates* : 8.1 hours

METABOLISM:

Bupivacaine is metabolized in the liver through conjugation with glucuronic acid. Patients with severe hepatic disease, are susceptible to the potential toxicities. The major metabolite of bupivacaine is N-desbutyl bupivacaine.

EXCRETION:

Excreted mainly by kidneys **.**Urinary excretion depends on renal perfusion and urinary pH . Only 5% of bupivacaine is excreted unchanged in the urine.

PHARMACODYNAMICS:

Bupivacaine when absorbed systemically can produce central nervous and cardiovascular effects. At therapeutic doses, following changes are seen in cardiovascular system – abnormality in cardiac conduction, excitability, contractility, and peripheral vascular resistance.

Due to depression of cardiac conduction and excitability, atrioventricular block, ventricular arrhythmias and even cardiac arrest can occur. Also there is decrease in myocardial contractility and peripheral vasodilation leading to decreased blood pressure.

Systemic absorption of bupivacaine can cause central nervous system stimulation, depression or both. Stimulation of central nervous system leads to agitation, shivering, tremors and convulsions later depression and coma , finally respiratory arrest.

DOSE:

The required dose of bupivacaine should be calculated based on -the type of procedure to be performed, the anatomical area to be anaesthetized, the vascularity of the tissues to be anaesthetized, the number of segments to be blocked, the depth of anaesthesia and quality of muscle relaxation required, duration of anaesthesia required, individual tolerance and the physical condition of the patient.

The recommended dose is plain bupivacaine 2mg/kg and with epinephrine 3 mg/kg.

USES OF BUPIVACAINE:

- Spinal anaesthesia (0.5%)
- Epidural anaesthesia(0.125% - 0.75%)
- Nerve blocks (0.25 %- 0.5 %)

- Local infiltrations (0.25 %)
- Retrobulbar and peribulbar blocks
- Caudal anaesthesia

ADVERSE EFFECTS:

- Allergic reactions to the drug – usually seen in less than 1 % of the individuals , characterized by rash ,urticaria , bronchospasm , laryngeal oedema , hypotension.
- Systemic toxicity – central nervous system toxicity and cardiovascular toxicity. Central nervous system toxicity occurs when the serum plasma concentration of the drug is 4.5 – 5.5 μ/ml. Characterized by circumoral numbness , restlessness, vertigo, tinnitus, slurred speech, twitching of facial muscles and convulsions.

Cardiovascular toxicity occurs when the plasma concentration of the drug is above 8μ/ml. Usually seen after accidental intravenous injection of bupivacaine. Characterized by sudden hypotension , atrioventricular block ,dysrythmias and sudden cardiac arrest. Cardiac arrest caused due to bupivacaine is very difficult to revive. Bertylium and intralipids can be used to treat both cardiovascular and neuro toxicity.

CONTRAINDICATIONS FOR BUPIVACAINE USE:

- Known hypersensitivity to the drug
- Heart block
- Severe Sepsis
- Intravenous regional anaesthesia – Biers block
- Obstetrical paracervical block

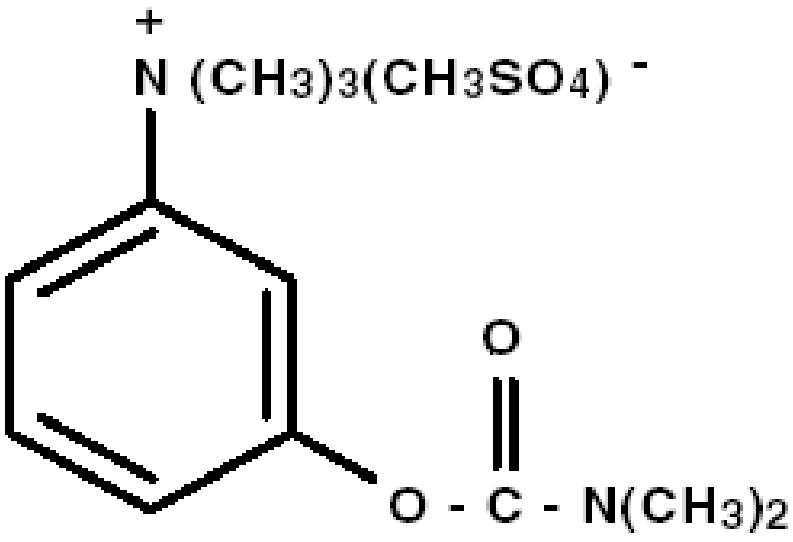
NEOSTIGMINE:

Neostigmine is a parasympathomimetic drug which act as reversible Acetylcholine inhibitor. It is first synthesised by Aeschlimann and Reinert in 1931.

CHEMICAL FORMULA:

3-dimethyl amino phenol with N- di methyl carbamate.

STRUCTURAL FORMULA:



MECHANISM OF ACTION OF NEOSTIGMINE:

Neostigmine acts by inhibiting the hydrolysis of acetylcholine by competitively binding to the esteric site of acetylcholinesterase. It causes accumulation of acetyl choline there by enchancing he cholinergic action and facilitates impulse transmission.

Neostigmine when given in subarachnoid block that is spinal anaesthesia it gets absorbed into cerebrospinal fluid. Neostigmine acts both on the muscarinic and nicotinic receptors. In spinal , neostigmine acts on the Lamina 2 Substantia Gelatinosa of Ronaldi and on Lamina 3 and 4, and cause stimulation of muscarinic receptors M1 and M2.

PHYSICAL PROPERTIES OF NEOSTIGMINE:

Molecular weight - 303.1

Protein binding – 15% -25%

PHARMACOKINETICS:

- ABSORPRION:

  When given in spinal anaesthesia ,it gets absorbed rapidly in the CSF, but the gastrointestinal route of absorption is poor. Intravenously administered neostigmine gets absorbed within minutes and the onset action time is 1-2 minutes. When given through intramuscular route the onset of action takes 20 – 30 minutes.

- DISTRIBUTION:

  Neostigmine is only 15 -25% protein bound. It is bound to albumin.

- HALF LIFE :

  Half life is 50 -90 minutes.

- METABOLISM:

  Neostigmine is metabolized by liver with microsomal enzymes. It also undergoes hydrolysis by cholinesterase.

- EXCRETION:

  Neostigmine , upto 50% is excreted unchanged in urine.

  Total body clearance is between 1.14 and 16.7 ml/kg/min.

DOSE :

- For reversing the effect of neuromuscular blocking agents , non depolarising muscle relaxants , the dose usually used is 40-80µ/kg. Usually atropine is given before giving neostigmine to prevent bradycardia. Neostigmine should be given slowly and dose should be titrated based on the response using nerve stimulator.

- In myasthenia gravis , neostigmine is given as oral tablets , dose ranges from 50 – 300 mg per day.

USES:

- Reversing the non depolarising block
- Treatment of myasthenia gravis
- Prevention and treatment of postoperative urinary retension

ADVERSE EFFECTS:

- Hypersensitivity
- Arrhythmia , AV blocks and cardiac arrest
- Convulsion
- Gastrointestinal cramps
- Urinary frequency

CONTRAINDICATIONS:

- Known allergy to drug
- Intestinal or urinary tract obstruction
- Bronchial asthma
- Patients with cardiac arrhythmias
- Neostigmine should be used with caution in patients with epilepsy , hyperthyroidism , peptic ulcer , recent myocardial infarction , av blocks.

DRUG INTERACTIONS:

- Neostigmine prolongs the phase 1 block produced by depolarising muscle relaxants. So it should not be used to reverse this type of blocks.
- Neostigmine has additive effects when used with opioids.
- Neostigmine also has additive effects with alpha adrenoreceptor agonists like clonidine.

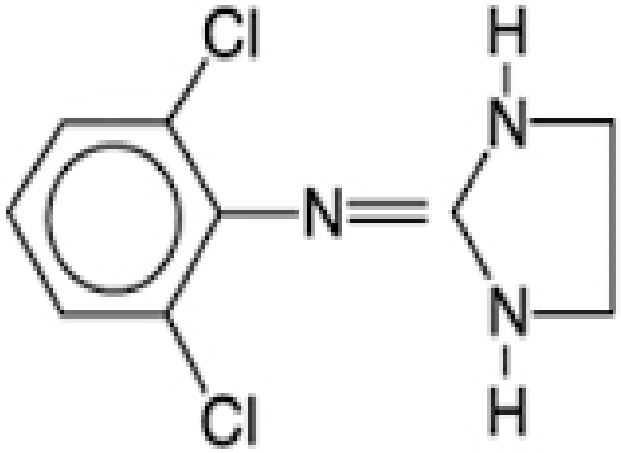
CLONIDINE:

Clonidine is a centrally acting alpha 2 adrenergic agonist and also imidazoline receptor agonist , having sympatholytic action. Clonidine is synthesised by Boehringer Ingelheim in 1966.

CHEMICAL FORMULA:

N-(2,6 -dichlorophenyl) -4,5 dihydro -1H imidazol -2 amine

STRUCTURAL OF CLONIDINE:



(Clonidine)

MECHANISM OF ACTION:

Clonidine is selective partial agonist of alpha 2 adrenergic receptors. Clonidine when administered intrathecally , that is in spinal anaesthesia , gets absorbed quickly in cerebrospinal fluid and acts on the post synaptic alpha 2 receptors(stimulation) in Substantia Gelatinosa present in dorsal horn of the spinal cord. Clonidine also has intrinsic property to block the conduction in C and Aδ fibers.

Clonidine stimulates alpha 2 receptors in brain and spinal cord and causes decrease in sympathetic outflow from the central nervous system resulting in decreased blood pressure and heart rate.

The anatomic site of action of clonidine is on the receptors present in spinal dorsal horn and supraspinally in nucleus coereleus in pons. The mechanism of sedative effects of clonidine is due to hyperpolarization of exitable neurons in nucleous coereleus. The analgesic property of clonidine has multiple mechanisms acting on brain , brain stem and spinal cord .The action at the spinal level are by activation of descending medullospinal noradrenergic pathways and by reduction of spinal sympathetic outflow at presynaptic ganglions. It also suppresses the generation of action potential in spinal dorsal horn cells. Clonidine also acts by opening the potassium channels , the mechanism by which local anaesthetic agents acts.

Clonidine has specificity towards binding to alpha 2 receptors in the vasomotor centre in brain stem and this binding causes decrease in presynaptic

calcium , inhibiting release of norepinephrine. Clonidine exerts its antihypertensive effects by acting as imidazoline I1 receptor agonist.

PHYSICAL PROPERTIES:

Molecular weight 230

Protein binding 20- 40 %

pka 8

PHARMACOKINETICS:

The pharmacokinetics of clonidine is dose proportional which lies in the range of 100 – 600 mcg. On oral administration clonidine is absorbed 70 -90% and the peak plasma clonidine levels are reached at 1-3 hours. After intravenous injection of clonidine , it shows biphasic disposition . the distribution half life is 20 minutes and that of elimination is 12-16 hours.

Clonidine crosses blood brain barrier and also crosses placenta. The half life is increased in patients with severe renal failure. The absorbed drug , after oral administration , of which 50% is recovered unchanged in urine. Clonidine is metabolized in liver and excreted through kidneys.

DOSAGE:

- For spinal anesthesia as an adjuvant dose ranges from 25µ - 150µ ,1-2 µ/ kg .Different doses have different effects which includes hypotension , sedation , bradycardia , long duration of analgesia.

- Anti hypertensive – usually administered orally. Usually started as 0.1 mg tablet twice a day and titrated by increasing the dose by 0.1 mg weekly after observing the response of the patient to the drug.

USES:

- As adjuvant in spinal and epidural analgesia
- Premedication agent
- Antihypertensive agent
- In Attention Deficit Hyperactivity Disorder
- Chronic diarrhoea
- Glaucoma
- Diagnosing pheochromacytom – clonidine suppression test
- Migraine
- Postmenopausal flushing
- Opioid withdrawal
- Anxiety disorder

CLONIDINE WITHDRAWAL:

As clonidine acts by decreasing the sympathetic outflow and there by decreasing the blood pressure , sudden withdrawal causes rebound hypertension due to sudden increase in sympathetic outflow. So clonidine therapy should be tapered

gradually to minimize the hypertension. Treatment of clonidine withdrawal hypertension consist of beta blockers and readministration of clonidine to decrease blood pressure and gradually decrease it.

ADVERSE EFFECTS:

- Cardiovascular : bradycardia , hypotension , raynaud's phenomenon , AV blocks.
- Central nervous system : insomnia , nervousness , vivid dreams , delusion and hallucinations
- Dermatological : allergic reaction , atopic eczema , rash , urticaria
- Gastrointestinal :abdominal pain , vomiting , transient changes in liver function tests , acute pancreatitis , pseudo obstruction of bowel.
- Haematological : thrombocytopenia
- Erectile dysfunction.

CONTAINDICATIONS:

- Patient with known hypersensitivity reaction
- Patients with sinoatrial disease and atrioventricular blocks.

DRUG INTERACTIONS:

- Clonidine increases the CNS depression effects of alcohol , antidepressants and sedative drugs.

- When clonidine is used along with cardiac drugs like digitalis , calcium channel blockers and beta blockers monitoring of heart rate is mandatory as it precipitates braycardia.
- Clonidine when used in high doses along with haloperidol can precipitate arrhythmias.

REVIEW OF LITERATURE

Elia et al (from april 2010 to jan 2011) , conducted a study including 1,445 patients , using intrathecal clonidine as adjuvant to bupivacaine and found that 15 – 150 µ prolonged , the time to two segment regression (mean 14 to 75 min), delay in regression time to L2 , the time to need for first rescue analgesic (median 101 min, range 35 – 310 min) and motor block(median 47 minutes , range 6 - 131) was extended without any relation to dose. Increased incidence of arterial hypotension without the effect of dose and the risk of bradycardia was unchanged.

Marrivirta et al (2010), in 60 ambulatory patients undergoing , added 75µ of clonidine to 6 mg spinal hyperbaric bupivacaine vs 6 mg bupivacaine alone. This study showed that motor block was prolonged in patients who received clonidine. Also these patients need more vasopressor and less post operative pain.

Yoganarasimha and co-worker in 2014 , compared intrathecal clonidine 75µ versus intrathecal neostigmine 50µ as adjuvant drug for spinal anaesthesia 0.5% hyperbaric bupivacaine 12.5 mg ;analgesia was prolonged with clonidine (362+/- 36 mins) compared with neostigmine (300+/-25 min).

Kanazi et al in 2006 , compared 'clonidine 30 µ versus dexmedetomidine 3µ added to 12 mg of spinal hyperbaric bupivacaine , versus bupivacaine alone in 60 transurethral resection of prostrate. Patient treated with alpha 2 agonist has rapid onset time of motor block and took longer time for sensory and motor regression . The mean time for sensory regression to reach level of S1 segment was 303+/-75

min for dexmedetomidine , 272 +/- 38 min in clonidine group , 190+/- 48 min in patients with bupivacaine alone.the regression of motor block to bromage 0 was 250+/- 76 min.

Andrieu et al in 2004 compared intrathecal morphine 4µ/kg with and without clonidine 4µ/kg in patients undergoing radical retropubic prostatectomy . adding clonidine to spinal morphine reduced intraoperative use of sufentanil , prolonged time for first rescue analgesia .

Strebel et al in 2004, compared three doses of clonidine (37.5,75 and 150 µg) added to spinal 0.5% bupivacaine 18 mg in 80 orthopaedics patients. In patients receiving intrathecal clonidine the duration of sensory block (regression below the level L1) was increased in patients receiving: 311±101 min in 37.5 µg (+8%), 325 ±69 min in 75 µg (+13%), and 337±78 min in those patients who received 150 µg (+17%) (estimated parameter for dose 0.23 [95% confidenceinterval-0.05-0.50]) versus control group 288 ±62 min. Time to first analgesic request was also prolonged: 343 ±75 min (+16%), 381±117 min (+29%), and 445±136 min (+51%) (estimated parameter for dose 1.02 [95% confidence interval 0.59-1.45]), respectively compared to control group 295±80 min. Hemodynamic stability of the was maintained throughout the procedure and they found no differences in sedation level'.

Tuijl et al, in 2013 investigated the effect of 0, 15 and 30 µg of clonidine added to 5 mg of 0.5% hyperbaric bupivacaine on the prolongation of motor block, analgesia and ability to void after knee arthroscopy. They found that clonidine

increased the duration of motor block duration by 25 and 34 min respectively. They also found better analgesic quality, and the mean time for spontaneous voiding was increased up to 18 and 44 min respectively.

Mahendru et al in 2013, conducted a prospective studystating that 'adding clonidine 30 μg, vs. dexmedetomidine 5 μg, vs. Fentanyl 25 μg to 12.5 mg spinal hyperbaric bupivacaine in cases of lower limb surgeries. They discovered that dexmedetomidine prolonged significantly sensory and motor block compared to clonidine, fentanyl and bupivacaine alone. The mean time of two segment sensory block regression was 147±21 min with dexmedetomidine, 117±22 with clonidine, 119±23 in those patients receiving fentanyl, and 102±17 in bupivacaine alone ($p > 0.0001$). The time taken for regression of motor block to reach modified Bromage scale grade 0 was 275±25, 199±26, 196±27, 161±20 respectively ($p > 0.0001$). The haemodynamic status of the patient was maintained. In patients aged 60 years or more who are undergoing orthopaedic surgeries for lower limb, intrathecally clonidine 15 μg or 30 μg was given along with 9 mg hyperbaric bupivacaine, which potentiated the sensory block levels and duration of analgesia without affecting the trend of systolic blood pressure as compared to bupivacaine alone. Clonidine in doses of 30 μg however facilitated the spread of sensory block to unexpectedly higher dermatomes for a longer time. Spinal postoperative analgesia can be improved by epidural infusion of 40 μg/h mixed with ropivacaine 4 mg/h-1in patient undergoing hip arthroplasty.

Gehling et al in 2008 ,studied 45 patients who are undergoing hip or knee replacement surgery with 15 mg of bupivacaine spinal anaesthesia and calculated a mean time for the first opioid request was for placebo group are 10.3±7.9 h, for 0.1 mg morphine group it was 23.0±3.9 h and for 0.1 mg morphine+50 μg clonidine group it was 21±6.9 h. Combination of pethidine 0.75 mg/kg and clonidine 75 μg in spinal anaesthesia provided good intraoperative anaesthesia for total hip replacement, but similar to plain isobaric 0.5% bupivacaine'.

Mercier et al in 1998 ,compared sufentanil 5 μg and clonidine 30 μg versus sufentanil 5 μg alone given intrathecally to reduce pain in the first stage of labour, they found that clonidine potentiate labour analgesia and side effects such as hypotension, maternal pruritus and sedation were equal in both groups.

Gautier et al in 2002 ,studied about the use of 30 μg of intrathecal clonidine with 5 μg of intrathecal sufentanil in labour analgesia. He found out that there is increase in the duration of analgesia during the first stage without any maternal or fetal sideeffects.

Chiari et al in 2011 'conducted a study by using clonidine alone in spinal anaesthesia for relieving pain during labour; in 36 parturients with cervical dilation < 6 cm; they compared 50, 100, and 200 μg intrathecal clonidine and found that labour pain was significantly reduced in all patients, analgesia duration was significantly longer with 200 μg (median 143; range of means75-210 min), with 100 μg (median 118; range of means 60-180 min) and using 50 μg (median 45;

range of means 25-150 min).Hypotension was associated with 200 μg and the need of intravenous ephedrine more often than in the other group'.

Rochette et al, studied 75 patients which were injected with increasing doses of clonidine (0.25, 0.5, 1 y 2 μg/kg) with plain spinal bupivacaine 0.5% (1 mg/kg) and concluded that clonidine 1 μg/kg produces improvement in spinal anaesthesia duration without significant side effects. Dose of 2 μg/kg produced transient hypotension. In a randomized investigation with 45 children aged 6 to 15 years, clonidine 2μg/kg prolonged motor block and improved postoperative analgesia. Hypotension and bradycardia were 54% and 30% respectively.

Lauretti GR et al in 1998 , studied in 45 patients the dose response of spinal morphine and intrathecal neostigmine, for postoperative analgesia in patients undergoing anterior and posterior vaginoplasty. 24-h visual analog scale score was analysed in both the groups. In group who receives spinal neostigmine the VAS score was significantly lower than in those who received morphine alone ($P = 0.00$). The durations of postoperative analgesia were longer for all patients in group receiving neostigmine compared with other groups. The incidence of nausea and vomiting was not increased in neostigmine group.

Hood DD, Mallak KA, Eisenach JC, Tong C in 1996, studied 'interaction between spinal neostigmine and epidural clonidine in human volunteers. A total of 58 volunteers received spinal injection of 5% dextrose in normal saline or neostigmine (50, 100, or 200 micrograms in D5NS), followed in 1 h by epidural saline or clonidine . Visual analog scale score for pain to a noxious cold stimulus,

nausea, weakness, sedation, and other safety variables was measured before and at specified intervals after drug administration.The first 21 volunteers who received spinal neostigmine rather than D5NS received the drug while in the sitting position, and had none-to-minimal analgesia 1 h later. The remaining volunteers received the drug in the lateral position, and demonstrated dose-dependent analgesia in the foot 1 h later. Epidural clonidine also caused dose-dependent analgesia. The combination of neostigmine and clonidine resulted in an additive enhancement for analgesia, but there is no enhancement of each drug's side effects, and also decreases clonidine-induced hypotension. Neostigmine injected into subjects in the lateral position diminished clonidine-induced reductions in blood pressure and plasma norepinephrine'.

Pan PM, Huang CT, Wei TT, Mok MS in 1998, conducted a study that states 'comparison of the analgesic effect of intrathecally administered neostigmine and clonidine along with bupivacaine in spinal anaesthesia for patients undergoing caesarean section. After explaining about the purpose of study and getting consents, 80 patients who were posted for cesarean section using spinal anesthesia were enrolled by a double-blind randomized design into four groups: bupivacaine group - received intrathecal ,10 mg of bupivacaine; bupivacaine + neostigmine group - received , 10 mg of bupivacaine + 50 microg of neostigmine; bupivacaine + clonidine group received - 10 mg of bupivacaine + 150 microg of clonidine; and bupivacaine + both (n = 21) received - 10 mg of bupivacaine + 50 microg of neostigmine + 150 microg of clonidine. The level spread of anesthesia , maximum duration of analgesia and motor block, pulse rate , blood pressure , oxygen

saturation, and side effects were recorded for 14 hours post injection. Fifty milligrams of intramuscular meperidine was given as a rescue analgesic whenever patient's pain score was greater than 5/10 by the visual analog scale.

Bupivacaine and the both group had a higher maximum spread of anesthesia of 23.3 +/- 2.9 segments than bupivacaine alone group of 20.5 +/- 2.9 segment. Bupivacaine + both group showed a delayed onset of postoperative pain of 6.5 +/- 1.5 hours as compared to bupivacaine group of 1.3 +/- 0.6 hours. The pain score in bupivacaine + both group was significantly lower than that of bupivacaine alone group during the first 10 hours. The 24-hour meperidine consumption also was lower in bupivacaine + both group than that of bupivacaine group. However, motor block was significantly prolonged from 3.5 +/- 1.1 hours in bupivacaine group to 7.1 +/- 1.6 hours in bupivacaine + both group. In addition, other side effects such as nausea and vomiting and dizziness were significantly increased in bupivacaine + both group'.

Klamt JG. Sluttitel A, Garcia IV, Prado WA in 1997 , conducted a study on postoperative analgesic effect of intrathecal neostigmine and its influence on spinal anaesthesia.

MATERIALS AND METHODS

This study was a prospective randomized double blinded control Trial. In this study, 60 patients from the Department of General Surgery and Department of Obstetrics and Gynecology , Chengalpattu Medical College Hospital was analysed .The study was done over a period of one year .Institutional ethical Committee approval obtained. Patients who were posted for lower abdominal surgery in the age group of 20 – 60 years were counselled about the purpose of study. The procedure was explained to the patient in their own language. Informed consent was obtained. Patients who fulfil the inclusion criteria and those who gave consent were then randomly allocated to one of the study groups based on computerized randomized list.

INCLUSION CRITERIA:

1. Age 18 to 60 years
2. ASA I and II
3. Patient posted for lower abdominal surgeries
4. Patient who are fit for spinal anaesthesia

EXCLUSION CRITERIA:

- Hypersensitivity to bupivacaine , neostigmine and clonidine
- Hemodynamic instability

- Patients with ischemic heart disease
- Infection at the site of lumbar puncture
- Patient refusal
- On anticoagulants
- Bronchial asthma
- Neuropathy
- Bleeding disorders
- Psychiatric illness
- Morbidly obese

MATERIALS REQUIRED FOR THE PROCEDURE:

1. 25 G Quinckes spinal needle
2. 5 ml sterile syringes
3. Hypodermic needles 18 G
4. Bowl, Sponge holding forceps, gauze, sterile towel, Chlorhexidine solution.
5. Sterile gown, Gloves, Cap & Mask
6. Local anaesthetic solution – 2% Lignocaine with adrenaline
7. 0.5% hyperbaric Bupivacaine , neostigmine , clonidine
8. Boyle's apparatus and oxygen cylinder

9. Emergency kit with working laryngoscope, endotracheal tubes of appropriate size, airway, suction apparatus with suction catheter.
10. Emergency drugs Inj. Adrenaline, Inj. Atropine, Inj.Thiopentone, Inj.Succinylcholine
11. Monitor for continuous monitoring of Pulse Rate, Oxygen saturation, Non-invasive blood pressure, ECG, Respiratory rate.

METHODOLOGY:

An 18G IV cannula was inserted and patient was started on an infusion of Ringer lactate solution at 10ml/kg and the patient connected to multi para monitor. The patient was made to lie in right lateral position, with a pillow.

Under strict aseptic precautions, the skin over the lumbar region was cleaned with the povidone-iodine solution and the area was covered with sterile drape. The space between the L3and L4 space was identified and the skin over that area was infiltrated with 2% lignocaine.The skin was pierced with 25G Quinckes needle at L3 – L4 intervertebral space. The Quinckes needle was advanced with the bevel facing upward till it pierces the dura. The stylet was removed and then observed for cerebrospinal to flow. After careful aspiration of cerebrospinal fluid , the desired drug is injected into subarachnoid space. Then the patient was made into the supine position immediately.

Vital signs were monitored at 2^{nd} minute and then every 5 minutes till completion of surgery. The surgery was started after obtaining adequate sensory block and adequate analgesia and surgical anaesthesia till T6 level assessed by

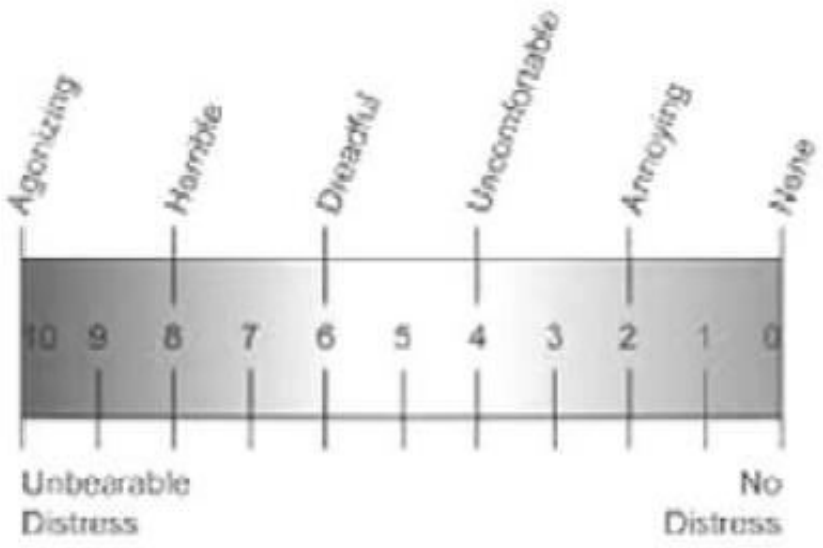
pinprick test. Vitals were monitored in the postoperative period. Pain was assessed using VAS (visual analogue scale) at the end of surgery during the recovery period when patient was awake. At the end of the surgery, motor block was assessed using modified Bromage scale for both lower limbs.

The study concluded at the end of the surgery. Both the patient and the anaesthesiologist who gave anaesthesia were blinded to the study solutions.

Following parameters are noted:

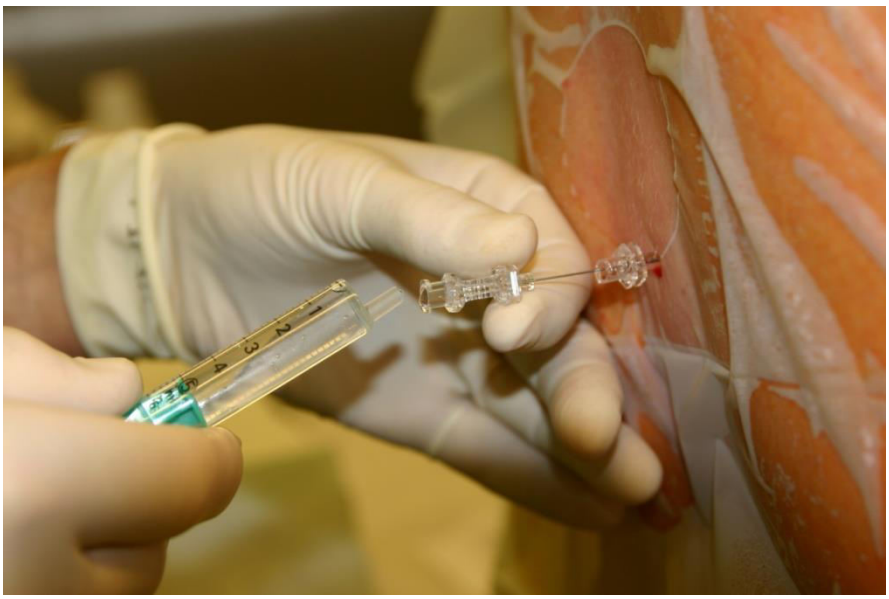
1. Heart Rate
2. Non invasive Blood Pressure
3. Oxygen saturation
4. Respiratory Rate
5. Sensory Block
    a. Onset time
    b. Duration
    c. Maximum level of sensory block
6. Motor Block
    a. onset time
    b. quality of motor block
7. Rescue Analgesia
8. VAS score
9. Postoperative Analgesia

Pain assessed using visual analogue scale:



'Assessment of motor block by using modified Bromage scale

Grade 0	No motor block
Grade 1	Inability to raise extended leg, able to move knees and feet
Grade 2	Inability to raise extended leg and move knee, able to move feet
Grade 3	Complete motor block of the lower limbs.



STATISTICAL ANALYSIS

The statistical analysis was done using SPSS (Statistical package for social sciences) version 16 for windows. Descriptive statistics are presented as mean± 1SD. Bar and line diagrams are drawn as and when required. Chi square test for association is used for comparison of categorical variables between treatment allocations.

RESULTS AND OBSERVATIONS:

Study includes 60 patients who were posted for lower abdominal surgeries. They were randomly allocated to either Group-A (0.5% hyperbaric bupivacaine) or Group-B (0.5% hyperbaric bupivacaine with 50µ neostigmine) , Group – C (0.5% hyperbaric bupivacaine with clonidine 50µ).The patient characteristics such as age, sex ,weight, ASA classification , comorbid conditions of the patients are noted.

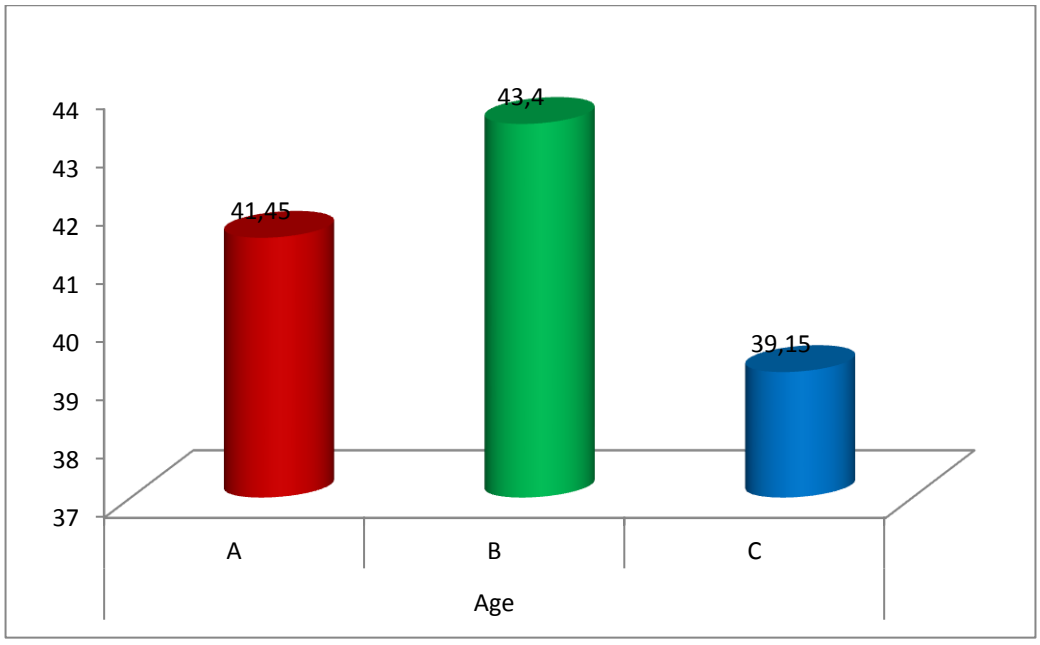
The outcomes measured were onset of sensory block , duration of the block, level of block achieved, haemodynamic status of the patient intra operatively, duration and quality of motor block, Rescue analgesia, VAS score and complications .

CHARACTERISTICS OF THE PATIENT:

- **AGE DISTRIBUTION:**

The average age between the three groups, does not varies much. The mean age of Group A is 41.45 ± 12.45, Group B is 43.4 ± 8.923, Group C is 39.15 ± 11.811. The difference between the groups in age distribution was not statistically significant. The p value is 0.489.

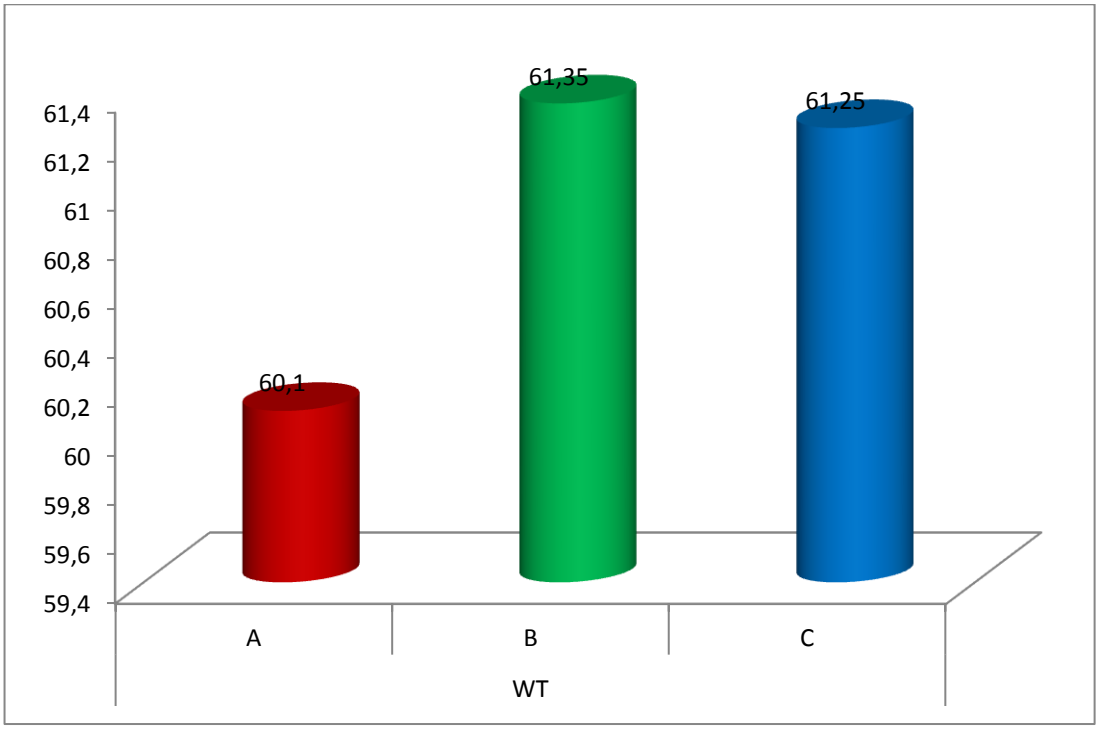
Descriptive	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Age	A	20	41.45	12.458	2.786	18	59
	B	20	43.4	8.923	1.995	25	62
	C	20	39.15	11.811	2.641	20	57
	Total	60	41.33	11.118	1.435	18	62



- **WEIGHT :**

The average weight of the patient in Group A is 60.1± 6.593 kg , Group B is 61.35 ± 9.213 and Group C is 61.25 ± 7.247 . The difference between the three groups in weight of the patients were not significant as the p value is 0.852.

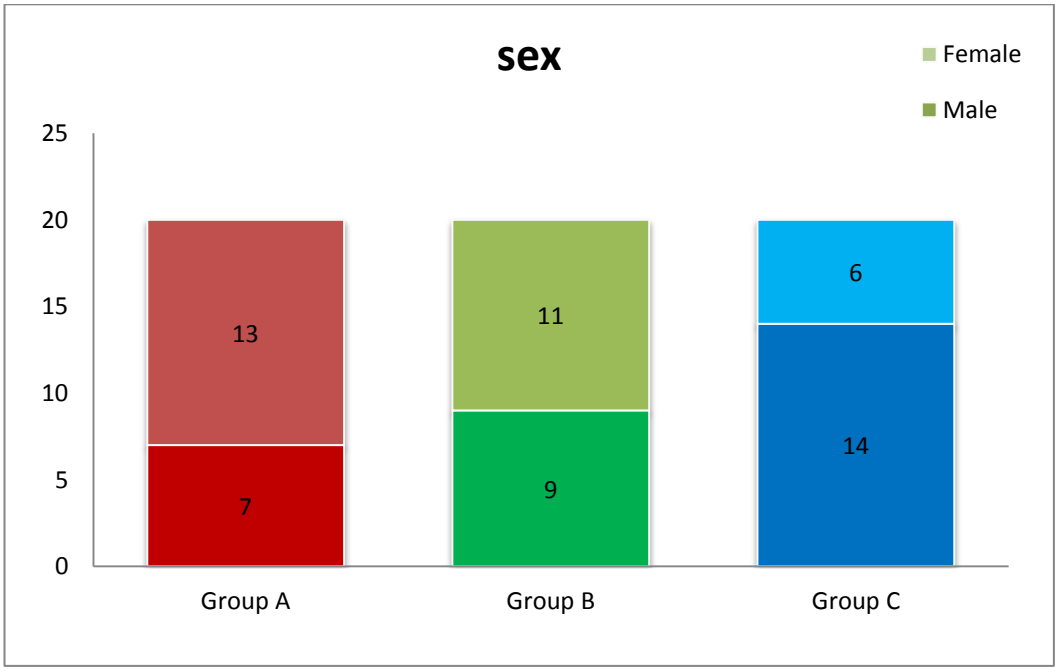
Descriptive	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
WT	A	20	60.1	6.593	1.474	47	71
	B	20	61.35	9.213	2.06	40	76
	C	20	61.25	7.247	1.62	49	78
	Total	60	60.9	7.653	0.988	40	78



- **GENDER DISTRIBUTION:**

In Group A consist of 7 male patients and 13 female patients. Group B has 9 male patients and 11 female patients. Group C had 14 male patients and 6 female patients. The gender distributions of all three groups are comparable.

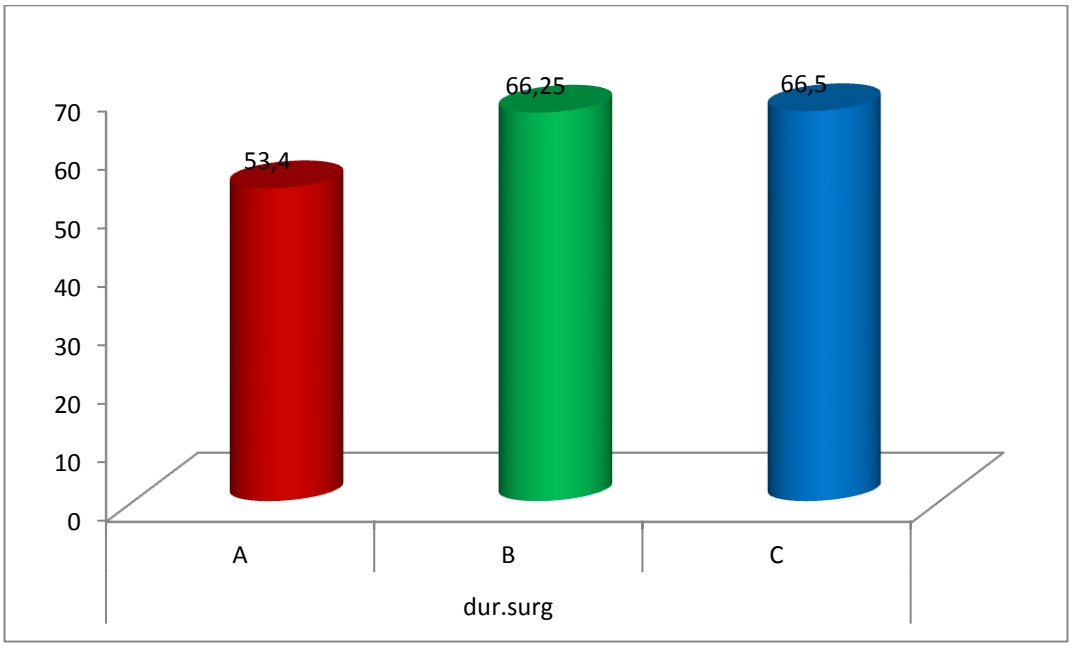
Sex	Group A		Group B		Group C	
	Frequency	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
Male	7	35	9	45	14	70
Female	13	65	11	55	6	30
Total	20	100	20	100	20	100



- **DURATION OF SURGERY:**

The mean duration of surgery were comparable between the three groups. The mean duration of surgery in Group A is 53.4 ± 8.217 , Group B is 66.25 ± 18.416 , Group C is 66.5 ± 14.336. The p value is 0.007 and is statistically significant.

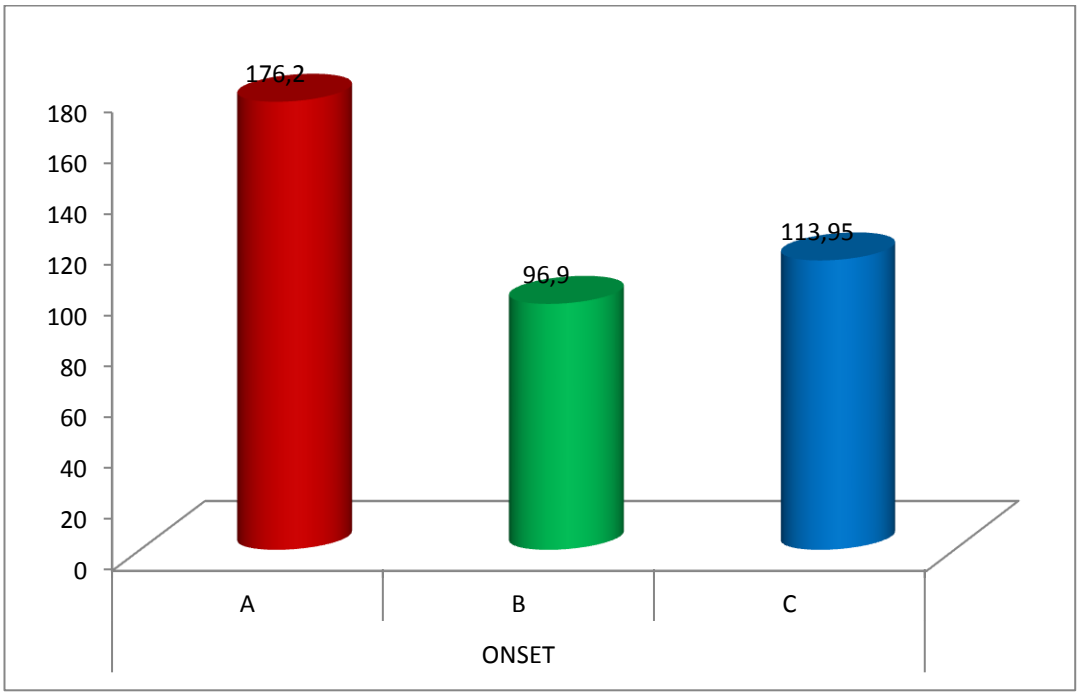
Descriptives	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Duration of surgery	A	20	53.4	8.217	1.837	35	70
	B	20	66.25	18.416	4.118	30	110
	C	20	66.5	14.336	3.206	45	90
	Total	60	62.05	15.336	1.98	30	110



- **ONSET OF SENSORY BLOCKADE:**

The mean onset time of sensory block in Group A is 176.2 ± 6.948, Group B is 96.9 ± 19.472 and Group C is 113.95 ± 14.666. The p value is statistically significant (p = 0.0001) between the three groups.

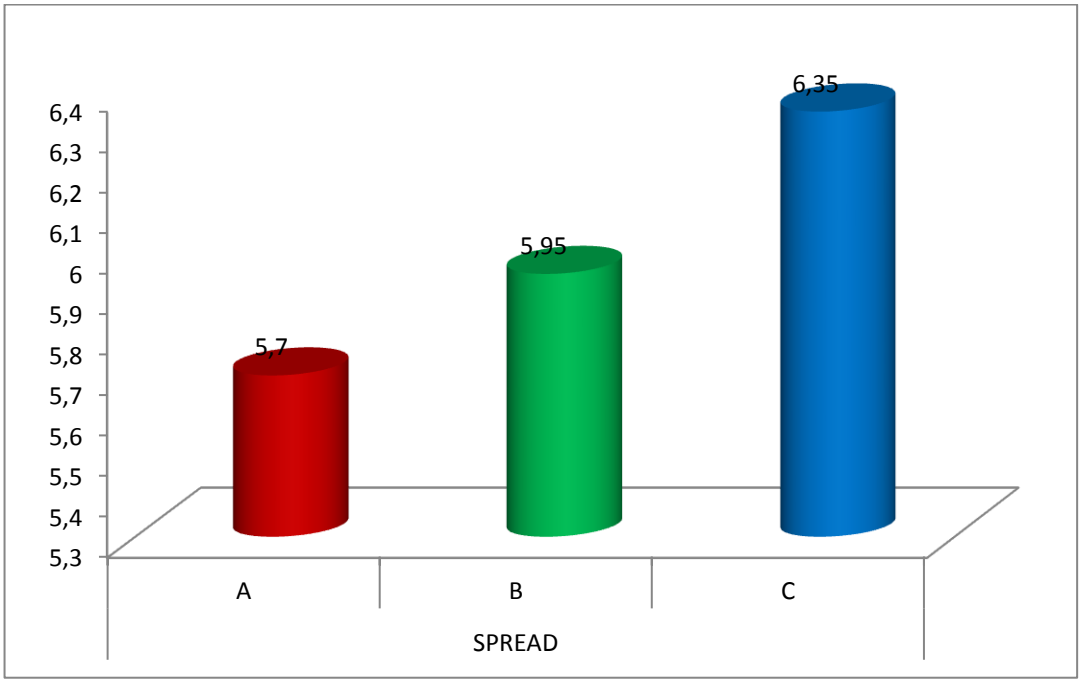
Descriptives	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
ONSET	A	20	176.2	6.948	1.554	164	186
	B	20	96.9	19.472	4.354	68	140
	C	20	113.95	14.666	3.28	80	154
	Total	60	129.02	37.258	4.81	68	186



- **MAXIMUM LEVEL OF SENSORY BLOCK ACHEIVED:**

The levels of sensory block achieved between the groups were not statistically significant. The p value is 0.199.

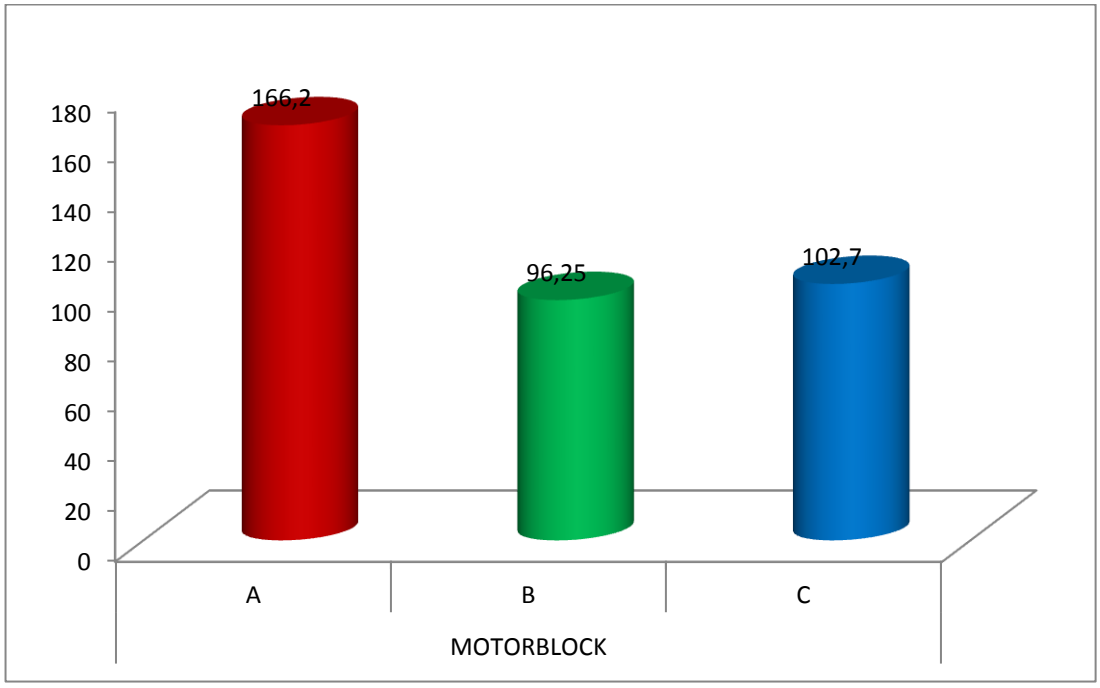
Descriptives	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
SPREAD	A	20	5.7	1.174	0.263	4	8
	B	20	5.95	1.395	0.312	4	8
	C	20	6.35	0.745	0.167	6	8
	Total	60	6	1.15	0.148	4	8



- **ONSET TIME OF MOTOR BLOCK:**

The mean onset time for motor block in each groups were as follows: Group A is 166.2 ± 7.824, Group B is 96.2 ± 29.243, Group C is 102.75 ± 29.993.

Descriptives	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
MOTOR BLOCK	A	20	166.2	7.824	1.75	150	178
	B	20	96.25	29.243	6.539	60	180
	C	20	102.75	29.993	6.707	60	190
	Total	60	121.72	39.975	5.161	60	190



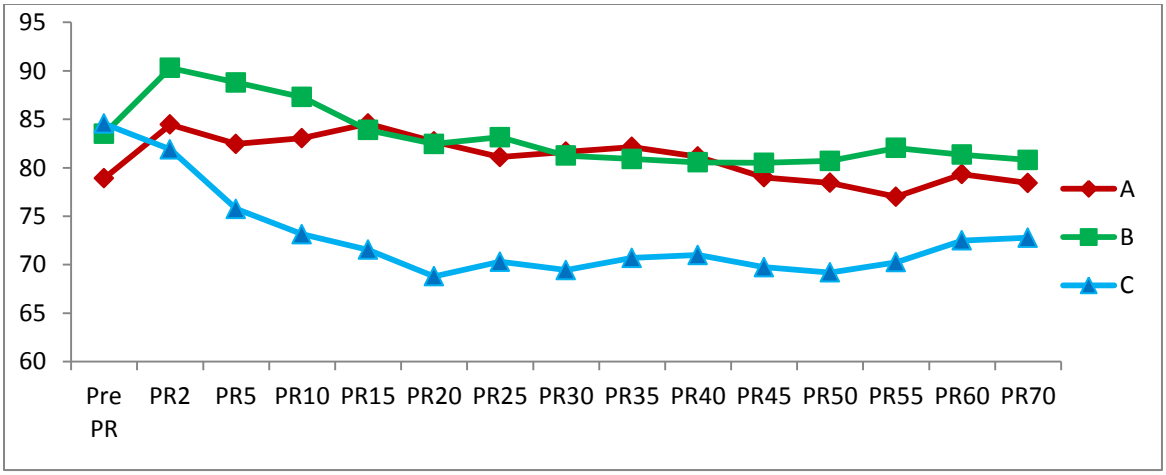
- **INTRAOPERATIVE HAEMODYNAMICS:**

In all the patients who are subjected to the study, the hemodynamic status was monitored. The parameters monitored were pulse rate, systolic blood pressure , diastolic blood pressure , oxygen saturation, the reading taken after two minutes after spinal anaesthesia there after vitals monitored every fifth minute till the end of surgery.

- PULSE RATE:

Variables	Group	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	Sig.
PR PREOP	A	20	78.9	9.968	2.229	60	100	1.394	0.256
	B	20	83.5	14.468	3.235	60	124		
	C	20	84.55	8.947	2.001	68	104		
	Total	60	82.32	11.459	1.479	60	124		
PR2	A	20	84.45	7.185	1.607	74	96	3.931	**0.025**
	B	20	90.3	11.815	2.642	74	124		
	C	20	81.9	9.586	2.143	64	107		
	Total	60	85.55	10.185	1.315	64	124		
PR5	A	20	82.45	8.338	1.864	68	96	8.464	**0.001**
	B	20	88.8	11.848	2.649	72	119		
	C	20	75.75	9.591	2.145	63	103		
	Total	60	82.33	11.229	1.45	63	119		
PR10	A	20	83.05	7.366	1.647	66	92	13.065	**0.0001**
	B	20	87.3	10.006	2.237	70	111		
	C	20	73.15	9.366	2.094	59	102		
	Total	60	81.17	10.663	1.377	59	111		
PR15	A	20	84.55	9.768	2.184	64	100	10.305	**0.0001**
	B	20	83.9	12.143	2.715	60	110		
	C	20	71.55	8.338	1.864	57	92		
	Total	60	80	11.704	1.511	57	110		
PR20	A	20	82.7	10.408	2.327	62	104	12.764	**0.0001**
	B	20	82.45	10.47	2.341	57	99		
	C	20	68.8	8.912	1.993	54	90		
	Total	60	77.98	11.775	1.52	54	104		
PR25	A	20	81.1	10.809	2.417	61	102	10.927	**0.0001**
	B	20	83.15	9.778	2.186	58	100		
	C	20	70.3	7.02	1.57	59	86		
	Total	60	78.18	10.798	1.394	58	102		
PR30	A	20	81.65	10.52	2.352	62	94	12.864	**0.0001**
	B	20	81.25	8.46	1.892	60	93		
	C	20	69.45	6.468	1.446	54	83		
	Total	60	77.45	10.234	1.321	54	94		
PR35	A	20	82.15	8.928	1.996	63	96	12.436	**0.0001**
	B	20	80.9	7.907	1.768	61	96		

Variables	Group	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	Sig.
	C	20	70.7	6.937	1.551	53	85		
	Total	60	77.92	9.383	1.211	53	96		
PR40	A	20	81.15	8.061	1.802	62	98	12.1	**0.0001**
	B	20	80.55	7.38	1.65	64	90		
	C	20	71	6.432	1.438	57	89		
	Total	60	77.57	8.589	1.109	57	98		
PR45	A	20	79	7.064	1.579	62	91	15.639	**0.0001**
	B	20	80.5	6.573	1.47	68	91		
	C	20	69.75	6.077	1.359	55	85		
	Total	60	76.42	8.053	1.04	55	91		
PR50	A	20	78.45	7.395	1.654	62	94	17.941	**0.0001**
	B	20	80.7	5.639	1.261	72	89		
	C	20	69.2	6.144	1.374	54	80		
	Total	60	76.12	8.074	1.042	54	94		
PR55	A	20	77	8.105	1.812	60	93	14.308	**0.0001**
	B	20	82.05	6.1	1.364	72	94		
	C	20	70.25	6.64	1.485	58	85		
	Total	60	76.43	8.432	1.089	58	94		
PR60	A	12	79.33	9.018	2.603	60	96	8.164	**0.001**
	B	17	81.35	4.676	1.134	72	90		
	C	16	72.5	5.967	1.492	58	79		
	Total	45	77.67	7.492	1.117	58	96		
PR70	A	7	78.43	8.886	3.358	60	85	4.184	**0.04**
	B	10	80.8	5.574	1.763	73	88		
	C	9	72.78	6.942	2.314	61	87		
	Total	26	77.38	7.627	1.496	60	88		

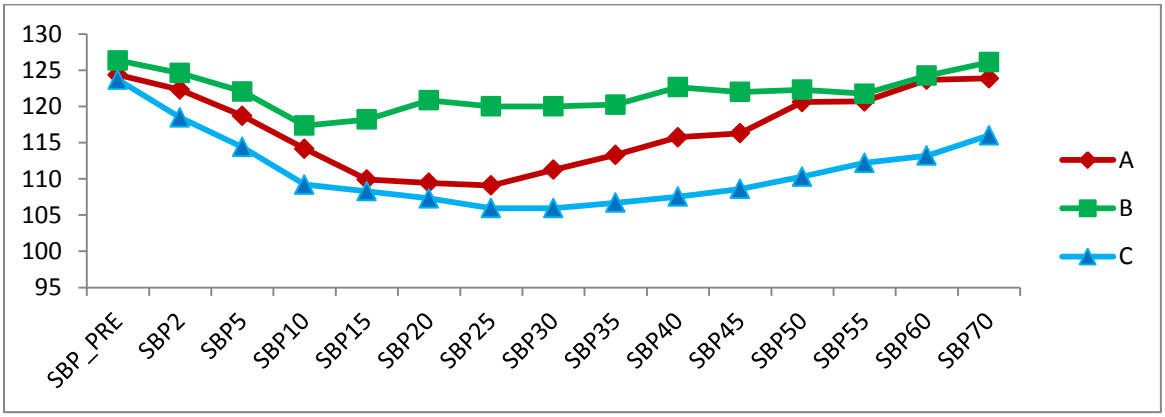


The preoperative pulse rate in three groups are not significant statistically where as the pulse rate after tenth minute of spinal anaesthesia were significant statistically.

- SYSTOLIC BLOOD PRESSURE:

Variables	Group	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	Sig.
SB PPREOP	A	20	124.35	10.07	2.252	110	159	0.301	0.741
	B	20	126.35	13.124	2.935	108	154		
	C	20	123.7	10.322	2.308	106	139		
	Total	60	124.8	11.123	1.436	106	159		
SBP2	A	20	122.3	8.467	1.893	108	150	1.523	0.227
	B	20	124.6	11.98	2.679	104	148		
	C	20	118.45	12.857	2.875	93	140		
	Total	60	121.78	11.362	1.467	93	150		
SBP5	A	20	118.7	8.578	1.918	104	147	2.715	0.075
	B	20	122.05	10.185	2.277	102	137		
	C	20	114.4	12.15	2.717	90	127		
	Total	60	118.38	10.706	1.382	90	147		
SBP10	A	20	114.15	8.887	1.987	100	139	3.561	0.035
	B	20	117.35	11.061	2.473	100	138		
	C	20	109.2	9.099	2.035	92	120		
	Total	60	113.57	10.145	1.31	92	139		
SBP15	A	20	109.9	8.867	1.983	94	132	5.25	0.008
	B	20	118.2	12.344	2.76	92	140		
	C	20	108.3	9.581	2.142	92	120		
	Total	60	112.13	11.095	1.432	92	140		
SBP20	A	20	109.45	10.4	2.325	94	142	8.803	0.0001
	B	20	120.85	12.214	2.731	94	146		
	C	20	107.3	10.204	2.282	90	126		
	Total	60	112.53	12.343	1.594	90	146		
SBP25	A	20	109.1	12.49	2.793	94	146	8.398	0.001
	B	20	120	11.734	2.624	96	143		
	C	20	105.95	9.73	2.176	90	126		
	Total	60	111.68	12.725	1.643	90	146		
SBP30	A	20	111.25	13.932	3.115	90	146	7.308	0.001
	B	20	120	12.439	2.782	96	147		
	C	20	105.95	8.029	1.795	90	120		
	Total	60	112.4	12.932	1.669	90	147		
SBP35	A	20	113.3	12.704	2.841	94	146	7.183	0.002
	B	20	120.25	12.212	2.731	90	146		
	C	20	106.7	8.542	1.91	90	120		
	Total	60	113.42	12.435	1.605	90	146		
SBP40	A	20	115.75	9.797	2.191	100	142	9.361	0.0001

Variables	Group	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	Sig.
	B	20	122.65	14.694	3.286	94	163		
	C	20	107.55	7.373	1.649	89	119		
	Total	60	115.32	12.518	1.616	89	163		
SBP45	A	20	116.3	9.274	2.074	100	146	9.244	0.0001
	B	20	122	12.057	2.696	102	158		
	C	20	108.6	7.883	1.763	90	118		
	Total	60	115.63	11.189	1.444	90	158		
SBP50	A	20	120.6	9.213	2.06	110	153	10.194	0.0001
	B	20	122.3	9.437	2.11	108	147		
	C	20	110.3	8.615	1.926	89	120		
	Total	60	117.73	10.417	1.345	89	153		
SBP55	A	20	120.7	8.682	1.941	110	150	6.751	0.002
	B	20	121.75	9.657	2.159	104	145		
	C	20	112.2	8.667	1.938	91	121		
	Total	60	118.22	9.853	1.272	91	150		
SBP60	A	12	123.67	7.608	2.196	118	140	8.899	0.001
	B	17	124.24	9.384	2.276	106	147		
	C	16	113.19	7.323	1.831	98	124		
	Total	45	120.16	9.603	1.432	98	147		
SBP70	A	7	123.86	7.798	2.947	118	140	7.461	0.003
	B	10	126.1	5.547	1.754	120	140		
	C	9	116	4.387	1.462	110	122		
	Total	26	122	7.244	1.421	110	140		

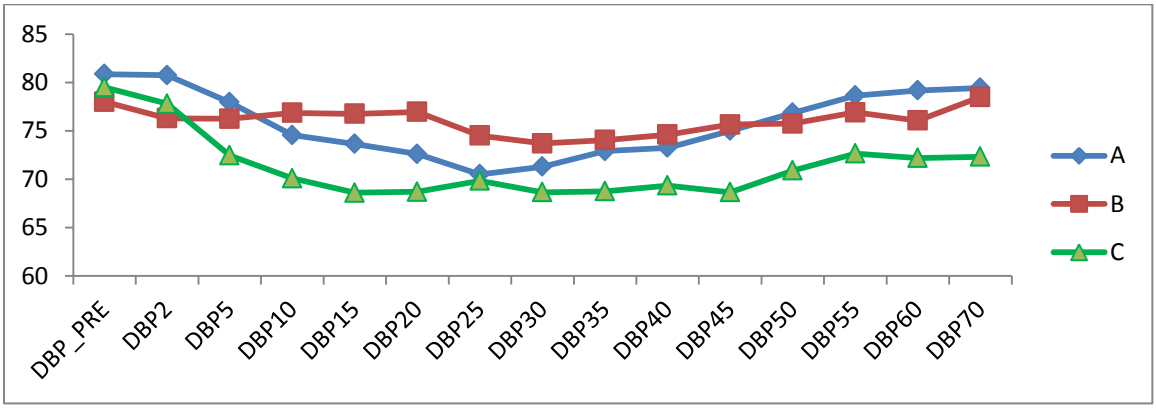


This variable shows statistical significance after tenth minute of spinal anaesthesia . the p value is 0.001.

- DIASTOLIC BLOOD PRESSURE:

DBPPREOP	A	20	80.85	6.753	1.51	70	92	0.59	0.558
	B	20	78	7.567	1.692	64	93		
	C	20	79.5	10.185	2.277	65	110		
	Total	60	79.45	8.241	1.064	64	110		
DBP2	A	20	80.75	7.999	1.789	69	102	1.365	0.264
	B	20	76.3	7.651	1.711	60	87		
	C	20	77.8	10.139	2.267	65	113		
	Total	60	78.28	8.72	1.126	60	113		
DBP5	A	20	77.95	6.245	1.396	70	96	2.015	0.143
	B	20	76.25	6.512	1.456	66	91		
	C	20	72.45	12.437	2.781	56	112		
	Total	60	75.55	9.022	1.165	56	112		
DBP10	A	20	74.55	8.062	1.803	64	98	4.34	**0.018**
	B	20	76.85	6.201	1.387	69	94		
	C	20	70.1	7.704	1.723	58	88		
	Total	60	73.83	7.773	1.003	58	98		
DBP15	A	20	73.65	6.491	1.451	64	87	8.398	**0.001**
	B	20	76.75	4.179	0.934	69	86		
	C	20	68.6	7.83	1.751	54	87		
	Total	60	73	7.1	0.917	54	87		
DBP20	A	20	72.6	5.725	1.28	64	84	9.3	**0.0001**
	B	20	76.95	2.665	0.596	72	81		
	C	20	68.7	8.367	1.871	53	88		
	Total	60	72.75	6.851	0.884	53	88		
DBP25	A	20	70.5	6.091	1.362	57	81	3.361	**0.042**
	B	20	74.5	5.463	1.222	68	91		
	C	20	69.85	6.8	1.521	58	88		
	Total	60	71.62	6.383	0.824	57	91		
DBP30	A	20	71.3	5.048	1.129	64	84	4.993	**0.01**
	B	20	73.7	5.017	1.122	61	83		
	C	20	68.65	5.102	1.141	55	78		
	Total	60	71.22	5.387	0.695	55	84		
DBP35	A	20	72.9	5.647	1.263	64	86	5.114	**0.009**
	B	20	74.05	5.605	1.253	64	86		
	C	20	68.75	5.28	1.181	52	76		
	Total	60	71.9	5.885	0.76	52	86		
DBP40	A	20	73.25	6.086	1.361	60	84	4.658	**0.013**
	B	20	74.6	6.286	1.406	61	91		
	C	20	69.35	4.38	0.979	55	74		
	Total	60	72.4	5.989	0.773	55	91		

DBP45	A	20	75	3.92	0.877	68	82	9.457	**0.0001**
	B	20	75.65	5.412	1.21	64	86		
	C	20	68.65	7.088	1.585	48	75		
	Total	60	73.1	6.38	0.824	48	86		
DBP50	A	20	76.85	4.837	1.082	70	87	5.77	**0.005**
	B	20	75.75	5.26	1.176	65	85		
	C	20	70.9	7.29	1.63	51	83		
	Total	60	74.5	6.353	0.82	51	87		
DBP55	A	20	78.65	4.095	0.916	72	89	7.044	**0.002**
	B	20	76.9	6.078	1.359	61	86		
	C	20	72.65	5.234	1.17	60	81		
	Total	60	76.07	5.707	0.737	60	89		
DBP60	A	12	79.17	2.368	0.683	76	84	7.572	**0.002**
	B	17	76.06	5.662	1.373	69	86		
	C	16	72.19	4.996	1.249	60	80		
	Total	45	75.51	5.417	0.808	60	86		
DBP70	A	7	79.43	1.512	0.571	76	80	8.081	**0.002**
	B	10	78.5	5.759	1.821	67	86		
	C	9	72.33	2.55	0.85	70	78		
	Total	26	76.62	4.981	0.977	67	86		

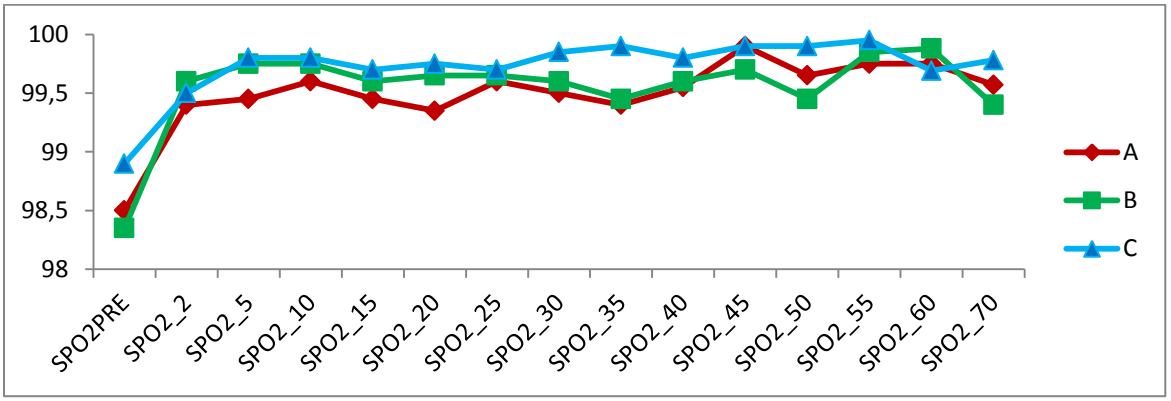


The diastolic blood pressure in all three groups were insignificant statistically during pre operative period. The diastolic blood pressure shows statistical significance in all three groups from tenth minute after spinal anaesthesia.

- OXYGEN SATURATION:

Variables	Group	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	Sig.
SPO_2PREOP	A	20	98.5	1.1	0.246	97	100	1.502	0.231
	B	20	98.35	0.933	0.209	97	100		
	C	20	98.9	1.071	0.24	97	100		
	Total	60	98.58	1.046	0.135	97	100		
$SPO_2$2	A	20	99.4	0.821	0.184	98	100	0.429	0.654
	B	20	99.6	0.598	0.134	98	100		
	C	20	99.5	0.607	0.136	98	100		
	Total	60	99.5	0.676	0.087	98	100		
$SPO_2$5	A	20	99.45	0.759	0.17	98	100	2.053	0.138
	B	20	99.75	0.55	0.123	98	100		
	C	20	99.8	0.41	0.092	99	100		
	Total	60	99.67	0.601	0.078	98	100		
$SPO_2$10	A	20	99.6	0.503	0.112	99	100	0.784	0.461
	B	20	99.75	0.55	0.123	98	100		
	C	20	99.8	0.523	0.117	98	100		
	Total	60	99.72	0.524	0.068	98	100		
$SPO_2$15	A	20	99.45	0.686	0.153	98	100	0.754	0.475
	B	20	99.6	0.681	0.152	98	100		
	C	20	99.7	0.571	0.128	98	100		
	Total	60	99.58	0.645	0.083	98	100		
$SPO_2$20	A	20	99.35	0.933	0.209	97	100	1.712	0.19
	B	20	99.65	0.587	0.131	98	100		
	C	20	99.75	0.55	0.123	98	100		
	Total	60	99.58	0.72	0.093	97	100		
$SPO_2$25	A	20	99.6	0.681	0.152	98	100	0.146	0.865
	B	20	99.65	0.587	0.131	98	100		
	C	20	99.7	0.47	0.105	99	100		
	Total	60	99.65	0.577	0.075	98	100		
$SPO_2$30	A	20	99.5	0.761	0.17	98	100	1.221	0.303
	B	20	99.6	0.94	0.21	96	100		
	C	20	99.85	0.366	0.082	99	100		
	Total	60	99.65	0.732	0.095	96	100		
$SPO_2$35	A	20	99.4	0.94	0.21	97	100	2.577	0.085
	B	20	99.45	0.887	0.198	97	100		
	C	20	99.9	0.308	0.069	99	100		
	Total	60	99.58	0.787	0.102	97	100		
$SPO_2$40	A	20	99.55	0.605	0.135	98	100	1.177	0.316
	B	20	99.6	0.598	0.134	98	100		

Variables	Group	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	Sig.
	C	20	99.8	0.41	0.092	99	100		
	Total	60	99.65	0.547	0.071	98	100		
$SPO_2$45	A	20	99.9	0.308	0.069	99	100	1.949	0.152
	B	20	99.7	0.47	0.105	99	100		
	C	20	99.9	0.308	0.069	99	100		
	Total	60	99.83	0.376	0.049	99	100		
$SPO_2$50	A	20	99.65	0.587	0.131	98	100	2.721	0.074
	B	20	99.45	0.826	0.185	97	100		
	C	20	99.9	0.308	0.069	99	100		
	Total	60	99.67	0.629	0.081	97	100		
$SPO_2$55	A	20	99.75	0.444	0.099	99	100	1.572	0.216
	B	20	99.85	0.366	0.082	99	100		
	C	20	99.95	0.224	0.05	99	100		
	Total	60	99.85	0.36	0.046	99	100		
$SPO_2$60	A	12	99.75	0.452	0.131	99	100	0.917	0.407
	B	17	99.88	0.332	0.081	99	100		
	C	16	99.69	0.479	0.12	99	100		
	Total	45	99.78	0.42	0.063	99	100		
$SPO_2$70	A	7	99.57	0.535	0.202	99	100	1.014	0.378
	B	10	99.4	0.699	0.221	98	100		
	C	9	99.78	0.441	0.147	99	100		
	Total	26	99.58	0.578	0.113	98	100		

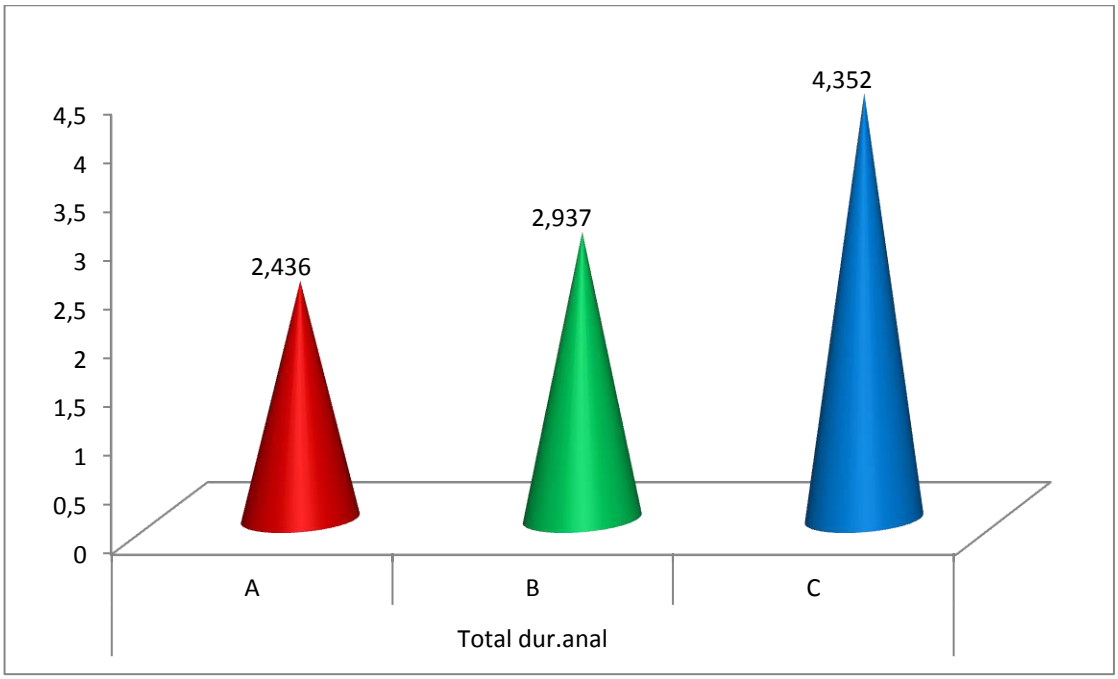


As the table mentioned above shows that oxygen saturation has no statistical significance between the groups.

- **TOTAL DURATION OF ANALGESIA:**

The total duration of analgesia were statistically significant in all three groups. In Group A the mean was 2.436 ± 0.2868 , in Group B it was 2.937 ± 0.3352, in Group C it was 4.352± 0.6231.

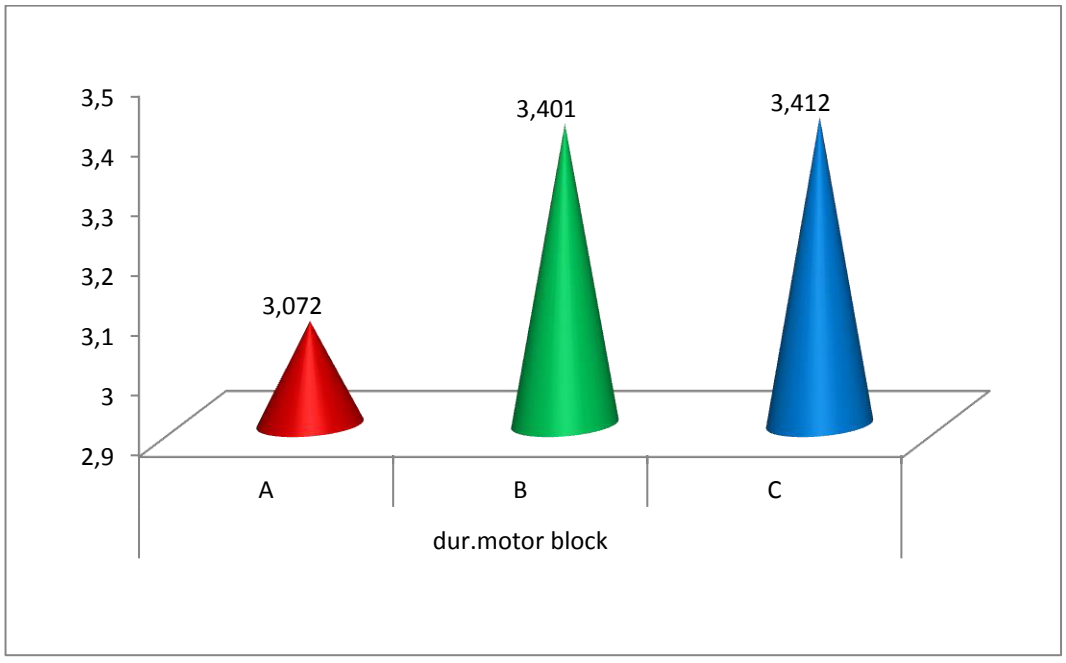
Descriptives	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Total dur. Of analgesia	A	20	2.436	0.2868	0.0641	2.1	3.1
	B	20	2.937	0.3352	0.0749	2.4	3.4
	C	20	4.352	0.6231	0.1393	3.4	5.2
	Total	60	3.242	0.9261	0.1196	2.1	5.2



- **TOTAL DURATION OF MOTOR BLOCK:**

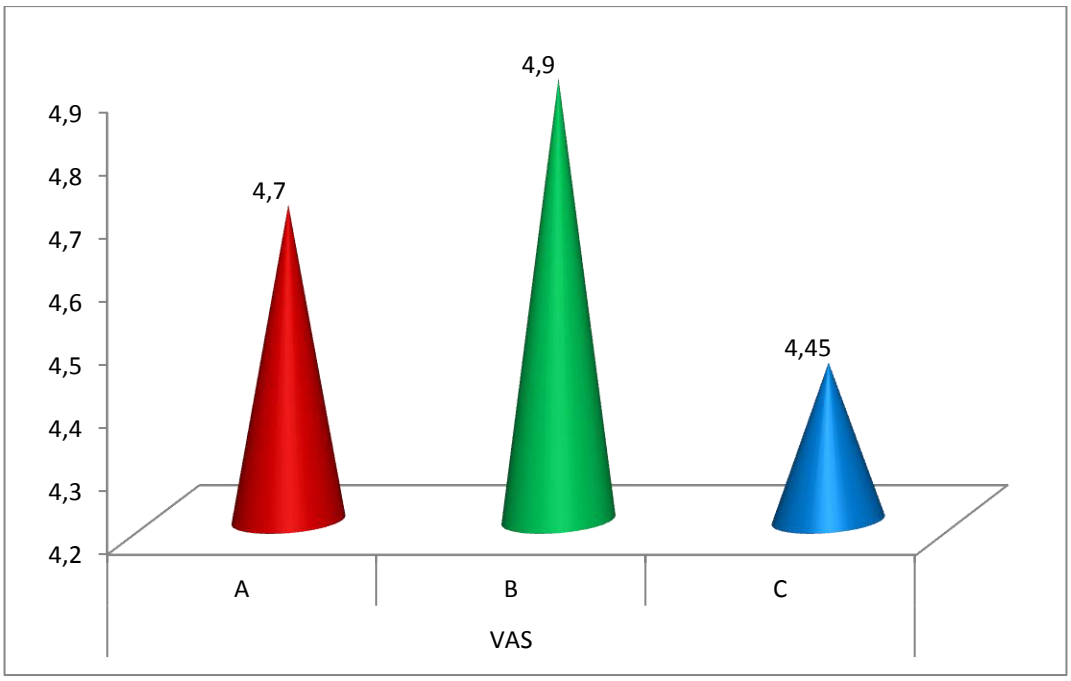
The total duration of motor block was found to be statistically significant between the groups. In Group A the mean was 3.072±0.3467 , in Group B it was 3.401± 0.2172, in Group C mean was 3.412± 0.2328.

Descriptives	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
dur.motor block	A	20	3.072	0.3467	0.0775	2.5	3.5
	B	20	3.401	0.2172	0.0486	3.2	4.2
	C	20	3.412	0.2328	0.052	3.1	4.2
	Total	60	3.295	0.3108	0.0401	2.5	4.2



- **VAS SCORE:**

Descriptives	Groups	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
VAS	A	20	4.7	0.47	0.105	4	5
	B	20	4.9	1.071	0.24	4	9
	C	20	4.45	0.51	0.114	4	5
	Total	60	4.68	0.748	0.097	4	9



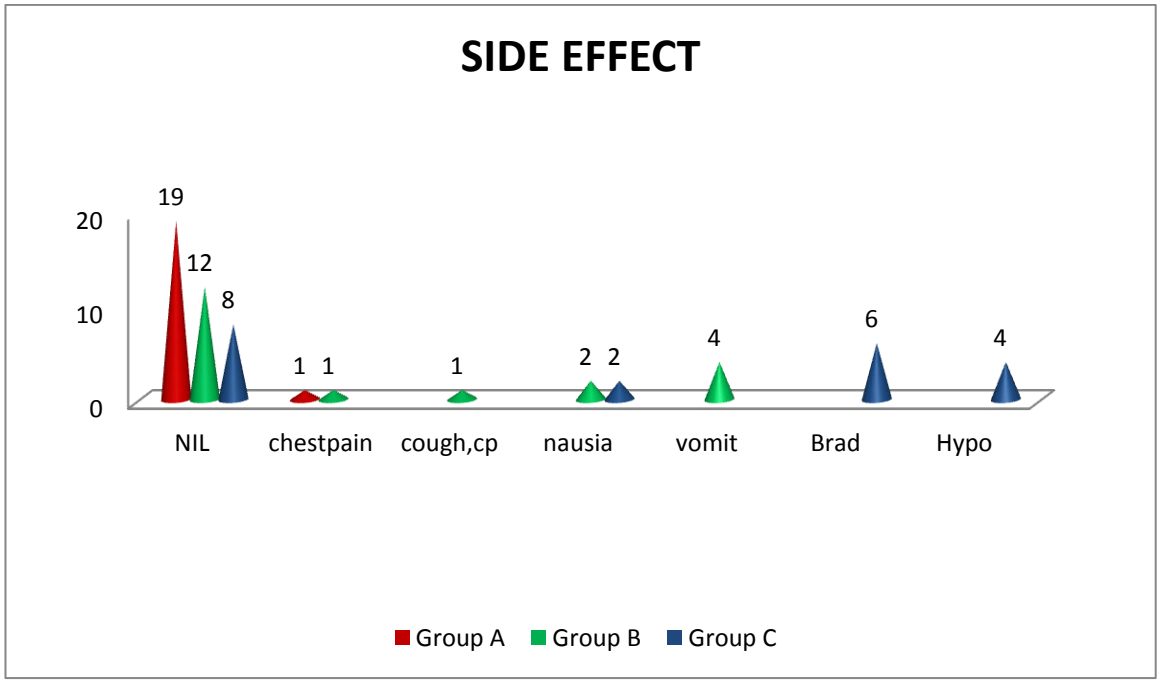
The mean VAS score was not significant statistically as the p value is 0.163.

- **SIDE EFFECTS:**

In Group A , out of 20 patients only one had complaints of mild chest pain . in Group B , out of 20 patients two patients had chest pain , one had cough 5 -6 episodes ,two patients had complaints of nausea and 4 patients had vomiting during intraoperative and postoperative period. In Group C , out of 20 patients 6 patients had bradycardia , 4 patients had hypotension with bradycardia and two patients had nausea.

Group	Side effect	Frequency	Percent
A	NIL	19	95
	chestpain	1	5
	Total	20	100
B	NIL	12	60
	chestpain	1	5
	cough,cp	1	5
	nausea	2	10
	Vomiting	4	20
	Total	20	100
C	NIL	8	40
	Brady	6	30
	Hypo	4	20
	Nausea	2	10
	Total	20	100

Side Effect	Group A	Group B	Group C
NIL	19	12	8
chestpain	1	1	
cough,cp		1	
nausea		2	2
vomit		4	
Brad			6
Hypo			4



DISCUSSION

Lower abdominal surgeries like hernioplasty , abdominal hysterectomy are commonly performed surgeries. Providing good analgesia with adequate muscle relaxation during intra operative period and managing pain in the post operative period is a good practice of anaesthesia. As pain influences the morbidity and mortality of the patients, it's important to ease pain due to surgery for better outcome of the patients.

Commonly, lower abdominal surgeries are performed under spinal anaesthesia , as it is easy to perform , single shot technique when compared to epidural anaesthesia and general anaesthesia. But the main problem of spinal anaesthesia is that postoperative analgesia lasts only for considerable period.

This study is conducted to analyse the effect of adding additives 50 μ of neostigmine and 50 μ of clonidine to 0.5% hyperbaric bupivacaine and evaluating the duration of postoperative analgesia with each drug and the intraoperative haemodynamic stability in patients undergoing lower abdominal surgeries.

After preanaesthetic check-up and getting informed consent, 60 patients of ASA I and II of both sexes, between 20-60 yrs of age, who were scheduled to undergo lower abdominal surgeries of duration less than 90 mins wereincluded in the study. They were randomly allocated into 3 groups of 20 patients each.

AGE:

The mean age in all groups were comparable , Group A is 41.45 ±12.458, Group B is 43.4± 8.923, Group C is 39.15± 11.118.

WEIGHT:

The mean body weight of the patient in Group A is 60.1± 6.593 kg , Group B is 61.35 ± 9.213 and Group C is 61.25 ± 7.247 and is comparable in all three groups.

SENSORY BLOCK:

- **ONSET TIME OF SENSORY BLOCK:**

In this study , the mean time for onset of sensory block was found to be 176.2 ±6.948 sec in Group A, 96.9± 19.472 sec in Group B, 113.95± 14.666 in Group C. This shows that there is statistical difference between the three groups.

Pan PM, Huang CT, Wei TT, Mok MS in 1998, conducted a study that compares the analgesic effect of intrathecally administered neostigmine and clonidine along with bupivacaine in spinal anaesthesia for patients undergoing caesarean section. They found that the onset of sensory block was rapid in neostigmine groups than clonidine groups.

Yoganarasimha and co-worker in 2014 , compared intrathecal clonidine 75µ versus intrathecal neostigmine 50µ as adjuvant drug for spinal anaesthesia 0.5% hyperbaric bupivacaine 12.5 mg ;they also found that onset of sensory and

motor block is faster in neostigmine when compared to clonidine and plain bupivacaine.

- **DURATION OF SENSORY BLOCK:**

In this study, the mean time for total duration of sensory block was found to be 2.436 ± 00.6231.2868 in Group A, 2.937 ± 0.3352 in Group B, 4.352 ± 0.6231 in Group C. This shows that there is statistical difference between the three groups.

Elia et al, conducted a study including 1,445 patients , used intrathecal clonidine as adjuvant to 0.5% hyperbaric bupivacaine and found that 15 – 150 μ prolonged , the time to two segment regression (mean 14 to 75 min), delay in regression time to L2 that the duration of analgesia, the time to need for first rescue analgesic and motor block was extended without any relationship to dose.

Andrieu et al in 2004 compared intrathecal morphine 4μ/kg with and without clonidine 4μ/kg in patients undergoing radical retropubic prostatectomy . adding clonidine to spinal morphine reduced intraoperative use of sufentanil and prolonged the total duration of analgesia.

Strebel et al in 2004, studied about the effect of three different doses of clonidine (37.5,75 and 150 μg) when added to spinal 0.5% bupivacaine 18 mg in 80 orthopaedics patients. The results showed that in group receiving intrathecal clonidine , the duration of sensory block was prolonged irrespective of the dose.

MOTOR BLOCK:

- **ONSET TIME:**

The mean onset time for motor block in Group A is 166.2 ± 7.824, Group B is 96.2 ± 29.243, Group C is 102.75 ± 29.993 and were comparable between the groups.

Kanazi et al in 2006 , compared clonidine 30 μ and dexmedetomidine 3μ added to 12 mg of 0.5% hyperbaric bupivacaine in spinal anaesthesia , versus 12 mg of hyperbaric bupivacaine alone in 60 transurethral resection of prostrate. Patient treated with alpha 2 agonist has rapid onset time of motor block and took longer time for sensory and motor regression .

- **DURATION OF MOTOR BLOCK:**

The total duration of motor block in Group A it was 3.072±0.3467 , in Group B it was 3.401± 0.2172, in Group C it was 3.412± 0.2328.

Marrivirta et al , conducted a study in 60 ambulatory patients undergoing surgery , added 75μ of clonidine to 6 mg spinal hyperbaric bupivacaine with 6 mg bupivacaine alone. It showed that motor block was prolonged in patients who received clonidine.

Tuijl et al, conducted a study in 2010 in which the effect of 0, 15 and 30 μg of clonidine along with 5 mg of 0.5% hyperbaric bupivacaine on the prolongation of motor block, analgesia and ability to void after knee arthroscopy. The study showed

that clonidine increased the duration of motor block duration by 25 and 34 min respectively.

Rochette et al, studied 75 patients who were given increasing doses of clonidine (0.25, 0.5, 1 y 2 μg/kg) with plain spinal bupivacaine 0.5% (1 mg/kg) and concluded that clonidine 1 μg/kg produces improvement in spinal anaesthesia duration without significant side effects.

Hood DD, Mallak KA, Eisenach JC, Tong C in 1996, studied the difference between spinal neostigmine and epidural clonidine. A total of 58 people received spinal injection of 5% dextrose in normal saline or neostigmine (50, 100, or 200 micrograms in D5NS), followed in 1 h by epidural saline or clonidine. The study showed that clonidine increased the duration of analgesia and motor block.

HAEMODYNAMIC VARIABLES:

Elia et al , studied 1,445 patients , using intrathecal clonidine as adjuvant to bupivacaine and found that there is increased incidence of arterial hypotension without the effect of dose and the risk of bradycardia.

Marrivirta et al (2010), in 60 ambulatory patients undergoing surgery , added 75μ of clonidine to 6 mg spinal hyperbaric bupivacaine with 6 mg bupivacaine alone. This study showed that there is more vasopressor requirement and less post operative pain.

Mercier et al in 1998 ,studied the effect of sufentanil 5 μg and clonidine 30 μg with sufentanil 5 μg alone given in spinal anaesthesia to reduce pain in the first

stage of labour, they stated that ‘clonidine potentiate labour analgesia and side effects such as hypotension, maternal pruritus and sedation were equal in both groups’.

Chiari et al in 2011,conducted a study by using clonidine alone in spinal anaesthesia for relieving pain during labour; in 36 parturients with cervical dilation < 6 cm; they compared 50, 100, and 200 μg intrathecal clonidine and found that labour pain was significantly reduced in all patients, analgesia duration was significantly longer with 200 μg (median 143; range of means75-210 min), with 100 μg (median 118; range of means 60-180 min) and using 50 μg (median 45; range of means 25-150 min).Hypotension was associated with 200 μg and the need of intravenous ephedrine more often than in the other group.

Rochette et al, studied 75 patients which were injected with increasing doses of clonidine with plain spinal bupivacaine 0.5% (1 mg/kg) and concluded that hypotension and bradycardia were seen in 54% and 30% of patients respectively.

Hood DD, Mallak KA, Eisenach JC, Tong C in 1996, studied the effects of spinal neostigmine and epidural clonidine in human volunteers. The study results were ‘combination of neostigmine and clonidine resulted in an additive enhancement for analgesia, with no enhancement of each drug's side effects, and also decreases clonidine-induced hypotension. Neostigmine injected into subjects in the lateral position diminished clonidine-induced reductions in blood pressure and plasma norepinephrine’.

COMPLICATIONS:

In Group A, the study showed that out of 20 patients only one had complaints of mild chest pain, in Group B , out of 20 patients only two patients had chest pain , one had cough 5 -6 episodes in itraoperative period ,two patients had complaints of nausea and 4 patients had vomiting during intraoperative and postoperative period and in Group C , out of 20 patients 6 patients had bradycardia, 4 patients had hypotension with bradycardia and two patients had nausea.

Pan PM, Huang CT, Wei TT, Mok MS in 1998, conducted a study that states 'comparison of the analgesic effect of intrathecally administered neostigmine and clonidine along with bupivacaine in spinal anaesthesia for patients undergoing caesarean section'. 80 patients who were posted for lower segment cesarean section using spinal anesthesia were divided into four groups: bupivacaine group - received 10 mg of bupivacaine alone; bupivacaine + neostigmine group - received 10 mg of bupivacaine + 50μ of neostigmine; bupivacaine + clonidine group received - 10 mg of bupivacaine + 150μ of clonidine; bupivacaine + both received - 10 mg of bupivacaine + 50μ of neostigmine + 150μ of clonidine. This study found that the side effects such as nausea and vomiting and dizziness were significantly high in bupivacaine + both group'.

SUMMARY

This study was done to compare the use of neostigmine 50µ , clonidine 50µ along with 0.5% hyperbaric bupivacaine in spinal anaesthesia in patients undergoing lower abdominal surgeries in providing postoperative analgesia with stable haemodynamic status.

A total of 60 patients were randomly allocated into three groups, 20 patients in each group. Group A received 2.5 ml of 0.5% hyperbaric bupivacaine, Group B received 50µ of neostigmine with 2.5 ml of 0.5% hyperbaric bupivacaine, Group C received 50µ of clonidine with 2.5 ml of 0.5% hyperbaric bupivacaine. Various haemodynamic parameters complications if any were recorded at second minute after spinal and every 5 minutes till the end of surgery.

The observations were noted as follows

Sensory block mean onset time for Group A is 176.2 ± 6.948, Group B is 96.9 ± 19.472 and Group C is 113.95 ± 14.666.

Motor block mean onset time is Group A is 166.2 ± 7.824, Group B is 96.2 ± 29.243, Group C is 102.75 ± 29.993 seconds.

Duration of surgical anaesthesia in Group A is 176.2 ± 6.948, Group B is 96.9 ± 19.472 and Group C is 113.95 ± 14.666.

Haemodynamic changes were significant between three groups.

No significant changes were observed with VAS score.

Complications were seen in Group B nausea, vomiting, cough and chest pain and in Group C bradycardia and hypotension were seen.

LIMITATIONS OF THE STUDY

The selected sample size is small.

Patients belong to ASAI/II only.

CONCLUSION

The observations of this study regarding the sensory and motor block onset time, duration of sensory and motor block, postoperative analgesia show that spinal neostigmine has faster onset in both sensory and motor blockade, but spinal clonidine has longer duration of sensory and motor blockade, and has good post operative analgesia.

The findings suggest that the use of clonidine 50µ along with 2.5 ml of 0.5% hyperbaric bupivacaine in lower abdominal surgeries has an added advantage in comparison with hyperbaric bupivacaine, as it provides longer duration of sensory and motor blockade, faster onset time of sensory block and good post operative analgesia, promotes early ambulation, shorter duration of hospital stay and thus reducing postoperative morbidity. Also it avoids multidrug exposure and its side effects.

This study concluded that spinal clonidine 50µ along with 0.5% hyperbaric bupicaine is better than 0.5% hyperbaric bupivacaine alone as a effective adjuvant , providing good postoperative analgesia.

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PROFORMA

Name : Age /sex: IP no :

Date of surgery :

- Diagnosis : Surgery :
- Weight : PR: BP:
- CVS: RS:
- ABDOMEN:CNS:
- Mallampati classification class: ASA PS class :
- Investigations :
  - ✓ CBC: ECG:
  - ✓ Platelets CXR:
  - ✓ RFT: ELECTROLYTES:
  - ✓ Urine routine: OTHERS:
- Premedication :
- Preloading:
- Spinal anaesthesia :
- Drugs given :
- Time of onset of analgesia:
- Cephalad spread of analgesia:
- Time taken for onset of motor blockade:
- Quality of motor blockade:

- Intraoperative haemodynamics:

TIME	PR	SPO2	NIBP
2nd min			
5th min			
10th min			
15th min			
20th min			
25th min			
30th min			
35th min			
40th min			
45th min			
50th min			
55th min			
60th min			
65th min			
70th min			
75th min			
80th min			
85th min			
90th min			

- Sedation:
- Total duration of analgesia:
- Time of first rescue analgesia given:
- Duration of motor block:
- Other side effects:

<u>ஆராய்ச்சி தகவல் தாள்</u>

செங்கல்பட்டு அரசு பொது மருத்துவமனையில் மயக்கவியல் துறையில ஆராய்ச்சி நடைபெற்று வருகின்றது.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்பிகிறோம். இதனால் உங்களுக்கு எந்த பாதிப்பும் ஏற்படாது என்பதை தெரிவித்துக் கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போது அல்லது ஆராய்ச்சியின்போது உங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

MASTER CHART

GROUP - A

S.No	Name	Age	Sex	WT	dur.surg	PRPREOP	PR2	PR5	PR10	PR15	PR20	PR25	PR30	PR35	PR40	PR45	PR50	PR55	PR60	PR70
1	Silambarasan	22	M	67	45	84	86	89	87	82	88	89	94	87	88	82	82	80		
2	Thirunavukarasu	58	M	59	55	78	79	74	72	73	66	64	67	74	82	76	74	75		
3	Kabali	50	M	51	50	78	74	72	78	78	84	88	90	87	84	87	86	84		
4	Elumalai	24	M	54	50	88	86	94	82	80	80	83	79	78	80	76	75	72		
5	Punithavel	39	M	68	40	84	96	94	89	89	92	86	89	84	81	80	78	76		
6	Kandidas	18	M	54	50	92	75	68	66	68	71	66	62	64	68	67	62	60		
7	subramani	50	M	53	60	78	78	82	71	64	62	61	66	63	62	62	63	60	60	60
8	Kavitha	37	F	64	58	94	91	84	88	86	79	86	87	82	78	81	74	78	76	80
9	Daulath	40	F	71	60	85	94	92	92	100	88	90	94	92	82	87	86	84	85	85
10	Kalaiselvi	41	F	59	55	70	80	82	85	88	84	82	80	81	84	82	81	79	84	84
11	Sathya	39	F	64	60	70	79	82	84	89	81	78	78	86	84	82	79	70	85	85
12	Panimalar	24	F	59	45	70	90	82	85	88	84	80	82	81	84	87	84	82		
13	Anjalai	59	F	62	60	75	92	90	87	98	104	96	94	92	89	84	79	78	81	80
14	Maduna	33	F	52	35	60	84	80	91	92	88	78	74	80	82	80	78	78	80	
15	Vijayakumari	48	F	68	60	80	84	86	87	90	78	80	84	82	81	79	84	89	85	
16	Agilandam	59	F	64	50	72	80	70	74	78	70	68	70	74	71	72	75	76	74	75
17	Bharani	45	F	58	70	75	92	82	84	76	79	81	84	96	89	76	74	70	72	
18	Kumari	41	F	63	55	100	95	96	92	94	98	102	94	96	98	91	94	93	96	
19	Bhuvaneswari	47	F	47	50	80	78	76	87	82	84	92	94	79	72	73	80	78		
20	Kuppammal	55	F	65	60	65	76	74	80	96	94	72	71	85	84	76	81	78	74	

SBPPREOP	SBP2	SBP5	SBP10	SBP15	SBP20	SBP25	SBP30	SBP35	SBP40	SBP45	SBP50	SBP55	SBP60	SBP70
120	124	127	120	117	110	112	110	112	116	120	120	120		
120	124	120	116	110	100	112	110	98	100	114	118	120		
130	134	124	120	118	118	114	110	117	120	113	120	120		
120	124	120	126	118	114	110	112	118	120	119	120	120		
126	124	121	124	120	117	120	124	123	120	120	120	120		
116	122	117	104	104	116	110	112	110	115	107	110	110		
159	150	147	139	132	142	146	146	146	142	146	153	150	140	140
128	120	116	110	108	100	106	117	124	118	114	121	124	121	121
130	124	116	112	94	108	100	114	112	120	120	124	117	118	118
110	108	106	104	104	106	102	98	100	112	110	118	114	120	120
126	124	120	106	108	102	98	106	112	118	124	126	130	128	128
128	120	116	110	108	106	94	90	96	110	112	120	120		
130	122	116	118	110	112	110	114	116	108	110	112	118	120	120
112	116	114	112	114	100	96	90	98	100	100	110	110	120	
126	124	118	112	110	106	104	108	112	117	114	119	124	120	
116	112	124	116	111	94	96	92	94	100	108	116	114	118	120
120	118	116	114	100	98	94	97	106	110	112	110	117	121	
124	116	114	110	94	116	124	127	126	121	124	128	130	138	
126	118	104	100	106	110	118	124	125	123	119	124	120		
120	122	118	110	112	114	116	124	121	125	120	123	116	120	

DBPPREOP	DBP2	DBP5	DBP10	DBP15	DBP20	DBP25	DBP30	DBP35	DBP40	DBP45	DBP50	DBP55	DBP60	DBP70
70	72	74	72	68	66	58	64	70	74	74	80	80		
84	82	79	70	70	70	68	70	64	70	72	74	80		
80	80	78	70	70	70	68	64	70	68	72	78	80		
70	72	70	73	68	68	72	74	70	70	76	70	80		
80	79	74	73	68	68	70	72	72	76	74	80	80		
74	69	82	64	64	64	57	65	70	64	69	70	76		
73	74	72	68	73	73	73	73	70	60	76	78	80	80	80
88	82	76	74	72	72	76	70	76	78	72	70	74	76	76
84	82	96	98	82	82	81	74	76	84	82	87	81	79	80
80	76	74	74	70	70	64	72	76	72	74	76	78	80	80
90	84	76	78	66	66	70	65	68	70	76	74	72	76	80

92	102	90	89	84	84	79	84	86	79	74	80	80		
84	80	76	74	70	70	76	79	80	84	80	81	79	78	80
70	74	76	72	78	68	66	67	70	71	70	80	80	80	
84	83	82	80	74	74	69	72	74	75	79	72	74	76	
82	96	74	72	76	73	71	68	64	71	77	78	80	84	80
78	74	74	69	71	80	74	73	78	81	82	84	89	80	
90	86	84	83	87	80	70	72	75	73	76	80	84	81	
84	82	76	64	80	78	74	76	81	75	77	73	72		
80	86	76	74	82	76	74	72	68	70	68	72	74	80	

SPO2PREOP	SPO22	SPO25	SPO210	SPO215	SPO220	SPO225	SPO230	SPO235	SPO240	SPO245	SPO250	SPO255	SPO260	SPO270
98	100	98	99	99	100	100	100	99	99	100	99	99		
99	100	99	99	98	100	100	98	99	100	100	99	99		
97	99	98	100	98	97	100	100	100	99	99	99	99		
98	100	100	99	99	100	99	100	100	100	100	98	99		
100	100	100	100	100	99	98	100	99	99	100	100	100		
100	100	100	100	100	100	100	100	100	99	100	100	100		
97	100	98	99	99	100	100	98	99	100	100	100	100	100	100
99	100	100	100	99	100	100	100	100	100	100	100	100	100	100
97	98	99	99	100	99	99	99	97	98	99	99	99	99	99
99	98	100	100	100	99	99	98	97	99	100	100	100	99	99
97	99	100	100	99	98	100	99	100	100	100	100	100	100	100
99	98	100	100	100	100	100	100	99	100	100	100	100		
100	100	99	99	100	100	100	100	100	100	100	100	100	99	99
97	100	99	99	100	98	100	99	99	99	100	100	100	100	
98	99	100	100	100	99	98	99	100	100	100	100	100	100	
99	100	100	100	99	100	100	100	100	100	100	99	100	100	100
98	99	100	100	100	98	99	100	100	99	100	100	100	100	
99	98	100	100	100	100	100	100	100	100	100	100	100	100	
100	100	99	99	100	100	100	100	100	100	100	100	100		

ONSET	SPREAD	MOTORBLOCK	Totaldur.anal	dur.motorblock	sideeffect	VAS
164	8	156	2.4	3.3		5
180	6	172	2.3	3.0	chestpain	4

184	6	178	2.5	3.1		5
179	6	170	2.6	3.3		4
168	6	150	2.4	3.1		5
186	8	174	2.1	3.4		5
182	6	172	2.4	3.2		5
179	6	176	3.0	3.5		4
174	6	167	2.3	2.6		5
182	4	172	3.1	3.5		5
164	6	160	2.3	3.2		5
180	4	164	2.5	3.4		4
176	6	159	2.3	2.6		5
168	6	154	2.5	3.4		5
170	4	162	2.2	2.6		5
174	6	168	2.5	3.2		5
186	4	172	2.3	3.4		4
176	6	159	2.3	2.6		5
170	4	167	2.2	2.5		4

GROUP – B

S.No	Name	Age	Sex	WT	dur.surg	PRPREOP	PR2	PR5	PR10	PR15	PR20	PR25	PR30	PR35	PR40	PR45	PR50	PR55	PR60	PR70
1	Vinayagam	34	M	70	55	68	78	84	88	94	89	91	85	86	82	87	89	92	90	
2	Durai	62	M	64	65	65	74	72	70	76	70	78	81	84	82	74	79	73	75	77
3	Elangovan	53	M	61	55	80	80	101	98	60	57	58	60	61	64	68	72	74	80	
4	Krishnan	46	M	40	60	89	97	96	91	87	81	78	83	87	85	80	77	80	86	86
5	Arumugam	60	M	65	110	78	91	82	80	78	72	71	77	74	75	71	74	72	80	75
6	Palani	42	M	60	90	100	87	74	79	73	80	75	70	76	73	74	73	80	72	73
7	Sadiq basha	39	M	68	55	124	124	119	111	110	99	96	84	87	90	89	87	85		
8	Ramadoss	25	M	58	80	83	78	83	74	68	79	82	81	79	86	84	87	81	81	82
9	Periasamy	46	M	65	70	74	96	84	83	80	79	79	75	77	74	72	77	83	76	75
10	Sirajbegum	32	F	76	60	98	94	90	94	96	92	90	85	82	87	84	81	85	81	
11	theboral	40	F	62	85	90	101	80	80	86	79	86	72	74	85	91	89	94	88	85
12	Shanthy	40	F	59	90	92	90	94	96	94	94	84	86	85	81	84	83	86	82	88
13	Vasuki	45	F	68	60	87	92	80	80	84	82	85	90	86	83	84	86	79	81	80
14	Kavitha	37	F	54	80	78	76	90	98	70	74	94	92	76	74	86	87	90	82	87
15	Daulath	40	F	49	55	60	98	94	90	100	96	100	92	96	90	86	84	87	85	
16	Selvi	40	F	59	45	75	88	84	85	87	90	88	84	85	86	80	80	80		
17	Jayanthy	43	F	67	65	68	76	72	75	73	72	72	71	68	67	76	72	74	78	
18	Maliga	54	F	45	50	82	96	94	87	81	82	82	85	87	76	74	81	80		
19	Jayakumari	45	F	61	30	87	89	96	91	87	88	83	79	82	87	85	77	84	86	
20	Mega	4	F	7	65	92	1	1	96	94	94	91	93	86	84	81	79	82	80	

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SBPPREOP	SBP2	SBP5	SBP10	SBP15	SBP20	SBP25	SBP30	SBP35	SBP40	SBP45	SBP50	SBP55	SBP60	SBP70
120	122	118	110	112	114	116	124	121	125	120	123	116	120	
117	124	120	126	125	120	124	121	120	123	127	125	124	120	
108	104	102	100	96	110	112	108	115	124	127	121	122	126	125
135	135	126	110	112	135	126	124	112	104	107	112	116	120	
140	143	135	125	137	134	135	147	146	163	158	147	145	147	140
148	131	136	100	107	128	117	111	112	108	108	111	116	119	122
154	142	134	138	140	146	143	143	141	146	133	140	137	137	128
118	115	123	121	121	123	130	134	133	137	123	118	122		
138	135	124	112	117	122	125	117	125	128	130	127	124	127	123
122	124	126	120	124	125	123	127	120	121	124	126	123	120	127
130	126	124	120	117	100	96	107	111	117	118	124	127	134	
126	118	120	120	116	118	112	117	120	122	120	124	121	126	125
126	120	118	118	120	116	111	118	124	120	125	127	124	127	123
110	117	108	106	105	104	104	107	112	115	117	115	110	116	120
140	148	137	135	136	131	128	127	129	124	126	127	132	130	128
124	122	120	124	126	120	125	121	120	123	127	119	124	120	
116	126	124	125	120	124	121	119	124	120	123	126	120		
125	126	130	127	120	124	126	120	121	126	106	112	104	116	
130	122	120	110	122	126	124	128	124	128	124	120	120		
110	106	102	100	92	94	98	96	90	94	102	108	104	106	
110	108	112	110	111	117	120	108	106	110	115	117	120	121	

DBPPREOP	DBP2	DBP5	DBP10	DBP15	DBP20	DBP25	DBP30	DBP35	DBP40	DBP45	DBP50	DBP55	DBP60	DBP70
80	86	76	74	82	76	74	72	68	70	68	72	74	80	
74	72	74	80	80	78	70	74	70	71	74	73	76	70	
74	82	78	80	80	76	71	76	73	75	74	73	74	70	76
78	79	91	94	81	80	91	61	65	61	69	65	61	70	
90	82	76	80	76	77	80	83	86	91	84	85	83	83	80
83	62	75	80	76	76	72	71	67	68	68	71	69	69	67
80	86	79	80	76	81	78	74	77	75	70	81	86	80	86
74	78	71	70	80	80	76	78	81	80	77	80	78		
93	82	90	76	74	76	72	70	77	80	81	85	83	80	81

81	87	74	76	80	77	74	76	73	76	73	73	74	75	79
84	72	79	78	78	72	69	76	77	75	86	84	81	83	
70	70	68	70	74	76	72	70	76	78	80	79	82	80	81
86	84	82	82	80	80	74	72	79	82	78	74	82	86	84
64	68	72	70	69	76	71	77	75	70	78	75	73	80	80
76	82	74	71	76	75	75	81	69	74	76	73	75	72	71
84	82	84	85	86	78	84	80	81	79	81	77	83	80	
69	72	74	76	76	75	75	74	72	71	74	75	80		
74	72	71	75	78	80	70	69	76	72	75	77	73	73	
70	74	75	69	70	72	75	71	73	75	77	72	80		
72	60	66	70	75	80	68	72	70	69	64	70	70	72	
84	80	72	75	70	74	73	69	64	70	74	73	75	70	

SPO2P REOP	SP O22	SP O25	SPO 210	SPO 215	SPO 220	SPO 225	SPO 230	SPO 235	SPO 240	SPO 245	SPO 250	SPO 255	SPO 260	SPO 270
99	100	100	100	99	100	100	100	100	100	100	100	100	100	
98	100	99	100	100	100	98	99	99	100	100	100	100	100	
99	99	100	100	100	99	100	100	98	99	99	99	100	100	99
97	100	100	99	98	100	99	100	100	100	100	100	100	100	
99	99	99	100	100	100	100	100	100	99	100	100	100	100	99
99	100	100	100	100	100	100	100	100	100	100	100	100	100	100
97	100	100	100	100	99	99	100	100	99	99	100	100	100	100
98	99	100	100	100	98	99	100	100	99	99	98	99		
99	100	100	98	99	100	100	100	99	99	100	100	100	100	98
97	99	100	100	100	100	100	99	98	100	100	99	100	100	100
99	100	100	99	100	100	100	100	100	100	100	99	100	100	
98	100	100	100	98	100	100	96	97	99	100	100	100	100	100
99	100	100	100	100	100	99	99	99	100	99	99	99	99	99
97	98	100	100	99	99	100	100	100	100	100	100	100	100	100
99	100	100	100	99	100	100	100	99	98	99	97	99	99	99
99	100	100	99	100	100	100	100	100	100	100	100	100	100	
99	100	100	100	100	100	100	99	100	100	100	99	100		
97	99	98	100	100	100	100	100	100	100	100	100	100	100	
99	100	99	100	99	99	100	100	100	100	99	99	100		
100	99	100	100	100	99	100	100	100	100	100	100	100	100	
98	100	100	100	100	100	99	100	100	100	100	100	100	100	

ONSET	SPREAD	MOTORBLOCK	Totaldur.anal	dur.motorblock	sideeffect	VAS
182	6	172	3.0	3.0		5
74	8	67	3.2	3.5	cough,cp	5
96	6	124	2.5	3.3		4
140	6	180	2.4	3.2	vomit	4
90	8	60	3.1	3.5	vomit	5
100	8	60	3.0	4.2		5
68	8	90	2.4	3.2		5
80	7	128	3.2	3.4	vomit	5
120	6	79	3.2	3.6		5
102	6	90	3.2	3.6	nausia	5
116	4	125	3.4	3.5		5
110	4	128	2.6	3.3	chestpain	5
104	6	96	3.0	3.2		4
80	6	82	3.2	3.4		5
94	4	70	3.3	3.5	nausia	9
106	6	94	2.4	3.4		5
74	6	80	3.0	3.2		4
120	4	110	3.1	3.4	vomit	4
70	6	90	3.2	3.5		5
110	4	95	3.2	3.5		4
84	6	77	2.6	3.2		5

GROUP – C

S.NO.	NAME	AGE	SEX	WT	DUR.OF. SURGERY	PREOP	PR2	PR5	PR10	PR15	PR20	PR25	PR30	PR35	PR40	PR45	PR50	PR55	PR60	PR65
1	Arunachalam	44	1	64	75	76	74	67	61	68	54	69	68	69	70	73	63	62	65	
2	Arumugam	25	1	57	80	88	89	84	79	77	74	78	76	79	72	70	65	63	64	
3	Parthasarathy	49	1	78	55	84	71	74	67	61	54	69	68	69	70	63	65	58		
4	Karthi	20	1	54	80	84	95	96	75	74	60	64	62	66	68	70	75	80	78	
5	Venkatesan	21	1	75	90	94	80	73	64	57	64	68	67	66	68	67	65	62	71	75
6	Kumar	30	1	55	70	104	107	103	102	92	90	86	83	85	89	85	80	85	79	73
7	Elumalai	56	1	68	90	72	77	69	76	80	71	70	68	64	70	68	62	61	58	61

8	Rama doss	25	1	56	80	83	78	83	74	68	65	60	62	53	57	55	54	71	79	87
9	Manic ham	52	1	68	65	92	86	73	72	66	64	66	68	72	66	64	69	72	71	69
10	Mano har	45	1	62	60	87	81	70	74	72	71	68	72	72	76	73	75	72	75	75
11	Sivapr akasa m	57	1	59	70	85	77	72	76	69	72	78	72	73	73	75	71	74	79	70
12	MD kaja	26	1	64	45	90	84	73	73	70	75	77	70	74	77	75	74	74		
13	Dinah aran	46	1	49	45	97	94	81	86	85	84	83	83	80	70	74	74	74	76	
14	Santha kumar	44	1	58	60	81	76	74	64	63	60	59	54	78	79	72	70	73	75	
15	Gandh imathy	30	2	62	70	84	89	72	74	76	70	68	70	74	72	71	71	70	72	75
16	Pushp a	49	2	56	60	92	84	70	71	69	64	67	68	68	72	69	63	72	72	
17	Jayach andra	44	2	67	80	79	79	74	77	69	67	72	70	71	68	72	75	73	71	70
18	Latha	47	2	57	60	68	64	63	59	74	72	70	71	69	64	65	73	72	75	
19	Chand ra	40	2	61	45	72	77	70	72	78	76	70	68	64	66	64	67	65		
20	Sudha devi	33	2	55	50	79	76	74	67	63	69	64	69	68	73	70	73	72		

SBPPREOP	SBP2	SBP5	SBP10	SBP15	SBP20	SBP25	SBP30	SBP35	SBP40	SBP45	SBP50	SBP55	SBP60	SBP70
106	93	98	97	92	93	97	90	90	91	90	89	91	100	
130	124	121	118	117	114	110	112	117	111	98	94	100	98	
107	100	93	98	97	92	93	97	98	100	106	117	120		
133	120	116	110	110	105	106	108	105	107	106	113	110	113	
139	140	127	120	114	117	116	114	110	111	115	118	118	124	122
134	138	126	120	120	126	126	111	116	115	108	114	119	117	121
120	127	126	110	116	113	104	115	113	108	105	106	98	106	111
138	126	121	110	103	111	109	105	107	110	109	111	111	116	112
110	107	106	100	93	97	98	93	91	89	94	96	100	107	110
124	121	124	116	115	115	110	109	107	110	106	110	112	109	120
130	123	120	115	109	109	104	109	108	113	117	112	110	114	116
116	114	117	112	111	113	109	105	107	110	116	120	120		
127	120	120	118	112	115	117	98	100	106	109	110	110	120	
127	120	117	114	118	110	121	120	120	119	117	119	115	117	
116	107	90	92	97	90	90	98	100	112	116	115	117	119	116

124	127	120	110	117	109	106	112	117	110	113	112	115	116	
118	107	105	98	94	90	90	96	98	110	118	120	121	120	116
134	130	127	120	114	114	107	108	108	110	116	115	117	115	
110	98	94	96	99	100	108	109	106	109	109	110	120		
131	127	120	110	118	113	98	110	116	100	104	105	120		

DBPPREOP	DBP2	DBP5	DBP10	DBP15	DBP20	DBP25	DBP30	DBP35	DBP40	DBP45	DBP50	DBP55	DBP60	DBP70
65	65	56	58	54	55	61	55	52	55	54	51	60	60	
70	78	70	70	68	64	60	63	68	64	60	64	67	70	
70	65	56	58	64	55	61	65	71	72	48	60	64		
75	73	58	59	55	53	58	62	68	69	64	70	71	69	
89	83	74	75	72	72	71	69	67	67	72	73	75	71	73
110	113	112	88	87	88	88	74	73	73	72	83	81	76	78
84	87	86	82	80	76	75	67	64	73	74	75	70	68	71
93	77	72	67	67	69	71	70	68	67	72	62	68	72	70
72	70	68	64	59	64	72	73	68	71	69	70	72	74	74
76	73	70	64	68	60	63	67	65	69	72	71	72	70	70
85	80	79	74	71	70	73	69	76	74	72	70	73	73	71
76	78	70	69	69	73	75	71	70	72	70	76	78		
87	83	70	78	74	70	73	72	75	71	74	76	78	80	
76	74	73	69	68	72	74	70	72	70	74	70	74	78	
82	79	75	73	69	68	68	70	72	74	73	75	72	70	71
75	75	72	70	74	75	71	65	63	65	68	70	72	70	
84	83	84	74	72	75	71	70	68	69	68	70	72	74	73
76	73	78	75	73	72	70	75	73	71	72	76	78	80	
72	70	64	68	60	74	72	78	73	72	70	78	78		
73	77	62	67	68	69	70	68	69	69	75	78	78		

SPO2P REOP	SP O22	SP O25	SPO 210	SPO 215	SPO 220	SPO 225	SPO 230	SPO 235	SPO 240	SPO 245	SPO 250	SPO 255	SPO 260	SPO 270
99	100	99	98	99	100	99	100	100	100	100	100	100	99	
99	99	100	99	100	99	100	100	100	99	99	99	99	99	
99	99	100	100	100	100	99	100	100	100	99	100	100		
99	100	100	100	100	100	100	100	100	100	100	99	100	100	
100	100	100	100	100	100	99	100	100	100	100	100	100	100	100
97	99	99	100	98	98	99	99	100	100	100	100	100	100	100
98	98	99	100	99	99	100	100	99	99	100	100	100	100	100
99	99	100	100	99	100	100	99	100	100	100	100	100	100	100
98	99	100	100	100	100	100	100	100	99	100	100	100	99	100
99	100	100	100	100	100	99	100	100	99	100	100	100	100	100
97	99	100	100	99	100	100	100	99	100	100	100	100	100	99
98	99	99	99	100	100	100	100	100	100	100	100	100		
99	100	100	100	100	100	99	99	100	100	100	100	100	100	
97	99	100	100	100	99	100	100	100	100	100	100	100	99	
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
100	100	100	100	100	100	100	100	100	100	100	100	100	100	
100	100	100	100	100	100	100	100	100	100	100	100	100	99	99
100	100	100	100	100	100	100	100	100	100	100	100	100	100	
100	100	100	100	100	100	100	100	100	100	100	100	100		
100	100	100	100	100	100	100	100	100	100	100	100	100		

ONSET	SPREAD	MOTORBLOCK	Totaldur.anal	dur.motorblock	sideeffect	VAS
120	6	68	5.2	3.5	brad	5
154	6	149	4.6	3.2	nausea	4
120	6	60	5.3	3.5	brad	5
110	6	84	4.2	3.4	hypo	5
120	6	190	5.1	3.5	hypo	4
100	6	90	4.4	3.1		4
80	6	65	5.1	3.4	brad	5
120	6	110	4.2	3.6	brad	4
113	8	95	4.3	3.4	hypo	4
106	8	90	3.4	3.3		5
117	6	130	4.1	3.6		4
110	6	115	5.0	3.4	nausea	4
130	6	124	4.2	3.3		5
110	8	100	3.4	3.2	brad	5
98	6	90	3.6	3.5		4
100	6	110	4.1	3.5		4
117	7	95	3.4	3.2	hypo	5
120	6	84	4.2	3.2	brad	4
110	6	110	5.3	3.5		4
124	6	95	4.4	4.2		5

GLOSSARY:

- IASP — International Association of the Study of Pain
- CSF — Cerebrospinal fluid
- PR — Pulse Rate
- SBP — Systolic Blood Pressure
- DBP — Diastolic Blood Pressure
- NIBP — Non invasive Blood Pressure
- CVS — Cardiovascular System
- RS — Respiratory System
- CNS — Central Nervous System
- WT — Weight
- ASA — American Society of Anaesthesiologist
- VAS — Visual Analogue Scale