"A COMPARATIVE STUDY OF DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUNCT TO INTRATHECAL BUPIVACAINE IN LOWER ABDOMINAL SURGERIES".

By

Dr. MALLIKA GANESH

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IN

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Under the guidance of

Dr. DINESH K M.D.

PROFESSOR AND HOD

DEPARTMENT OF ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY AND CRITICAL CARE
SRI DEVARAJ URS MEDICAL COLLEGE
TAMAKA, KOLAR-563101

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SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR- 563101

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Date:

Place: Kolar

Signature of the Guide

Dr. DINESH K. **M.D**

Professor and HOD

Department Of Anesthesiology

Sri Devaraj Urs Medical College

Tamaka, Kolar.

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA,

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Dr. Dinesh K. M.D

Professor and HOD

Department of Anesthesiology
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:

Place: Kolar

Dr. HARENDRA KUMAR. M. L

Principal

Sri Devaraj Urs Medical College.
Tamaka, Kolar.

Date:

Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA,

ETHICAL COMMITTEE CERTIFICATE

This is to certify that the Ethical committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved **Dr. MALLIKA GANESH,** Postgraduate student in the subject of ANAESTHESIOLOGY at Sri Devaraj Urs Medical College, Kolar to take up the Dissertation work entitled **"A COMPARATIVE STUDY OF DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUNCT TO INTRATHECAL BUPIVACAINE IN LOWER ABDOMINAL SURGERIES" t**o be submitted to **SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTRE, TAMAKA, KOLAR, KARNATAKA.**

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Place: Kolar

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Sri Devaraj Urs Medical College,

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Dr. MALLIKA GANESH

LIST OF ABBREVIATIONS USED

Abbreviation	Full Form
α	Alpha
A	Appendicectomy
ASA	American society of Anesthesiologists
b/w	Between
C	Cervical vertebra
cc	Cubic centimeter
cm	Centimeters
CNS	Central nervous system
CSF	Cerebrospinal fluid
CVS	Cardiovascular system
DBP	Diastolic blood pressure
ECG	Electrocardiogram
G	Grams
HR	Heart Rate
hr	Hours
IH	Inguinal hernioplasty
Inj	Injection

IV	Intravenous
kg	Kilograms
L	Lumbar Vertebra
M	Myomectomy
MAP	Mean arterial pressure
µg	Micrograms
µl	Microliters
ml	Milliliters
mg	Milligrams
min	Minutes
mm of Hg	Millimeter of mercury
PACU	Post anesthesia care unit
PCA	Patient controlled analgesia
PR	Pulse rate
SBP	Systolic blood pressure
SpO_2	Percentage of oxygen saturation
SPSS22	Statistical package for the social sciences
T	Thoracic vertebra

TAH	Total abdominal hysterectomy
TURP	Transurethral resection of prostate
TURBT	Transurethral resection of bladder tumor
VAS	Visual analogue scale

ABSTRACT

BACKGROUND AND OBJECTIVES

Spinal block has been the choice of anaesthesia for lower abdominal surgeries because it has a rapid onset, better blockade, and is cost effective. But the drawback is its shorter duration of analgesia. Local anesthetic commonly used is bupivacaine. Adjuncts are used to prolong the duration of action [1]. Alpha 2 agonists dexmedetomidine and clonidine have shown to be effective. In this study we compared effect of addition of clonidine and dexmedetomidine to intrathecal hyperbaric bupivacaine with respect to onset and duration of sensory and motor blockade [2].

MATERIALS AND METHODS

After obtaining permission from Institutional Ethics Committee, and informed consent from patients, 150 patients of ASA 1 and 2 posted for lower abdominal surgeries were randomly divided into three groups of 50 each. Each group 3.5 ml 0.5% hyperbaric bupivacaine and 0.5ml saline, clonidine(30 μg) and dexmedetomidine(3 μg) respectively in group B, C, D.

RESULTS

Mean Time for rescue analgesia in Group B was 167.9 ± 20.6 min, in Group C was 344.4 ± 28.9 min and in Group D was 366.6 ± 37.5 min. This difference in mean Time for rescue analgesia b/w three groups was statistically significant. Highest Time for rescue analgesia was seen in Group D and lowest in Group B.

CONCLUSION

Hence, it is concluded from our study that dexmedetomidine in the dose of 3 μg or clonidine in the dose of 30 μg when added to the bupivacaine 0.5% heavy prolongs the duration of sensory and motor blockade, time taken for sensory regression by two segments and duration of post operative analgesia.

KEYWORDS

Bupivacaine, Lower abdominal surgeries, Spinal anaesthesia

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INTRODUCTION

INTRODUCTION

Anaesthesia technique of choice for most of lower abdominal surgeries is neuraxial blockade [1]. It avoids the complications of general anaesthesia like airway manipulation, polypharmacy and allows the patient to remain awake. Biggest advantage is the post operative analgesia. Amongst that spinal anaesthesia is an easier technique to perform, the onset of anaesthesia is faster favoring the surgical incision to be made sooner [2].

James Leonard Corning injected cocaine inadvertently for the first time intrathecally [3]. Later August Bier in 1898 performed surgery under spinal anaesthesia.

Initially for a long time local anesthetic used was lignocaine as the drug of choice for spinal anaesthesia. It had a faster onset of action and good muscle relaxation. But the use of it got limited because its duration of action was short. Also it was implicated in transient neurologic symptoms and cauda equina syndrome post spinal anaesthesia [4, 5].

Bupivacaine has more potency and longer duration of action than lignocaine [6]. Hyperbaric bupivacaine 0.5% is now the most commonly used drug for spinal anaesthesia. Though it has a prolonged duration of action, it is not sufficient enough to produce adequate post operative analgesia. Hence adjuncts were started being used with bupivacaine intrathecally.

Opioids became commonly used as intrathecal adjuncts with the discovery of their receptors along with endorphins in spinal and supraspinal regions [7]. Opiods prolong the effect of bupivacaine and have an effective post operative analgesic effect without causing significant motor or autonomic blockade [8]. The first opioid used for spinal anaesthesia was morphine [9]. However, side effects like pruritus, nausea, vomiting, urinary retention, and delayed respiratory depression are seen with opiods. This has prompted the need for further research towards non-opioid analgesics with less serious side effects [10].

Other adjuncts tried include benzodiazepines like midazolam, neostigmine, magnesium, epinephrine and ketamine [10, 11].

Alpha2 adrenoreceptor agonists have sedative, analgesic and haemodynamic stabilizing effect. Hence they are now being used as adjuncts to bupivacaine. They prolong the duration of the block produced following their administration intrathecally [12].

Clonidine, a α2 adrenergic agonist, is one of the drugs used. Clonidine was used orally to prolong the analgesic effect of lignocaine, tetracaine and bupivaine used intrathecally [13-15]. Hypotension was severe after oral administration of clonidine than intrathecal clonidine.

Clonidine intrathecally with bupivacaine prolongs analgesia and decreases post operative consumption of opioid analgesics [16]. Also reduces the local anesthetic requirement. Large doses upto 450µg without local anesthetics provide sedation and adequate postoperative analgesia. But this is inadequate for surgical anaesthesia though clonidine has motor blockade property. Hence clonidine is not used alone and only as an adjunct to bupivacaine intrathecally [17].

Dexmedetomidine another α2 adrenergic agonist in 1999 came into practice as a short term medication for analgesia and sedation in intense care unit [18]. Dexmedetomidine is a highly specific and selective α2 adrenoceptor agonist. Its potency is 8 times more for α2 adrenoceptor than clonidine. The ratio of α1:α2 receptor binding selectivity for dexmetomidine is 1:1620 compared to 1:220 for clonidine.

It provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects [19].

While clonidine has been in use as an adjunct to bupivacaine in subarachnoid block, there are only a few studies upon intrathecal uses of dexmedetomidine.

Therefore we designed this study to compare the synergestic effect of addition of clonidine and dexmedetomidine to intrathecal hyperbaric bupivacaine with respect to duration of sensory block, motor block and associated side effects if any in elective lower abdominal surgeries.

OBJECTIVES

OBJCTIVES

To study and compare the efficacy of intrathecal dexmedetomidine 3µg with intrathecal clonidine 30µg as an adjunct to 0.5% bupivacaine heavy 15mg for spinal anesthesia with respect to

1) Time taken for onset of sensory blockade.
2) Maximum level of sensory blockade attained and time taken for the same.
3) Time taken for onset of motor blockade.
4) Maximum grade of motor blockade attained and time taken for the same.
5) Time taken for sensory block regression by two segments.
6) Duration of analgesia.
8) Duration of sensory blockade
9) Duration of motor blockade.
10) Adverse effects.

APPLIED ANATOMY

VERTEBRAL CANAL [20]

The spine has 33 vertebrae which include 7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral, and 4 fused coccygeal vertebrae. All the vertebrae have a body anteriorly, two pedicles posteriorly project from the body, and two laminae connecting the pedicles. All of these form the vertebral canal that contains the spinal cord. The transverse processes arise from the laminae and it projects laterally. The spinous process project posteriorly. The pedicles have the superior and inferior vertebral notch. The spinal nerves exit the vertebral canal through this. At the junction of the lamina and pedicles, superior and inferior articular processes arise. They form joints with the adjoining vertebrae.

The first cervical vertebra (atlas) is an exception to this typical structure. It does not have a body or a spinous process. The first prominent spinous process is that of C7. This is followed by T1spinous process. T12 vertebra is identified by tracing the 12th rib back to its attachment to it. An imaginary transverse line can be drawn connecting the tops of the iliac crests. This crosses the body of L5 or the 4th and 5th inter vertebral space. This is called Tuffier's line.

Spinous process of C7	First prominent spinous process in the back of the neck
Spinous process of T1	Most prominent spinous process; immediately follows C7
Spinous process of T12	Palpate the 12th rib and trace back to its attachment of T12
Spinous process of L5	Line drawn between the iliac crests crosses the body of L5 or the L4–L5 interspace

Table 1: Landmarks for vertebral interspaces

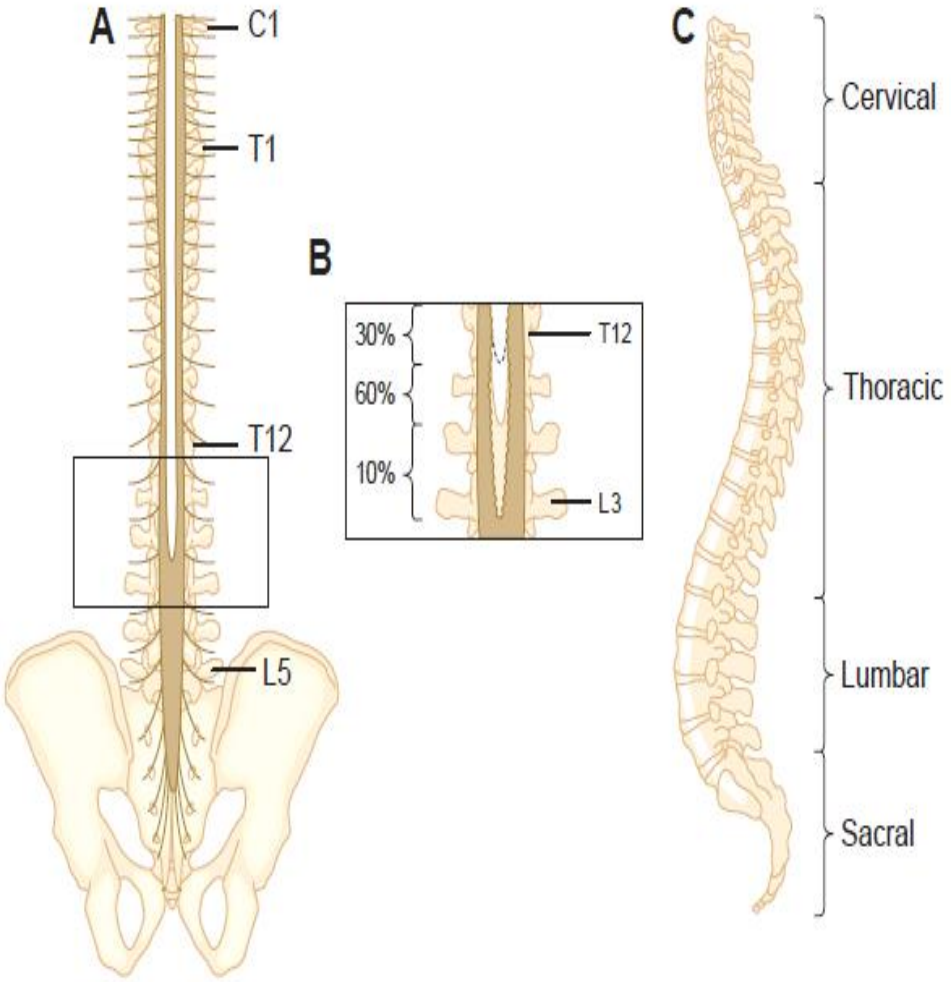


Fig 1: Vertebral column anatomy

31 pairs of spinal nerves arise from the spinal cord. Each nerve has an anterior motor root and a posterior sensory root. The nerve roots are made up of multiple rootlets. Cord segment is the part of the spinal cord that gives all of the rootlets of a single spinal nerve. The skin area that a particular spinal nerve and its cord segment innervate is a dermatome.

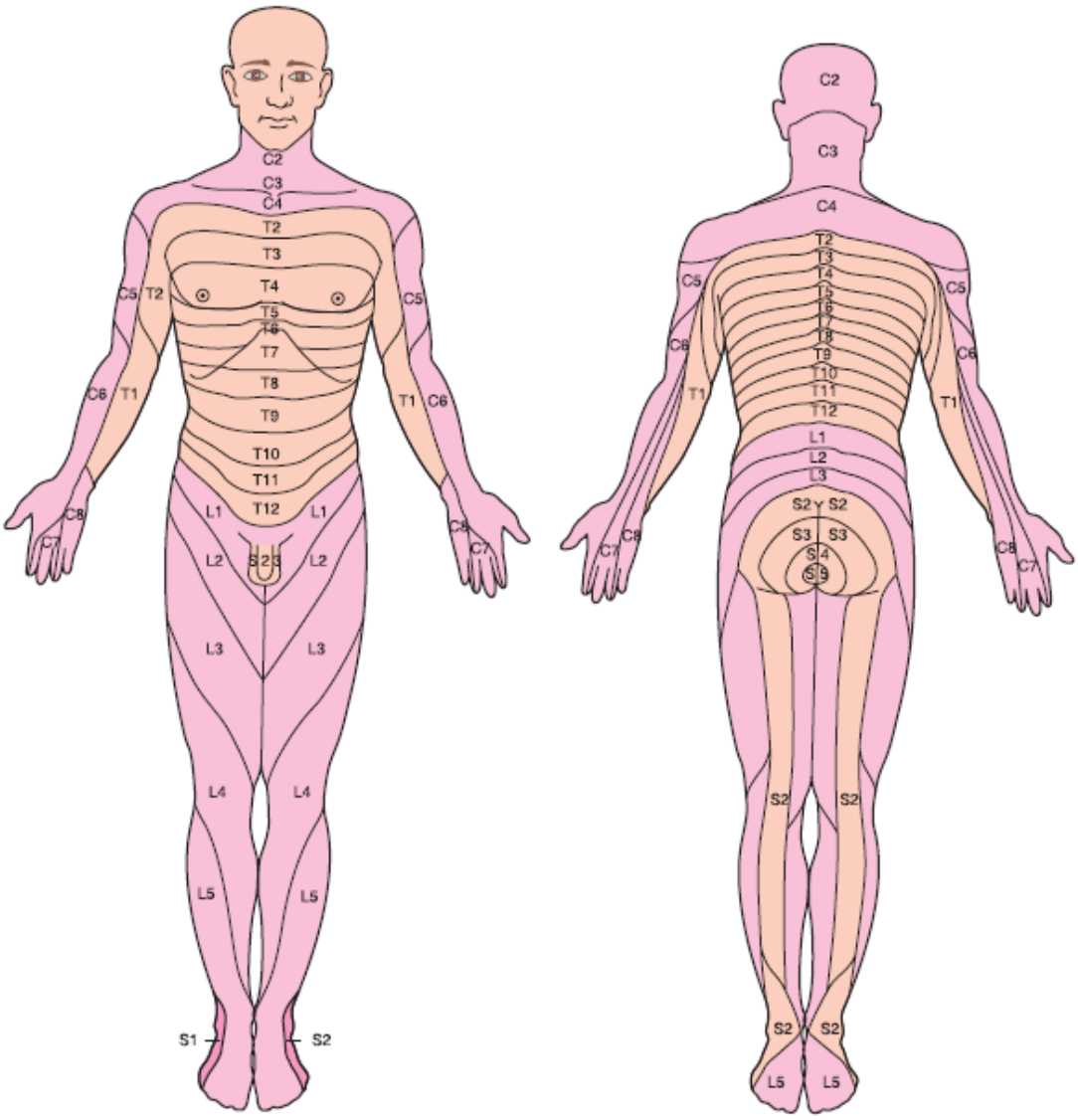


Fig 2: Sensory dermatomes

Spinal cord in adults ends between L1 and L2.The thoracic, lumbar, and sacral nerve roots run longer in the subarachnoid space from their spinal cord segment of origin to the intervertebral foramen where they exit. Nerves that extend beyond where the spinal cord ends are known as the cauda equina.

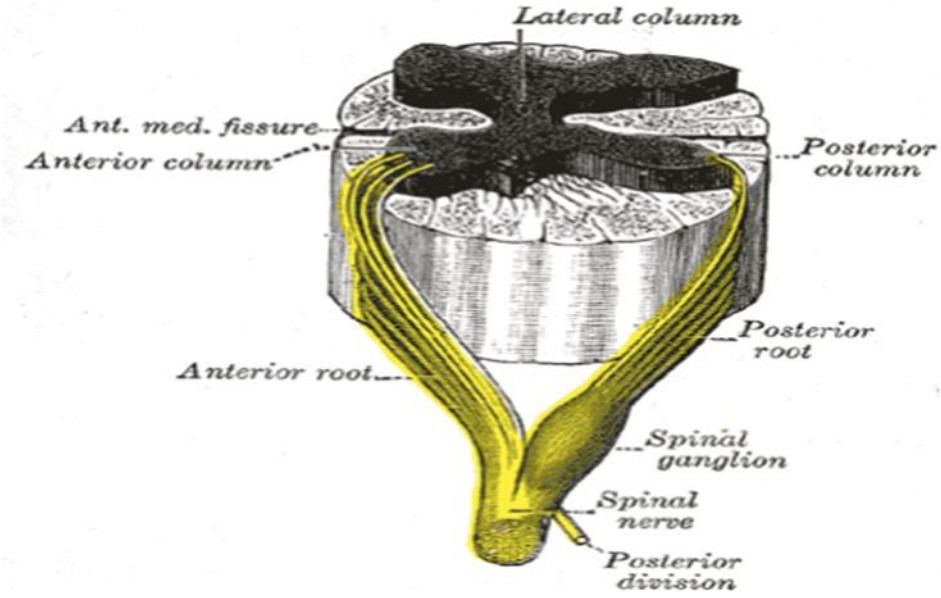


Fig 3: A spinal nerve with its anterior and posterior roots

LUMBAR VERTEBRAE

The lumbar vertebrae bodies are large and kidney-shaped. The vertebral foramen is triangular, larger thoracic but smaller than cervical. Pedicles are thick and have shallow superior notches. Transverse processes are slender. Length increases from L1 to L3, again becomes short hence third transverse process is the longest.

Each vertebra has an accessory process posteroinferiorly at its base and a mammillary process next to the superior articular process. The laminae are short, broad and strong. They do not overlap each other. The superior articular facets face backwards and inwards and the inferior facets face forwards and outwards. The spines are horizontally placed. The 5th lumbar vertebra is wedge-shaped. It produces the lumbosacral angle as it is in front than behind. The transverse process is short, thick and strong. They arise from both the arch and the side of the vertebral body. The laminae and spines overlap and interdigitate with each other such that the spinal canal is hidden. This is not so in the lower lumbar region. This interlaminar gap increases by forward flexion of the spine that makes lumbar puncture possible.

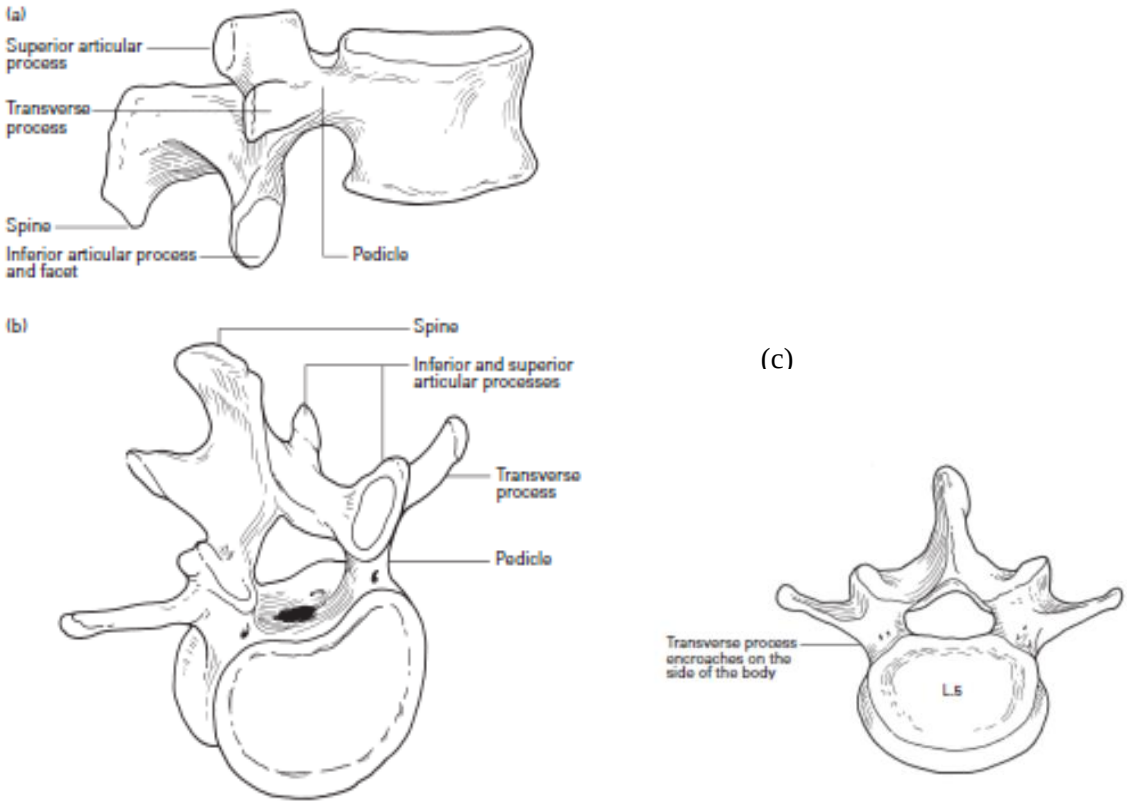


Fig 4: Lumbar vertebra in (a) lateral and (b) anterosuperior (c) superior view.

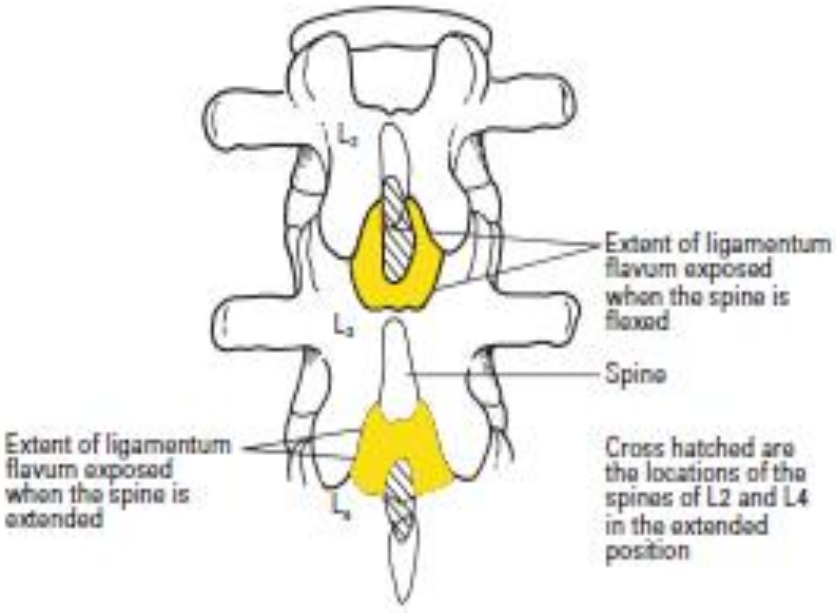


Fig 5: The lumbar interlaminar gap

LIGAMENTS OF VERTEBRAL COLUMN [21]

1) Supraspinous ligament: This is a powerful fibrous tissue that connects the tips of the spines from C7 to the sacrum. It is thicker and broader at the lumbar region and blends with neck ligaments in the cervical region. This ligament becomes ossified in elderly patients making a midline spinal puncture difficult.

2) Interspinous ligament: This is a thin fibrous structure which connects the shafts of adjacent spines. These fibres are membranous and extending from the apex and upper surface of a lower spine till the root and inferior surface of the next higher vertebra. This ligament meets the supraspinous ligament posteriorly and the ligamentum flavum anteriorly.

3) Ligamentum flavum: This is a yellow elastic tissue with perpendicularly aligned elastic fibres that connect the adjacent laminae. Thickness increases progressively from above downwards. Due to this the elastic recoil is more obvious in the lumbar than in the thoracic region that is transmitted to a syringe attached to an epidural needle inserted into the ligamentum flavum. In the elderly the elasticity is lost and it becomes calcified.

4) Posterior longitudinal ligament: This extends along the posterior surfaces of the vertebral bodies. Its attachment corresponds to that of the anterior ligament.

5) Anterior longitudinal ligament: This runs along the anterior surfaces of the vertebral bodies. It becomes progressively wider from above downwards. It is attached to the anterior aspect of each intervertebral disc and to the adjacent margins of the vertebral bodies.

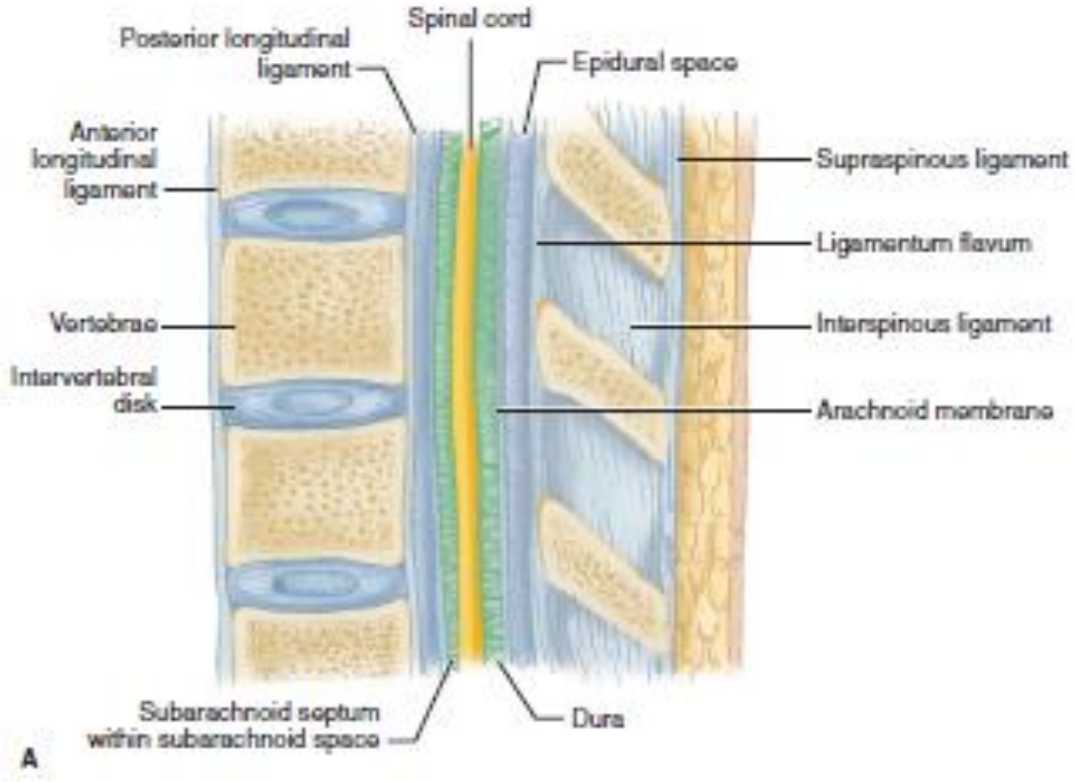


Fig 6: Median sagittal section of two lumbar vertebrae and their ligaments

MENINGEAL COVERINGS OF THE SPINAL CORD [20]

The brain and spinal have are three membranes (from inside out) the pia mater, arachnoid mater, and dura mater.

1) Dura mater - This is a direct extension of the cranial dura mater. The dural covering in the brain is a double membrane containing the cerebral venous sinuses between its walls. The dura mater has the continuation of the inner meningeal layer of the cerebral dura. This is cerebral dura ends at the foramen magnum. Here it merges with the periosteum and encloses the skull and from there it is the periosteal lining of the vertebral canal. It extends from the foramen magnum to S2 as spinal dura mater. Here the filum terminale blends with the periosteum on the coccyx. Sometime can be upto S3, because of which there is a chance of inadvertent spinal tap during a caudal injection. The sac is wider at the cervical and lumbar regions where it corresponds to the cervical and lumbar enlargements of the spinal cord. The sac is present loosely in the canal, within the epidural fat. But it is attached at the following points to its bony surroundings:

a) Superiorly: above the edges of the foramen magnum and posteriorly to the C2 and C3 vertebral bodies.
b) Anteriorly: to the posterior longitudinal ligament by thin filaments fibrous tissue.
c) Laterally: by prolongations along the dorsal and ventral nerve roots. These fuse into a common sheath that blends with the epineurium of the resultant spinal nerves.
d) Inferiorly: by the filum terminale to the coccyx.
e) Posteriorly: completely free.

2) Arachnoid mater - This is the middle covering of the brain and spinal cord. It is a delicate non-vascular membrane very closely attached to the dura. It ends at S2 lower border. Above, it continues with the cerebral arachnoid where it loosely invests the brain and dips into the longitudinal fissure between the hemispheres.

3) Pia mater – this is the inner most of the three membranes. It is highly vascular membrane closely investing the spinal cord and brain. Pia matter folds and extends laterally along the lines of attachments of the anterior and posterior roots and these are called denticulate ligaments. They hold the spinal cord within the subdural space. It is thickened anteriorly along the length of the anterior median fissure into the linea splendens. On both sides, it forms a series of triangular fibrous strands called the ligamentum denticulatum. It is attached at their apices to the dural sheath. They lie between the spinal nerves till the gap between the T12 and L1root. They are 21 in number. Posteriorly the subarachnoid septum has an incomplete sheet which passes from the posterior median sulcus of the cord backwards till the dura in the midline. Inferiorly, it continues downwards as the filum terminale. This pierces the lower end of the dural sac continuing till the coccyx with a covering sheath of dura.

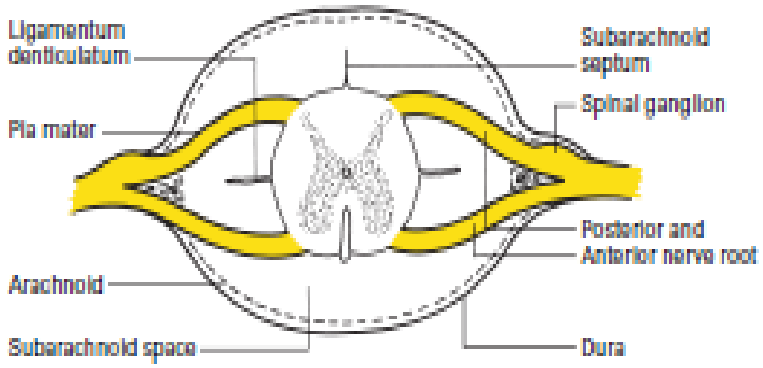


Fig 7: The spinal cord and meninges in transverse section.

DURAL SPACES [2]

The subarachnoid space has the CSF, spinal nerves, blood vessels that supply the spinal cord, the lateral extensions of the pia mater and the dentate ligaments, which provide lateral support to the dura mater. This space communicates with tissue spaces in the pia mater that are accompanied by vessels as they penetrate into the cord. These continuations are described the Virchow–Robin spaces and these are pathways by which drug injected intrathecally permeates the cord.

Though the spinal cord ends at the L1 lower border, the subarachnoid space continues to S2. The potential space between the dura and the arachnoid is the subdural space. This small amounts of serous fluid which allows the dura and arachnoid to move over each other. The injection of local anesthetic here can be associated with patchy anaesthesia, often unilateral.

ANATOMY OF THE SPINAL CORD [20]

The length of the spinal cord is 45 cm in males, and 42 cm in females on an average. The weight is approximately 30 g. It is elongated and cylindrical shape. It is flattened anteroposteriorly in the lumbar region. The spinal cord tapers to form the conus medullaris, from this a glistening thread called the filum terminale comes down and gets attached to the coccyx. The filum terminale is piamater in a sheath of dura, but its upper part has no prolongation of the central canal of the cord.

The relationship of the cord to the vertebral column has major difference in fetal, infant and adult life. Till the third month of fetal life, the cord is lengthier than the vertebral canal. Later the vertebrae grow faster than the cord such that

the cord ends at L3 lower border in the newborn. At one year of age, the conus medullaris is at L2 lower border and the dural sac at the S2 vertebra. This difference in growth rate leads to formation of epidural space and the caudal canal. The adult relations are attained by 12-16 years and the spinal cord is at the lower border of the L1. However, there is a frequent and considerable variation in this level where the cord ends opposite the body of L1 or L2, or, rarely, T12 or even L3. This differential growth results in the lumbar and sacral nerve roots becoming considerably elongated to reach their corresponding intervertebral foramina, hence forming the cauda equina.

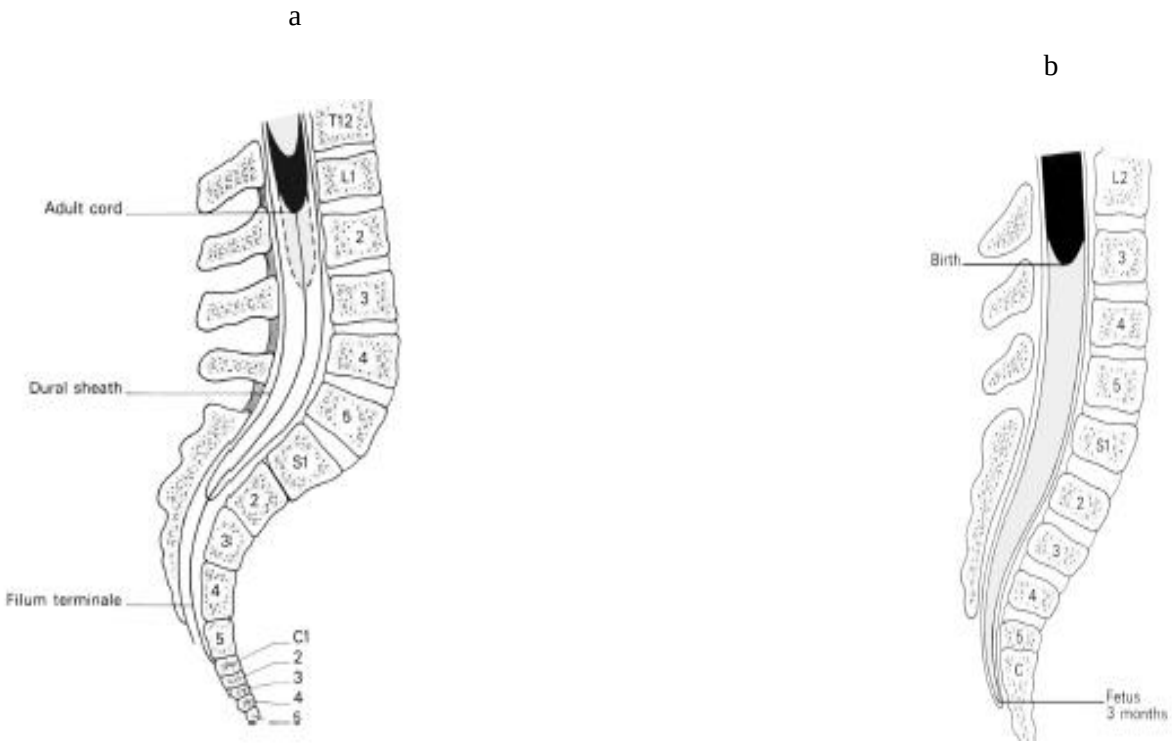


Fig 8 (a): The relationship between the spinal cord and the vertebrae in a 3 month fetus and in a newborn child.

(b): The range of variation in the termination of the spinal cord in the adult.

THE STRUCTURE OF THE CORD

The spinal cord has an anterior median fissure and a posterior median sulcus. On both sides of the posterior sulcus posterior nerve roots emerge. The anterior nerve roots emerge by a number of nerve tufts.

Transverse section of the cord has a central canal, H shaped zone of grey matter which has the nerve cells and an outer zone of white matter that has the nerve fibres.

The white matter amount reduces from the cervical down to the lumbar region. This is because the afferent nerve fibres are progressively added to the cord from below upwards and the efferent fibres are progressively given off from above downwards. The grey matter is more in both the cervical and lumbar enlargements. These correspond to the zones of origin of the motor nerves to the upper and lower limbs.

The central canal continues from the forth ventricle downwards as a narrow tube. It is lined with ciliated ependymal cells and contains the CSF. It is present in the whole length of the cord, dilates in the conus medullaris, and continues within the filum terminale for a short distance. The H of grey matter has a crosslimb which is called the transverse commissure.

Each lateral limb has a short and broad anterior column that contains large motor cells and a thinner and pointed posterior column which is capped by the substantia gelatinosa. These are the anterior and posterior horns, respectively.

The thoracic and uppermost lumbar segments have the lateral grey column. This projects outwards from the grey matter at the junction of the anterior and posterior horns. It contains the spinal cells of origin of the sympathetic system.

The white matter consists of longitudinally disposed medullated nerve fibres to a large extent. This can be divided into the posterior, lateral and anterior white columns based on their central grey matter relationship.

The important tracts in the white matter are:

1) Descending tracts
    a) The lateral cerebrospinal or pyramidal tract
    b) Anterior cerebrospinal, direct pyramidal or uncrossed motor tract
2) Ascending tracts
    a) The posterior column
    b) The spinothalamic tracts
    c) The anterior and posterior spinocerebellar tracts

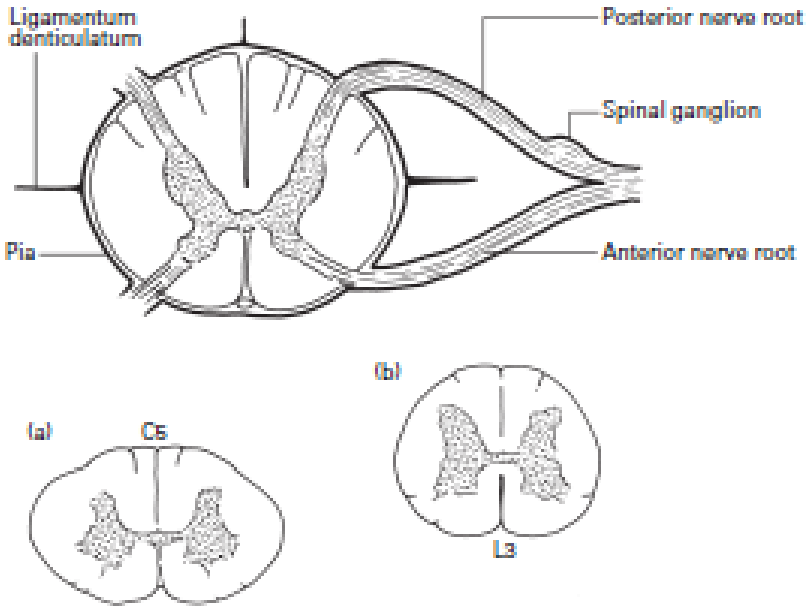


Fig 9: The spinal cord in transverse section from a thoracic segment.

(a) A section from the cervical cord

(b) A section from the lumbar cord.

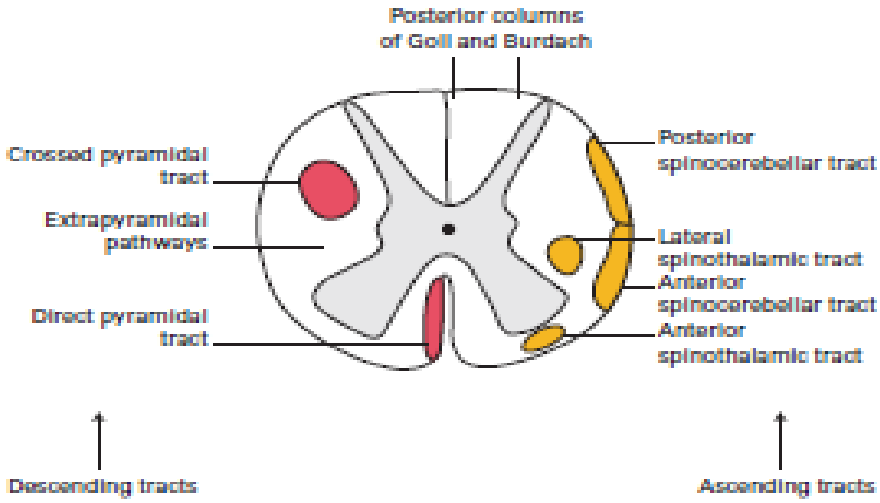


Fig 10: The spinal tracts shown diagrammatically in a transverse section of the thoracic cord.

CIRCULATION OF THE SPINAL CORD [20]

Arterial supply

Two arteries supply the spinal cord- the anterior and posterior spinal arteries. Both these descend at the level of the foramen magnum.

The anterior spinal artery is formed at the foramen magnum by the union of a branch from each vertebral artery. This is in the midline on the anterior median fissure. It is the larger of the two vessels. It supplies the whole of the cord in front of the posterior grey columns.

The posterior spinal arteries consist of four longitudinal running vessels, one on either side. They are derived from the posterior inferior cerebellar arteries. They supply the posterior grey and white columns on either side. These arteries are reinforced serially by spinal branches of the vertebral, deep cervical, intercostal, lumbar, iliolumbar and lateral sacral arteries. The lower branches being responsible for the blood supply of the cauda equina.

Each spinal branch divides into an anterior radicular and posterior radicular artery. They approach the cord along the ventral and dorsal roots.

Anterior radicular arteries are small and they terminate within the ventral nerve roots. Sometimes one of the anterior radicular artery is relatively large compared to others. This is termed as the arteria radicularis magna, or the artery of Adamkiewicz. It comes from the intersegmental branches of the descending aorta. This supplies the lower two-thirds of the spinal cord.

The arterial supply to the spinal cord is very prone to minor trauma and vasoconstrictor drugs. Occlusion of the anterior spinal artery causes the anterior spinal artery syndrome presented with lower limb paralysis without loss of posterior column sensation. It can also be manifested as cauda equina syndrome characterized by sphincter disturbances.

Venous supply

The veins are in the pia mater. After draining the parenchyma of the cord they form longitudinal plexiform channels. They are six in number. It consists of two median longitudinal veins and four lateral longitudinal veins. These veins drain into the internal vertebral plexus that further drain into the intervertebral veins. These exit through the intervertebral foramina to the segmental veins and finally to the external vertebral plexus.

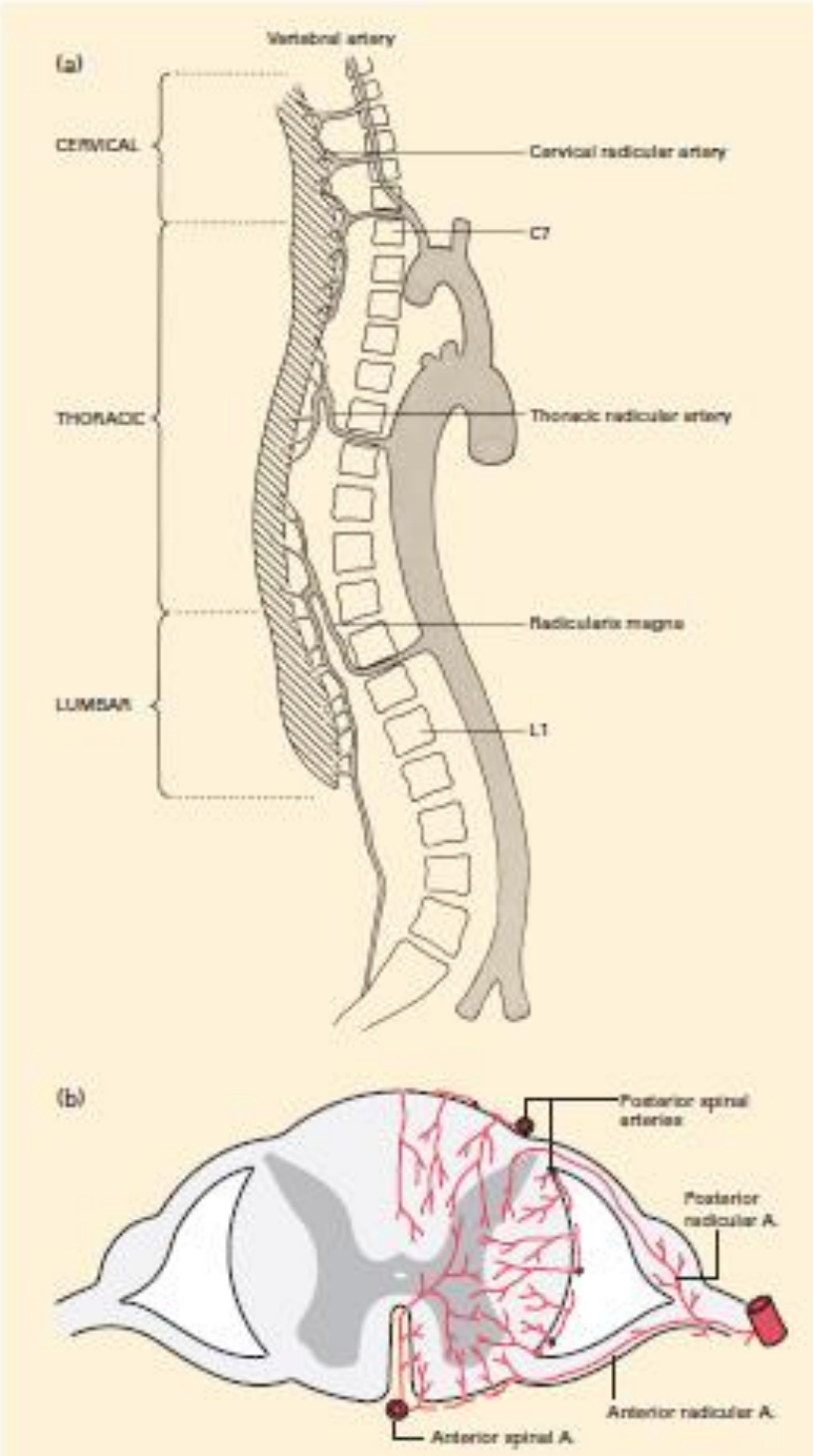


Fig 11: The arterial supply of the spinal cord. (a) In schematic lateral view. (b) In transverse section.

CEREBROSPINAL FLUID [20]

The CSF is a clear watery fluid within the cerebral ventricles and the subarachnoid space. The total volume of CSF in the adult is approximately 150 ml out of which 25 ml is in the spinal theca. Its composition includes electrolytes, proteins, glucose, neurotransmitters, neurotransmitter metabolites, cyclic nucleotides, amino acids. CSF is produced in the choroid plexus by ultra filtration of plasma. It is a true dialysate of plasma. It is produced at the rate of 20 to 25 ml/hr. Entire CSF volume is replaced every 6 hr. CSF escapes from the forth ventricle through the median foramen of Magendie and the lateral foramina of Luschka into the cerebral subarachnoid space, at the cisterna cerebello-medullaris and cisterna pontis, respectively. This absorption is depending on its higher hydrostatic pressure than that of the venous blood. Hence it is passive. There is a constant circulation of CSF. This results in drugs injected intrathecally being carried cephalad. Intrathecal opiods injected in the lumbar region may cause late respiratory depression on reaching the medulla. This may occur up to 16 hr after the intrathecal injection.

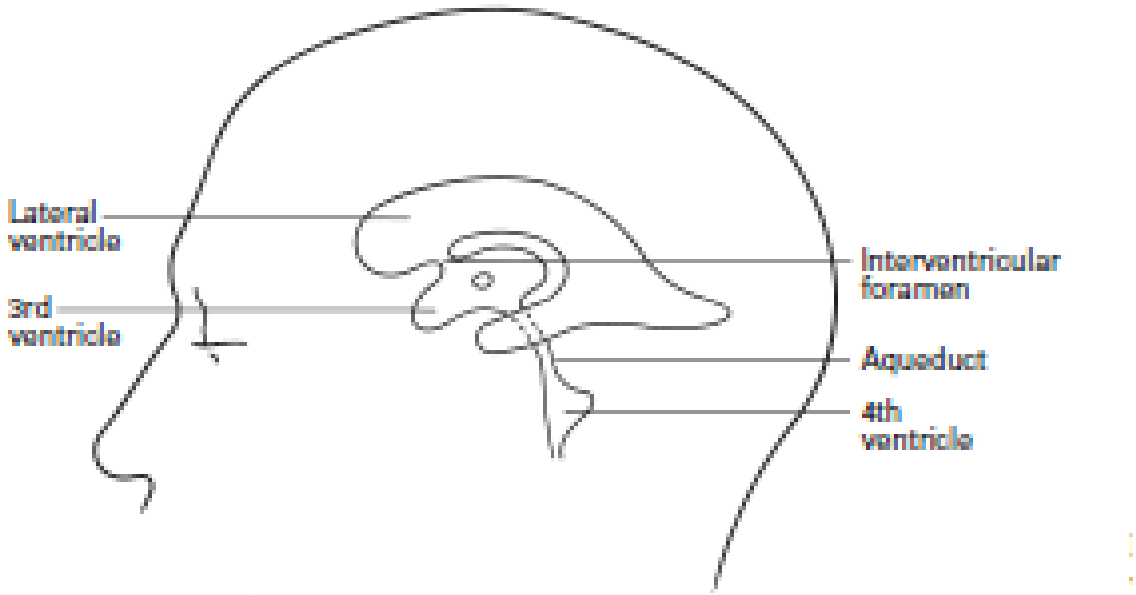


Fig 12: The ventricular system

PHYSIOLOGICAL EFFECTS TO SPINAL ANAESTHESIA [2]

1) Cardiovascular system

The cardiovascular effects include a decrease in heart rate and arterial blood pressure. The sympathetic blockade depends on the height of the block and extends two to six dermatomes above the sensory level. Due to which there is venous and arterial vasodilatation. The venodilation effect predominates because there is limited smooth muscle in venules. During high spinal anaesthesia heart rate decreases because the cardioaccelerator fibres from T1 to T4 are blocked. Fall in right atrial filling causes the bradycardia. This is due to decrease in the outflow from intrinsic chronotropic stretch receptors located in the right atrium and great veins.

2) Respiratory system

Tidal volume remains may remain unchanged. Vital capacity reduces due to decrease in expiratory reserve volume caused by the paralysis of abdominal muscles which are used during forced exhalation.

The respiratory arrest due to spinal anaesthesia is because of the hypoperfusion of the respiratory centres in the brainstem rather than ted to phrenic nerve dysfunction. This immediately responds to fluid therapies which restore the cardiac output and blood pressure.

The consideration with muscle paralysis after spinal anaesthesia focuses on the expiratory muscles that are needed for effective coughing and clearing of intrapulmonary secretions.

3) Gastrointestinal system

Nausea and vomiting is associated with spinal anaesthesia. This is majorly due to gastrointestinal hyperperistalsis caused by unopposed parasympathetic activity. This gastrointestinal hyperperistalsis provides a good surgical condition because of the contracted gut.

4) Renal system

Through autoregulation renal blood flow gets maintained. There is minimal effect on renal function. Neuraxial anesthesia blocks both sympathetic and parasympathetic control of bladder function. Due to this there is urinary retention till the block wears off. Patients should be checked for bladder distention after spinal anesthesia.

5) Metabolic and endocrine system

There is neuroendocrine response because of activation of somatic and visceral afferent nerve fibres and due to localized inflammatory response caused by surgical trauma. This includes increased adrenocorticotropic hormone concentrations, cortisol, norepinephrine, epinephrine, and vasopressin levels,and activation of the renin–angiotensin–aldosterone system. Clinical manifestations include intraoperative and postoperative tachycardia, hypertension, protein catabolism, hyperglycemia, suppressed immune responses, and altered renal function. Spinal anesthesia suppresses this neuroendocrine stress response.

DETERMINANTS OF SPREAD OF LOCAL ANAESTHETICS INTRATHECALLY [21]

1) Characteristics of the local anaesthetic solution

* Baricity
* Volume injected
* Local anaesthetic dose
* Local anaesthetic concentration

2) Patient characteristics

* Age
* Weight
* Height
* Gender
* Pregnancy
* Patient position
* Technique

3) Site of injection

* Barbotage
* Direction of needle bevel
* Addition of vasoconstrictors
* Speed of injection

BARICITY

Baricity is the ratio of the density of the local anesthetic by the density of CSF. This is about 1.0003±0.0003 g/mL at 37°C. Solutions with same density of CSF have a baricity of 1.0000 and are isobaric. Solutions that are more dense than CSF are hyperbaric, and solutions that are less dense than CSF are hypobaric.

Baricity is the most important determinant for the local anesthetic spread and block height.

Hyperbaric solutions are prepared by mixing the local anesthetic solution with 5% to 8% dextrose. After giving spinal in lateral position with a hyperbaric drug at the height of lumbar lordosis and turning the patient, the drug tends to flow cephalad and caudad to pool in the thoracic kyphosis and in the sacrum. This is because of the normal spine curvature causing the subsequent movement of the drug injected.

Hypobaric solutions rise in CSF. Gravity has no effect on isobaric solutions. Thus the choice of anesthetic solution and proper patient positioning can have a considerable influence on the block height.

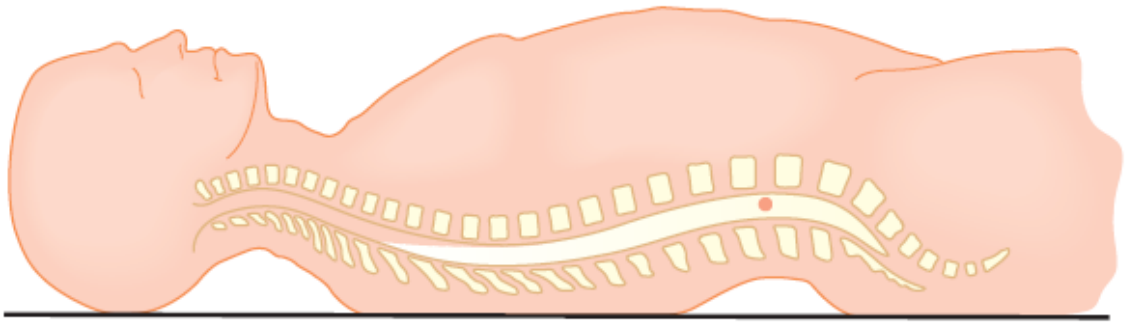


Fig 13: Distribution of the hyperbaric drug injected at the lumbar lordosis (circle)

SEQUENCE OF NERVE MODALITY BLOCK

1) Vasomotor block - Dilation of skin vessels and increased cutaneous blood flow.
2) Block of cold temperature fibres.
3) Temperature discrimination.
4) Slow pain.
5) Fast pain.
6) Tactile senses.
7) Motor paralysis.
8) Pressure senses.
9) Proprioception and joint senses.

INDICATIONS

1) Lower abdominal surgeries
2) Urogenital surgeries
3) Anorectal surgeries
4) Caesarean sections
5) Lower limb surgeries

CONTRAINDICATIONS

Absolute

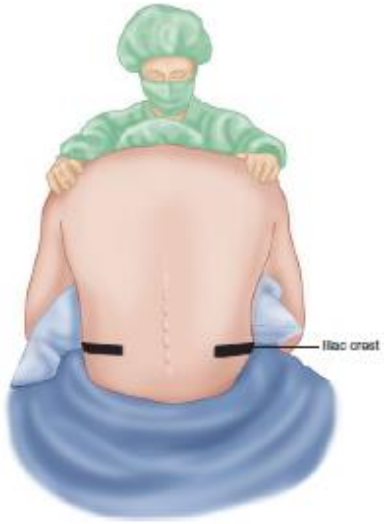
1) Infection at the site of injection
2) Patient refusal
3) Coagulopathy or other bleeding diathesis
4) Severe hypovolemia
5) Increased intracranial pressure
6) Severe aortic stenosis
7) Severe mitral stenosis

Relative

1) Sepsis
2) Uncooperative patient
3) Preexisting neurological deficits
4) Demyelinating lesions
5) Stenotic valvular heart lesions
6) Left ventricular outflow obstruction (hypertrophic obstructive cardiomyopathy)
7) Severe spinal deformity

POSITIONING

1) Sitting Position
2) Lateral Decubitus
3) Buie's (Jackknife) Position



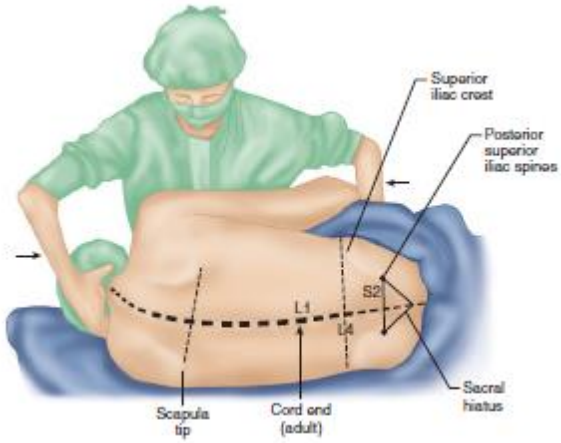


Fig 14: Sitting posture

Fig 15: Lateral decibitous position

Fig 16: Jack knife position

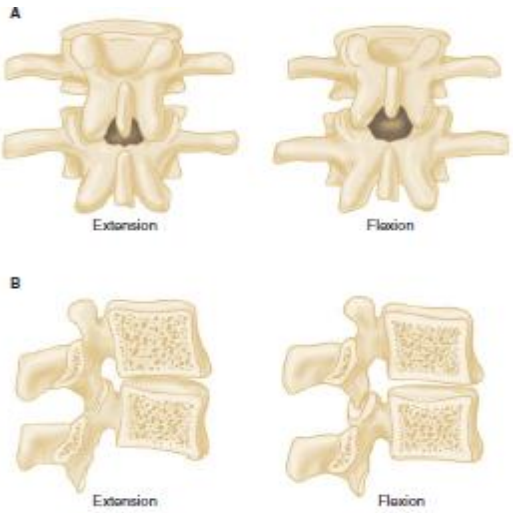


Fig 17: The effect of flexion on adjacent vertebrae. A: Posterior view.

B: Lateral view.

APPROACH

- Midline
- Paramedian

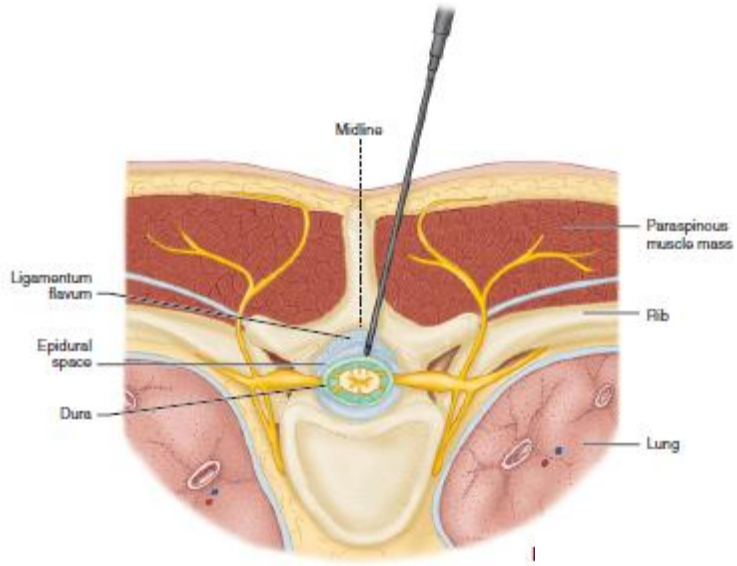


Fig 18: Paramedian approach

COMPLICATIONS

1) Adverse or exaggerated physiological responses
a) Urinary retention
b) High block
c) Total spinal anesthesia
d) Cardiac arrest
e) Anterior spinal artery syndrome
f) Horner's syndrome
2) Complications related to needle/catheter placement
a) Backache
b) Dural puncture/leak
   i. Postdural puncture headache
   ii. Diplopia
   iii. Tinnitus
c) Neural injury
   i. Nerve root damage
   ii. Spinal cord damage
   iii. Cauda equina syndrome

d) Bleeding
    i. Intraspinal/epidural hematoma
e) Misplacement
    i. Misplacement
    ii. No effect/inadequate anesthesia
    iii. Subdural block
    iv. Inadvertent subarachnoid block
    v. Inadvertent intravascular injection
f) Catheter shearing/retention
g) Inflammation ad infection
    i. Arachnoiditis
    i. Meningitis
    ii. Epidural abscess

3) Drug toxicity
    a) Systemic local anesthetic toxicity
    b) Transient neurological symptoms
    c) Cauda equina syndrome

PHYSIOLOGY OF PAIN [22]

Pain is an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage. The term nociception which is derived from a latin word noci that means harm or injury. All nociception produces pain, but not all pain results from nociception.

Clinically pain can be categorized into two types:

1) Acute pain primarily due to nociception is defined as pain caused by noxious stimulation due to injury, a disease process, or the abnormal function of muscle or viscera. Four physiological processes are involved: transduction, transmission, modulation, and perception.

   Acute pain can be somatic or visceral, which are differentiated based on origin and features. Somatic pain can be further classified as superficial or deep.

   Superficial somatic pain is due to nociceptive input arising from skin, subcutaneous tissues, and mucous membranes. It is characteristically well localized and described as a sharp, pricking, throbbing, or burning sensation.

Deep somatic pain arises from muscles, tendons, joints or bones. In contrast to superficial somatic pain, it usually has a dull, aching quality and is less well localized.

The visceral form of acute pain is due to a disease process or abnormal function of an internal organ or its covering. The visceral pain is dull, diffuse, and usually midline. Parietal pain is typically sharp and often described as a stabbing sensation that is either localized to the area around the organ or referred to a distant site. The phenomenon of visceral or parietal pain referred to cutaneous areas results from patterns of embryological development and migration of tissues, and the convergence of visceral and somatic afferent input into the central nervous system.

Four subtypes are described:

a) True localized visceral pain
b) Localized parietal pain
c) Referred visceral pain
d) Referred parietal pain.

2) Chronic pain which may be due to nociception but in which psychological and behavioural factors often play a major role.

PAIN PATHWAYS

Pain gets conducted along from three neuronal pathways which transmit painful stimuli from the periphery to the cortex. Primary afferent neurons have their cell bodies in the dorsal root ganglia. These lie at each spinal cord level in the vertebral foramina. Each of these neurons has a single bifurcating axon. One end of it goes to the innervating peripheral tissue and the other to the dorsal horn of the spinal cord. In the dorsal horn, the primary afferent neuron synapses with a second-order neuron whose axon crosses the midline and ascends in the contralateral spinothalamic tract to reach the thalamus. Second-order neurons synapse in thalamic nuclei with third-order neurons, which inturn send projections through the internal capsule and corona radiata to the postcentral gyrus of the cerebral cortex.

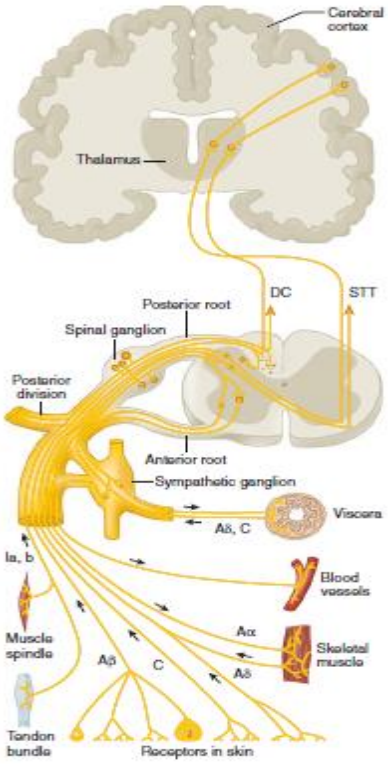


Fig 19: Pain pathway

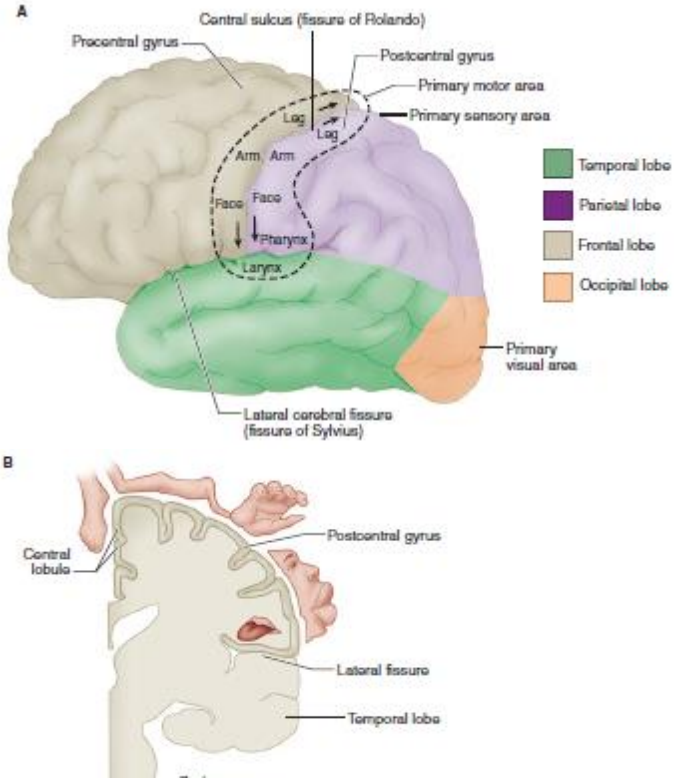


Fig 20: Primary sensory cortex area

A: Lateral view B: Coronal view

NOCICEPTORS

Nociceptors are free nerve endings with a high threshold for activation. As the stimulus intensity increases these in a graded manner increase their discharge rates. With repeated stimulus they have delayed adaptation, sensitization, and after discharges.

Noxious sensations include two types. First pain is a fast, sharp, and well localized sensation. This is the first pain and is conducted A fibres. It has a shorter latency (0.1s) and is tested by pinprick. Second pain is a dull, poorly localized sensation with a delayed onset. It is the second pain and is conducted by C fibres.

Different types of nociceptors include

a) Mechanoceptors: respond to pinch and pinprick
b) Silent nociceptors: respond in the presence of inflammation
c) Polymodal mechanoheat nociceptors.
d) Cutaneous nociceptors: present in skin

e) Deep somatic nociceptors: present in deeper tissues like muscle, tendons fascia and bone

f) Visceral nociceptors: in internal organs

CHEMICAL MEDIATORS OF PAIN

Several neuropeptides and excitatory amino acids function as neurotransmitters for afferent neurons sub serving pain. The afferent neurons contain more than one neurotransmitter that is simultaneously released. The most important of these peptides are substance P and calcitonin gene-related peptide. Glutamate is the most important excitatory amino acid.

Substance P is an 11 amino acid peptide that is synthesized and released by the first order neurons both peripherally and in the dorsal horn. It facilitates transmission in pain pathways via NK-1 receptor activation.

In the periphery, substance P neurons send collaterals that are closely associated with blood vessels, sweat glands, hair follicles and mast cells in the dermis. Substance P sensitizes nociceptors, degranulates histamine from mast cells and serotonin (5-HT) from platelets, and is a potent vasodilator and a chemoattractant for leukocytes.

PHARMACOLOGY OF BUPIVACAINE [23]

CHEMICAL STRUCTURE

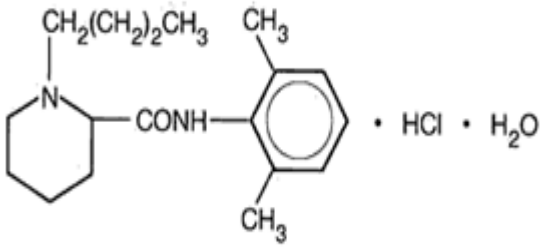


Fig 21: Chemical structure of bupivacaine

Local anaesthetics consist of a lipophilic portion which is usually an unsaturated aromatic ring such as paraaminobenzoic acid and a hydrophilic portion which is usually a tertiary amine such as diethylamine separated by a connecting hydrocarbon chain. The lipophilic portion is essential for

anaesthetic activity and therapeutically useful local anaesthetics require a delicate balance between lipid solubility and water solubility.

In mepivacaine adding a butyl group to the piperidine nitrogen results in bupivacaine. It is 35 highly lipid soluble. It has a higher potency and duration of action comparative to mepivacaine.

Bupivacaine is a pipecoloxylidide local anaesthetic. It is a chiral drug because its molecule possesses an asymmetric carbon atom which is available for clinical use as racemic mixture of the enantiomers.

CHEMICAL NAME

Bupivacaine hydrochloride is an amide type of local anaesthetic drug that is chemically 1-butyl-2', 6' pipecoloxylidide hydrochloride. It was synthesized by Ekenstam AF in 1957 and used clinically in 1963.

PHYSICOCHEMICAL PROPERTIES

a) Molecular weight- 288 (base) 325 (chloride salt)
b) pKa- 8.1
c) Plasma protein binding- 95%
d) Solubility: The base is sparingly soluble, but the hydrochloride is readily soluble in water.
e) Stability and sterilization: Bupivacaine is highly stable and can withstand repeated autoclaving.
f) Melting point: 258^0C.
g) Potency: Bupivacaine is approximately three to four times more potent than lidocaine.

MECHANISM OF ACTION

Local anaesthetics cause conduction blockade. They prevent transmission of nerve impulses by inhibiting passage of sodium ions through ion selective sodium channels in nerve membranes. They occlude the open sodium channels. Failure of sodium ion channel permeability slows the rate of

depolarization such that threshold potential is not reached and thus an action potential is not propagated.

PHARMACOKINETICS

Local anaesthetics are weak bases that have pKa values above physiologic pH. As a result the local anaesthetic exists in a lipid soluble non-ionized form at physiologic pH.

ABSORPTION AND DISTRIBUTION

Absorption from site of injection into the systemic circulation is influenced by factors like site of injection and dosage, use of epinephrine, pharmacologic characteristics of the drug, the rate of tissue distribution and the rate of clearance of the drug.

Lipid solubility is important in redistribution and protein binding of local anaesthetic will influence their distribution and excretion. Bupivacaine is highly protein bound.

METABOLISM

They undergo varying rates of metabolism by microsomal enzymes located primarily in the liver. Bupivacaine undergo the slowest metabolism among the amide local anaesthetics. Bupivacaine is metabolized by aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation.

SYSTEMIC TOXICITY

Systemic toxicity of a local anaesthetic is due to an excess plasma concentration of the drug. Plasma concentrations are determined by the rate of drug entrance into the systemic circulation relative to their redistribution to inactive tissue sites and clearance by metabolism.

Central Nervous System toxicity

Symptoms include perioral tingling and numbness, restlessness, vertigo, tinnitus and difficulty in focusing occurs initially.

Further increase in concentration results in slurred speech and skeletal muscle twitching. Skeletal muscle twitching is often first evident in the face and extremities and signals the imminence of tonic-clonic seizures. Drowsiness precedes the onset of seizures. Seizures are classically followed by CNS depression which may be accompanied by hypotension and apnea.

The typical plasma concentration associated with seizures is 4.5 to 5.5 µg/ml.

Cardiac toxicity:

After accidental IV injection of bupivacaine the protein binding sites alpha1 acid glycoprotein and albumin are quickly saturated, leaving a significant mass of unbound drug available for diffusion into the conducting tissue of the heart. This may result in precipitous hypotension, cardiac dysrhythmias and atrioventricular heart block. Cardiotoxic plasma concentration of bupivacaine is 8 to 10 µg/ml.

Bupivacaine depresses the maximal depolarization rate of cardiac action potential. The resulting slowed conduction of the cardiac action potential in ECG is seen as prolongation of the P-R and QRS intervals and reentry ventricular cardiac dysrhythmias. The R enantiomer of bupivacaine is more toxic than the S enantiomer.

PHARMACOLOGY OF DEXMEDETOMIDINE

Dexmedetomidine hydrochloride is an imidazole compound. It is the pharmacologically active s-enantiomer of medetomidine which is an old anaesthetic agent. It is described chemically as (+)-4-(s) 2 3-(dimethylphenyl) ethyl -11 H-imidazole monohydrochloride. Its empirical formula is C13H16N2HCl and has a molecular weight is 236.7. [24]

STRUCTURAL FORMULA

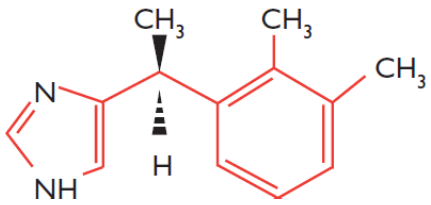


Figure 22: Chemical structure of dexmedetomidine

PHYSIOCHEMICAL PROPERTIES

It is a white powder and is freely soluble in water. It has a Pka of 7.1 and a partition coefficient in octanol:water at pH 7.4 of 2.89. Preservative free dexmedetomidine is available in 0.5, 1 and 2 ml ampoule as Dexmedetomidine Hydrochloride for intravenous use in a dose of 100µg/ml. It can be used both intrathecally and for epidural anaesthesia.

MECHANISM OF ACTION

Dexmedetomidine is the methylated derivative of etomidine. It has a specificity for the α2 receptor and is 8 times more than that of clonidine. Its α2:α1 binding affinity ratio of 1620:1. [25]

Effects of dexmedetomidine are sedation, hypnosis, analgesia, sympatholysis, neuroprotection and inhibition of insulin secretion. [26, 27] agonism at the alpha 2B receptor suppresses shivering centrally, promotes analgesia at spinal cord sites and induces vasoconstriction in peripheral arteries. The alpha 2C receptors are associated with modulation of cognition, sensory processing, mood and stimulant-induced locomotor activity and regulation of epinephrine outflow from the adrenal medulla. Inhibition of nor

epinephrine release appears to be equally affected by all three alpha-2 receptor subtypes. [28]

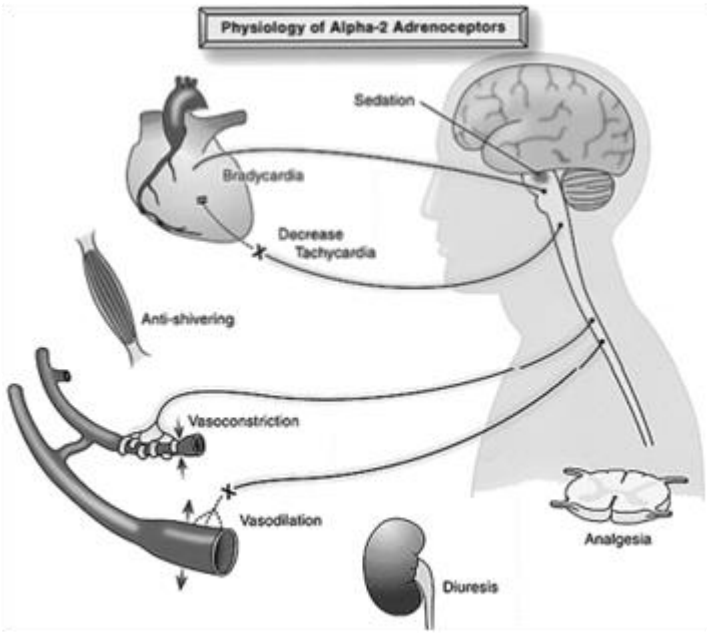


Figure 23: Responses that can be mediated by α2 adrenergic receptors

α2 adrenoceptors are found in highest densities in CNS in the locus ceruleus, the predominant noradrenergic nuclei of the brainstem and also an important modulator of vigilance. Activation this inhibits the release of norepinephrine resulting in the sedative and hypnotic effects. [29] Stimulation this area terminates the propagation of pain signals leading to analgesia. Postsynaptic activation of α2 receptors in the CNS decreases the sympathetic activity causing hypotension and bradycardia. [30]

In the spinal cord at the substantia gelatinosa of the dorsal horn, α2 receptors stimulation leads to inhibition of the nociceptive neurons and release of substance P. Also the alpha-2 adrenoceptors located at the nerve endings have a possible role in the analgesic mechanism by preventing norepinephrine release. The spinal mechanism is the principal mechanism for the analgesic action of dexmedetomidine. There is a clear evidence for both supraspinal and peripheral sites of action. [31]

Alpha-2 receptors are also present in the blood vessels and on sympathetic terminals, where they mediate vasoconstriction inhibit norepinephrine release respectively. The other responses of activation of alpha-2 receptors include contraction of vascular and other smooth muscles, decreased

salivation and decreased bowel motility in the gastrointestinal tract, inhibition of renin release, increased glomerular filtration and increased secretion of sodium and water in the kidney, decreased release of insulin from the pancreas, decreased intraocular pressure, decreased platelet aggregation and decreased shivering threshold by 2^{o}C. [18]

PHARMACODYNAMICS

Dexmedetomidine is considered as the complete α2 agonist. At low to medium doses or on slow infusion, the selectivity is high than with high doses or rapid infusions with of low doses. [12]

Central nervous system

1. Sedation, anxiolysis, hypnosis and amnesia

Dexmedetomidine provides anxiolysis and sedation in a dose dependent manner. There is a good corelation between the level of sedation and the bispectral EEG. Arousability is maintained at deep levels of sedation. The sedation caused resembles normal sleep. Dexmedetomidine activates endogenous non-rapid eye movement pathways inducing sleep. Stimulation of alpha-2A receptors in the nucleus ceruleus inhibits nor adrenergic neurons and disinhibits GABAnergic neurons in the ventrolateral preoptic nucleus (VLPO). [32]

Patient will be cooperative or arousable, that differs it from the sedation caused drugs acting on the GABA system. [33] Sedation is dose dependant, but can cause adequate sedation at low doses. [34] Amnesia is seen with dexmedetomidine at high plasma levels more than 1.9 ng/ml. [35]

2. Analgesia

Dexmedetomidine has analgesic effects both at spinal cord level and supraspinal sites. It significantly decreases opioid requirement. [36, 37] Administration during knee surgery intra articularly has a good postoperative analgesia with less sedation. [38] Mechanisms are activation of alpha-2A receptors, inhibition of the conduction of nerve signals through C and A fibres and the local release of encephalin. [39]

Respiratory effects

Dexmedetomidine does not cause respiratory depression like opioids. The changes in ventilation appeared similar to those observed during natural sleep. [35] It exhibites hypercarbic arousal phenomenon which is a safety feature. [40]

Dexmedetomidine is very useful during fibreoptic intubation or other difficult airway procedures where it causes good sedation without respiratory depression. [41, 42] Also it favours intubation as it reduces airway secretions. [25]

Cardiovascular effects

A biphasic cardiovascular response is seen. [34] Initially it causes a transient increase of the blood pressure and a reflex decrease in heart rate because of peripheral alpha 2B adrenoceptors stimulation of vascular smooth muscles. [34] This lasts for 5-10 min which is followed by a fall in blood pressure caused by the inhibition of the central sympathetic outflow. [43]

Effect on thermoregulation

Dexmedetomidine has lesser rates of shivering. It suppresses shivering because of alpha-2B receptor action in the hypothalamic thermoregulatory centre of the brain. Hence it helps in postoperative shivering. [32]

Effects on renal function

Has diuretic effect due to inhibition of antidiuretic action of arginine vasopressin at the collecting duct. This causes reduced expression of aquaporin-2 receptors and decreased salt and water absorption. [18]

PHARMACOKINETICS

Dexmedetomidine intravenous has an onset at about15 min. Peak concentrations are within an hr continuous infusion. It has a rapid distribution half life of 6 min and a terminal elimination half life of between 2 and 2.5 hr. 94% of drug is protein bound. It has a steady state volume of

distribution. Dexmedetomidine is rapidly distributed and metabolized mainly in the liver by conjugation, n-methylation or hydroxylation followed by conjugation. Concentration ratio between blood and plasma is 0.66. [44]

Dexmedetomidine is absorbed through transdermal, buccal or intramuscular routes, bioavailability of 82% and 104% respectively. [45]

PERIOPERATIVE USES

1. Premedication

Being an anxiolytic, sedative, analgesic, antisialogogue it is suitable as a premedication agent. IV doses 0.33 to 0.67 µg/kg 15 min before surgery.

2. Uses in regional anaesthesia

a. Epidural dexmedetomidine at a dose of 100 µg prolongs analgesia. [46]

b. Intrathecal dexmedetomidine at a dose of 3 to 10 µg causes significant prolongation of sensory and motor blockade. [47]

c. Addition of 0.5µg/kg body weight of dexmedetomidine to lidocaine for intravenous regional anaesthesia improves the quality of anaesthesia and perioperative analgesia. [48]

3. Use in monitored anaesthesia care: it confers arousable sedation orientation, anxiolysis, and analgesia without significant respiratory depression. [24]

4. Dexmedetomidine has also been used as sole anaesthetic agent upto doses of 10µg/kg/hr. [42]

5. Use of dexmedetomidine in postoperative period for sedation and sympatholytic. [24]

6. Addition of dexmedetomidine 2µg/kg body weight to bupivacaine for caudal analgesia promotes analagesia after anaesthetic recovery without increasing the incidence of side effects. [49]

7. Use of dexmedetomidine in intensive care unit as provides adequate sedation with minimal respiratory depression and can be used for weaning patients from ventilator. [50]

ADVERSE EFFECTS

Side effects of dexmedetomidine includes dystonic movements, atelectasis, nausea and vomiting, dry mouth, atrial fibrillation, haemorrhage, acidosis, confusion, agitation and rigors which are rare. Withdrawal after abrupt discontinuation can lead to development of hypertension, tachycardia, emesis, agitation, dilated pupils, diarrhea, and increased muscle tone and tonic clonic seizures. [51, 52]

DOSAGE AND ADMINISTRATION

The dexmedetomidine IV bolus 1µg/kg body weight over a 10 min period, followed by a continuous IV infusion of 0.2-0.7µg/kg/hr. The maintenance dose is titrated until the sedation goal is reached. [18]

DRUG INTERACTIONS

Dexmedetomidine inhibits CYP2 D6 but the clinical significance of this inhibition is not well established. Dexmedetomidine has a little potential for interactions with drugs metabolized by the cytochrome p450 system.

Co-administration of Dexmedetomidine with sevoflurane, isoflurane, propofol, alfentanil and midazolam may result in enhancement of sedative, hypnotic or anaesthetic effects.

PHARMACOLOGY OF CLONIDINE HYDROCHLORIDE

Clonidine is a centrally acting selective partial α2adrenergic agonist. α2:α1 ratio is 220:1. It acts as an antihypertensive drug because of its ability to decrease sympathetic nervous system output from central nervous system. [53]

STRUCTURAL FORMULA

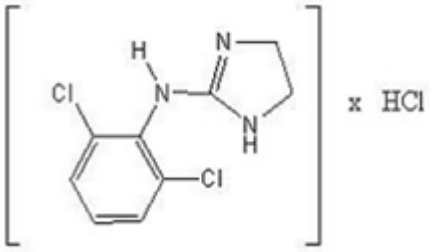


Figure 24: Chemical structure of Clonidine hydrochloride

PHARMACOKINETICS

Clonidine is completely absorbed from gastrointestinal tract. The bioavailability is nearly hundred percent. On oral administration, peak plasma concentration is within 60 to 90 min. The elimination half life is between 9 and 12 hr. 50% of the drug is metabolized in the liver whereas the rest is excreted unchanged in urine. The transdermal route requires about 48 hr to produce therapeutic plasma concentrations. Various routes of administration of clonidine are nasal, oral, intravenous, intramuscular, transdermal, epidural and intrathecal route. Clonidine is metabolized mainly by the liver to its metabolite P-hydroxy clonidine which subsequently undergoes glucuronidation and is excreted in urine.

Preservative free clonidine is available in 1 ml ampoule as clonidine hydrochloride for intravenous use in a dose of 150µg/ml.

PHARMACODYNAMICS

Analgesic effects

Its analgesic effect is due to activation of post synaptic α2 receptors in the substantia gelatinosa of the spinal cord.

α2 receptors are located on primary afferent terminals both at peripheral and spinal endings, on neurons in the superficial laminae of the spinal cord, and within several brainstem nuclei. This is implicated in analgesia, supporting the possibility of analgesic action at peripheral, spinal, and brainstem sites. [12]

The cardiovascular effects

Clonidine action blood pressure is complex after neuraxial or systemic administration because of opposing actions at multiple sites. Activation of postsynaptic α2 receptors reduces sympathetic drive in the nucleus tractus solitarius and locus ceruleus of the brainstem. Clonidine is not a pure α adrenergic agonist. It also activates nonadrenergic imidazoline preferring binding sites in the lateral reticular nucleus, producing hypotension and an antiarrythmogenic action. [54, 55]

In the periphery, activation of presynaptic α2 receptors at sympathetic terminals reduces their release of norepinephrine by the sympathetic nerve terminals, which could cause vasorelaxation and reduced chronotropic drive. These brainstem and peripheral effects are counter-balanced by direct peripheral vasoconstriction from circulating concentrations of clonidine. As a result, the dose response for clonidine by neuraxial or systemic administration is U-shaped, with peripheral vasoconstriction from circulating drug concentrations at high doses opposing central sympatholysis. [12]

Clonidine causes bradycardia by a presynaptically mediated inhibition of norepinephrine release at the neuroreceptor junction and vagomimetic effect. Clonidine depresses atrioventricular nodal conduction. [12]

IV clonidine administration before laryngoscopy and intubation, in the dose of 3μg/kg to 6 μg/kg effectively attenuated the haemodynamic response to intubation.

Respiratory effects

Clonidine has minimal respiratory depressant effect. [53] It must be considered that drugs acting on the central nervous system to alleviate pain, relieve anxiety, and produce sedation are almost always accompanied by some reduction in alveolar ventilation.

Central nervous system [56]

Clonidine causes sedation and increases stage I and stage II sleep. It causes anxiolysis. Anaesthetic-sparing properties of alpha2-adrenergic agonists by inhibitory actions in the locus ceruleus via a G-protein mediated mechanism that involves inhibition of adenylate cyclase and decreases requirement for inhaled anaesthetic (MAC) and injected drugs. Clonidine produces dose-dependent sedation over the dose range 50-900 µg with rapid onset (< 20 min) regardless of route of administration.

Renal system

Clonidine causes early micturition after spinal anaesthesia. [57, 58] Clonidine causes diuresis by inhibition of release of antidiuretic hormone, antagonism of renal tubular action of ADH and increase in glomerular filtration.

Gastrointestinal system

Clonidine reduces secretion and hence a good premedicant.

Hormonal effects

Clonidine decreases plasma catecholamine levels. In stress situations, it reduces, but does not suppress, the neurohormonal secretion. [59]

USES

1. in the treatment of patient with severe hypertension or renin dependant disease.

2. as a premedicant.

a. Produces sedation and decreases anesthetic requirement. [56]

b. Attenuates the blood pressure and heart rate response to laryngoscopy and intubation. [9]

c. Decreases intra operative liability of blood pressure and heart rate.

d. Decrease plasma concentration of catecholamines. [59]

3. Preservative free clonidine administered into the epidural or subarachnoid space (150 to 450 µg) produces dose dependent analgesia. [12]

4. Addition of clonidine 1 μg/kg, to lidocaine for Bier's block enhances postoperative analgesia.

5. Clonidine protects against perioperative myocardial ischemia.

6. Clonidine used for the diagnosis of pheochromocytoma.

7. Used for the treatment of opioid and alcohol withdrawal syndrome.

8. Used in the treatment of shivering

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORICAL REVIEW OF LITERATURE

Leonard J Corning was the first person to perform spinal anesthesia. He did it inadvertently with cocaine1885.

August Bier on August 16 1898 performed the spinal anesthesia at the Royal Surgical Hospital of the University of Kiel, Germany. He performed did for the resection of a tuberculous ankle joint on a 34 year old laborer by injecting 15 mg cocaine intrathecally. August Bier has mentioned in his article the detailed descriptions of the first six patients he performed spinal anesthesia. Bier performed self experiments to solve the problems faced during his initial administration in patients. In 1898, Bier performed the lumbar puncture on Hildebrandt who had previously failed in spinal anaesthesia while performing on Bier himself. He injected 0.5 cc of 1 percent solution of cocaine. The anaesthetic effect lasted for a very short time. [4]

The local anesthetic available for spinal anaesthesia until 1904 was cocaine. In 1905 Einhorn introduced procaine. In 1943 lignocaine was introduced by Lofgren. Bupivacaine was introduced by Ekenstam in 1957.

Duration of action for lignocaine is shorter and may cause transient radicular irritation. Bupivacaine is about four times more potent than lignocaine and has duration of action more than lignocaine. [5]

Although it has prolonged duration bupivacaine does not produce post operative analgesia. Due to this in recent times, adjuncts have started being used for post operative pain relief. [61]

CLINICAL REVIEW OF LITERATURE

Filos KS et al. [62] in 1992 conducted a double blinded study with intrathecal clonidine as a sole agent for pain relief in cesarean section.

This study consisted of 20 ASA physical status I parturient posted for elective cesarean section. They were randomly assigned divided into two groups of ten each. All sections were under general anesthesia. Patients were induced with thiopental 6 mg/kg, paralysed with atracurium 0.3 mg/kg and

intubated. Anaesthesia was maintained with oxygen, nitrous and halothane upto 0.5%.

With 23 gauge disposable spinal needle at L2-L3 or L3-L4 interspace, lumbar puncture was done 45 min after extubation to all patients.

In group 1 normal saline and in group 2 150 µg clonidine hydrochloride (same volume 3 ml) was injected. Duration of analgesia was the time until the patient requested for supplemental analgesia. It was provided with 50 mg IV meperidine and the study was stopped. Assessment of pain was made using a visual pain linear analog intensity scale. Blood pressure, central venous pressure, heart rate, respiratory rate and PaCO2 were monitored. Adverse effects like nausea, vomiting and pruritus were noted during each assessment. Sedation was assessed.

Onset of analgesia was faster in the clonidine group. Duration of analgesia was upto 181.5±168.9 min in normal saline group, whereas in the clonidine group it was 414±127.9 min. Five of ten patients in clonidine group reported a no pain state of duration varying between 60-135 min. Clonidine showed significant reduction of arterial blood pressure and sedation produced in clonidine group was significant than in normal saline group.

So from the study authors concluded that 150µg intrathecal clonidine had effective analgesia of medium duration after cesarean section, but with adverse effects like hypotension and sedation.

Benhamou D et al. [63] in 1998 did a study where they compared analgesic effect of intrathecal clonidine and fentanyl with hyperbaric bupivacaine during elective cesarean section.

Study group included of 78 pregnant women posted for elective cesarean section. It included ASA physical status I or II patients. Patients were kept fasting overnight and premedicated with acid aspiration prophylaxis that included sodium citrate 30 ml or effervescent cimetidine 200 mg 15 min before the spinal anaesthesia. Patients were preloaded with 20 ml/kg of lactated Ringer solution. Lumbar puncture was done with 25 gauge Whitacre needles with patient in sitting posture. Group B patients were injected with hyperbaric bupivacaine and 1 ml saline, Group BC patients with hyperbaric bupivacaine with clonidine 75µg (0.5 ml) and saline (0.5 ml) and Group

BCF with fentanyl 12.5 µg (0.5 ml) and clonidine 75 µg. Bupivacaine dose was 0.06 mg/cm of body height.

Analgesic duration was evaluated with two segment regression time and time for first rescue analgesia post opearively. Motor block was evaluated intraoperatively every 5 min and every 15 min postoperatively using Bromage scale. Adverse effects such as nausea, vomiting, pruritus and shivering if any were noted. Sedation was recorded intra and postoperatively till the block wore off.

Heart rate and noninvasive blood pressure were recorded every 5 min from prior to preloading till the first request for additional analgesia. A fall in SBP to less than 100 mmHg, ephedrine 5 mg was given.

Combined spinal epidural anaesthesia was performed in 34 patients out of 78. In group BC and BCF the upper sensory level achieved was higher compared with group B. To achieve T4 sensory level in group B additional epidural top up was required. When patients who received only the initial spinal injection were compared, two segment regression time and time for first rescue analgesic were significantly longer only in group BCF.

They concluded the study saying that small dose of intrathecal clonidine with bupivacaine improved intraoperative analgesia and side effects were not increased. Combination of clonidine and fentanyl further improved analgesia but moderately increased sedation and pruritis.

De Kock M et al. [64] in 2001 studied the effect of intrathecal ropivacaine and clonidine in knee arthroscopies.

In this double blinded study, 120 patients of ASA grade I scheduled for knee arthroscopy were randomly divided into group 1who received 8 mg of ropivacaine and group 2 patients received 8 mg of ropivacaine plus 15µg clonidine, group 3 received 8 mg ropivacaine with 45µg clonidine and group 4 received ropivacaine 8 mg plus 75µg clonidine. All were in the volume of 4 ml.

A combined spinal epidural technique was performed. Midline approach was used with patients in the lateral position at L3-L4 interspace. Lumbar puncture was performed using a 29 gauge pencil point needle. Motor block was assessed with modified Bromage scale. During surgery, the surgeon

assessed the motor blockade quality and the same surgeon performed all procedure.

The motor blockade intensity was significantly low in group 1and significantly high in patients in group 4. There was no statistical difference in the heart rate among the groups. Mean arterial blood pressure was significantly low in group 3 and 4. Two patients in group 4, were asleep but arousable with oral commands.

Intrathecal ropivacaine alone had a shorter sensory block and motor blockade (132±38 min) than other groups. Ropivacaine with 75µg clonidine produced significantly longer sensory anesthesia (195±40 min) but was associated with side effects such as sedation and hypotension but without bradycardia. Ropivacaine with 45µg clonidine had a sensory blockade of 183±52 min and had no change in motor blockade but had delayed micturition and relative hypotension. Ropivacaine with 15µg clonidine did not prolong sensory or motor blockade, but produced anaesthesia better than ropivacaine alone.

Thus the authors concluded that low dose clonidine 15µg with 8 mg ropivacaine for ambulatory arthroscopy significantly improved the quality of intraoperative analgesia without compromising early mobilization or causing systemic side effects.

Dobrydnjov I et al. [65] in 2003 studied clonidine combined with small dose bupivacaine during spinal anesthesia for inguinal herniorrhaphy surgeries.

This study included 45 patients of ASA physical status I and II posted for open inguinal herniorrhaphy as a day case procedure. These patients were divided randomly to one of the three groups, each comprising 15 patients. Group B patients received 0.5% hyperbaric bupivacaine 6 mg. Patients in group BC15 along with bupivacaine received clonidine 15 µg and in group BC30 received clonidine 30 µg along with bupivacaine. Total volume of the drug was made to 3ml in all the groups. The drug was injected intrathecally over 3 min.

Patients were premedicated with midazolam 1-2 mg IV and paracetamol 1g rectally. They were preloaded with lactated Ringers solution of 250 ml followed by an infusion of 250 ml during the operation.

Lumbar puncture was done using 27 guage Whitacre spinal needles between L2-L3 interspace using midline approach in lateral position. The patients remained in the same position after drug administration for 15 min.

The time at which the intrathecal injection was completed was considered as zero. Patients were asked to stand and walk when Bromage grade 0 and full skin sensibility at the S1 segment was noticed. The time to standing and to walking were recorded.

Surgeons assessed the quality of spinal anesthesia during surgery using four point scale, 4 = excellent, 3=good, 2=inadequate, 1=poor.

Post operative pain intensity at rest and on movement was assessed with the visual analogue scale. Paracetamol 1g orally every 6 hr in all patients was given. Sedation was assessed with 4 point verbal rating scale.

Adverse effects such as pruritis, postoperative nausea and vomiting, headache and low back pain were recorded.

Authors noted that the sensory block on the dependent side in groups BC15 was T6 and BC30 was T8 compared with group B where it was T10. The maximum level in BC15 on dependent side was higher by four segments. Five patients in group B had insufficient level of analgesia for surgery and were converted to general anesthesia.

The two segment regression time, total analgesic duration and duration of motor block was significantly short in group B. Mean duration of motor blockade was significantly longer in Group BC30.

VAS score was significantly low in groups BC15 and BC30 when compared with group B during. All patients in group B, 11 patients in group BC15 and 10 patients in group BC 30 needed supplementary analgesics in PACU. The time for rescue analgesic was significantly short in group B than group BC15 and group BC30.

The MAP was significantly lower during the first 45-120 min after spinal injection in clonidine groups. Hypotensive episodes that required ephedrine were not seen in group B during surgery or PACU. 1 patient was given ephedrine during surgery in group BC30. One patient in group BC15 and three patients in group BC30 had mild orthostatic hypotension initially while standing and walking.

One patients each in group B and group BC30 and two patients in group BC15 complained of postoperative nausea and vomiting. One patient in group B experienced dizziness. One in each groups B and BC30 had headache but neither were typical postdural puncture headache. Two patients in group B complained of back pain. No significant difference in sedation was found among the groups.

The authors concluded clonidine as an adjunct to bupivacaine is effective for ambulatory inguinal herniorrhaphy. It also increased the spread and duration of analgesia.

Strebel S et al. [66] in 2004 did a study on the effect of small dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery.

The study included 80 ASA physical status I to III patients scheduled for elective hip or knee arthroplasties. They were randomly divided and administered isobaric 0.5% bupivacaine 18 mg with saline (Group 1) or clonidine 37.5µg (Group 2) or clonidine 75µg (Group 3) or clonidine 150µg (Group 4). Total volume of the drug was 4.6ml.

Baseline heart rate, ECG, NIBP and peripheral oxygen saturation were noted. All patients had spinal anaesthesia according to a standard protocol. Patients were placed in the supine position for surgery after drug administration. Pain intensity was assessed with VAS score. Duration of analgesia was the time between the intrathecal clonidine administration to the request for supplemental analgesia by PCA. Motor blockade was with Bromage scale. Sedation was scored on a 5 point scale ranging from 0 to 5 (0 = fully awake, alert. 5 = deeply asleep).

The sensory block duration was prolonged with intrathecal clonidine when added in a dose dependent manner. Time to regression of spinal anaesthesia below level L1 was 288±62 min in control group, 311±101 min in group 2, 325±69 min in group 3 and 337±78 min in group 4.

The time for first rescue analgesia was more in all clonidine groups was 295±80 min in control group, 343±75 min in group 2, 381±117 min in group 3 and 445±136 min in group 4.

The range of the upper level of sensory blockade was similar in all groups. A complete motor blockade of the lower extremities was observed in all

patients. After 4, 5, 6 and 7 hr, the Bromage grade was significantly higher in group 4 compared in the group 1.

There were no differences in patients having hypotension between the groups. The maximal decrease in MAP was 21±13% in control group and 25±14%, 26±12% and 25±13%, who received clonidine 37.5µg, 75µg and 150µg respectively.

There was no significant difference in sedation scores among the groups.

The study concluded that intrathecal clonidine at a dose of 150µg to isobaric bupivacaine prolongs sensory blockade of spinal anesthesia. Also the time for rescue analgesia is also more. The study also concluded that 150 µg of clonidine is the preferred dose, in terms of effect versus side effects in patients scheduled for long, lower extremity orthopedic procedures.

Kanazi GE et al. [47] in 2006 did a study where they compared the effects of low dose dexmedetomidine or clonidine with bupivacaine in spinal anaesthesia.

In the study they included 60 patients of ASA physical status I to III posted for transurethral resection of prostrate or bladder tumour under spinal anesthesia. The patients were randomly divided into 3 groups. Each patient received hyperbaric (0.75%) bupivacaine 12 mg with 3µg dexmedetomidine in Group D and 30µg of clonidine in group C.

Patients were premedicated with 5 mg diazepam orally and preloaded with 500 ml of ringer lactate solution. Lumbar puncture was done in sitting position at L3-4 interspace with 25-gauge Whitacre needle. Following which patients were put to lithotomy position. The parameters noted were highest sensory level using pin prick test, motor block grade using Bromage scale, the time to reach T10 level, time to reach the highest sensory level, time for two segment regression, time taken for regression to the S1 level, time to reach Bromage scale 3, time taken for regression to Bromage 0, sedation level using the sedation scale, pain score using the 10 cm VAS and rescue doses of analgesics.

The MAP, HR and SpO2 were noted at every min for the first 10 min after intrathecal injection and taken every 5 min till the discharge of the patient from the PACU.

It was observed that the time to reach T10 sensory block was least in clonidine group followed by dexmedetomidine and then control group. The mean time of sensory regression to S1 was highest in group D (303±75 min), than C (272±38 min) and then Group B (190±48 min). The two segment regression time and time taken to regress to S1 segment were significant between groups B and D and between groups B and C.

The time to reach to Bromage scale 3 was significantly less in group D followed by C and B. The regression of motor block to Bromage 0 was 250±76 min in Group D, Group C was 216±35 min and Group B was 163±47 min. The mean arterial pressure, heart rate and level of sedation were similar in the three groups intraoperatively and postoperatively.

From the study the authors concluded that addition of low dose dexmedetomidine or clonidine intrathecally with bupivacaine produced significantly shorter onset of motor block and a significantly longer sensory and motor block than bupivacaine alone. Dexmedetomidine 3µg and clonidine 30µg had the same effect on block characteristics.

Kaabachi O et al. [67] in 2007 conducted a study on spinal anesthesia with bupivacaine and clonidine 1µg/kg regarding the safety and efficacy.

The study group had 83 children aged between 10 to 16 years, posted for lower limb orthopedic surgeries. Patients were divided into groups. Both received spinal anaesthesia in sitting position. Isobaric bupivacaine 0.5%, at a dose of 0.2 to 0.4 mg/kg of body weight up to 15 mg was given intrathecally to control group. Clonidine group received the same with clonidine 1µg/kg.

Noninvasive blood pressure, heart rate and arterial oxygen saturation were assessed at baseline and every 2 min for the first 10 min after spinal injection, and thereafter, every 5 min during the surgery. Fall in SBP more than 20% from baseline was treated with normal saline 20 ml/kg infusion and IV ephedrine 3 mg boluses. Fall in heart rate more than 20% from baseline was treated with atropine IV 0.6mg bolus.

Sensory and motor blocks were assessed from intrathecal injection till in post anaesthesia care unit. Postoperative pain was assessed using a 100 mm visual analog scale. Rescue analgesia was tramadol 1-2 mg/kg IV if the VAS score was 3 or more. The observations made were that the time taken for two

segment regression was significantly longer in the clonidine group. Also the total duration of analgesia was more with clonidine group which was 461±147 min and in control group was 330±138 min. There was no difference in the motor blockade between the two groups, although the motor block recovery was longer with clonidine group.

There was no difference in the need for rescue analgesics between the two groups. But, the first rescue analgesia was asked faster in the placebo group. Hypotension and bradycardia was seen more with the clonidine group.

Hence the authors concluded the study saying clonidine 1µg/kg as an adjunct in spinal anaesthesia to bupivacaine prolongs the analgesia.

Sethi BS et al. [68] in 2007 did a study on effects of low dose intrathecal clonidine with bupivacaine.

The study had 60 ASA physical status I and II patients who were to lower abdominal surgery. They were randomly divided into two groups of 30 each. Patients in clonidine group were given bupivacaine 12.5 mg 0.5% hyperbaric with clonidine 1µg/kg. Patients in the control group received bupivacaine with identical volume of saline. All patients were followed with the routine procedure of elective surgeries.

Spinal anaesthesia was given in lateral position between L2-L3 level. Sensory block was when there was loss of pin prick sensation. Motor blockade was assessed with Bromage scale. Heart rate, noninvasive blood pressure and ECG were recorded. Nausea, vomiting and shivering if any was noted as adverse effects. Hypotension was treated with fluid boluses and incremental doses of mephenteramine iv. Bradycardia was treated with atropine IV. Post operative pain was assessed with VAS score.

It was seen that the two segment regression mean time was of 218 min in the clonidine group and 136 min in the control group. The mean duration of motor blockade was mean of 205 min in clonidine group and 161 min in control group. Duration of analgesia was 614 min in clonidine group and 223 min in control group. The numbers of rescue ananlgesics used in 24 hr were higher in control group than clonidine group.

The sedation score were higher in clonidine group than control group. The differences in number of patients having dryness of mouth or nausea in the

two groups were not significant. Hypotension and bradycardia was significant in clonidine group.

The authors concluded telling that clonidine as an adjunct to bupivacaine intrathecally significantly increases the duration of analgesia.

Grandhe RP et al. [69] did a study in 2008 on the effect of clonidine with bupivacaine for unilateral spinal anaesthesia in lower limb orthopedic surgery.

The study was on 45 patients ASA physical status I and II posted for unilateral lower limb surgery. Patients were randomly divided to receive 1.5 ml of 0.5% bupivacaine hyperbaric combined with either 1 ml of normal saline (group B) or clonidine 1 g/kg (group BC1) or 1.5 g/kg (group BC2) intrathecally. The total volume was 2.5 ml.

The patients were given 5 mg oral diazepam previous night and the morning of surgery. Preloading was done with 10 ml/kg of normal saline over 15-20 min preoperatively. Lumbar puncture was done with 25 guage Quincke spinal needle at L3-4 interspace in lateral position with the affected limb being dependent. Patient was kept in the same position for 15 min after the administration of drug.

HR, BP, RR and SpO2 were recorded before the block, every 5 min after the block for 30 min, every 15 min thereafter until the end of surgery and then every 30 min until 8 hr after the intrathecal administration.

The level of sensory block (pin prick test), grade of motor block (Bromage scale), level of sedation (sedation scale) and pain score (10 cm VAS) were recorded before block, every 5 min until 30 min after the block and later at hourly intervals until 8 hr after injection.

It was seen that the time for sensory block upto T11 level was 7.6±2.2 min in control group and 7.1±4.2 min and 8.2±3.4 min in clonidine groups (clonidine 1 µg/kg and 1.5 µg/kg respectively). The maximum sensory level was seen at 19±2.1 min in the control group and 18±4.6 min and 21±3.9 min in clonidine groups (clonidine 1 µg/kg and 1.5 µg/kg respectively). The duration of analgesia was 3.8±0.7 hr in control group, 6.3±0.8 hr when using clonidine of 1 µg/kg and 7.3±0.9 hr when using clonidine of 1.5 µg/kg.

Hypotension was seen in 4/15 patients in control group, 10/15 patients in group BC1 and 8/15 patients in group BC2.

Hence it was concluded that clonidine with bupivacaine effectively prolonged the sensory and motor block and postoperative analgesia.

Al Ghanem SM et al. [70] in 2009 conducted a study on the effect of dexmedetomidine and fentanyl with bupivacaine intrathecally in gynaecological procedures.

The study size was 76. ASA physical status I-III posted for vaginal hysterectomy were included in the study. After randomization patients were divided into two groups. Each group received 10 mg of isobaric bupivacaine with 5µg dexmedetomidine in group D and 25 µg of fentanyl in group F.

After routine preparation of patients preoperatively, in the OR patients were given spinal ananesthesia at L3-4 interspace with 25-gauge Quincke needle. The above drug was injected. Following which patients were put to lithotomy position. The parameters seen were level of sensory block assessed by cold alcohol swab, grade of motor block using modified Bromage scale, the time taken to attain T10 level, time to reach peak sensory level, two segment regression, regression to the S1 dermatome, time to reach Bromage 3, regression to Bromage 0, level of sedation using sedation scale and pain score with 10 cm VAS.

In case of hypotension 6 mg of intra venous ephedrine with fluid bolus was given. In case of bradycardia boluses of 0.3-0.5 mg of intravenous atropine was given.

At the end of the study the authors noted that to reach T10 level time taken was 7.5±7.4 min in Group D and 7.4±3.3 min in Group F. The maximum sensory block was reached in 19.34±2.87 min in Group D and 18.39±2.46 min in Group F. The time taken to reach S1 segment in group D was 274.8±73.4 min and in Group F 179.5±47.4 min. The motor block onset had no statistical significance but the regression of the motor block was longer in group D than F.

MAP and HR changes and the sedation score were similar in both the groups. Side effects were significantly more with fentanyl than dexmedetomidine.

At the study it was concluded from the study that, dexmedetomidine was a better alternative as an adjunct to spinal bupivacaine in surgical procedures.

The post operative analgesia seen with this was very long compared to the other adjuncts and also had lesser side effects.

Al-Mustafa MM et al. [71] in 2009 did a study on dexmedetomidine with isobaric bupivacaine intrathecally for urological procedures.

66 patients belonging to ASA physical status I-III posted for TURP, TURBT and placement of tension free vaginal tape for urinary incontinence control were included. The patients were randomised into three groups of 22 each. In group N patients were injected with received isobaric bupivacaine 12.5 mg with normal saline, in Group D5 5 µg dexmedetomidine was the adjunct and Group D10 10 µg dexmedetomidine. Lumbar puncture was performed at L3-4 inter space in sitting position with 25-gauge Quincke needle. All patients received a volume of 3 ml.

The parameters observed were onset of sensory block with cold alcohol swab, time taken to reach level T10, peak level and time taken for it, two segment regression, time taken for regression to S1, sedation score.

The results of the study showed that the sensory blockade onset was in 4.7±2.0 min in group D10, 6.3±2.7 min in group D5 and in group N it was 9.5±3.0 min. Motor blockade in Group D 10 was 10.4±3.4 min, Group D5 was 13.0±3.4 min and Group N was 18.0±3.3 min.

Time to reach S1 sensory level in Group D10 was 338.9±44.8 min, Group D5 was 277.1±23.2 min and Group N was 165.5±32.9 min. The duration of motor blockade was 302.9±36.7 min in Group D10, 246.4±25.7 min in group D5 and 140.1±32.3 min in group N.

There was no significant difference in MAP and HR between 3 groups intraoperatively and postoperatively. Ramsay sedation scores were 2 in all patients in the 3 groups.

The conclusion was that with dexmedetomidine the onset of sensory and motor blockade was faster and it prolonged the sensory and motor block when used with bupivacaine in spinal anaesthesia in a dose dependent manner.

Saxena H et al. [72] in 2010 did a study on the effect of low dose intrathecal clonidine with bupivacaine with regards to onset and duration of block.

The study group had 80 patients of ASA of physical status I and II, posted for elective lower abdominal surgeries. The patients were divided into 4 groups. Group1 received bupivacaine hyperbaric 0.5% 13.5 mg and 0.3 ml saline. Group 2 received 15 µg, group 3 received 30 µg and group 4 received 37.5 µg clonidine added to bupivacaine. In all the groups total volume of drug was 3 ml.

Parameters observed were onset of sensory block assessed by pinprick test, time taken to reach T10 level, peak level and time taken to reach that, two segment regression, motor block onset and duration assessed by Bromage scale, total duration of analgesia.

Hypotension described as 30% reduction in mean arterial BP from baseline value and was treated with 300 ml of additional fluids and IV ephedrine.

The time taken for onset of sensory block was low in all clonidine groups in a dose dependant manner. The time taken for sensory block upto level T10 6.57±0.49 min in control group and 2.58±0.33 min, 2.54±0.34 min and 2.09±0.89 min in 15 µg, 30 µg and 37.5 µg clonidine group respectively. The mean time for maximum sensory level was 7.3±1.25 min in control group and 6.8±1.20 min, 7.4±1.31 min and 6.7±1.12 min in clonidine group 15µg, 30µg and 37.5µg respectively. The onset of motor block was fastest in group 4.

The duration of sensory block was assessed with time for two segment regression, mean VAS scores at 3.5 hr and analgesia time. All three criteria were best in group 4. The duration of analgesia was 99.75±21.91 min in control group, 164.5±23.9 min, 264.75±44.3 min and 285.60±36.59 min in clonidine group (15µg, 30µg and 37.5µg respectively).

The haemodynamic parameters were similar in all the groups. Eighteen patients (90%) had grade 2 sedation in group 4 as compared to only 8 in group 3.

Authors concluded that addition of clonidine to bupivacaine, even in very small doses, significantly improves the onset and duration of sensory and motor block with relative haemodynamic stability. The 30 µg provides maximum benefit and minimum side effects.

Gupta R et al. [73] in 2011conducted a study on dexmedetomidine with ropivacaine intrathecally. Sixty patients were randomized into 2 groups.

Group R were injected with 3 ml of 0.75% isobaric ropivacaine and 0.5 ml normal saline, Group D patients with ml of 0.75% isobaric ropivacaine and 0.5 ml dexmedetomidine (5µg). All patients were given diazepam 0.2 mg/kg orally previous night. Patients were preloaded with ringer lactate solution at 15 ml/kg. With patient in sitting position, lumbar puncture was performed at L3-4 interspace with 23 or 25-gauge Quicke needle.

Parameters observed were sensory onset with pin prick test, peak level, two segment regression, regression to S2 and total duration of ananlgesia using Vas score. Hypotension was treated with 6 mg of intravenous ephedrine in increments. Bradycardia was treated with 0.6 mg of intravenous atropine.

The results showed that the onset of sensory blockade was faster in group D and two segment regression time was significantly prolonged in group D. Time for rescue analgesia in Group D was 478.4±20.9 min compared with Group R which was 241.7±21.7 min.

Intraoperative hypotension and bradycardia was more in group D patients.

Authors concluded that 5µg dexmedetomidine prolonged the effect of ropivacaine when given intrathecally.

Eid HEA et al. [74] in 2011 conducted a study on dose related effect of intrathecal dexmedetomidine with bupivacaine. It was a prospective randomized double blind study.

48 patients of ASA physical status I and II posted for anterior cruciate ligament reconstruction were included in the study. These patients were randomized into three groups. Group D1 was given 10 µg dexmedetomidine, group D2 15 µg dexmedetomidine and group B normal saline with 3 ml of 0.5% hyperbaric bupivacaine to all patients. In all the groups total volume of drug was 3.5 ml.

Parameters observed were sensory onset with pin prick test, peak level, two segment regression, regression to S2 and total duration of ananlgesia using Vas score, motor block onset and duration with Bromage scale, sedation with Ramsay sedation scale scores and adverse events if any.

Hypotension was treated with 6 mg of intravenous ephedrine in increments. Bradycardia was treated with 0.3-0.5 mg of intravenous atropine.

The results of the study showed that the time of sensory block to reach T10 was similar in all the groups. Two segments regression was faster with plain bupivacaine group and prolonged with dexmedetomidine group in a dose dependent manner. There was a dose dependent prolongation of the duration of sensory block and motor block by the addition of intrathecal dexmedetomidine. Two segment regression time, total duration of motor block were significantly prolonged in Group D2 than in Group D1 and Group B and in Group D1 than in Group B. rescue analgesic was highest required in group B. Pain scores at 24 hr were significantly low in Group D2 than in Group D1 and Group B and in Group D1 than in Group B. The mean values of MAP and HR were comparable between the three groups throughout the study.

The authors concluded that intrathecal dexmedetomidine significantly prolonged the anesthetic and analgesic effects of spinal hyperbaric bupivacaine in a dose dependent manner.

Gupta R et al. [75] in 2011 did a study to compare the effects of intrathecal dexmedetomidine and fentanyl with bupivacaine.

Sixty patients posted for lower abdominal surgeries were included in the study. Patients were randomly divided to receive 12.5 mg hyperbaric bupivacaine with either 5µg dexmedetomidine in group D or 25µg fentanyl in group F intrathecally.

Parameters observed were sensory onset with pin prick test, peak level, two segment regression, regression to S2 and total duration of ananlgesia using Vas score, motor block onset and duration with Bromage scale, sedation with Ramsay sedation scale scores and adverse events if any.

Hypotension was treated with incremental intravenous doses of 5 mg ephedrine and intravenous fluids as required. Bradycardia was treated with 0.3-0.6 mg of intravenous atropine.

The study showed that there was no difference maximum level of block achieved in the two groups and in the time to reach peak level. Block regression was significantly slow with the addition of intrathecal dexmedetomidine. Both two segment regression and regression to S2 were significantly more with dexmedetomidine. Regression of motor block was significantly slow dexmedetomidine group. Rescue analgesia needed was

less in group D than group F. The sedation score was more in group D patients. Intraoperative hypotension was more in group D.

Authors concluded that dexmedetomidine was a better adjunct than fentanyl to spinal bupivacaine. It provides longer duration of analgesia.

Shukla D et al. [76] in 2011 did a study to compare the effects intrathecal dexmedetomidine and magnesium sulfate used as adjuncts to bupivacaine.

Study included 90 patients posted for lower abdominal and lower limb surgeries. After randomization, patients received 15 mg hyperbaric bupivacaine 3cc with either 10 µg (0.1 ml) dexmedetomidine (group D) or 50 mg (0.1 ml) magnesium sulfate (group M) or 0.1 ml saline (group C).

Patients were preloaded with ringer lactate solution 500 ml, with patient in sitting position, lumbar puncture was performed at L3-4 interspace with 25-gauge Quincke needle.

Parameters observed were sensory onset with pin prick test, peak level, two segment regression, regression to S2 and total duration of ananlgesia using Vas score, motor block onset and duration with Bromage scale, sedation with Ramsay sedation scale scores and adverse events if any.

Hypotension was treated with incremental intravenous doses of 5 mg ephedrine and IV fluids as required. Bradycardia was treated with 0.3-0.6 mg of IV atropine.

The study showed that the duration of onset of sensory and motor blockade was faster in group D and was statistically significant. The regression time of both sensory and motor block was prolonged in group D and in group M in comparison with the control group C and was statistically significant. There was no significant difference in the mean values of mean arterial pressure and heart rate intraoperatively and postoperatively.

Authors concluded that dexmedetomidine intrathecally as an adjunct produces a faster block and prolonged duration of sensory and motor block compared to magnesium sulphate.

Nayagam HA et al. [82] did a study in 2014 to quality of anaesthesia with low dose bupivacaine and fentanyl or with low dose bupivacaine and dexmedetomidine.

This prospective randomised double-blinded study was carried out in a tertiary health care centre on 150 patients by randomly allocating them into two groups using a computer generated randomisation table. Group F (n = 75) received bupivacaine 0.5% heavy (0.8 ml)+fentanyl 25 μg (0.5 ml) + normal saline 0.3 ml and Group D (n = 75) received bupivacaine 0.5% heavy (0.8 ml) + dexmedetomidine 5 μg (0.05 ml) + normal saline 0.75 ml, aiming for a final concentration of 0.25% of bupivacaine (1.6 ml), administered intrathecally.

Time to reach sensory blockade to T10 segment, peak sensory block level (PSBL), time to reach peak block, time to two segment regression (TTSR), the degree of motor block, side-effects, and the perioperative analgesic requirements were assessed.

There were no significant differences between the groups in the time to reach T10 segment block and time to two segment regression. Time to reach peak sensory block level and modified Bromage scales were significant. Peak sensory block level and time to first analgesic request were highly significant. All patients were haemodynamically stable and no significant difference in adverse effects was observed.

Both groups provided adequate anaesthesia for all lower abdominal surgeries with haemodynamic stability. It was concluded that dexmedetomidine is superior to fentanyl since it facilitates the spread of the block and offers longer post-operative analgesic duration.

Nethra SS et al. [83] did a study in 2015 using intrathecal dexmedetomidine as adjunct for spinal anaesthesia for perianal ambulatory surgeries.

The study investigated effects of addition of 5 μg of dexmedetomidine to 6 mg of hyperbaric bupivacaine on duration of analgesia, sensory and motor block characteristics for perianal ambulatory surgeries.

This study was a prospective randomised controlled double blind study. Forty adult patients between 18 and 55 years of age were divided into 2 groups. Group D received intrathecal 0.5% hyperbaric bupivacaine 6 mg (1.2 ml) with injection dexmedetomidine 5 μg in 0.5 ml of normal saline and Group N received intrathecal 0.5% hyperbaric bupivacaine 6 mg (1.2 ml) with 0.5 ml of normal saline. The parameters assessed were time to regression of sensory blockade, motor blockade, ambulation, time to void,

first administration of analgesic. Statistical analysis was done using appropriate tests.

It was observed that the time for regression of sensory level and time for first administration of analgesic were prolonged in Group D (430.05 ± 89.13 min, 459.8 ± 100.9 min, respectively) in comparison to Group N (301.10 ± 94.86 min, 321.85 ± 95.08 min, respectively). However, the duration of motor blockade, time to ambulation, and time to void were also significantly prolonged in Group D (323.05 ± 54.58 min, 329.55 ± 54.06 min, 422.30 ± 87.59 min) than in Group N (220.10 ± 63.61 min, 221.60 ± 63.84 min, 328.45 ± 113.38 min).

It was concluded that intrathecal dexmedetomidine 5 μg added to intrathecal bupivacaine 6 mg as adjunct may not be suitable for ambulatory perianal surgeries due to prolongation of motor blockade.

Kurhekar P et al. [84] did a study in 2014 on intrathecal morphine and intrathecal dexmedetomidine in patients undergoing gynaecological surgeries under spinal anaesthesia.

The study was designed to evaluate analgesic efficacy, haemodynamic stability and adverse effects of both these adjuncts in patients undergoing gynaecological surgeries.

This was a prospective, randomised, double blind study involving 25 patients in each group. Group M received 15 mg of 0.5% hyperbaric bupivacaine with 250 μg of morphine while Group D received 15 mg of 0.5% hyperbaric bupivacaine with 2.5 μg of dexmedetomidine.

Characteristics of spinal block, time for first rescue analgesic and total dose of rescue analgesics were noted. Vital parameters and adverse effects were noted perioperatively. Data analysis was done with independent two sample t-test and Mann–Whitney U test.

Time for first rescue analgesic and total analgesic demand were similar in both groups. Duration of sensory and motor block was significantly higher in dexmedetomidine group. Itching was noticed in 36% and nausea in 52% of patients in the morphine group, either of which was not seen in dexmedetomidine group.

It was concluded that intrathecal dexmedetomidine produced prolonged motor and sensory blockade without undesirable side effects but intraoperative hypotension was more frequent in dexmedetomidine group.

MATERIALS & METHODS

METHODOLOGY

Our study was titled a comparative study of dexmedetomidine and clonidine as an adjunct to intrathecal bupivacaine in lower abdominal surgeries. Study group included patients posted for elective lower abdominal surgeries in R L Jalappa Hospital attached to Sri Devaraj Urs Medical College, Kolar. Period of study was January 2016 to January 2017. The study was started after taking ethical committee clearance as well as informed consent from all patients.

150 patients of ASA physical status I and II between age group of 18 to 60 years of either sex scheduled for elective lower abdominal surgeries were included in the study. The patients were divided into 3 groups after randomization which was done using simple sealed envelope technique.

Preoperative assessment was done for each patient and written informed consent was taken. All the routine investigations required for pre operative evaluation and the proposed surgery was done. All the patients were pre-medicated with Tab. alprazolam 0.5 mg and Tab. ranitidine 150mg overnight and the morning of surgery and were kept nil per oral for a period of at least 8 hr.

On arrival in the operating room, intravenous line was secured with 18G Intravenous cannula preloaded with lactated ringer's solution at 15ml/kg. Patients received one of the following for the subarachnoid block:

1. Group B (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml normal saline.

2. Group C (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. clonidine (30 μg).

3. Group D (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. dexmedetomidine (3 μg).

Monitoring was done using multiparameter monitor having pulse oximetry, ECG and NIBP.

Patient was placed in lateral position. Under all aseptic precautions lumbar puncture was done between L3-L4 space with 25 guage quincke’s spinal needle and the total volume of 4ml of drugs was deposited intrathecally.

The doses were chosen according to a 1:10 ratio found to be equipotent and would produce similar effects on the characteristics of bupivacaine spinal anaesthesia. [47, 70, 74, 77]

INCLUSION CRITERIA

Patients belonging to ASA physical status 1 and 2 between age group 18 and 60 posted for lower abdominal surgeries.

EXCLUSION CRITERIA

1) Contraindications to neuraxial blockade
2) Pregnancy
3) Patients having history of allergic reactions to local anaesthetics, dexmedetomidine or clonidine.
4) Patients of ASA physical status III, IV

The following parameters are noted,

1) Onset of sensory blockade and motor blockade.
2) Maximum level of sensory blockade attained and the time taken for the same.
3) Maximum level of motor blockade attained and the time taken for the same.
4) Two segments sensory regression time.
5) Total for recue analgesia.
6) Total duration of sensory blockade and motor blockade.

DEFINITIONS

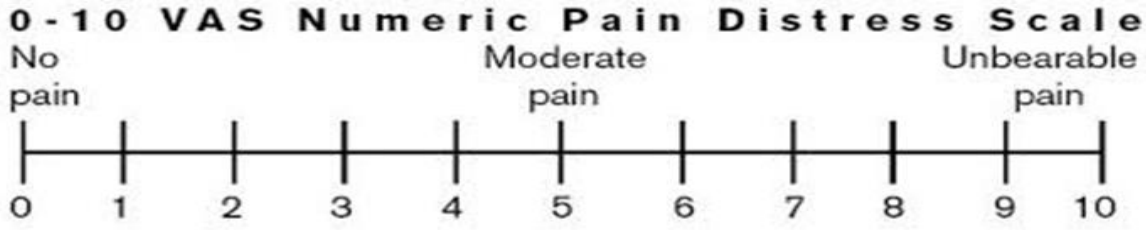
1. Time of onset of sensory blockade: is the time in minutes to achieve loss of pinprick sensation to 23 G hypodermic needle.

2. Time to achieve maximum dermatome level of sensory blockade: is the time in minutes for loss of pinprick sensation to 23 G hypodermic needle tested every 2 min until the highest level is stabilized for four consecutive tests.

3. Time of onset of motor blockade: is the time in minutes taken from the time of injection till patient is not able to flex the ankle i.e. modified Bromage 3 muscle power.

4. Time to two segment regression from highest sensory level: is the time in minutes taken for for sensory block to regress to two lower sensory dermatomal levels as assessed by loss of pin prick sensation.

5. Time for rescue analgesia/duration of sensory blockade: is the time in minutes from the time of injection to the time when the patient complains of pain at surgical site. Pain is assessed by Visual Analogue Scale.



0 No pain

1-3 Mild pain

4-6 Moderate pain

7-10 Severe pain

Patients with score more than 4 will be treated with Inj. tramadol 50mg and Inj. ondensetron 4mg IV.

6. Duration of motor blockade: is the time in minutes from the time of injection till the patient attains complete motor recovery of lower limb i.e. modified Bromage 0 muscle power.

MODIFIED BROMAGE SCALE

0- Able to perform a full straight leg raise over the bed for 5sec.

1- Unable to perform a leg raise but can flex the leg on knee.

2- Unable to flex knee but can flex ankle.

3- Unable to flex ankle but can move toes.

4- Unable to move toes.

7. Sedation: measured by Ramsay Sedation Scale and the patient is considered sedated if the score is ≥ 4

RAMSAY SEDATION SCALE

1. Patient anxious, agitated or restless
2. Patient cooperative, oriented, and tranquil alert
3. Patient responds to commands
4. Asleep, but with brisk response to light glabellar tap or loud auditory stimulus
5. Asleep, sluggish response to light glabellar tap or loud auditory stimulus
6. Asleep, no response to light glabellar tap or loud auditory stimulus
7. Haemodynamic monitoring (heart rate, mean arterial pressure and oxygen saturation) was done at 0, 2, 5, 10 and every five min after that till 30 min and every ten min till end of surgery.
8. Hypotension: defined as a decrease in systolic blood pressure by more than 30% from baseline or less than 80 mm Hg will be treated with incremental intravenous doses of Inj. mephentermine 6 mg and further intravenous fluid as required.
9. Bradycardia: defined as heart rate less than 50 beats per min will be treated with Inj. atropine 0.6mg.
10. Oxygen will be administrated through a mask if the pulse oximetry reading is decreased below 90%.
11. Adverse effects: patients will be monitored for any cardiovascular side effects like changes in blood pressure, heart rate and rhythm, central nervous system depression, respiratory depression, nausea, vomiting, shiverring and any hypersensitivity reactions for drugs.

STATISTICAL ANALYSIS

Data will be entered into the Microsoft excel data sheet and will be analyzed using SPSS 22 version software, categorical data will be represented in the form of frequencies and proportions. Chi-square will be the test of significance. Continuous data will be represented as mean and standard deviation. Independent t test will be the test of significance to identify the mean difference between two groups. ANOVA test will be done to find the mean difference between three groups. p value <0.05 was considered as statistically significant.

Sample Size: Was estimated by using the Mean time to reach T10 Sensory block from the study by G.E.Kanazi et.al. using this values at 95% Confidence limit and 80% power sample size of 46 was obtained in each group. With 10% nonresponse sample size of 46 + 4.6 ≈ 50 cases will be included in each group.

Single calculation: sample size estimation

Probability of Type I Error (α)	0.05
Power (1-β)	0.8
Number of Groups in the Analysis	3
Largest Difference between any Two Means	2.1
Expected Background Standard Deviation	3.7

Example: Calculate Sample Size from Data

Sample Size for Analysis of Variance

Probability of Type I Error (α) = 0.05

Power (1-β) = 0.8

Number of groups (between group df+1) = 3

Largest Difference to be detected = 2.1

Within group Standard Deviation = 3.7

Calculated parameters

beta (β) = 0.2

between group df (u) = 2

effect size (Diff/SD) = 0.5676

effect size (Cohen f) = 0.2676

Sample size required (per group) = 46 taken to be 50

STATISTICAL METHODS APPLIED

Frequencies

The Frequencies procedure provides statistics and graphical displays that are useful for describing many types of variables. The Frequencies procedure is a good place to start looking at your data.

Descriptives

The Descriptives procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which you select the variables (the default).

Independent-Samples T Test

The Independent-Samples T Test procedure compares means for two groups of cases. Ideally, for this test, the subjects should be randomly assigned to two groups, so that any difference in response is due to the treatment (or lack of treatment) and not to other factors.

One-Way ANOVA

The One-Way ANOVA procedure produces a one-way analysis of variance for a quantitative dependent variable by a single factor (independent) variable. Analysis of variance is used to test the hypothesis that several means are equal. This technique is an extension of the two-sample t test.

Repeated Measures ANOVA

GLM Repeated Measures analyzes groups of related dependent variables that represent different measurements of the same attribute. This dialog box lets you define one or more within-subjects factors for use in GLM Repeated Measures. Note that the order in which you specify within subjects factors is important. Each factor constitutes a level within the previous factor.

All the statistical calculations were done through SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) to analyze data.

RESULTS

RESULTS

Our study was titled a comparative study of dexmedetomidine and clonidine as an adjunct to intrathecal bupivacaine in lower abdominal surgeries. Study group included patients posted for elective lower abdominal surgeries in R L Jalappa Hospital attached to Sri Devaraj Urs Medical College, Kolar. Period of study was January 2016 to January 2017. The study was started after taking ethical committee clearance as well as informed consent from all patients.

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On arrival in the operating room, intravenous line was secured with 18G Intravenous cannula preloaded with lactated ringer's solution at 15ml/kg. Patients received one of the following for the subarachnoid block:

1. Group B (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml normal saline.

2. Group C (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. clonidine (30 μg).

3. Group D (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. dexmedetomidine (3 μg).

Monitoring was done using multiparameter monitor having pulse oximetry, ECG and NIBP. Patient was placed in lateral position. Under all aseptic precautions lumbar puncture was done between L3-L4 space with 25 G quincke’s spinal needle and the total volume of 4ml of drugs was deposited intrathecally.

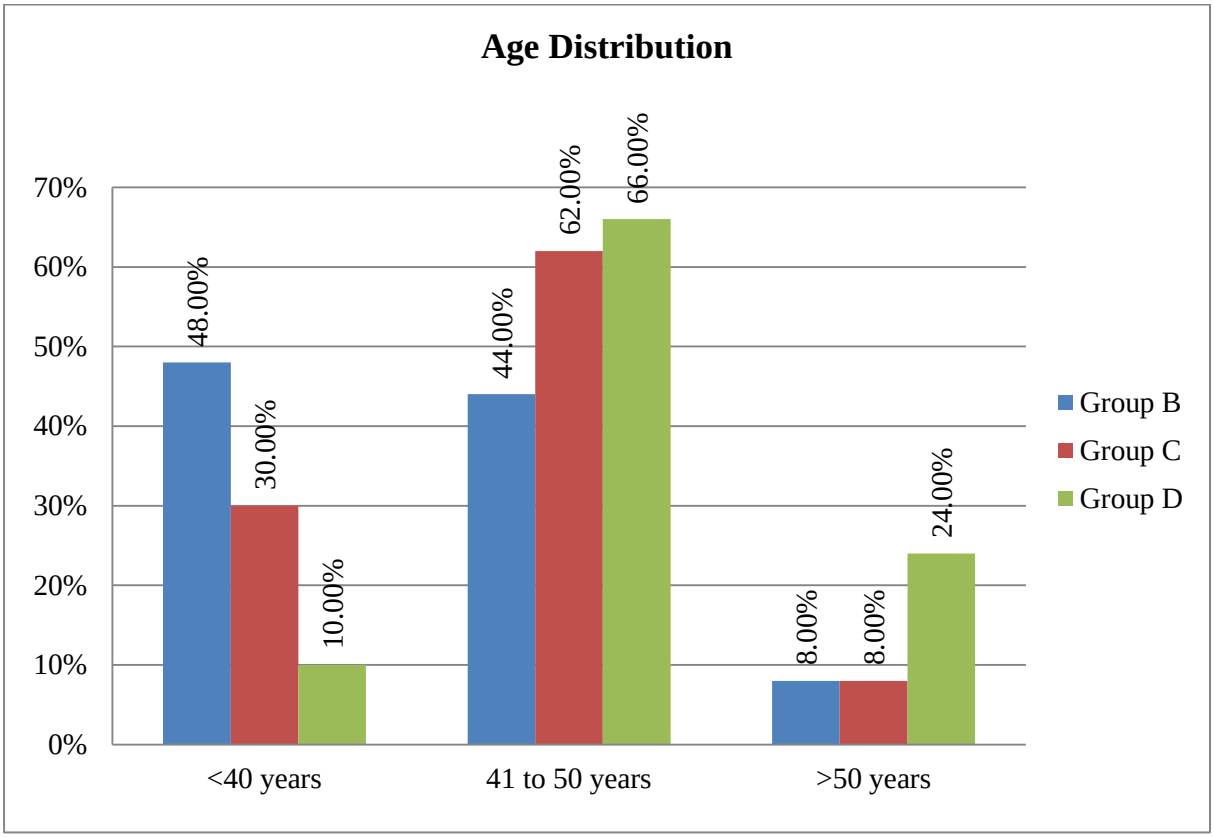
Table 2: Age distribution of subjects in three groups

		Group					
		Group B		Group C		Group D	
		Count	%	Count	%	Count	%
Age	<40 years	24	48.0%	15	30.0%	5	10.0%
	41 to 50 years	22	44.0%	31	62.0%	33	66.0%
	>50 years	4	8.0%	4	8.0%	12	24.0%
	Mean ± SD	42 ± 6.1		43.3 ± 5.1		46.3 ± 4.9	

χ 2 = 21.11, df = 4, p <0.001*

F= 8.171, p <0.001* B vs C = 0.715, B vs D <0.001*, C vs D = 0.02*

In Group B majority of subjects were in the age group <40 years (48%), in Group C and Group D majority of subjects were in the age group 41 to 50 years, 62% and 66% respectively.



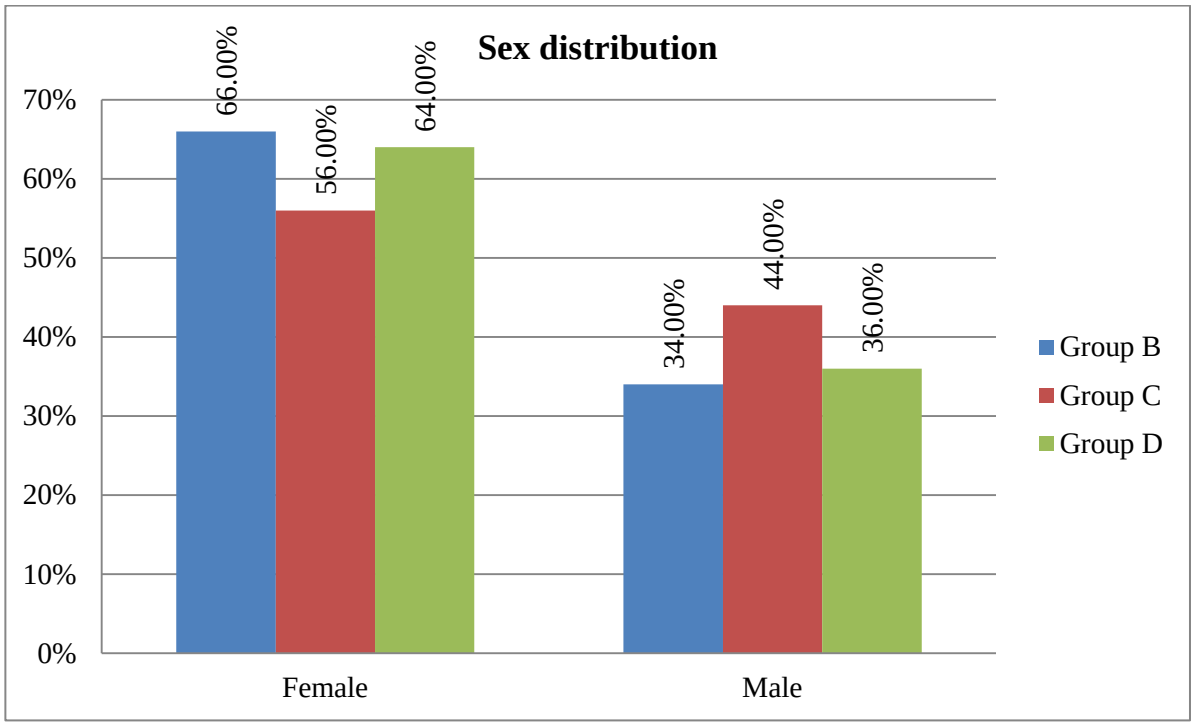
Graph 1: Bar diagram showing Age distribution of subjects in three groups

Table 3: Sex distribution of subjects in three groups

		Group					
		Group B		Group C		Group D	
		Count	%	Count	%	Count	%
Sex	Female	33	66.0%	28	56.0%	32	64.0%
	Male	17	34.0%	22	44.0%	18	36.0%
	Total	50	100.0%	50	100.0%	50	100.0%

$\chi 2 = 1.188$, df = 2, p = 0.552

In all the three groups majority of subjects were females, 66% in Group B, 56% in Group C and 64% in Group D respectively. There was no significant difference in gender distribution between three groups.

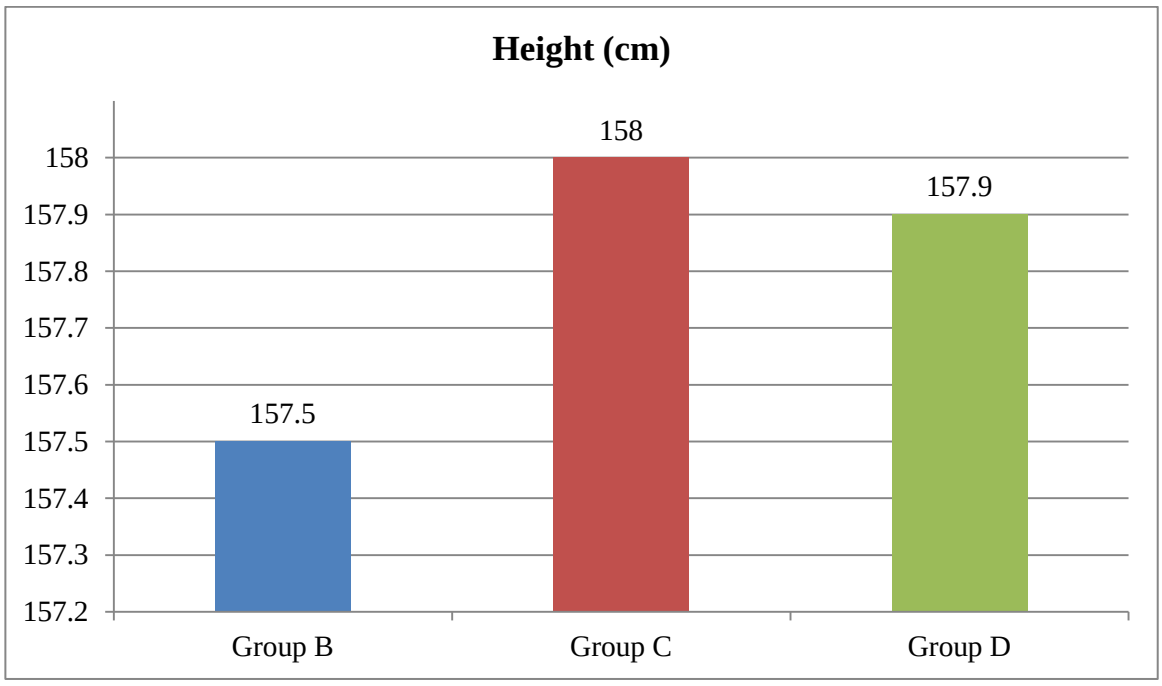


Graph 2: Bar diagram showing Sex distribution of subjects in three groups

Table 4: Height distribution of subjects in three groups

		Group			P value b/w three groups
		Group B	Group C	Group D	
Height (cm)	Mean	157.5	158.0	157.9	0.825
	SD	4.7	4.7	3.8	
	Minimum	150	150	150	
	Maximum	167	167	164	

Mean Height of subjects in Group B was 157.5 ± 4.7 cm, in Group C was 158 ± 4.7 cm and in Group D was 157.9 ± 3.8 cm. There was no significant difference in mean Height between three groups.

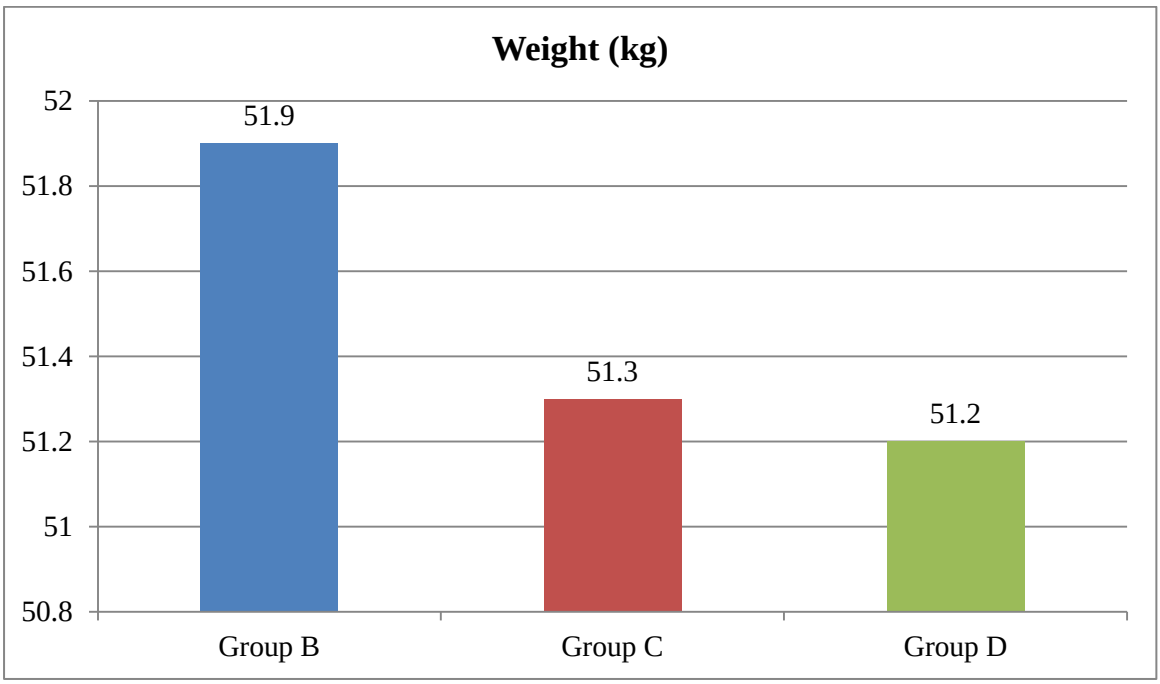


Graph 3: Bar diagram showing Height distribution of subjects in three groups

Table 5: Weight distribution of subjects in three groups

		Group			P value b/w three groups
		Group B	Group C	Group D	
Weight (kg)	Mean	51.9	51.3	51.2	0.308
	SD	2.8	2.2	2.3	
	Minimum	48	48	46	
	Maximum	60	56	55	

Mean Weight of subjects in Group B was 51.9 ± 2.8 kg, in Group C was 51.3 ± 2.2 kg and in Group D was 51.2 ± 2.3 kg. There was no significant difference in mean Weight between three groups.



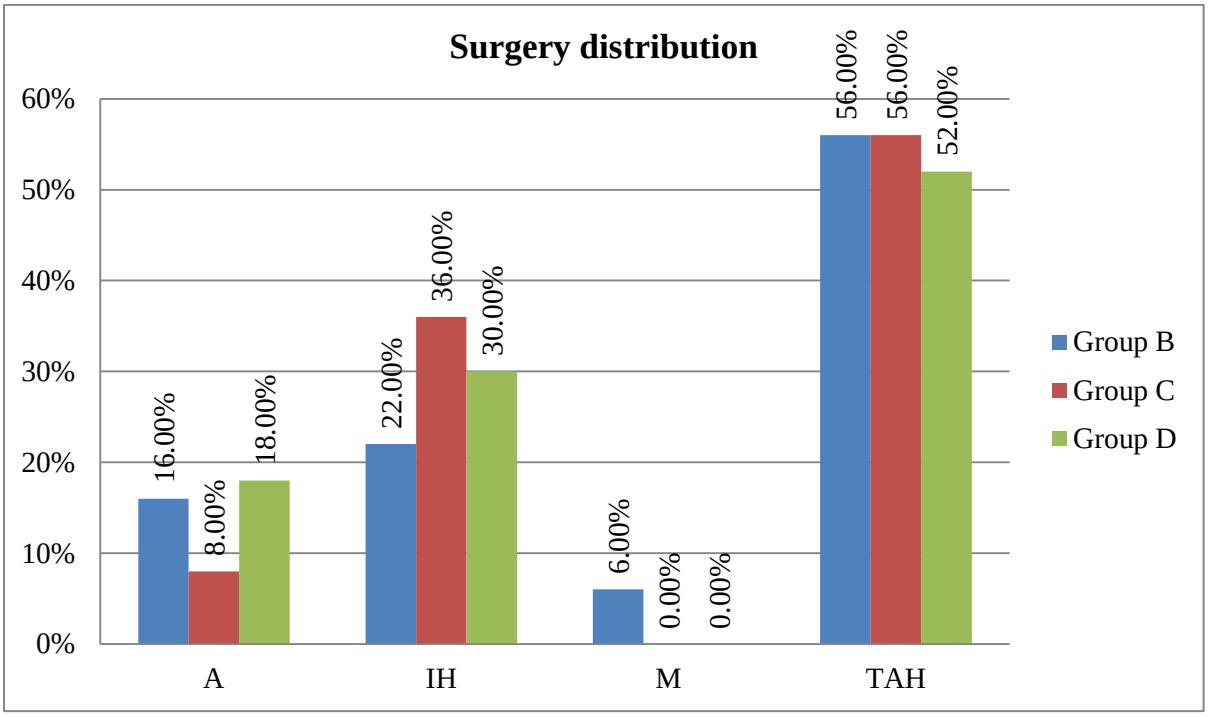
Graph 4: Bar diagram showing Weight distribution of subjects in three groups

Table 6: Surgery distribution of subjects in three groups

		Group					
		Group B		Group C		Group D	
		Count	%	Count	%	Count	%
Surgery	A	8	16.0%	4	8.0%	9	18.0%
	IH	11	22.0%	18	36.0%	15	30.0%
	M	3	6.0%	0	0.0%	0	0.0%
	TAH	28	56.0%	28	56.0%	26	52.0%

$\chi 2 = 9.779$, df = 6, p = 0.134

In all the three group most common surgery done was TAH, 56% in Group B and Group C respectively and 52% in Group D. There was no significant difference in Surgery between three groups.

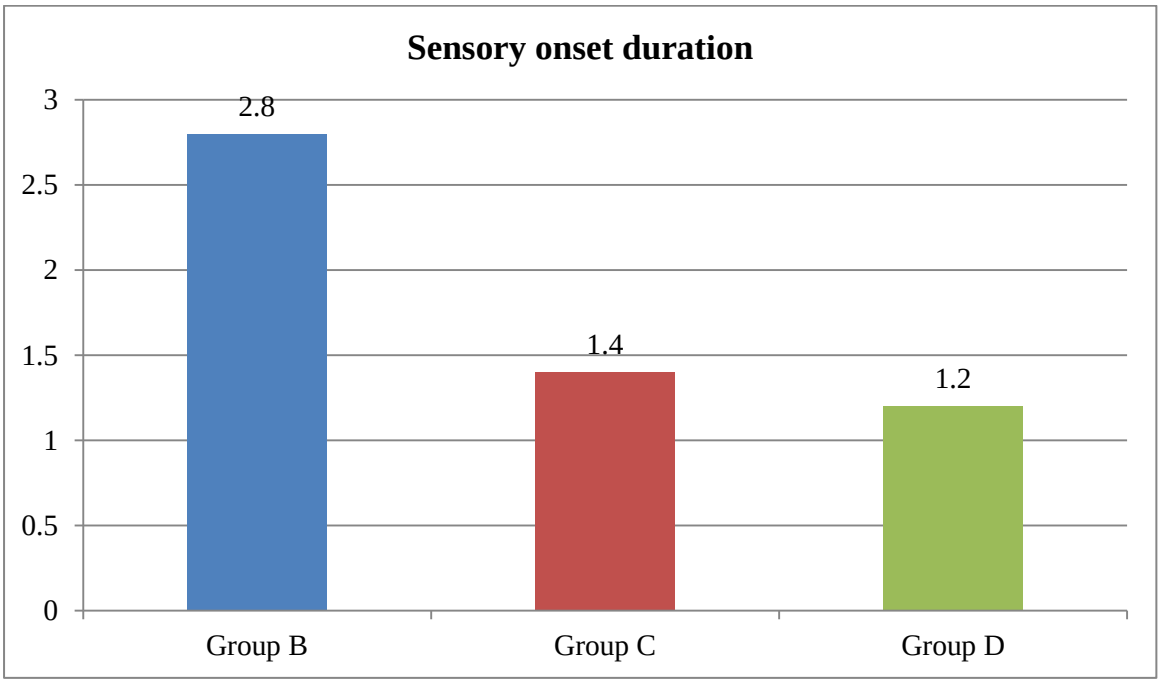


Graph 5: Bar diagram showing Surgery distribution of subjects in three groups

Table 7: Sensory onset duration comparison between three groups

		Group			P value b/w three groups	B vs C	B vs D	C vs D
		Group B	Group C	Group D				
Sensory onset duration (min)	Mean	2.8	1.4	1.2	<0.001*	<0.001*	<0.001*	0.045*
	SD	.7	.5	.4				
	Minimum	2	1	1				
	Maximum	4	2	2				

Mean Sensory onset in Group B was 2.8 ± 0.7 min, in Group C was 1.4 ± 0.5 min and in Group D was 1.2 ± 0.4 min. This difference in mean duration of sensory onset b/w three groups was statistically significant. Sensory onset was faster in Group D and slowest in Group B.



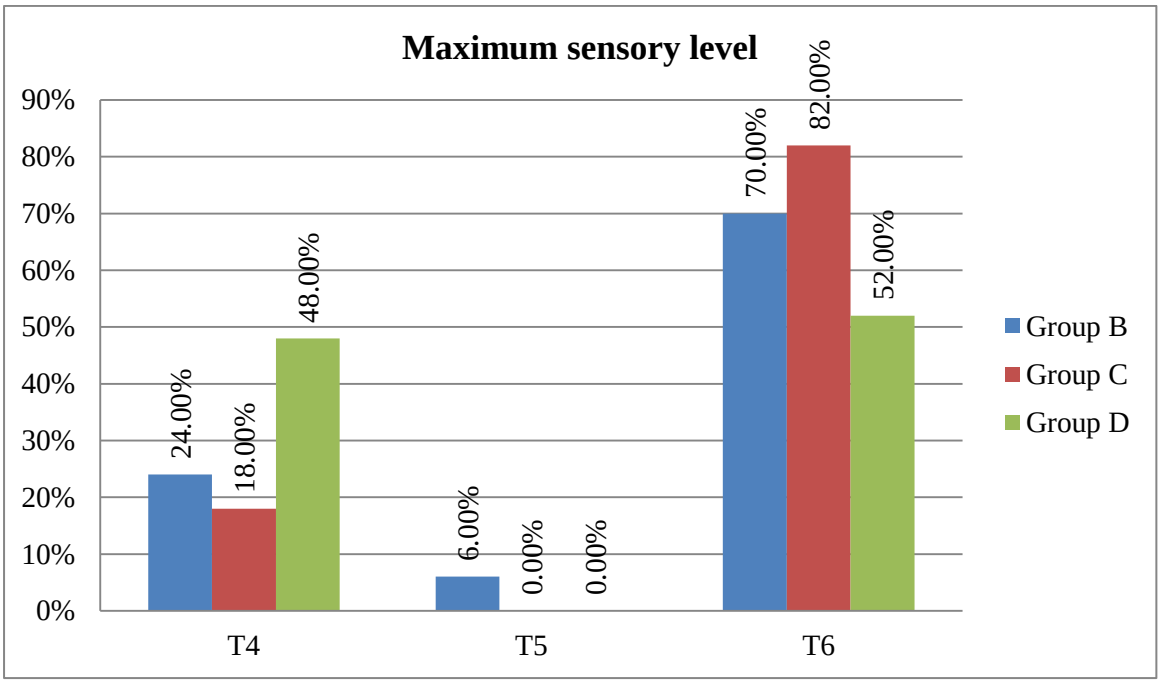
Graph 6: Bar diagram showing Sensory onset duration comparison between three groups

Table 8: Maximum sensory level comparison between three groups

		Group					
		Group B		Group C		Group D	
		Count	%	Count	%	Count	%
Maximum sensory level	T4	12	24.0%	9	18.0%	24	48.0%
	T5	3	6.0%	0	0.0%	0	0.0%
	T6	35	70.0%	41	82.0%	26	52.0%

χ 2 = 17.75, df = 4, p = 0.001*

Maximum sensory level reached in Group B was T6 in 70%, in Group C was T6 in 82% and in Group D was T6 in 52%. Hence highest percentage of T6 sensory level was seen in Group C and lowest percentage in Group D. This difference in maximum sensory level was statistically significant.

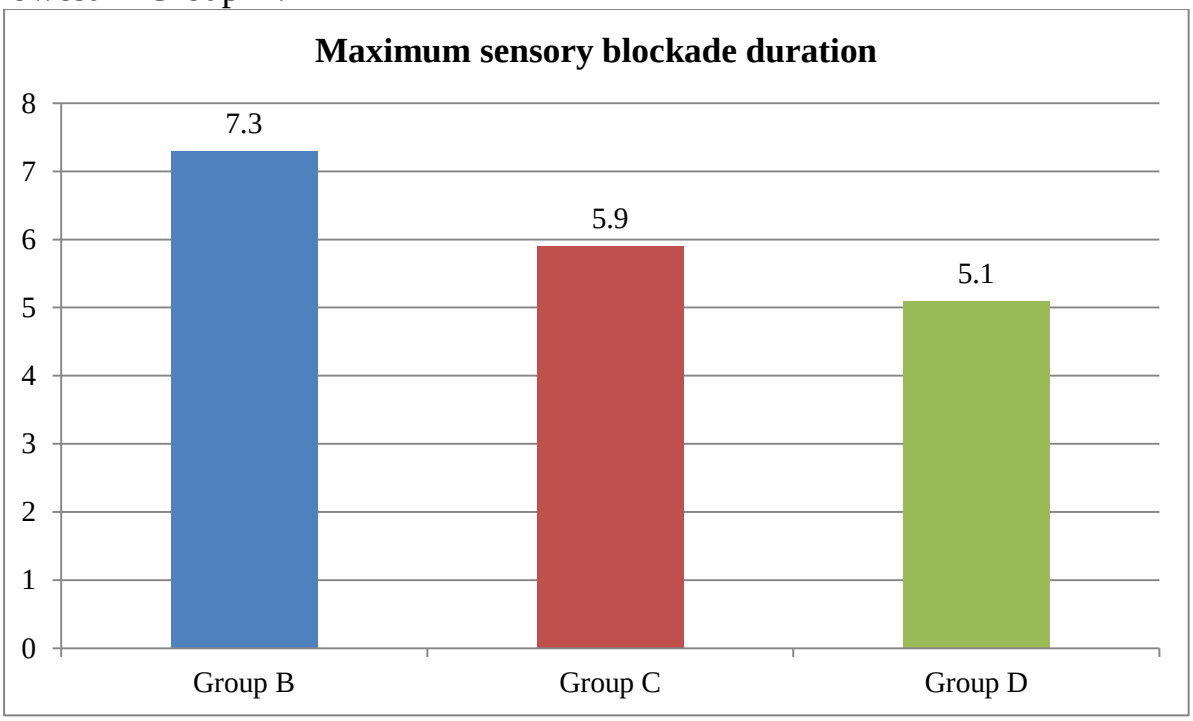


Graph 7: Bar diagram showing Maximum sensory level comparison between three groups

Table 9: Maximum sensory blockade duration comparison between three groups

		Group			P value b/w three groups	B vs C	B vs D	C vs D
		Group B	Group C	Group D				
Maximum sensory blockade duration (min)	Mean	7.3	5.9	5.1	<0.001*	<0.001*	<0.001*	<0.001*
	SD	1.1	.8	.7				
	Minimum	6	5	4				
	Maximum	9	7	7				

Mean duration of Sensory blockade in Group B was 7.3 ± 1.1 min, in Group C was 5.9 ± 0.8 min and in Group D was 5.1 ± 0.7 m min in. This difference in mean duration of sensory blockade b/w three groups was statistically significant. Highest duration of sensory blockade was seen in Group B and lowest in Group D.

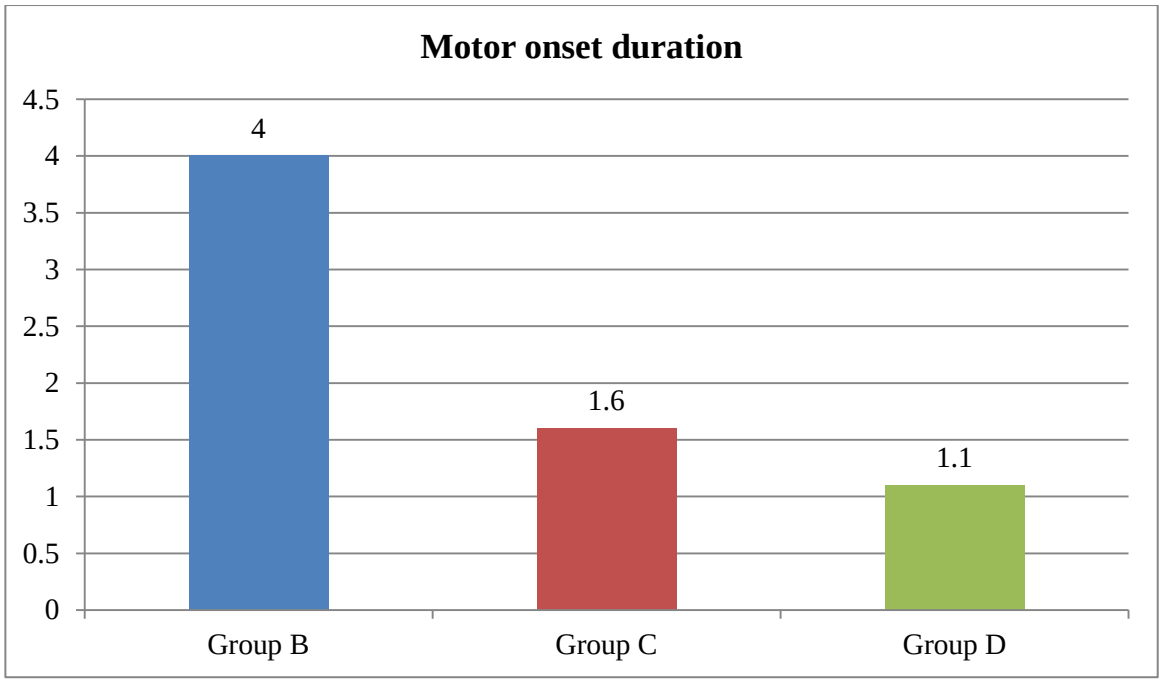


Graph 8: Bar diagram showing Maximum sensory blockade duration comparison between three groups

Table 10: Motor onset duration comparison between three groups

		Group			P value b/w three groups	B vs C	B vs D	C vs D
		Group B	Group C	Group D				
Motor onset duration (min)	Mean	4.0	1.6	1.1	<0.001*	<0.001*	<0.001*	<0.001*
	SD	0.7	0.5	0.4				
	Minimum	3	1	1				
	Maximum	5	2	2				

Mean Motor onset in Group B was 4 ± 0.7 min, in Group C was 1.6 ± 0.5 min and in Group D was 1.1 ± 0.4 min. This difference in mean duration of motor onset b/w three groups was statistically significant. Motor onset was faster in Group D and slowest in Group B.

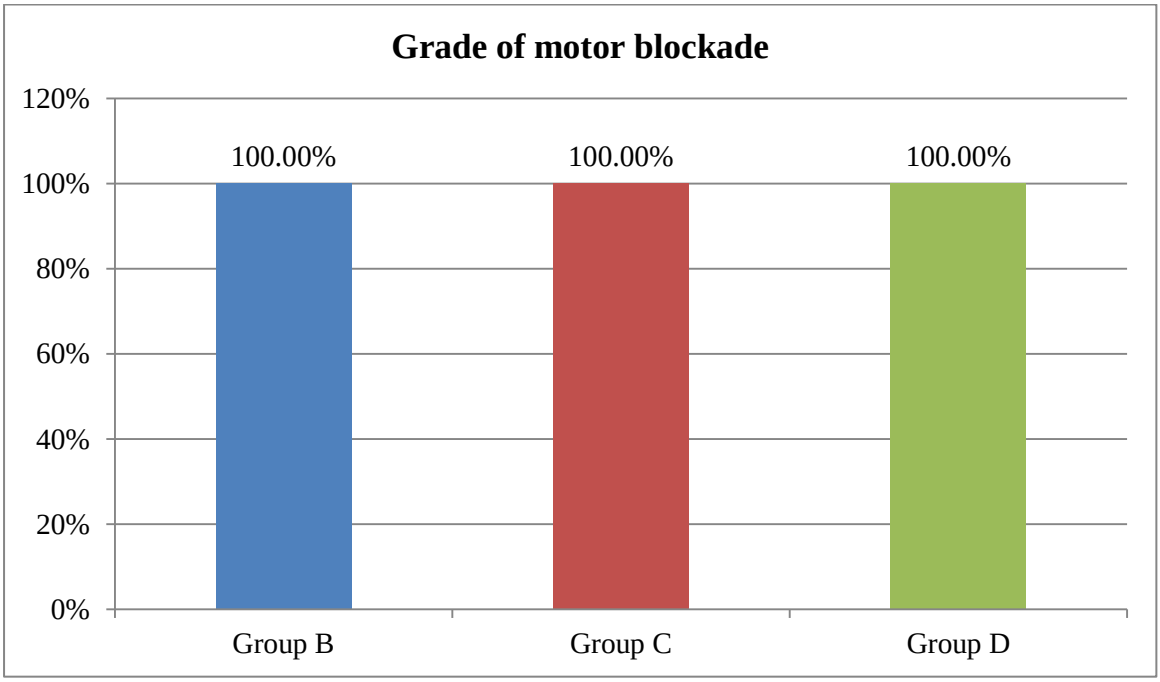


Graph 9: Bar diagram showing Motor onset duration comparison between three groups

Table 11: Grade of motor blockade comparison between three groups

		Group					
		Group B		Group C		Group D	
		Count	%	Count	%	Count	%
Grade of motor blockade (Bromage scale in grades)	3	50	100.0%	50	100.0%	50	100.0%

In all the three groups Motor blockade grade was 3. There was no difference.

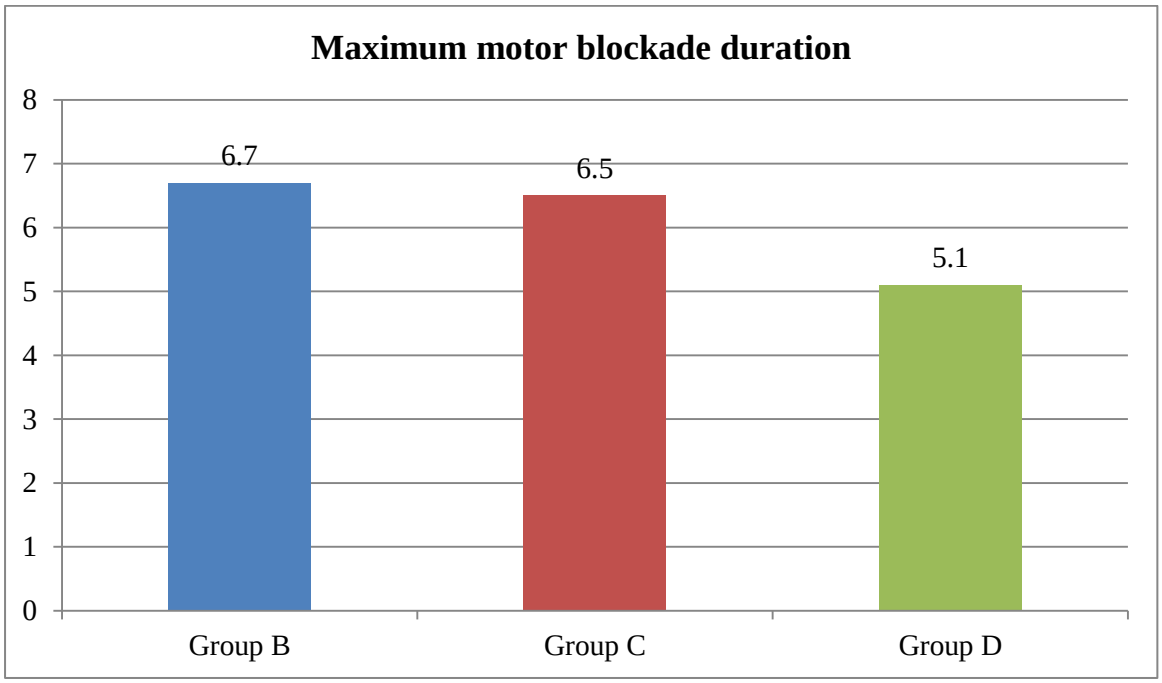


Graph 10: Bar diagram showing grade of motor blockade

Table 12: Maximum motor blockade duration comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
Maximum motor blockade duration (min)	Mean	6.7	6.5	5.1	<0.001*	0.851	<0.001*	<0.001*
	SD	.9	1.0	.9				
	Minimum	5	5	4				
	Maximum	9	8	7				

Mean duration of maximum motor blockade in Group B was 6.7 ± 0.9 min, in Group C was 6.5 ± 1 min and in Group D was 5.1 ± 0.9 min. This difference in mean duration of motor blockade b/w three groups was statistically significant. Highest duration of motor blockade was seen in Group B and lowest in Group D.

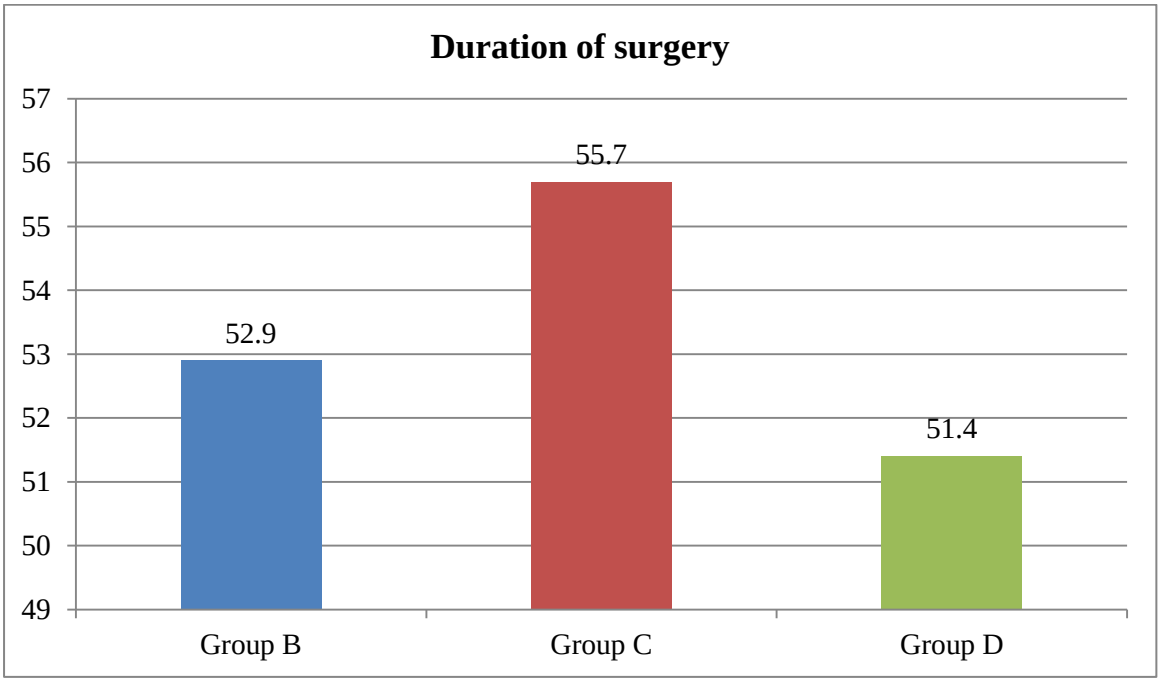


Graph 11: Bar diagram showing Maximum motor blockade duration comparison between three groups

Table 13: Duration of surgery comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
Duration of surgery (min)	Mean	52.9	55.7	51.4	0.059	0.375	1.000	0.057*
	SD	6.9	12.1	7.3				
	Minimum	40	40	40				
	Maximum	60	90	70				

Mean duration surgery in Group B was 52.9 ± 6.9 min, in Group C was 55.7 ± 12.1 min and in Group D was 51.4 ± 7.3 min. This difference in mean duration surgery b/w three groups was not statistically significant. Difference b/w Group C and Group D was statistically significant. Highest duration of duration surgery was seen in Group C and lowest in Group D.

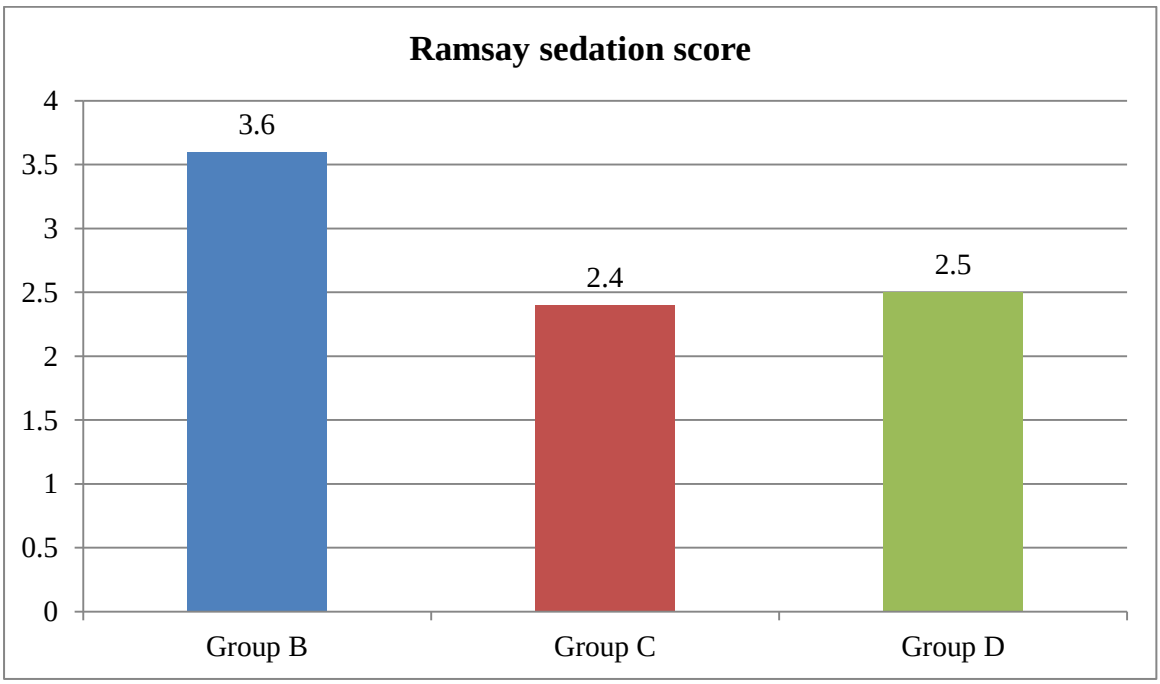


Graph 12: Bar diagram showing Duration of surgery comparison between three groups

Table 14: Ramsay sedation score comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
Ramsay sedation score	Mean	3.6	2.4	2.5	<0.001*	<0.001*	<0.001*	1.000
	SD	.7	.6	.7				
	Minimum	2	1	2				
	Maximum	4	4	5				

Mean Ramsay sedation score in Group B was 3.6 ± 0.7, in Group C was 2.4 ± 0.6 and in Group D was 2.5 ± 0.7. This difference in mean Ramsay sedation score b/w three groups was statistically significant. Highest Ramsay sedation score was seen in Group B and lowest in Group C.

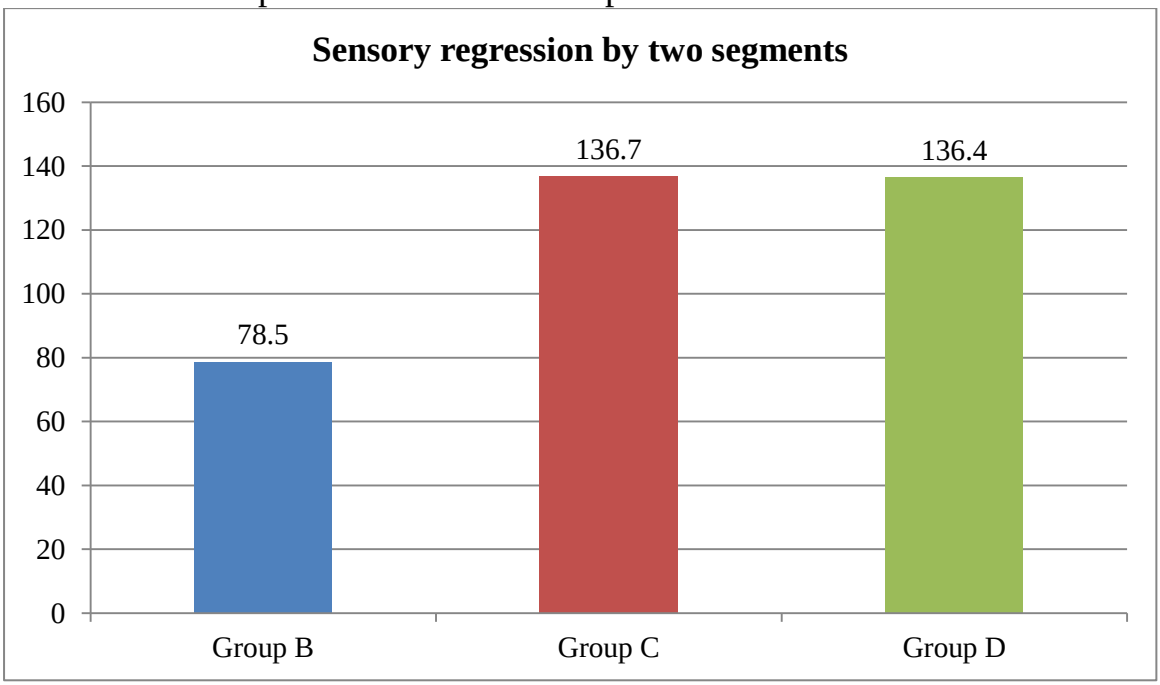


Graph 13: Bar diagram showing Ramsay sedation score comparison between three groups

Table 15: Sensory regression by two segments comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
Sensory regression by two segments (min)	Mean	78.5	136.7	136.4	<0.001*	<0.001*	<0.001*	1.000
	SD	9.9	10.7	11.7				
	Minimum	60	120	120				
	Maximum	95	155	150				

Mean Sensory regression by two segments in Group B was 78.5 ± 9.9 min, in Group C was 136.7 ± 10.7 min and in Group D was 136.4 ± 11.7 min. This difference in mean Sensory regression by two segments b/w three groups was statistically significant. Difference b/w Group C and Group D was not statistically significant. Highest duration of Sensory regression by two segments was seen in Group C and lowest in Group B.

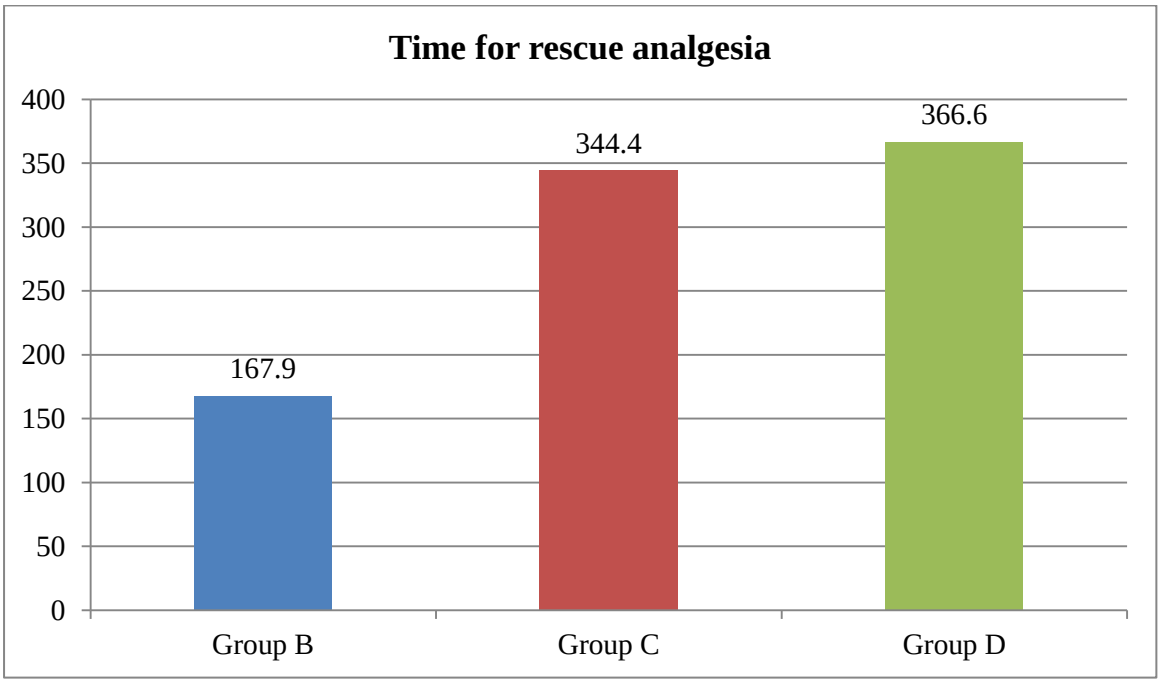


Graph 14: Bar diagram showing Sensory regression by two segments comparison between three groups

Table 16: Time for rescue analgesia comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
Time for rescue analgesia (min)	Mean	167.9	344.4	366.6	<0.001*	<0.001*	<0.001*	0.001*
	SD	20.6	28.9	37.5				
	Minimum	135	300	300				
	Maximum	210	390	420				

Mean Time for rescue analgesia in Group B was 167.9 ± 20.6 min, in Group C was 344.4 ± 28.9 min and in Group D was 366.6 ± 37.5 min. This difference in mean Time for rescue analgesia b/w three groups was statistically significant. Highest Time for rescue analgesia was seen in Group D and lowest in Group B.

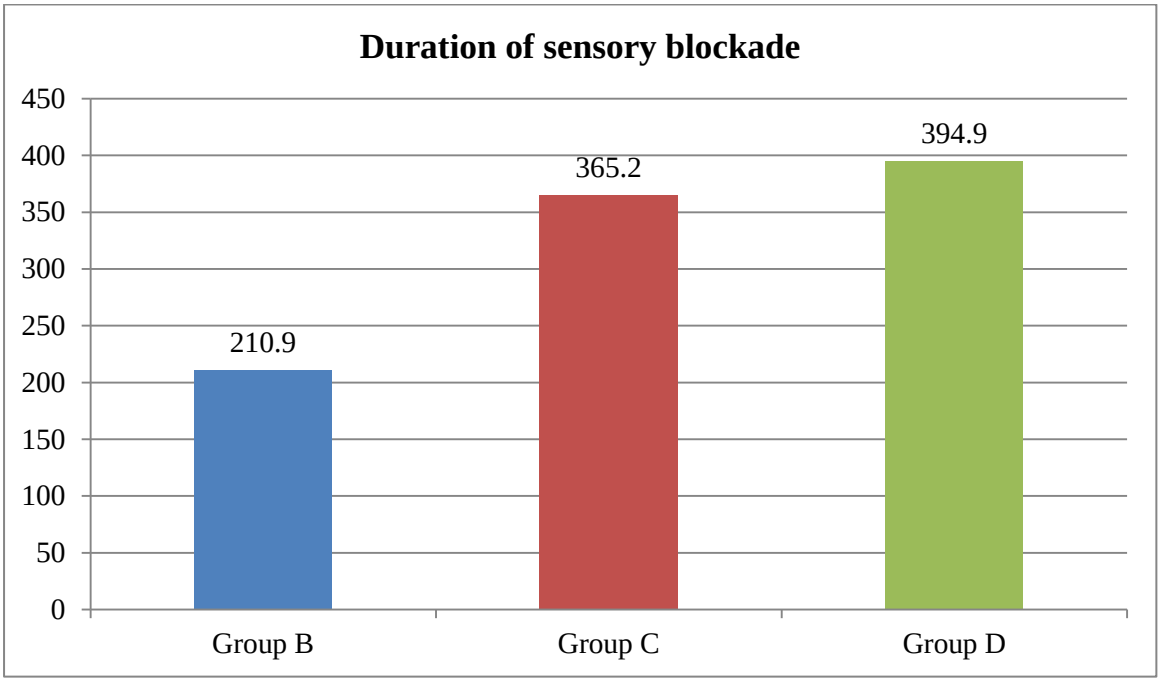


Graph 15: Bar diagram showing Time for rescue analgesia comparison between three groups

Table 17: Duration of sensory blockade comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
Duration of sensory blockade (min)	Mean	210.9	365.2	394.9	<0.001*	<0.001*	<0.001*	<0.001*
	SD	23.0	24.8	31.6				
	Minimum	170	320	335				
	Maximum	260	410	445				

Mean Duration of sensory blockade in Group B was 210.9 ± 23.0 min, in Group C was 365.2 ± 24.8 min and in Group D was 394.9 ± 31.6 min. This difference in mean Duration of sensory blockade b/w three groups was statistically significant. Highest Duration of sensory blockade was seen in Group D and lowest in Group B.

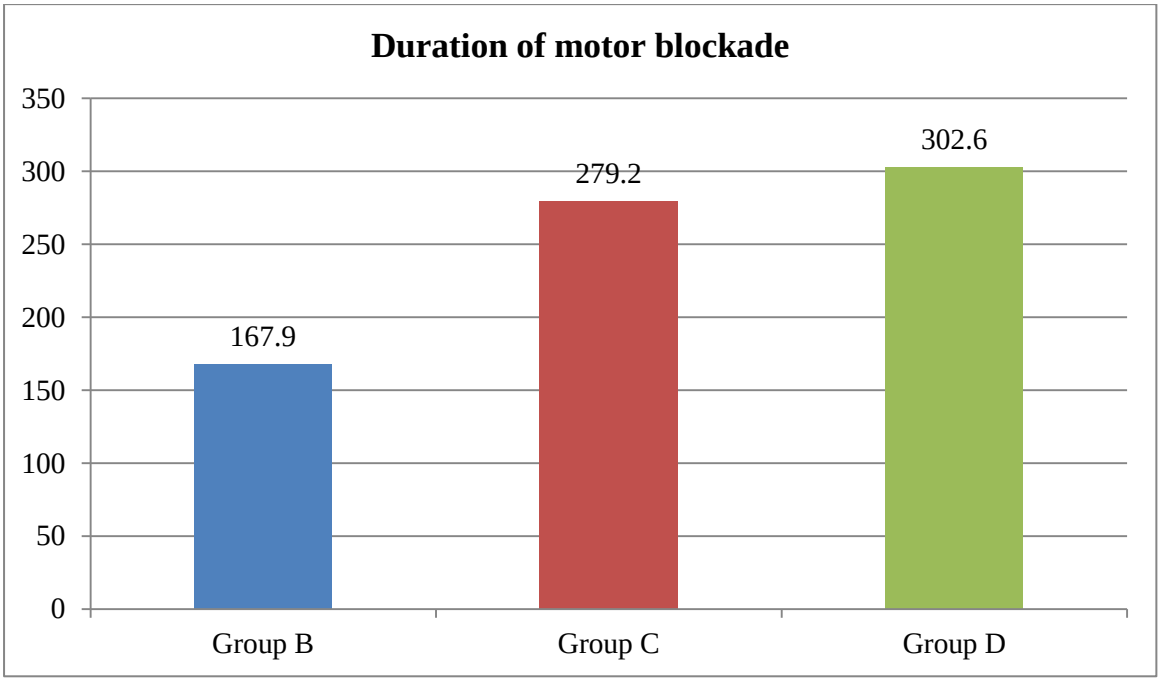


Graph 16: Bar diagram showing Duration of sensory blockade comparison between three groups

Table 18: Duration of motor blockade comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
Duration of motor blockade (min)	Mean	167.9	279.2	302.6	<0.001*	<0.001*	<0.001*	<0.001*
	SD	20.6	24.1	36.6				
	Minimum	135	240	240				
	Maximum	210	330	360				

Mean Duration of motor blockade in Group B was 167.9 ± 20.6 min, in Group C was 279.2 ± 24.1 min and in Group D was 302.6 ± 36.6 min. This difference in mean Duration of motor blockade b/w three groups was statistically significant. Highest Duration of motor blockade was seen in Group D and lowest in Group B.

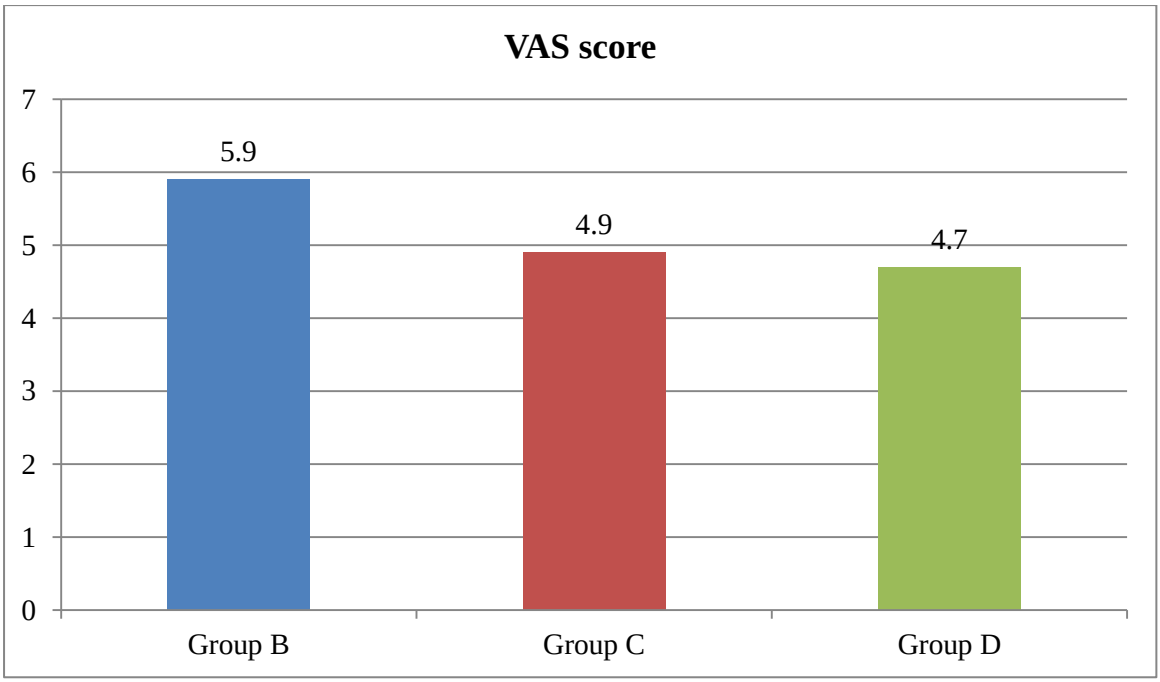


Graph 17: Bar diagram showing Duration of motor blockade comparison between three groups

Table 19: VAS score comparison between three groups

		Group			P value b/w three groups	B vs C	Bvs D	C vs D
		Group B	Group C	Group D				
VAS score	Mean	5.9	4.9	4.7	<0.001*	<0.001*	<0.001*	0.907
	SD	.8	.8	.7				
	Minimum	4	4	4				
	Maximum	7	7	6				

Mean VAS Score in Group B was 5.9 ± .8, in Group C was 4.9 ± .8 and in Group D was 4.7 ± .7. This difference in mean VAS Score b/w three groups was statistically significant. Highest VAS Score was seen in Group B and lowest in Group D.



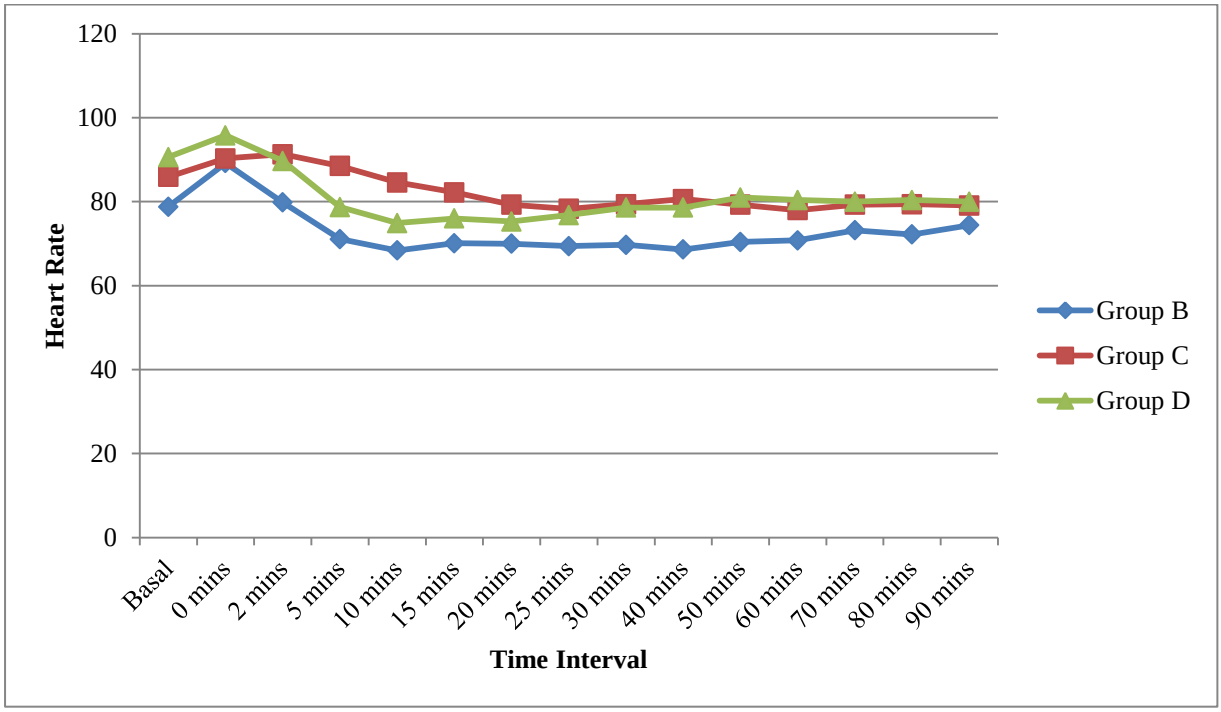
Graph 18: Bar diagram showing VAS score comparison between three groups

Table 20: Heart rate comparison between three groups at different time intervals of Follow up

HR	Group									
	Group B		Group C		Group D		P value b/w three groups	B vs C	Bvs D	C vs D
	Mean	SD	Mean	SD	Mean	SD				
Basal	78.8	6.3	85.9	16.7	90.6	17.4	<0.001*	0.042*	<0.001*	0.310
0 min	89.2	7.4	90.3	11.5	95.8	16.7	0.019*	1.000	0.026*	0.085
2 min	79.8	7.2	91.3	15.2	89.7	19.0	<0.001*	<0.001*	0.003*	1.000
5 min	71.1	7.6	88.5	18.4	78.7	17.9	<0.001*	<0.001*	0.045*	0.006*
10 min	68.4	5.8	84.6	19.5	74.9	14.5	<0.001*	<0.001*	0.077	0.003*
15 min	70.1	7.9	82.2	13.9	76.0	11.9	<0.001*	<0.001*	0.035	0.021*
20 min	70.0	7.5	79.3	14.7	75.3	9.4	<0.001*	<0.001*	0.051	0.210
25 min	69.4	5.6	78.3	13.0	76.8	9.7	<0.001*	<0.001*	0.001*	1.000
30 min	69.7	4.2	79.4	9.8	78.6	11.7	<0.001*	<0.001*	<0.001*	1.000
40 min	68.6	4.4	80.6	9.6	78.6	12.0	<0.001*	<0.001*	<0.001*	0.813
50 min	70.4	2.9	79.3	9.6	81.0	11.8	<0.001*	<0.001*	<0.001*	1.000
60 min	70.8	4.4	78.0	10.5	80.4	11.3	<0.001*	<0.001*	<0.001*	0.570
70 min	73.2	4.5	79.3	11.1	80.0	10.3	<0.001*	0.003*	0.001*	1.000
80 min	72.2	5.3	79.4	9.6	80.4	11.3	<0.001*	<0.001*	<0.001*	1.000
90 min	74.4	4.7	79.1	9.9	80.0	10.3	0.003*	0.022*	0.004*	1.000

In the study there was significant difference in mean Heart rate between three groups at all the intervals of follow up. Mean HR was highest in Group C and Lowest in Group B. Between Group B and Group C, significant difference in mean HR was seen at all the intervals except at 0 min. B/w Group B vs D,

significant difference in mean HR was seen at all the intervals except at 10 min, 15 min and 20 min. B/w Group C and D, significant difference in mean HR was observed at 5 min, 10 min and 15 min, at other intervals there was no significant difference in mean HR between Group C and Group D.

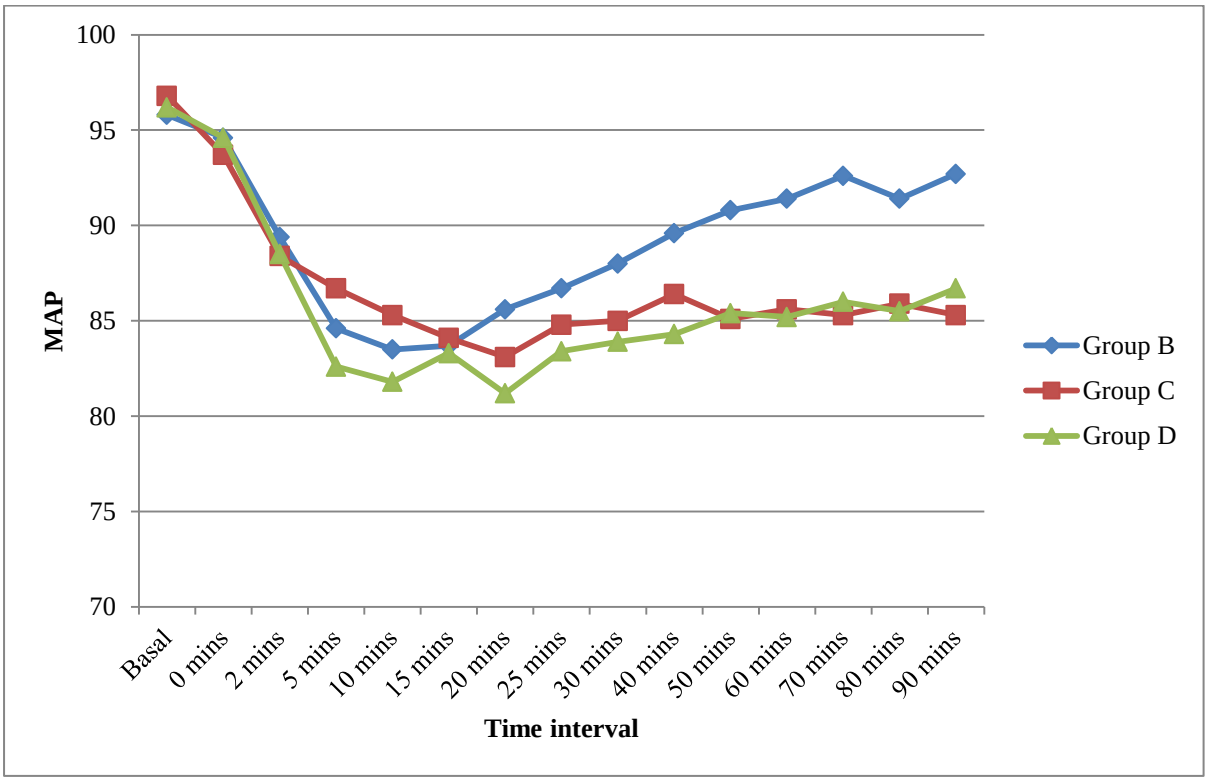


Graph 1: Line diagram showing heart rate comparison between three groups

Table 21: MAP comparison between three groups at different time intervals of Follow up

	Group									
	Group B		Group C		Group D		P value b/w three groups	B vs C	Bvs D	C vs D
	Mean	SD	Mean	SD	Mean	SD				
Basal	95.8	6.9	96.8	7.2	96.2	9.4	0.827	1.000	1.000	1.000
0 min	94.6	5.8	93.7	7.3	94.6	8.3	0.734	1.000	1.000	1.000
2 min	89.4	7.2	88.4	9.2	88.5	9.8	0.828	1.000	1.000	1.000
5 min	84.6	6.6	86.7	9.6	82.6	11.0	0.094	0.789	0.860	0.090
10 min	83.5	6.1	85.3	8.4	81.8	10.6	0.117	0.872	0.920	0.116
15 min	83.7	6.4	84.1	7.4	83.3	10.1	0.874	1.000	1.000	1.000
20 min	85.6	5.6	83.1	7.8	81.2	9.7	0.022*	0.344	0.018*	0.689
25 min	86.7	6.6	84.8	12.5	83.4	8.1	0.220	0.915	0.251	1.000
30 min	88.0	6.1	85.0	11.0	83.9	7.8	0.044*	0.221	0.048	1.000
40 min	89.6	6.2	86.4	9.5	84.3	6.7	0.002	0.106	0.002	0.106
50 min	90.8	5.6	85.1	8.2	85.4	7.0	<0.001*	<0.001*	0.001*	<0.001*
60 min	91.4	5.9	85.6	9.6	85.2	6.0	<0.001*	<0.001*	<0.001*	1.000
70 min	92.6	6.0	85.3	9.7	86.0	6.0	<0.001*	<0.001*	<0.001*	1.000
80 min	91.4	5.9	85.9	9.0	85.5	5.4	<0.001*	<0.001*	<0.001*	1.000
90 min	92.7	5.8	85.3	8.6	86.7	5.0	<0.001*	<0.001*	<0.001*	0.904

In the study there was significant difference in mean SBP between three groups at 20 min, 30 min and from 50 min to 90 min intervals of followup. Mean SBP was highest in Group B and Lowest in Group D. Between Group B and Group C, significant difference in mean SBP was seen from 50 min to 90 min intervals. Between Group B and Group C, significant difference in mean SBP was seen at 20 min and from 50 min to 90 min intervals. B/w Group C and D, significant difference in mean SBP was observed at 50 min, at other intervals there was no significant difference in mean SBP between Group C and Group D.



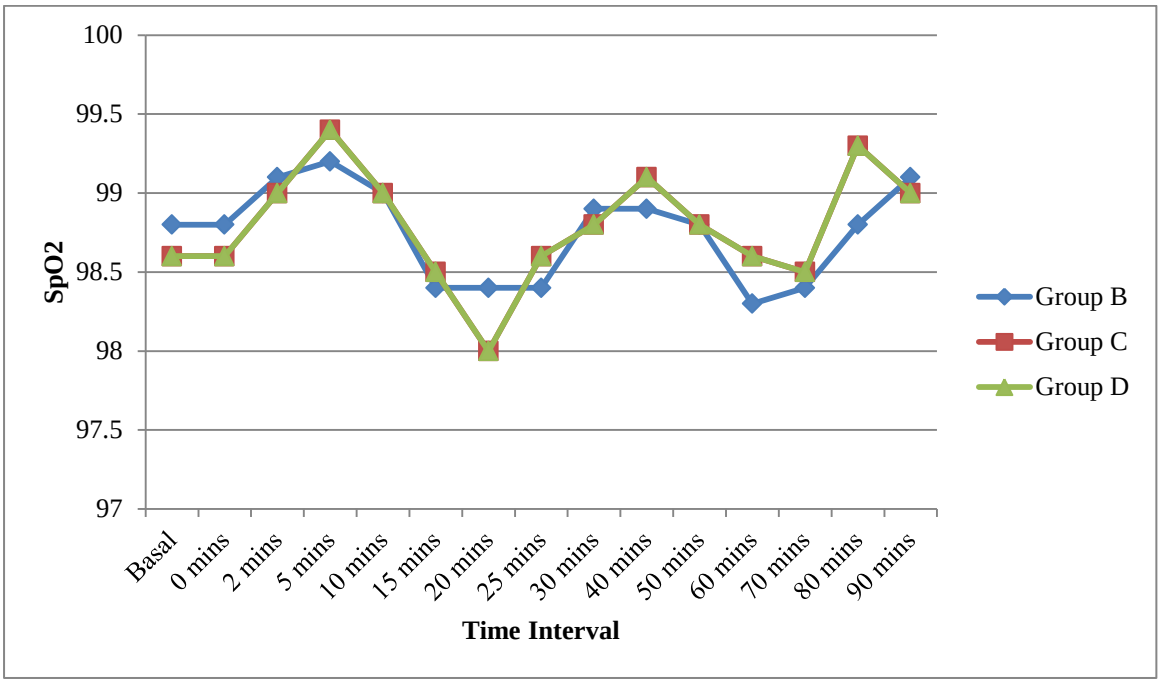
Graph 202: Line diagram showing MAP comparison between three groups at different time intervals of Follow up

Table 22: SpO2 comparison between three groups at different time intervals of Follow up

	Group									
	Group B		Group C		Group D		P value b/w three groups	B vs C	Bvs D	C vs D
	Mean	SD	Mean	SD	Mean	SD				
Basal	98.8	1.6	98.6	1.8	98.6	1.8	0.800	0.042*	<0.001*	0.310
0 min	98.8	1.5	98.6	1.7	98.6	1.7	0.785	1.000	0.026*	0.085
2 min	99.1	1.2	99.0	1.4	99.0	1.4	0.967	<0.001*	0.003*	1.000
5 min	99.2	1.1	99.4	.8	99.4	.8	0.351	<0.001*	0.045*	0.006*
10 min	99.0	1.2	99.0	1.2	99.0	1.2	0.995	<0.001*	0.077	0.003*
15 min	98.4	1.7	98.5	1.7	98.5	1.7	0.963	<0.001*	0.035*	0.021*
20 min	98.4	1.7	98.0	1.8	98.0	1.8	0.537	<0.001*	0.051	0.210
25 min	98.4	1.6	98.6	1.7	98.6	1.7	0.889	<0.001*	0.001*	1.000
30 min	98.9	1.4	98.8	1.5	98.8	1.5	0.972	<0.001*	<0.001*	1.000
40 min	98.9	1.4	99.1	1.4	99.1	1.4	0.854	<0.001*	<0.001*	0.813
50 min	98.8	1.5	98.8	1.4	98.8	1.4	0.997	<0.001*	<0.001*	1.000
60 min	98.3	1.7	98.6	1.6	98.6	1.6	0.573	<0.001*	<0.001*	0.570
70 min	98.4	1.6	98.5	1.6	98.5	1.6	0.913	0.003*	0.001*	1.000
80 min	98.8	1.4	99.3	.8	99.3	.8	0.056	<0.001*	<0.001*	1.000
90 min	99.1	.9	99.0	1.1	99.0	1.1	0.852	0.022*	0.004*	1.000

In the study there was no significant difference in mean SpO2 between three groups at all the intervals. However b/w Group B and Group C, there was significant difference in mean SpO2 at all the intervals except at 0 min. B/w Group B vs Group D, significant difference in mean SpO2 was observed at all the intervals except at 10 min and 20 min. B/w Group C vs Group D, significant

difference in mean SpO2 was observed at 10 min, 15m in and 20 min, at other intervals there was no significant difference in mean SpO2.



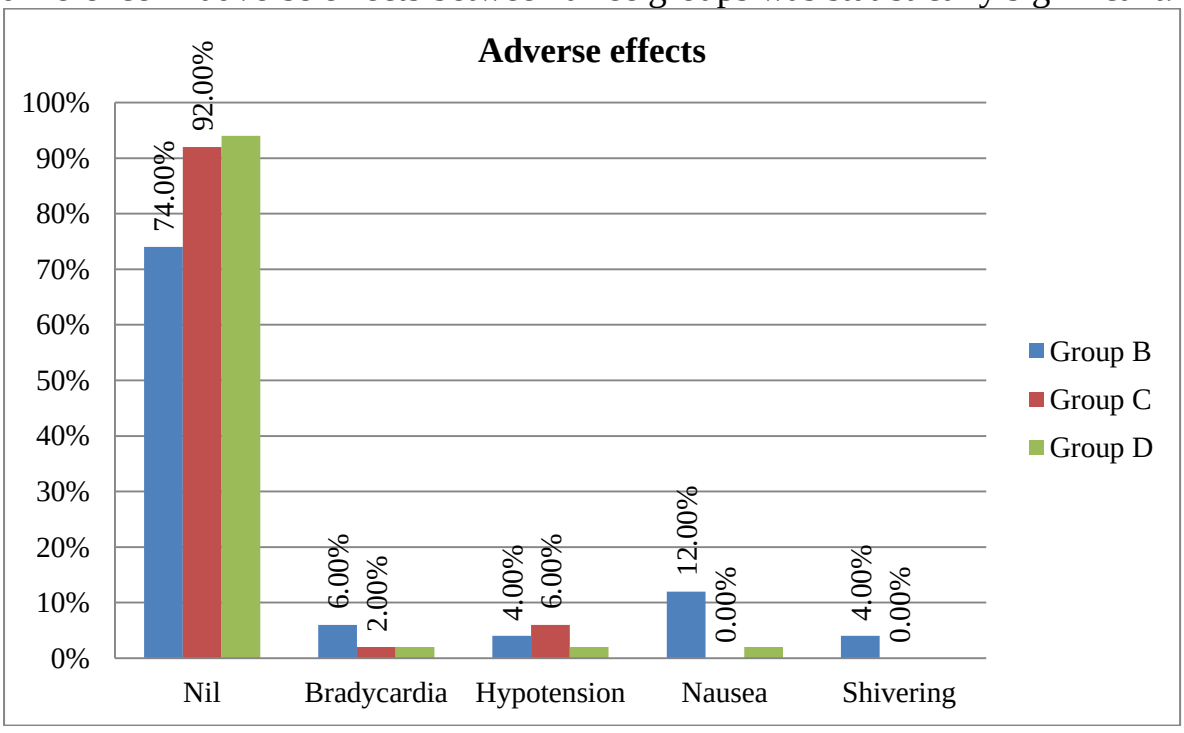
Graph 21: Line diagram showing SpO2 comparison between three groups at different time intervals of Follow up

Table 23: Adverse effects comparison between three groups

		Group					
		Group B		Group C		Group D	
		Count	%	Count	%	Count	%
Adverse effects	Nil	37	74.0%	46	92.0%	47	94.0%
	Bradycardia	3	6.0%	1	2.0%	1	2.0%
	Hypotension	2	4.0%	3	6.0%	1	2.0%
	Nausea	6	12.0%	0	0.0%	1	2.0%
	Shivering	2	4.0%	0	0.0%	0	0.0%

χ 2 = 16.85, df = 8, p = 0.032*

In Group B, 6% had Bradycardia, 4% had Hypotension, 12% had Nausea and 4% had Shivering. In Group C, 2% had Bradycardia and 6% had hypotension, in Group D, 2% had Bradycardia, hypotension and nausea respectively. This difference in adverse effects between three groups was statistically significant.



Graph 22: Bar diagram showing adverse effects comparison between three groups

DISCUSSION

DISCUSSION

Post operative analgesia must be long lasting, effective with minimum side effects. For spinal anaesthesia bupivacaine 0.5% hyperbaric is most common local anaesthetic used. But its post operative analgesic duration is limited. Hence, an additive to these local anaesthetics is a reliable method to prolong the duration of anaesthesia. This is a simpler technique has been widely accepted.

Many drugs like opioids (fentanyl, nalbufen, pethidine and buprenorphine), benzodiazepines (midazolam), ketamine and neostigmine have been used.

The most common are opioids and they have been the mainstay for post operative pain. [47] Opiods intrathecally prolong the duration of analgesia, but can have late and unpredictable respiratory depression, pruritus, nausea, vomiting and urinary retention. [62, 75, 76] Hence there was requirement for better adjuncts which prolongs analgesia without the above side effects of opioids.

Intrathecal alpha 2 agonists are found to have antinociceptive action for both somatic and visceral pain. [12] Hence these are used as adjuncts to bupivacaine for spinal anaesthesia. [47]

Clonidine being a partial α2 adrenergic agonist potentiate both sensory and motor block of local anesthetics. Its analgesic effect is mediated through activation of post synaptic alpha-2 receptors in substantia gelantinosa of spinal cord. It decreases the release of nociceptive substances from substantia gelatinosa by activating the descending inhibitory medullospinal pathways [12]

Many studies are there regarding clonidine when used intrathecally. It has been found to be a definitive adjunct to prolong the duration of analgesia.

Dexmedetomidine is also an alpha2 receptor agonist more specific than clonidine. [18] It is commonly used as a premedicant in general anaesthesia. It reduces opioid and inhalational anaesthetic requirements. [18]

There are very few studies available for dexmedetomidine and its intrathecal efficacy. So there is a need to compare its effectiveness as a spinal adjunct to bupivacaine.

Hence, we have undertaken this study to evaluate and compare the effect of adding clonidine versus dexmedetomidine with hyperbaric 0.5% bupivacaine in spinal anaesthesia for elective lower abdominal surgeries.

150 patients of ASA physical status I and II between age group of 18 to 60 years of either sex scheduled for elective lower abdominal surgeries were included in the study. The patients were divided into 3 groups after randomization which was done using simple sealed envelope technique.

Demographic data: comparing age, sex, height, weight shows no statistical difference among the groups.

Hypothesis done before the study: it was hypothesised that both clonidine and dexmedetomidine will prolong duration of postoperative analgesia compared to the control. Duration of analgesia between clonidine and dexmedetomidine will not be different as equipotent doses are used.

Dosages of drugs selected

Clonidine

Various authors have used different doses of clonidine for intrathecal blockade starting from 15 µg to 300 µg along with local anesthetics. [66]

Table 24: Various studies, dosages and the effects of intrathecal clonidine

Authors	Year	Dose of clonidine used	Onset of sensory block in clonidine group	Max sensory level attained	Duration of analgesia in clonidine group	Quality of motor block attained	Duration of motor blockade in clonidine group	Side effects
Benhamou D et al	1998	75µg	----	----	183±80 min	Bromage grade 3	137±35 min	Moderate sedation in 40% of patients.
De Kock Marc et al	2001	15µg 45µg 75µg	-----	T8 T8 T6	160±37 min 183±80 min 194±40 min	Bromage grade 3	137±32 min 138±34 min 164±38 min	Fall in MAP in clonidine group of 45µg,75µg
Dobrydnjov I et al	2003	15µg 30µg	-----	T6 T8	274±94 min 253±71 min	Bromage grade 3	155±37 min 182±55 min	11- 19 mm Hg 15-20 mm Hg (fall in MAP in clonidine group)
Strebel S et al	2004	37.5µg 75µg 150µg	-----	T1-T10	343±75 min 381±117 min 445±136 min	Bromage grade 3	------	1/17 0/18 1/20 (Mean arterial BP decrease 30% in clonidine group)
vanTuijl I et al [77]	2006	75µg	-----	---	129±13.8 min	---	------	No deleterious side effects

Kaabachi O et al	2007	1µg/kg	-----	---	461±147 min	Bromage grade 3	252±79 min	Hypotension (12/42 patients) and Bradycardia (9/42 patients) in clonidine group
Sethi BS et al	2007	1µg/kg	----	----	614 min	Bromage grade 3	205 min	16 out of 30 patients had sedation in clonidine group
Grandhe RP et al	2008	1µg/kg 1.5µg/kg	7.1±4.2 min 8.2±3.4min	T6 T5	6.3±0.8 hr 7.3±0.9 hr	Bromage grade 3 ---	142±37.1min 191.7±38.5min	Hypotension 10/15 patients Hypotension 8/15 patients
Saxena H et al	2010	15µg 30µg 37.5µg	1.48±0.39 min 0.95±0.09 min 0.92±0.08 min	---	164.53±23.9 min 264.75±44.3 min 285.6±36.5 min	Bromage grade 3	206.75±20.16 min 220±47.43 min 235±31.9 min	Mean arterial BP decrease 20% in clonidine group37.5µg
Kanazi GE et al	2006	30µg	7.6±4.4 min	T6.5	272±38min	Bromage grade 3	216±35 min	Hypotension 3/16 patients

(------) are the parameters not studied by the authors

Dexmedetomidine

Variours studies with different doses of dexmedetomidine for intrathecal blockade starting from 3 µg to 15µg along with local anaesthetics.

Table 25: Various studies, dosages and the effects of intrathecal clonidine

Authors	Year	Dose of medetomidine used	Onset of sensory block in Dexmedetomidine group	Max sensory level attained in Dexmedetomidine group	Duration of analgesia in Dexmedetomidine group	Quality of motor block attained in Dexmedetomidine group	Duration of motor blockade in Dexmedetomidine group	Side effects
Kanazi GE et al	2006	3µg	8.6±3.7 min	T6	303±75min	Bromage grade 3	250±76 min	Hypotension 1/16 patients
Al-Ghanem SM et al	2009	5µg	7.5±7.4min	T6	274±73min	Bromage grade 3	240±60 min	Mild-moderate Hypotension 4/38 patients
Al-Mustafa MM et al	2009	5µg 10µg	6.3±2.7 min 4.7±2 min	-----	277.1±23min 338.9±44.8 min	Bromage grade 3	246.4±25.7 min 302.9±36.7 min	Bradycardia 1/21 patients Hypotension 1/21 patients
Gupta R et al	2011	5µg	4.8±1.2 min	T5	478.4±20.9 min	Bromage grade 3	------	Bradycardia 2/16 patients Hypotension 2/16 patients
Gupta R et al	2011	5µg	11.6±1.8 min	T5	251.77±30.69 min	Bromage grade 3	421±21 min	No deleterious side effects
E id HEA et al	2011	10µg 15µg	---	T5 T7	320±65.8min 336±58 min	Bromage grade 3	280±46 min 336±58 min	Hypotension 3/15 patients Hypotension 2/16 patients

Shukla D et al	2011	10µg	2.27±1.09 min	----	352±45 min	Bromage grade 3	331±35 min	No deleterious side effects

(------) are the parameters not studied by the authors

We selected 3µg dexmedetomidine as it was studied by only a few studies.

Kalso E et al. [78] and Post C et al. [79] did a study and told that 1:10 dose ratio between dexmedetomidine and clonidine intrathecal produces a similar effect in animal models.

Asano T et al. [80] also told that binding affinity to spinal alpha-2 receptors of dexmedetomidine compared with clonidine is approximately 1:10. Hence dexmedetomidine dose was taken as 30 µg.

Selection of route of administration

Initially before availability of parentral form of clonidine oral clonidine was used. Various studies were done with oral clonidine to prolong the duration of analgesia by spinal anaesthesia. After availability of parentral form of α2 adrenergic agonists it became possible to do its study. Many studies were done with clonidine and only a few with intrathecal dexmedetomidine.

Intrathecal administration of α2 adrenergic agonists achieves a high drug concentration in the α2 adrenoreceptor in the spinal cord and acts by blocking the conduction through C and A delta fibres, increases potassium conductance and intensifies the conduction block of local anesthetics. [12, 62]

Dobrydnjov I et al. [15] did a study on analgesic effect following intrathecal bupivacaine with intrathecal or oral clonidine (150 µg). They found that with intrathecal clonidine analgesia was prolonged. Hypotension was more pronounced after oral than intrathecal clonidine.

Al-Mustafa MM et al. [81] found that intravenous dexmedetomidine prolonged effect of isobaric bupivacaine spinal anaesthesia. The dose used was 1µg/kg bolus and an infusion of 0.5µg/kg/hr.

Dexmedetomidine intrathecally the total dose ranged from 3 µg to 15 µg. it suggests that intrathecal route is more specific and low doses may be used. Hence in our study we chose to give intrathecally.

Analysis of data between the groups

Sensory block characteristics

1. Onset of sensory blockade

In our study mean sensory onset in Group B was 2.8 ± 0.7 min, in Group C was 1.4 ± 0.5 min and in Group D was 1.2 ± 0.4 min. This difference in mean duration of sensory onset between three groups was statistically significant. Sensory onset was faster in Group D and slowest in Group B.

Saxena H et al. [72] observed in their study that the onset of sensory blockade was 6.57±0.49 min in control group and 2.58±0.33 min, 2.54±0.34 min and 2.09±0.89 min in clonidine group (15 µg, 30 µg and 37.5 µg respectively).

There was a significant reduction in the onset time that was seen in our study as well. When compared to our study the onset time was higher.

Al-Mustafa MM et al. [71] observed that the onset of sensory blockade was 9.5±3min in control group and 6.3±2.7 min and 4.7±2 min in dexmedetomidine group (5 µg and 10 µg respectively). Just like in our study the onset time for sensory block was reduced.

In studies by Benhamou D et al., [63] Dobrydnjov I et al., [65] Grandhe RP et al. [69] and De Kock M et al. [64] with clonidine and study by Shukla D et al [76] with dexmedetomidine, it is found that there is significant reduction significant reduction in the onset time of sensory blockade as seen in our study.

2. Time taken for maximum sensory blockade

Mean duration of Sensory blockade in Group B was 7.3 ± 1.1 min, in Group C was 5.9 ± 0.8 min and in Group D was 5.1 ± 0.7 min. This difference in mean duration of sensory blockade between three groups was statistically significant. Highest duration of sensory blockade was seen in Group B and lowest in Group D.

Saxena H et al. [72] observed in their study that the mean time to achieve maximum sensory level was 7.3±1.25 min in control group which is the same as our study and 7.4±1.31 min and 6.7±1.12min in clonidine groups (15µg, 30µg, 37.5µg respectively).

Shukla D et al [76] also saw a significant decrease in the mean time taken for the maximum sensory blockade in the dexmedetomidine group.

3. Maximum level of sensory blockade achieved

Maximum sensory level reached in Group B was T6 in 70%, in Group C was T6 in 82% and in Group D was T6 in 52%. Hence highest percentage of T6 sensory level was seen in Group C and lowest percentage in Group D. This difference in maximum sensory level was statistically significant.

Studies by Kanazi GE et al., [47] Al-Ghanem SM et al., [70] Gupta R et al., [73] Gupta R et al. [75] and Eid HEA et al. [74] in dexmedetomidine group and study conducted by Strebel S et al. [66] in the clonidine group showed no statistically significant difference in the maximum level of sensory blockade.

4. Time taken for regression of sensory block by two segments

Mean Sensory regression by two segments in Group B was 78.5 ± 9.9 min, in Group C was 136.7 ± 10.7 min and in Group D was 136.4 ± 11.7 min. This difference in mean Sensory regression by two segments between three groups was statistically significant. Difference b/w Group C and Group D was not statistically significant. Highest duration of Sensory regression by two segments was seen in Group C and lowest in Group B.

Kanazi GE et al. [47] observed that the time taken for two segment regression of sensory block was prolonged with dexmedetomidine group then clonidine group than the control group which compares with our study.

Our study also matches with studies done by Dobrydnjov I et al., [65] Saxena H et al., [72] Sethi BS et al. [68] in clonidine group and studies done by Gupta R et al. [75] and Eid HEA et al. [74] in dexmedetomidine group where authors have observed statistically significant increase in the two segment regression time.

5. Duration of analgesia

Mean Time for rescue analgesia in Group B was 167.9 ± 20.6 min, in Group C was 344.4 ± 28.9 min and in Group D was 366.6 ± 37.5 min. This difference in mean Time for rescue analgesia b/w three groups was statistically significant. Highest Time for rescue analgesia was seen in Group D and lowest in Group B.

Our study concurs with the study conducted by Grandhe RP et al., [69] here authors observed the mean duration of analgesia of 3.8 ±0.7 hr in the control group and 6.3±0.8 hr when using clonidine of 1µg/kg with a mean weight of 60.6±19.4 kg.

In studies conducted by Gupta R et al., [73] Gupta R et al. [75] and Eid HEA et al. [74] in dexmedetomidine group and studies conducted by Saxena H et al., [72] Strebel S et al., [66] Dobrydnjov I et al. [65] and Benhamou D et al. [63] in the clonidine group authors observed a statistically significant increase in the mean duration of analgesia.

Motor block characteristics

1. Onset of motor blockade

Mean Motor onset in Group B was 4 ± 0.7 min, in Group C was 1.6 ± 0.5 min and in Group D was 1.1 ± 0.4 min. This difference in mean duration of

motor onset b/w three groups was statistically significant. Motor onset was faster in Group D and slowest in Group B.

In studies by Kanazi GE et al., [47] Gupta R et al., [75] Al-Mustafa MM et al., [71] and Shukla D et al. [76] in the dexmedetomidine group and Saxena H et al. [70] and De Kock M et al. [62] in the clonidine group authors saw that there was a significant decrease in the mean time for onset of motor blockade.

2. Time taken for maximum motor blockade and grade of motor blockade

Mean duration of maximum motor blockade in Group B was 6.7 ± 0.9 min, in Group C was 6.5 ± 1 min and in Group D was 5.1 ± 0.9 min. This difference in mean duration of motor blockade b/w three groups was statistically significant. Highest duration of motor blockade was seen in Group B and lowest in Group D. In all the three groups Motor blockade grade was 3. There was no difference.

Study conducted by Kanazi GE et al., [47] Al-Mustafa MM et al. [71] and Shukla D et al. [76] found that the time taken for maximum motor blockade is lesser in dexmedetomidine group when compared to the control group. Similarly studies done by Sethi BS et al., [68] and Saxena H et al. [72] also observed complete motor blockade in clonidine group.

Dobrydnjov I et al. [81] found that a better quality of block was there in all the three clonidine groups, where no supplementation with general anaesthesia for relaxation request from surgeons was needed intraoperatively.

3. Duration of motor blockade

Mean Duration of motor blockade in Group B was 167.9 ± 20.6 min, in Group C was 279.2 ± 24.1 min and in Group D was 302.6 ± 36.6 min. This difference in mean Duration of motor blockade b/w three groups was statistically significant. Highest Duration of motor blockade was seen in Group D and lowest in Group B.

Kanazi GE et al., [47] Kaabachi O et al., [67] Al-Mustafa MM et al., [71] Al-Ghanem SM et al., [70] Gupta R et al., [75] Gupta R et al., [73] Eid HEA et al. [76] and Shukla D et al. [74] in dexmedetomidine group and in studies conducted by Saxena H et al., [72] Strebel S et al., [66] Dobrydnjov I et al., [65] Sethi BS et al., [68] Grandhe RP et al. [69] and Benhamou D et al. [63] in the clonidine group observed that the mean duration of motor blockade was high in

dexmedetomidine group followed by clonidine group and then control group.

Hemodynamic effects

1. Heart rate

In the study there was significant difference in mean Heart rate between three groups at all the intervals of followup. Mean HR was highest in Group C and Lowest in Group B. Between Group B and Group C, significant difference in mean HR was seen at all the intervals except at 0 min. B/w Group B vs D, significant difference in mean HR was seen at all the intervals except at 10 min, 15 min and 20 min. B/w Group C and D, significant difference in mean HR was observed at 5 min, 10 min and 15 min, at other intervals there was no significant difference in mean HR between Group C and Group D.

Bradycardia was easily reversed with 0.6mg intravenous atropine in all the patients. It was seen in three patients in group B, one each in group D and C.

Kaabachi O et al. [42] observed bradycardia to be 30% in clonidine (2 µg/kg) group.

Kanazi GE et al., [47] Al-Ghanem SM et al. [70] and Al-Mustafa MM et al. [71] who observed that there was no significant difference in mean value of heart rate throughout the intraoperative and postoperative period.

2. Mean arterial pressure

In the study there was significant difference in mean MAP between three groups at 20 min, 30 min and from 50 min to 90 min intervals of followup. MAP was highest in Group B and Lowest in Group D. In between Group B and Group C, significant difference in mean SBP was seen from 50 min to 90 min intervals. Between Group B and Group C, significant difference in MAP was seen at 20 min and from 50 min to 90 min intervals. B/w Group C and D, significant difference in MAP was observed at 50 min, at other intervals there was no significant difference in MAP between Group C and Group D.

Two patients in control group, three patients in clonidine group and one patient in dexmedetomidine group developed hypotension and were managed with intravenous fluids and vasopressor.

Sethi BS et al. [68] observed that the lowest mean MAP was 70 mmHg in clonidine group (1 µg/kg, mean weight 57.93±4.75 kg).

Strebel S et al. [66] saw the maximum decrease in MAP was 25%±14%, 26%±12% and 25±13%, in clonidine group of 37.5 µg, 75 µg and 150 µg respectively.

Grandhe RP et al. [69] saw that the incidence of hypotension was 10/15 patients in clonidine group (clonidine 1 µg/kg, mean weight 60.6±19.4 kg) and 8/15 patient in clonidine group (clonidine 1.5 µg/kg, mean weight 62.7±18 kg).

Al-Ghanem SM et al. [70] observed that the hypotension was seen in both dexmedetomidine and fentanyl group. 4/38 patients in dexmedetomidine group and 9/38 patient in fentanyl group had hypotension.

3. Oxygen saturation

In the study there was no significant difference in mean SpO2 between three groups at all the intervals. However b/w Group B and Group C, there was significant difference in mean SpO2 at all the intervals except at 0 min. B/w Group B vs Group D, significant difference in mean SpO2 was observed at all the intervals except at 10 min and 20 min. between group C and D, significant difference in mean SpO2 was observed at 10 min, 15m in and 20 min, at other intervals there was no significant difference in mean SpO2.

4. Sedation

Mean Ramsay sedation score in Group B was 3.6 ± 0.7, in Group C was 2.4 ± 0.6 and in Group D was 2.5 ± 0.7. This difference in mean Ramsay sedation score b/w three groups was statistically significant. Highest Ramsay sedation score was seen in Group B and lowest in Group C.
Saxena H et al. [72] observed higher incidence of sedation in clonidine group (37.5 µg). It was seen that the patients were asleep but arousable.

Gupta R et al. [75] found that there was significance in mean sedation scores among the groups.

Strebel S et al., [66] Al-Ghanem SM et al. [70] and Al-Mustafa MM et al. [71] saw that there was no significance in mean sedation scores among the groups.

In Group B, 6% had Bradycardia, 4% had Hypotension, 12% had Nausea and 4% had Shivering. In Group C, 2% had Bradycardia and 6% had

hypotension, in Group D, 2% had Bradycardia, hypotension and nausea respectively. This difference in adverse effects between three groups was statistically significant.

CONCLUSION

CONCLUSION

From the present study we concluded that dexmedetomidine 3µg or clonidine 30µg with bupivacaine, 0.5% heavy intrathecally in patients undergoing elective lower abdominal surgeries,

Decreases the onset time for sensory blockade

Decreases the onset time for motor blockade

Produces higher level of sensory blockade

Produces prolonged postoperative analgesia

Produces prolonged sensory blockade

Produces prolonged motor blockade

Produces sedation in which patients were asleep and easily arousable

And the haemodynamic changes could be easily managed.

It is associated with minimal side effects change in rate and rhythm, respiratory depression and hence can be an attractive alternative for opioids for prolonging spinal analgesia.

There was no clinically significant difference between clonidine and dexmedetomidine on spinal block characteristics. Cost of dexmedetomidine is 5 times the cost of clonidine. In order to reduce the total cost, use of clonidine as an adjunct along with bupivacaine intrathecally is more cost effective

SUMMARY

SUMMARY

The present study entitled a comparative study of dexmedetomidine and clonidine as an adjunct to intrathecal bupivacaine in lower abdominal surgeries was done to evaluate the efficacy of dexmedetomidine or clonidine as adjunct to intrathecal hyperbaric 0.5% bupivacaine.

150 subjects will be randomly allocated into three groups, 50 in each group by computer generated table to receive one of the following for the subarachnoid block:

1. Group B (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml normal saline.

2. Group C (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. clonidine (30 μg).

3. Group D (n=50) – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. dexmedetomidine (3 μg).

Patients belonging to ASA physical status 1 and 2 between age group 18 and 60 posted for lower abdominal surgeries were included in the study.

The onset, maximum level and duration of sensory blockade, motor blockade and haemodynamic parameters were studied.

From our study we can say that in dexmedetomidine group and clonidine group there is an early onset of both sensory and motor blockade and a higher level of sensory blockade compared to control group and duration of sensory, motor blockade and duration of analgesia is significantly prolonged in the dexmedetomidine group and clonidine group compared to the control group.

Haemodynamics were preserved both intraoperatively and postoperatively. However few patients developed significant fall in blood pressure and bradycardia which were easily managed without any untowards effect.

No patient had any respiratory depression, nausea, vomiting or shivering in either of the groups.

In the present study the efficacy of intrathecal dexmedetomidine and clonidine were compared and we noticed that intrathecal dexmedetomidine was better than clonidine with regards to onset and duration of both sensory

and motor blockade as well as duration of analgesia. Hence dexmedetomidine is a better neuraxial adjunct compared to clonidine for providing early onset of sensory and motor blockade, adequate sedation and prolonged post operative analgesia.

Table 26: Results obtained in our study

Spinal block characteristics	Group B	Group C	Group D
Time taken for onset of sensory blockade	2.8 ± 0.7 min	1.4 ± 0.5 min	1.2 ± 0.4 min
Time taken for maximum sensory blockade	7.3 ± 1.1 min	5.9±0.8 min	5.1±0.71 min
The time taken for regression of sensory block by two segments	78.5±9.9 min	136.7±10.7 min	136.4±11.7 min
Duration of analgesia	167±9.9 min	344.4±28.9 min	366.6±37.5 min
Onset of motor blockade	4±0.7 min	1.6±0.5 min	1.1±0.4 min
Time taken for maximum motor blockade	6.7±0.9 min	6.5±1 min	5.1±0.9 min
Duration of motor blockade	167.9±20.6 min	279.2±24.1 min	302.6±36.6 min

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ANNEXURES

PROFORMA

A COMPARATIVE STUDY OF DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUNCT TO INTRATHECAL BUPIVACAINE IN LOWER ABDOMINAL SURGERIES

INVESTIGATOR- Dr. MALLIKA GANESH **GUIDE-** Dr. DINESH K.

NAME: AGE: SEX:

DEPT: HOSPITAL NO:

PRE OPERATIVE EXAMINATION:

PR	BP	RR	TEMP	HEIGHT	WEIGHT	SPINE	AIRWAY

SYSTEMIC EXAMINATION:

CVS: RS:

INVESTIGATIONS:

HAEMOGLOBIN: PLATELET COUNT:

BLEEDING TIME: CLOTTING TIME:

BLOOD UREA: SERUM CREATNINE:

SERUM SODIUM: SERUM POTASSIUM:

ECG: CHEST X-RAY:

RANDOM BLOOD SUGAR: OTHERS:

DIAGNOSIS:

PROPOSED SURGERY:

ASA PHYSICAL STATUS:

PREMEDICATION: Tab. alprazolam 0.5mg, Tab. ranitidine 150mg

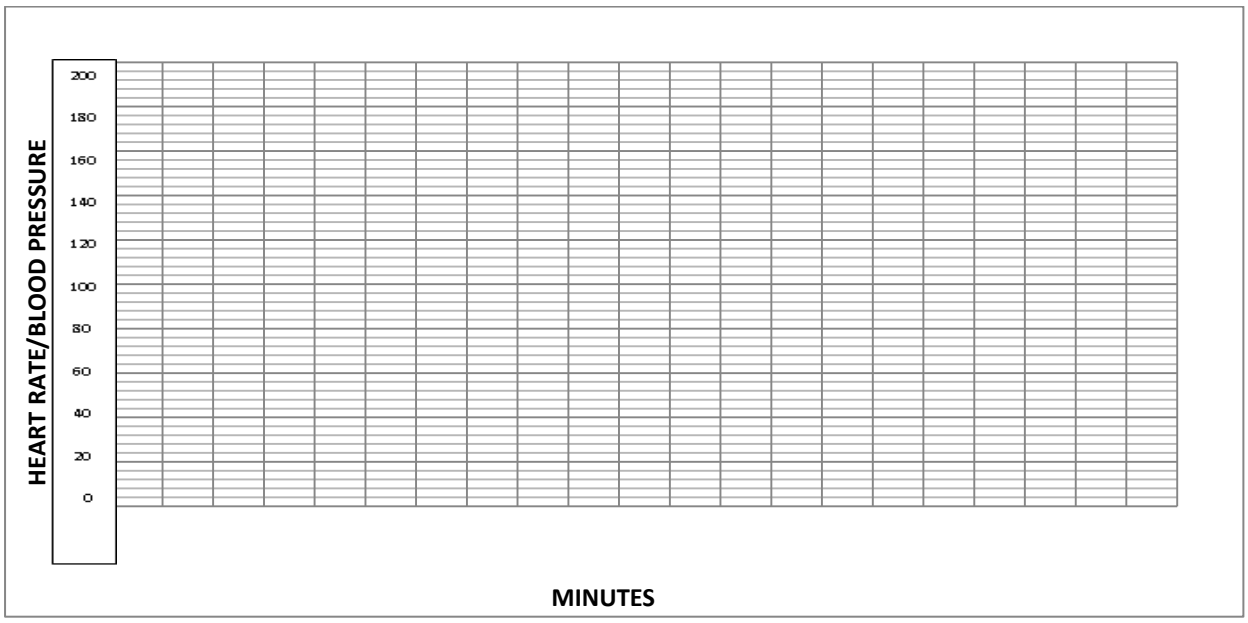
DRUG USED IN SUBARACHNOID BLOCK:

- Group B – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml normal saline.
- Group C – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. clonidine (30 μg).

- Group D – 3.5 ml volume of Inj. bupivacaine 0.5% hyperbaric and 0.5ml of Inj. dexmedetomidine (3 μg).

OBSERVATION:

1. Time of administration:
2. Onset of sensory block:
3. Time to achieve maximum dermatome level of sensory blockade:
4. Time for motor blockade:
   Modified Bromage scale 0:
   Modified Bromage scale 1:
   Modified Bromage scale 2:
   Modified Bromage scale 3:
5. Intraoperative Observation:



• Pulse ∧ Systolic BP ∨ Diastolic BP

6. Time to two segment regression of sensory level:
7. Sedation:

Ramsay sedation scale:

1. Anxious or agitated
2. Cooperative, oriented and tranquil

3. Responds to oral command only
4. Brisk response to glabellar tap
5. Sluggish reponse to glabellar tap
6. No response

8. Post operative vitals:

HR: BP: SPO_2:

9. Adverse effects if any:
10. Time for complete motor recovery:
11. Time for rescue analgesia:

VAS score:

GROUP B																																																																
																				HEART RATE															MEAN ARTERIAL PRESSURE															SPO2															
sl no	IP no	age(years)	sex	height(cm)	weight(kg)	surgery	Sensory onset duration (mins)	Maximum sensory level	Maximum sensory blockade duration(mins)	Motor onset duration (mins)	Grade of motor blockade (Bromage scale in grades)	Maximum motor blockade duration(mins)	duration of surgery (min)	Ramsay sedation score	Sensory regression by two segments (mins)	time for rescue analgesia (mins)	Duration of sensory blockade(mins)	Duration of motor blockade(mins)	VAS score	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins	adverse effects
1	245703	40	female	155	60	TAH	3	T6	8	4	3	6	40	4	80	165	195	165	4	84	98	88	78	74	72	72	70	70	72	72	70	74	76	74	99	97	92	85	82	84	86	83	88	87	91	91	92	91	92	99	99	99	99	99	99	99	100	100	100	100	100	99	99	99	
2	238178	50	male	150	55	IH	2	T6	7	3	3	5	60	4	95	150	210	150	6	86	98	90	86	80	82	70	68	66	66	68	66	70	68	72	99	97	92	87	82	79	80	81	83	83	83	84	85	84	85	96	99	100	100	100	100	100	100	100	99	99	99	99	99	99	
3	245360	40	female	152	52	TAH	2	T4	8	4	3	6	50	4	75	210	260	210	5	78	88	82	80	64	60	74	76	72	70	68	68	66	68	68	95	93	89	83	75	81	83	85	85	83	87	89	88	89	88	98	97	96	99	98	99	96	97	98	96	96	96	96	96	99	
4	237272	45	female	156	56	TAH	3	T6	6	5	3	6	60	4	65	165	200	165	5	80	94	82	70	70	76	66	66	64	66	68	64	68	68	70	99	95	90	84	79	81	85	83	83	85	85	89	86	89	86	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	nausea
5	243438	45	female	150	52	TAH	4	T4	9	5	3	7	45	4	90	135	170	135	5	88	86	80	74	74	74	72	74	76	70	72	76	74	70	72	95	93	89	87	85	85	89	93	89	87	91	88	87	88	87	95	94	96	99	98	99	99	100	100	100	100	100	100	99	99	
6	237114	45	female	155	49	TAH	3	T6	9	4	3	7	50	4	80	150	195	150	6	74	86	78	70	68	70	68	70	70	72	70	70	74	70	70	95	93	90	84	81	77	83	83	81	85	87	85	88	85	88	99	99	99	99	99	97	96	99	98	94	96	99	98	99	99	
7	244269	44	male	156	50	IH	2	T6	7	3	3	6	50	4	75	165	200	165	6	82	90	86	80	70	72	72	70	72	70	70	72	76	74	78	95	94	89	85	83	84	86	84	84	88	86	85	89	85	89	96	99	100	100	100	100	100	100	100	99	99	99	99	99	98	
8	180274	55	male	165	48	IH	3	T4	6	3	3	6	60	4	80	150	190	150	6	78	86	80	70	68	70	70	72	70	70	76	72	74	74	78	101	95	91	85	81	83	85	88	91	93	92	93	93	93	93	98	97	96	99	98	94	96	99	98	99	96	99	100	100	100	
9	247076	56	female	162	52	TAH	2	T6	8	4	3	7	55	4	65	150	195	150	5	70	80	76	68	68	78	64	60	70	66	70	68	70	66	70	95	93	89	83	80	78	81	79	81	79	83	83	85	83	85	99	99	100	100	100	99	99	99	99	96	98	97	96	99	98	
10	196917	35	female	155	51	TAH	3	T6	8	4	3	8	60	4	85	165	200	165	5	70	92	76	62	60	60	62	64	66	74	68	66	64	62	66	101	99	98	87	88	90	88	93	95	94	91	91	94	91	94	100	100	100	100	99	99	96	99	100	100	100	99	99	99	99	
11	249143	40	male	153	52	A	3	T4	7	4	3	6	60	4	95	210	255	210	5	80	88	78	70	70	72	72	70	74	72	78	80	82	86	84	96	89	86	85	83	85	85	87	90	89	91	95	98	95	98	99	96	97	98	96	96	98	97	96	99	98	94	96	99	98	nausea
12	247827	42	female	160	60	TAH	2	T6	6	3	3	6	50	4	70	135	170	135	5	84	98	86	80	76	74	74	76	72	64	72	76	78	80	80	93	90	70	65	63	60	65	70	83	93	95	97	96	97	96	100	100	100	100	100	100	100	99	99	100	100	100	100	99	99	hypotension
13	247451	50	female	167	55	TAH	4	T6	6	5	3	9	55	4	80	185	225	185	6	80	80	50	46	80	100	98	80	72	76	68	70	76	80	82	66	72	70	68	95	89	86	83	83	84	85	86	85	86	85	97	96	99	98	100	99	99	99	100	100	100	99	96	99	100	bradycardia
14	241080	46	male	162	52	A	3	T6	9	4	3	6	40	4	75	195	230	195	6	68	94	82	76	72	70	74	72	76	60	70	76	74	78	84	95	93	89	84	84	84	86	90	95	97	96	95	96	95	96	100	100	100	100	99	99	100	100	100	100	99	96	98	97	96	
15	251751	35	female	152	56	M	3	T6	8	5	3	8	60	4	65	165	195	165	5	86	80	72	62	64	62	64	60	60	76	66	60	62	68	80	103	98	94	92	93	97	94	99	97	97	97	97	100	97	100	94	96	99	98	99	100	99	96	97	98	96	96	100	100	99	
16	250965	35	female	155	52	M	2	T4	6	4	3	7	60	4	90	180	225	180	5	76	92	82	76	74	78	72	70	76	72	74	80	80	78	80	93	91	84	82	84	85	87	88	87	91	93	93	97	93	97	99	99	99	99	97	96	100	100	100	100	100	100	99	99	98	
17	257638	45	female	150	49	TAH	2	T6	7	3	3	6	45	4	85	150	195	150	4	84	90	78	70	70	70	72	70	70	78	70	71	70	72	72	93	93	89	86	84	83	85	91	93	96	97	99	99	99	99	99	99	100	100	100	100	99	99	99	99	99	99	99	100	100	
18	244250	42	male	158	50	IH	3	T6	7	4	3	8	40	4	75	180	230	180	6	70	96	86	80	78	80	78	70	80	62	78	80	80	78	76	97	97	93	89	88	87	91	92	91	95	92	96	100	96	100	100	100	100	100	99	99	96	99	100	100	100	100	100	100	100	
19	257078	37	female	159	48	M	4	T6	8	5	3	8	60	4	80	210	260	210	5	78	88	72	66	60	62	62	60	64	62	66	68	70	72	76	93	93	90	86	83	84	89	87	88	95	99	101	101	101	101	99	96	97	98	96	96	98	97	96	99	98	99	96	97	98	
20	250770	40	female	164	52	TAH	3	T6	6	4	3	7	55	4	95	180	225	180	7	86	90	76	66	68	70	70	70	70	70	70	72	70	70	74	103	100	97	91	91	91	94	94	91	95	96	97	100	97	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	nausea
21	204931	39	male	160	51	A	3	T6	8	4	3	6	55	4	60	165	195	165	6	86	98	90	80	66	68	72	72	70	72	70	76	78	80	78	98	95	65	60	62	66	65	62	63	70	72	75	72	75	75	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	hypotension
22	256364	30	female	157	52	TAH	2	T6	9	4	3	7	55	4	75	150	225	150	7	78	88	80	66	60	56	102	90	78	76	70	80	74	80	82	95	93	89	81	80	81	85	83	89	87	93	97	101	97	101	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	bradycardia
23	251675	35	male	158	52	IH	2	T5	6	3	3	6	50	4	80	180	230	180	6	68	60	60	56	50	48	60	66	60	60	66	70	72	70	76	97	98	92	90	85	82	85	87	88	89	92	91	92	91	92	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	bradycardia
24	256714	45	female	154	56	TAH	3	T4	9	5	3	6	50	4	70	180	225	180	6	88	100	84	68	66	62	66	66	68	66	70	68	72	70	74	100	97	92	88	82	84	86	85	87	88	91	91	92	91	92	96	99	98	99	100	99	98	97	96	99	98	94	96	99	98	
25	257153	35	female	159	52	TAH	3	T6	7	4	3	6	50	4	90	150	195	150	7	80	90	80	70	68	70	70	76	70	70	70	74	72	76	74	101	100	93	87	87	88	90	93	92	96	98	97	96	97	96	99	99	99	97	96	99	99	99	100	100	100	99	99	99	99	
26	260197	40	male	164	49	IH	4	T5	7	5	3	7	60	4	65	165	200	165	7	70	92	76	62	60	66	62	60	66	62	68	66	84	62	66	101	101	98	87	88	90	88	93	95	94	91	91	91	91	91	99	100	100	100	100	100	100	99	99	99	99	96	99	100	100	nausea
27	259957	38	female	150	50	A	3	T5	8	4	3	6	60	4	75	150	195	150	7	78	86	80	70	68	70	70	72	70	70	76	72	74	74	78	101	101	91	95	81	83	85	88	91	93	92	93	93	93	93	99	100	99	100	100	100	100	99	99	99	99	98	97	96	99	
28	261129	52	female	155	48	TAH	3	T4	6	4	3	6	55	4	90	150	195	150	6	70	80	76	68	68	72	64	66	70	64	70	68	70	66	70	95	101	89	83	80	78	81	79	81	79	83	83	85	83	85	100	100	100	100	100	99	99	96	99	100	100	100	100	100	100	shiverring
29	261091	42	male	156	52	IH	2	T6	7	3	3	5	50	3	85	150	200	150	6	74	86	78	70	68	70	68	66	70	68	70	70	74	70	70	95	95	90	84	81	77	83	83	81	85	87	85	88	85	88	96	97	96	97	98	96	96	98	97	96	99	95	94	96	99	
30	260864	52	female	165	51	TAH	3	T6	9	4	3	7	50	4	80	150	195	150	6	82	96	86	80	70	72	72	70	72	70	70	72	76	74	78	95	95	99	85	83	84	86	84	88	86	85	85	89	85	89	100	100	100	100	100	100	100	100	100	100	100	99	99	99	99	shiverring
31	262811	46	female	162	52	TAH	3	T6	7	4	3	6	40	2	75	165	200	165	6	84	98	88	78	74	72	72	70	70	72	72	70	74	76	74	95	93	89	83	80	78	81	79	81	79	83	83	85	83	85	100	100	100	100	100	100	99	95	94	96	99	96	99	100	100	
32	222853	46	male	155	52	IH	2	T6	6	3	3	7	60	4	80	150	190	150	6	86	98	90	86	80	82	70	68	66	66	68	64	70	68	72	101	99	98	87	88	90	88	93	95	94	91	91	94	91	94	99	98	99	98	100	99	99	99	99	99	99	98	97	96	99	
33	264678	43	female	153	56	TAH	4	T4	8	3	3	8	50	4	65	150	195	150	6	78	88	82	80	64	60	74	76	72	70	68	68	66	68	68	96	89	86	85	83	85	85	87	90	89	91	95	98	95	98	100	100	100	100	99	99	99	96	99	100	100	99	99	100	100	
34	190680	50	female	160	52	TAH	3	T6	8	4	3	6	60	4	85	165	200	165	5	80	94	82	70	70	76	66	66	64	66	68	64	68	68	70	66	72	70	68	95	89	86	83	83	84	85	86	85	86	85	99	98	99	98	99	100	99	98	97	96	99	99	99	99	99	
35	256929	40	male	167	49	IH	3	T4	7	4	3	6	45	4	95	210	255	210	5	88	86	80	74	74	74	72	74	76	70	72	76	74	70	72	93	90	85	83	83	83	86	87	89	93	95	97	96	97	96	99	99	99	99	97	96	99	99	99	100	100	99	99	99	99	
36	269660	45	female	162	50	TAH	2	T6	6	4	3	9	50	3	70	135	170	135	5	74	86	78	70	68	70	68	70	70	72	70	70	74	70	70	95	93	89	84	84	84	86	90	95	97	96	95	96	95	96	100	100	100	100	100	99	99	99	99	99	99	100	100	100	100	
37	224633	35	female	152	48	A	2	T6	6	3	3	6	50	2	80	185	225	185	6	82	90	86	80	70	72	72	70	72	70	70	72	76	74	78	103	98	94	92	93	97	94	99	97	97	97	97	100	97	100	99	100	100	100	100	99	99	99	99	99	99	96	99	100	100	
38	267049	38	male	155	52	A	3	T4	9	5	3	8	60	2	75	195	230	195	7	78	86	80	70	68	70	70	72	70	70	76	72	74	74	78	93	91	84	82	84	85	87	88	87	91	93	93	97	93	97	100	100	100	99	99	96	99	100	100	100	100	98	97	96	99	
39	268111	36	female	150	51	TAH	4	T6	8	4	3	7	55	3	65	165	195	165	6	70	80	76	68	68	78	64	60	70	66	70	68	70	66	70	93	93	89	86	84	83	85	91	93	96	97	99	99	99	99	96	97	98	96	96	98	97	96	99	98	99	100	100	100	100	
40	269860	45	female	158	52	TAH	3	T6	6	5	3	6	60	4	90	180	225	180	7	86	90	76	66	68	70	70	70	70	70	70	72	70	70	74	97	97	93	89	88	87	91	92	91	95	92	96	100	96	100	100	100	100	100	100	100	100	100	100	100	100	95	94	96	99	
41	268702	48	male	159	52	A	3	T4	7	4	3	8	60	4	85	150	195	150	6	86	98	90	80	66	68	72	72	70	72	70	76	78	80	78	93	93	90	86	83	84	89	87	88	95	99	101	101	101	101	100	100	100	100	99	95	94	96	99	98	99	99	99	99	99	nausea
42	268992	40	female	164	56	TAH	2	T6	7	3	3	8	50	4	75	180	230	180	6	78	88	80	66	64	62	66	66	66	66	70	68	74	80	82	98	95	89	88	91	95	98	97	97	99	100	101	97	101	97	99	98	100	99	99	99	99	99	99	99	97	96	99	100	100	
43	249659	40	female	160	52	TAH	2	T6	8	4	3	7	55	3	80	210	260	210	7	68	76	70	62	60	62	60	66	60	60	66	70	72	70	76	97	98	92	90	85	82	85	87	88	89	92	91	92	91	92	100	100	99	99	99	96	99	100	100	100	100	98	97	96	99	nausea
44	269031	45	male	157	49	A	3	T6	6	5	3	6	40	3	95	180	225	180	7	88	100	84	68	66	62	66	66	68	66	70	68	72	70	74	100	97	92	88	82	84	86	85	87	88	91	91	92	91	92	99	98	99	100	99	98	97	96	99	98	94	99	99	100	100	
45	268571	35	female	158	50	TAH	3	T6	8	4	3	7	60	2	60	165	195	165	7	80	90	80	70	68	70	70	76	70	70	70	74	72	76	74	101	100	93	87	87	88	90	93	92	96	98	97	96	97	96	99	99	97	96	99	99	99	100	100	100	99	99	99	99	99	
46	271072	32	female	154	48	TAH	4	T4	9	4	3	6	60	2	75	150	225	150	7	70	92	76	62	60	66	62	60	66	62	68	66	84	62	66	101	101	98	87	88	90	88	93	95	94	91	91	91	91	91	100	100	100	100	100	100	100	100	100	100	100	99	99	99	99	
47	266348	30	male	159	52	IH	3	T6	6	4	3	6	45	2	80	180	230	180	7	78	86	80	70	68	70	70	72	70	70	76	72	74	74	78	101	101	91	95	81	83	85	88	91	93	92	93	93	93	93	100	100	100	100	99	95	94	96	99	98	99	100	100	100	100	
48	268097	42	female	164	51	TAH	3	T6	9	3	3	6	40	4	70	180	225	180	6	70	80	76	68	68	72	64	66	70	64	70	68	70	66	70	95	101	89	83	80	78	81	79	81	79	83	83	85	83	85	99	98	100	99	99	99	99	99	99	99	97	100	100	100	96	
49	277520	40	female	155	52	TAH	2	T6	7	5	3	7	60	3	90	150	195	150	6	74	86	78	70	68	70	68	66	70	68	70	70	74	70	70	95	95	90	84	81	77	83	83	81	85	87	85	88	85	88	100	100	99	99	99	96	99	100	100	100	100	99	98	99	100	
50	275926	50	male	156	55	IH	3	T6	7	4	3	6	55	4	65	165	200	165	6	84	98	88	78	74	72	72	70	70	72	72	70	74	76	74	95	95	99	85	83	84	86	84	88	86	85	85	89	85	89	99	98	99	100	99	98	97	96	99	98	94	99	99	97	99	

GROUP C

																				HEART RATE															MEAN ARTERIAL PRESSURE															SPO2															
sl no	IP no	age(years)	sex	height (cm)	weight(kg)	surgery	Sensory onset duration (mins)	Maximum sensory level	Maximum sensory blockade duration(mins)	Motor onset duration (mins)	Grade of motor blockade (Bromage scale in grades)	Maximum motor blockade duration(mins)	duration of surgery (min)	Ramsay sedation score	Sensory regression by two segments (mins)	time for rescue analgesia (mins)	Duration of sensory blockade(mins)	Duration of motor blockade(mins)	VAS score	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins	adverse effects
1	278287	43	male	164	48	IH	1	T6	5	1	3	5	60	4	145	340	350	270	5	90	97	102	97	82	86	80	73	74	76	72	70	72	70	72	100	92	84	83	80	77	78	77	77	83	84	85	84	80	80	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
2	220691	34	female	150	52	TAH	1	T4	6	1	3	6	50	2	150	330	320	240	5	118	115	114	110	104	96	94	92	90	92	86	84	88	88	86	98	92	62	62	64	67	78	62	61	80	83	85	85	82	80	95	94	96	99	98	99	99	100	100	100	100	100	100	99	99	hypotension
3	276449	51	female	155	51	TAH	2	T4	5	2	3	5	50	2	120	360	375	300	5	104	102	106	112	107	105	110	105	102	106	104	106	110	102	106	104	102	96	92	84	88	87	83	85	88	90	90	89	92	90	99	99	99	99	99	97	96	99	98	94	96	99	98	99	99	
4	280391	41	female	156	52	TAH	1	T6	6	2	3	5	90	2	135	390	350	290	4	95	96	90	81	72	73	68	67	65	69	68	66	66	70	70	108	109	104	106	98	90	88	86	86	82	88	82	81	86	84	96	99	100	100	100	100	100	100	100	99	99	99	99	99	98	hypotension
5	284469	40	male	165	52	A	2	T6	7	2	3	8	70	2	120	300	410	300	4	98	98	93	102	108	95	83	78	77	76	75	71	74	72	78	98	99	60	60	62	80	66	72	70	66	70	72	74	72	70	98	97	96	99	98	94	96	99	98	99	96	99	100	100	100	
6	285244	38	female	162	56	TAH	1	T6	6	2	3	6	50	2	155	330	350	270	4	90	97	102	97	82	86	80	73	74	76	72	70	72	70	72	99	99	85	74	94	74	81	75	77	79	80	81	80	80	82	99	99	100	100	100	99	99	99	99	96	98	97	96	99	98	
7	282258	37	female	155	52	TAH	1	T6	5	1	3	7	70	2	145	360	380	300	4	76	80	87	85	79	77	73	72	74	76	72	70	74	76	76	94	81	80	77	80	87	85	81	86	88	85	85	82	85	85	100	100	100	100	99	99	96	99	100	100	100	99	99	99	99	
8	296110	46	male	153	49	IH	1	T6	5	1	3	7	60	2	130	330	350	290	4	80	78	74	70	72	78	76	82	80	84	80	78	76	80	78	94	93	90	86	84	87	89	96	94	93	91	93	92	93	91	99	96	97	98	96	96	98	97	96	99	98	94	96	99	98	
9	281286	45	male	160	50	A	2	T6	5	2	3	6	45	4	125	300	325	240	4	100	102	120	119	125	105	102	98	85	80	86	80	74	80	82	90	91	87	84	85	78	68	70	77	77	72	71	71	77	72	100	100	100	100	100	100	100	99	99	100	100	100	100	99	99	
10	285231	45	female	167	48	TAH	1	T6	5	1	3	5	70	2	145	360	380	270	4	78	90	95	93	66	68	60	62	74	76	74	78	80	82	88	100	92	84	83	80	77	78	73	77	83	84	85	83	83	84	97	96	99	98	100	99	99	99	100	100	100	99	96	99	100	
11	288315	42	female	162	52	TAH	1	T6	6	2	3	6	80	2	140	330	360	270	5	95	96	90	81	72	73	68	67	65	69	68	66	66	66	68	108	109	104	106	98	90	88	86	86	82	88	82	81	82	88	100	100	100	100	99	99	100	100	100	100	99	96	98	97	96	
12	286140	45	male	152	51	A	2	T6	7	2	3	8	60	2	150	340	360	300	5	78	73	73	61	64	65	69	61	90	89	89	87	90	88	88	100	92	92	93	93	93	90	106	102	104	97	108	108	104	97	94	96	99	98	99	100	99	96	97	98	96	96	100	100	99	
13	288652	51	female	155	52	TAH	2	T6	6	2	3	7	70	2	130	360	375	270	5	70	66	64	60	66	70	73	78	80	82	80	84	85	80	78	96	91	91	91	93	90	93	103	101	103	96	94	91	103	96	99	99	99	99	97	96	100	100	100	100	100	100	99	99	98	
14	287058	30	female	150	55	TAH	2	T6	7	2	3	8	45	2	135	390	405	300	4	84	82	80	76	78	80	82	84	80	82	84	83	82	80	80	98	94	89	90	88	90	92	97	99	95	93	90	92	95	93	99	99	100	100	100	100	99	99	99	99	99	99	99	100	100	
15	241369	45	male	158	48	A	2	T6	7	2	3	7	50	1	130	330	350	270	4	98	98	93	102	108	95	83	78	77	76	75	71	74	70	68	96	98	92	96	88	90	83	91	80	80	72	73	70	80	72	100	100	100	100	99	99	96	99	100	100	100	100	100	100	100	
16	286625	45	female	159	52	TAH	1	T4	6	1	3	7	45	3	135	360	380	300	5	70	86	80	70	68	68	56	84	84	82	74	72	74	80	82	93	93	97	84	82	81	75	73	75	78	79	80	80	78	79	99	96	97	98	96	96	98	97	96	99	98	99	96	97	98	
17	289939	45	female	164	51	TAH	1	T6	6	2	3	6	40	2	125	340	360	270	5	80	94	80	72	68	66	66	68	66	68	70	68	68	68	68	96	93	90	87	83	81	76	71	79	82	87	90	91	82	87	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
18	2945643	42	male	160	52	IH	1	T6	5	1	3	5	60	3	145	300	330	240	5	78	92	95	93	66	68	59	63	73	76	74	78	80	80	82	100	92	84	83	80	77	78	73	77	83	84	85	84	83	84	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	
19	293421	56	female	157	52	TAH	2	T6	6	2	3	7	65	3	150	360	380	270	5	70	66	64	59	66	70	74	78	80	82	80	84	85	84	84	96	91	91	91	93	90	98	103	101	103	96	94	91	103	96	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
20	295278	50	female	158	56	TAH	1	T6	5	1	3	5	70	3	135	390	410	330	6	80	92	96	93	68	66	60	64	74	76	76	78	80	78	80	100	92	84	83	80	77	78	73	77	83	84	85	83	83	84	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
21	287760	45	male	154	52	IH	2	T6	7	2	3	7	80	3	135	300	330	240	5	98	98	93	102	108	95	83	78	77	76	75	71	74	70	70	98	99	98	92	96	88	90	86	91	80	80	75	94	80	80	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
22	287788	31	female	159	49	TAH	1	T6	6	2	3	6	50	2	140	360	360	270	6	90	97	102	97	82	86	80	73	74	76	72	70	72	72	70	98	98	85	74	68	74	81	75	77	78	81	80	80	81	75	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	
23	296482	45	female	164	50	TAH	2	T4	6	2	3	6	40	2	120	390	380	300	6	104	102	106	112	107	105	110	105	102	106	104	106	110	108	106	104	102	96	92	84	88	87	83	85	88	90	90	89	87	83	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
24	296927	45	female	155	48	TAH	1	T6	5	1	3	7	50	3	130	300	350	270	4	76	80	87	85	79	77	73	72	74	76	72	70	74	76	72	94	81	80	77	80	91	85	83	86	88	85	85	82	85	83	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
25	295266	38	male	156	52	IH	1	T6	5	1	3	7	45	3	150	320	360	290	5	30	78	74	70	72	78	76	82	80	84	80	78	76	84	80	94	93	90	86	84	87	89	96	94	93	91	93	92	89	96	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	
26	296913	39	male	164	51	IH	2	T6	5	2	3	6	60	2	120	360	380	270	6	100	102	120	119	125	105	102	98	85	80	86	80	74	76	72	58	90	91	87	87	85	78	86	70	77	72	72	71	78	86	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
27	297440	45	female	150	52	TAH	2	T6	7	2	3	8	45	3	135	300	350	240	5	78	73	73	61	64	65	69	61	90	89	89	87	90	84	80	100	92	92	93	93	93	90	106	102	104	97	108	108	90	106	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
28	295268	50	female	155	55	TAH	2	T4	7	1	3	8	50	2	145	360	360	300	4	84	82	80	76	78	80	82	84	80	82	84	83	82	76	72	98	94	89	90	88	90	92	97	99	94	93	90	92	92	97	98	97	96	99	98	94	96	99	98	99	96	99	100	100	100	
29	190873	42	male	156	48	IH	1	T6	6	2	3	5	50	3	150	340	380	270	5	80	82	84	76	64	64	66	68	66	68	70	68	72	84	80	96	93	91	85	81	80	75	77	78	80	81	82	85	75	77	99	99	100	100	100	99	99	99	99	96	98	97	96	99	98	
30	259824	36	female	165	52	TAH	1	T6	7	2	3	7	60	2	120	390	410	330	6	70	82	60	52	98	90	92	88	90	84	80	82	88	80	82	90	85	79	77	78	79	79	82	82	83	85	82	84	79	82	100	100	100	100	99	99	96	99	100	100	100	99	99	99	99	bradycardia
31	245302	43	male	162	51	IH	2	T6	7	2	3	7	45	3	145	340	350	270	5	118	115	114	110	104	96	94	92	90	92	86	84	88	88	86	99	99	85	74	94	74	81	75	77	79	80	81	80	80	82	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	
32	300255	40	female	155	52	TAH	1	T4	6	1	3	7	50	2	150	330	320	240	6	104	102	106	112	107	105	110	105	102	106	104	106	110	102	106	94	81	80	77	80	87	85	81	86	88	85	85	82	85	85	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
33	296936	45	male	153	55	IH	1	T6	6	2	3	6	45	2	120	360	375	300	5	95	96	90	81	72	73	68	67	65	69	68	66	66	70	70	94	93	90	86	84	87	89	96	94	93	91	93	92	93	91	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
34	201270	40	male	160	50	IH	1	T6	5	1	3	5	40	2	135	390	350	290	4	98	98	93	102	108	95	83	78	77	76	75	71	74	72	78	90	91	87	84	85	78	68	70	77	77	72	71	71	77	72	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
35	301805	43	male	167	48	IH	2	T6	6	2	3	7	60	3	120	300	410	300	4	90	97	102	97	82	86	80	73	74	76	72	70	72	70	72	100	92	84	83	80	77	78	73	77	83	84	85	83	83	84	95	94	96	99	98	99	99	100	100	100	100	100	100	99	99	
36	301632	45	female	162	52	TAH	1	T6	5	1	3	5	65	3	155	330	350	270	4	76	80	87	85	79	77	73	72	74	76	72	70	74	76	76	108	109	104	106	98	90	88	86	86	82	88	82	81	82	88	99	99	99	99	99	97	96	99	98	94	96	99	98	99	99	
37	299197	56	female	152	51	TAH	2	T6	7	2	3	7	70	2	145	360	380	300	4	80	78	74	70	72	78	76	82	80	84	80	78	76	80	78	100	92	92	93	93	93	90	106	102	104	97	108	108	104	97	96	99	100	100	100	100	100	100	100	99	99	99	99	99	98	
38	300561	45	male	155	52	IH	1	T6	6	2	3	6	80	3	130	330	350	290	4	100	102	120	119	125	105	102	98	85	80	86	80	74	80	82	96	91	91	91	93	90	93	103	101	103	96	94	91	103	96	98	97	96	99	98	94	96	99	98	99	96	99	100	100	100	
39	295782	45	female	150	55	TAH	2	T4	6	2	3	6	50	3	125	300	325	240	6	78	90	95	93	66	68	60	62	74	76	74	78	80	82	88	98	94	89	90	88	90	92	97	99	95	93	90	92	95	93	99	99	100	100	100	99	99	99	99	96	98	97	96	99	98	
40	303900	40	male	158	48	IH	1	T6	5	1	3	7	40	2	145	360	380	270	5	95	96	90	81	72	73	68	67	65	69	68	66	66	66	68	96	98	92	96	88	90	83	91	80	80	72	73	70	80	72	100	100	100	100	99	99	96	99	100	100	100	99	99	99	99	
41	304394	40	female	159	52	TAH	1	T6	5	1	3	7	50	3	140	330	360	270	7	80	92	96	93	68	66	60	64	74	76	76	78	80	78	80	93	93	97	84	82	81	75	73	75	78	79	80	80	78	79	99	96	97	98	96	96	98	97	96	99	98	94	96	99	98	
42	303301	40	male	164	51	IH	2	T6	5	2	3	6	45	3	150	340	360	300	6	98	98	93	102	108	95	83	78	77	76	75	71	74	70	70	96	93	90	87	83	81	76	71	79	82	87	90	91	82	87	100	100	100	100	100	100	100	99	99	100	100	100	100	99	99	
43	304386	45	female	160	50	TAH	2	T6	7	2	3	8	60	2	130	360	375	270	5	90	97	102	97	82	86	80	73	74	76	72	70	72	72	70	90	91	87	84	85	78	68	70	77	77	72	71	71	77	72	97	96	99	98	100	99	99	99	100	100	100	99	96	99	100	
44	303485	45	male	157	48	IH	2	T4	7	1	3	8	45	2	135	390	405	300	4	104	102	106	112	107	105	110	105	102	106	104	106	110	108	106	100	92	84	83	80	77	78	73	77	83	84	85	83	83	84	100	100	100	100	99	99	100	100	100	100	99	96	98	97	96	
45	307109	48	female	158	52	TAH	1	T6	6	2	3	5	50	2	130	330	350	270	5	76	80	87	85	79	77	73	72	74	76	72	70	74	76	72	108	109	104	106	98	90	88	86	86	82	88	82	81	82	88	94	96	99	98	99	100	99	96	97	98	96	96	100	100	99	
46	305279	40	male	154	51	IH	1	T6	7	2	3	7	50	2	135	360	380	300	6	30	78	74	70	72	78	76	82	80	84	80	78	76	84	80	100	92	92	93	93	93	90	106	102	104	97	108	108	104	97	99	99	99	99	97	96	100	100	100	100	100	100	99	99	98	
47	310851	45	female	159	52	TAH	2	T4	6	2	3	6	60	2	125	340	360	270	5	100	102	120	119	125	105	102	98	85	80	86	80	74	76	72	96	91	91	91	93	90	93	103	101	103	96	94	91	103	96	99	99	100	100	100	100	99	99	99	99	99	99	99	100	100	
48	314619	45	male	164	55	IH	1	T6	5	1	3	7	45	2	145	300	330	240	5	78	73	73	61	64	65	69	61	90	89	89	87	90	84	80	98	94	89	90	88	90	92	97	99	95	93	90	92	95	93	100	100	100	100	99	99	96	99	100	100	100	100	100	100	100	
49	315533	43	female	155	48	TAH	1	T6	5	1	3	7	60	3	150	360	380	270	5	84	82	80	76	78	80	82	84	80	82	84	83	82	76	72	96	98	92	96	88	90	83	91	80	80	72	73	70	80	72	99	96	97	98	96	96	98	97	96	99	98	99	96	97	98	
50	308690	45	male	156	52	IH	2	T6	5	2	3	6	45	2	135	390	410	330	5	80	82	84	76	64	64	66	68	66	68	70	68	72	84	80	90	68	62	76	66	60	72	68	62	76	72	76	78	72	78	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	hypotension

GROUP D

sl no	IP no	age(years)	sex	height (cm)	weight(kg)	surgery	Sensory onset duration (mins)	Maximum sensory level	Maximum sensory blockade duration(mins)	Motor onset duration(mins)	Grade of motor blockade (Bromage scale in grades)	Maximum motor blockade duration(mins)	duration of surgery (min)	Ramsay sedation score	Sensory regression by two segments (mins)	time for rescue analgesia (mins)	Duration of sensory blockade(mins)	Duration of motor blockade(mins)	VAS score
1	314473	43	female	150	52	TAH	1	T6	5	1	3	6	50	2	120	390	420	300	5
2	311976	40	male	158	55	IH	1	T6	5	1	3	6	45	2	135	420	440	360	5
3	319625	46	female	159	48	TAH	1	T4	6	1	3	6	60	2	140	390	420	300	5
4	319573	45	female	164	52	TAH	1	T4	6	1	3	6	40	3	145	360	395	300	4
5	318660	55	male	160	51	IH	1	T6	7	1	3	7	50	2	130	330	360	270	4
6	319524	45	female	157	52	TAH	1	T6	6	2	3	5	50	3	145	360	380	270	4
7	319976	52	female	158	55	A	2	T6	5	2	3	4	45	2	150	420	440	290	4
8	321880	41	female	154	50	A	1	T6	5	1	3	5	55	2	120	360	385	300	4
9	323367	45	male	159	48	A	1	T6	5	1	3	6	60	3	150	390	415	360	4
10	323611	46	female	164	52	TAH	1	T4	5	1	3	4	50	2	130	330	360	270	4
11	91141	42	female	155	51	TAH	1	T6	5	1	3	6	60	2	150	360	390	330	4
12	320900	56	male	156	52	IH	2	T4	6	1	3	6	50	3	135	420	440	360	4
13	25854	55	male	150	55	IH	1	T6	6	1	3	6	45	5	120	390	415	300	5
14	310304	55	female	158	48	TAH	2	T6	5	1	3	6	60	2	145	360	390	300	5
15	334897	43	male	159	52	IH	1	T4	6	2	3	5	50	3	135	420	445	360	5
16	339386	40	female	164	51	TAH	1	T4	5	1	3	5	70	2	135	360	385	300	5
17	342470	46	female	160	50	TAH	1	T4	4	1	3	4	60	3	150	390	410	300	5
18	336624	45	male	157	48	IH	1	T6	6	1	3	6	40	2	120	330	360	270	5
19	331031	55	female	158	52	TAH	1	T4	5	1	3	4	50	2	130	360	390	300	6
20	332257	45	male	154	51	IH	1	T4	5	1	3	5	50	3	150	300	335	240	6
21	337091	52	male	159	52	IH	2	T6	5	2	3	5	45	2	140	300	375	270	6
22	329921	41	male	164	55	IH	1	T4	5	1	3	4	50	2	150	390	410	330	5
23	259233	45	female	155	48	TAH	1	T6	5	1	3	4	45	2	150	360	380	270	6
24	347168	46	male	156	52	IH	1	T6	4	1	3	4	45	3	120	420	440	360	5
25	348157	43	male	159	52	IH	1	T4	5	1	3	6	45	2	130	300	335	240	4

sl no	HEART RATE														
	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins
1	84	82	78	76	75	72	77	80	78	76	82	84	80	84	80
2	88	88	86	84	85	86	88	88	90	90	88	84	86	84	86
3	80	80	76	73	74	76	80	84	82	86	84	83	86	83	86
4	68	67	64	56	54	65	73	72	74	76	72	78	74	78	74
5	73	81	68	69	72	76	67	68	66	70	72	68	66	68	66
6	80	82	56	53	62	60	62	64	66	64	66	64	66	64	66
7	72	90	78	68	60	60	62	64	62	60	66	68	74	68	74
8	76	84	72	64	62	64	66	68	64	66	64	66	68	66	68
9	110	114	110	112	114	95	90	92	93	94	91	96	94	96	94
10	120	123	117	60	67	93	80	86	90	84	88	91	85	91	85
11	84	82	78	76	75	72	77	80	78	76	82	84	80	84	80
12	88	88	86	84	85	86	88	88	90	90	88	84	86	84	86
13	73	81	68	69	72	76	67	68	66	70	72	68	66	68	66
14	68	67	64	56	54	65	73	72	74	76	72	78	74	78	74
15	80	96	78	70	62	60	62	64	66	64	66	64	66	64	66
16	120	123	117	60	67	93	80	86	90	84	88	91	85	91	85
17	118	120	119	100	80	77	86	82	90	92	94	86	84	86	84
18	106	108	108	110	77	79	75	80	90	90	95	92	94	92	94
19	79	78	80	81	80	78	76	70	72	74	76	78	78	78	78
20	98	107	97	91	84	62	70	84	89	92	91	96	100	96	100
21	72	90	78	68	60	60	62	64	62	60	66	68	70	68	70
22	90	94	110	104	96	84	90	87	88	86	90	84	82	84	82
23	84	94	78	70	68	70	70	68	70	70	92	74	76	74	76
24	100	105	110	105	106	97	89	90	92	98	100	98	96	98	96
25	82	94	80	78	76	72	64	62	62	60	60	62	66	62	66

sl no	MEAN ARTERIAL PRESSURE														
	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins
1	104	104	99	98	95	98	94	99	96	95	93	92	93	92	93
2	100	99	99	94	98	94	100	100	103	99	100	99	98	99	98
3	99	98	94	91	92	91	92	95	94	92	94	91	95	91	95
4	83	85	86	84	85	84	82	78	89	84	83	80	83	80	83
5	98	99	93	96	91	96	86	89	86	91	89	91	86	91	86
6	94	95	89	85	80	85	77	78	81	81	81	81	83	81	83
7	104	98	92	89	82	89	77	78	81	83	83	83	85	83	85
8	94	95	89	85	80	85	77	78	81	81	81	81	83	81	83
9	92	105	90	83	80	83	82	81	81	83	81	82	80	82	80
10	109	105	97	79	85	79	85	87	84	86	92	86	88	86	88
11	104	104	99	98	95	98	94	99	96	95	93	92	93	92	93
12	100	99	99	94	98	94	100	100	103	99	100	99	98	99	98
13	98	99	62	60	70	76	60	72	68	70	72	72	70	80	86
14	85	86	84	77	82	77	78	84	84	83	80	83	83	83	83
15	94	95	89	85	80	85	77	78	81	81	81	81	83	81	83
16	109	105	97	79	85	79	85	87	84	86	92	86	88	86	88
17	94	82	79	63	71	63	84	85	80	79	84	84	85	84	85
18	104	84	81	66	66	66	66	75	89	87	81	84	83	84	83
19	103	86	88	90	74	90	81	80	79	83	82	85	85	85	85
20	72	90	83	76	66	76	65	73	77	81	81	87	90	87	90
21	104	98	92	89	82	89	77	78	81	83	83	83	85	83	85
22	88	103	104	100	90	100	87	83	84	83	87	87	88	87	88
23	85	86	82	80	77	80	75	75	73	75	77	77	79	77	79
24	97	98	95	93	109	93	97	93	91	93	98	96	97	96	97
25	83	81	73	75	71	75	75	77	78	77	80	81	83	81	83

sl no	SPO2															
	basal	0 mins	2 mins	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	40 mins	50 mins	60 mins	70 mins	80 mins	90 mins	adverse effects
1	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
2	95	94	96	99	98	99	99	100	100	100	100	100	100	99	99	
3	99	99	99	99	99	97	96	99	98	94	96	99	98	99	99	
4	96	99	100	100	100	100	100	100	100	99	99	99	99	99	98	
5	98	97	96	99	98	94	96	99	98	99	96	99	100	100	100	
6	99	99	100	100	100	99	99	99	99	96	98	97	96	99	98	bradycardia
7	100	100	100	100	99	99	96	99	100	100	100	99	99	99	99	
8	99	96	97	98	96	96	98	97	96	99	98	94	96	99	98	
9	100	100	100	100	100	100	100	99	99	100	100	100	100	99	99	
10	97	96	99	98	100	99	99	99	100	100	100	99	96	99	100	
11	100	100	100	100	99	99	100	100	100	100	99	96	98	97	96	
12	94	96	99	98	99	100	99	96	97	98	96	96	100	100	99	
13	99	99	99	99	97	96	100	100	100	100	100	100	99	99	98	hypotension
14	99	99	100	100	100	100	99	99	99	99	99	99	99	100	100	
15	100	100	100	100	99	99	96	99	100	100	100	100	100	100	100	
16	99	96	97	98	96	96	98	97	96	99	98	99	96	97	98	
17	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	nausea
18	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	
19	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
20	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
21	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
22	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	
23	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
24	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
25	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	

26	349716	40	male	164	55	IH	1	T4	4	1	3	5	60	3	120	330	360	270	4	120	123	110	59	66	93	80	86	90	84	88	91	85	91	85	109	105	97	79	85	79	85	87	84	86	92	86	88	86	88	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
27	349498	46	female	155	48	TAH	1	T4	4	1	3	4	45	2	145	360	390	300	4	118	120	119	100	80	70	86	82	90	92	94	86	84	86	84	94	82	79	63	71	63	84	85	80	79	84	84	85	84	85	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
28	348504	45	female	156	52	TAH	2	T6	5	1	3	5	50	3	150	390	410	360	4	76	84	72	64	62	64	66	68	64	66	66	64	66	64	66	94	95	89	85	80	85	77	78	81	81	81	81	83	81	83	98	97	96	99	98	94	96	99	98	99	96	99	100	100	100	
29	351822	55	female	150	51	A	1	T6	6	1	3	6	60	4	130	390	420	330	4	106	108	108	110	77	79	75	80	90	95	92	94	98	94	98	84	81	66	65	66	65	75	89	87	81	82	84	83	84	83	99	99	100	100	100	99	99	99	99	96	98	97	96	99	98	
30	349064	45	female	158	52	TAH	1	T4	5	1	3	5	50	3	120	360	390	300	5	79	78	80	82	80	78	76	70	72	74	76	78	78	78	78	103	86	88	90	74	90	81	80	79	83	82	85	85	85	85	100	100	100	100	99	99	96	99	100	100	100	99	99	99	99	
31	351702	52	female	159	55	A	2	T6	5	2	3	4	45	2	150	420	440	290	4	72	90	78	68	60	60	62	64	62	60	66	68	74	68	74	104	98	92	89	82	89	77	78	81	83	83	83	85	83	85	100	100	100	100	100	99	95	94	96	99	98	99	99	100	100	
32	351884	41	female	164	50	TAH	1	T6	5	1	3	5	55	2	120	360	385	300	4	76	84	72	64	62	64	66	68	64	66	64	66	68	66	68	94	95	89	85	80	85	77	78	81	81	81	81	83	81	83	96	99	98	100	99	99	99	99	99	99	99	97	96	99	98	
33	350056	45	female	160	48	A	1	T6	5	1	3	6	60	3	150	390	415	360	4	110	114	110	112	114	95	90	92	93	94	91	96	94	96	94	92	105	90	83	80	83	82	81	81	83	81	82	80	82	80	100	100	100	99	99	99	96	99	100	100	100	100	100	100	100	
34	353043	46	female	157	52	TAH	1	T4	5	1	3	4	50	2	130	330	360	270	4	120	123	117	60	67	93	80	86	90	84	88	91	85	91	85	109	105	97	79	85	79	85	87	84	86	92	86	88	86	88	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
35	353863	43	female	158	51	TAH	1	T6	5	1	3	6	60	2	150	360	390	330	4	84	82	78	76	75	72	77	80	78	76	82	84	80	84	80	104	104	99	98	95	98	94	99	96	95	93	92	93	92	93	95	94	96	99	98	99	99	100	100	100	100	100	100	99	99	
36	350606	40	male	154	52	A	2	T4	6	1	3	6	50	3	135	420	440	360	4	88	88	86	84	85	86	88	88	90	90	88	84	86	84	86	100	99	99	94	98	94	100	100	103	99	100	99	98	99	98	99	99	99	99	99	97	96	99	98	94	96	99	98	99	99	
37	329939	46	male	159	55	A	1	T6	6	1	3	6	45	5	120	390	415	300	5	73	81	68	69	72	76	67	68	66	70	72	68	66	68	66	98	99	62	60	70	76	60	72	68	70	72	72	70	80	86	96	99	100	100	100	100	100	100	100	99	99	99	99	99	98	
38	330042	45	female	159	48	TAH	2	T6	5	1	3	6	60	2	145	360	390	300	5	68	67	64	56	54	65	73	72	74	76	72	78	74	78	74	85	86	84	77	82	77	78	84	84	83	80	83	83	83	83	98	97	96	99	98	94	96	99	98	99	96	99	100	100	100	
39	330305	55	female	164	52	TAH	1	T4	6	2	3	5	50	3	135	420	445	360	5	80	96	78	70	62	60	62	64	66	64	66	64	66	64	66	94	95	89	85	80	85	77	78	81	81	81	81	83	81	83	99	99	100	100	100	99	99	99	99	96	98	97	96	99	98	
40	321848	45	female	155	51	A	1	T4	5	1	3	5	70	2	135	360	385	300	5	120	123	117	60	67	93	80	86	90	84	88	91	85	91	85	109	105	97	79	85	79	85	87	84	86	92	86	88	86	88	100	100	100	100	99	99	96	99	100	100	100	99	99	99	99	
41	329145	52	female	156	50	TAH	1	T4	4	1	3	4	60	3	150	390	410	300	5	118	120	119	100	80	77	86	82	90	92	94	86	84	86	84	94	82	79	63	71	63	84	85	80	79	84	84	85	84	85	99	96	97	98	96	96	98	97	96	99	98	94	96	99	98	
42	330995	41	female	150	48	TAH	1	T6	6	1	3	6	40	2	120	330	360	270	5	106	108	108	110	77	79	75	80	90	90	95	92	94	92	94	104	84	81	66	66	66	66	75	89	87	81	84	83	84	83	100	100	100	100	100	100	100	99	99	100	100	100	100	99	99	
43	328054	45	female	158	52	TAH	1	T4	5	1	3	4	50	2	130	360	390	300	6	79	78	80	81	80	78	76	70	72	74	76	78	78	78	78	103	86	88	90	74	90	81	80	79	83	82	85	85	85	85	97	96	99	98	100	99	99	99	100	100	100	99	96	99	100	
44	333042	46	female	159	51	TAH	1	T4	5	1	3	5	50	3	150	300	335	240	6	98	107	97	91	84	62	70	84	89	92	91	96	100	96	100	72	90	83	76	66	76	65	73	77	81	81	87	90	87	90	100	100	100	100	99	99	100	100	100	100	99	96	98	97	96	
45	322598	43	female	164	52	TAH	2	T6	5	2	3	5	45	2	140	300	375	270	6	72	90	78	68	60	60	62	64	62	60	66	68	70	68	70	104	98	92	89	82	89	77	78	81	83	83	83	85	83	85	94	96	99	98	99	100	99	96	97	98	96	96	100	100	99	
46	334002	40	male	160	55	IH	1	T4	5	1	3	4	50	2	150	390	410	330	5	90	94	110	104	96	84	90	87	88	86	90	84	82	84	82	88	103	104	100	90	100	87	83	84	83	87	87	88	87	88	99	99	99	99	97	96	100	100	100	100	100	100	99	99	98	
47	335749	46	male	157	48	IH	1	T6	5	1	3	4	45	2	150	360	380	270	6	84	94	78	70	68	70	70	68	70	70	92	74	76	74	76	85	86	82	80	77	80	75	75	73	75	77	77	79	77	79	99	99	100	100	100	100	99	99	99	99	99	99	99	100	100	
48	324567	45	female	158	52	TAH	1	T6	4	1	3	4	45	3	120	420	440	360	5	100	105	110	105	106	97	89	90	92	98	100	98	96	98	96	97	98	95	93	109	93	97	93	91	93	98	96	97	96	97	100	100	100	100	99	99	96	99	100	100	100	100	100	100	100	
49	324516	55	female	154	50	TAH	1	T4	5	1	3	6	45	2	130	300	335	240	4	82	94	80	78	76	72	64	62	62	60	60	62	66	62	66	83	81	73	75	71	75	75	77	78	77	80	81	83	81	83	99	96	97	98	96	96	98	97	96	99	98	99	96	97	98	
50	324678	45	male	159	46	IH	1	T4	4	1	3	5	60	3	120	330	360	270	4	120	123	110	59	66	93	80	86	90	84	88	91	85	91	85	109	105	97	79	85	79	85	87	84	86	92	86	88	86	88	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	