"RANDOMISED CLINICAL TRIAL TO ASSESS THE EFFICACY OF ADDITION OF FEMORAL NERVE BLOCK WITH 0.2% ROPIVACAINE TO EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN RELIEF AFTER TOTAL KNEE ARTHROPLASTY"

BY

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Dissertation

Submitted to

KAHER, Belagavi, Karnataka,

In partial fulfilment of the requirements for the degree of

M.D.

In

ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY,

JAWAHARLAL NEHRU MEDICAL COLLEGE,

BELAGAVI, KARNATAKA

DECEMBER 2024/JANUARY 2025

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With reference to the above, we wish to inform you that your proposed research project titled **"RANDOMISED CLINICAL TRIAL TO ASSESS THE EFFICACY OF ADDITION OF FEMORAL NERVE BLOCK WITH 0.2% ROPIVACAINE TO EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN RELIEF AFTER TOTAL KNEE ARTHROPLASTY."** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

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ABBREVIATIONS

TKA	**–**	**TOTAL KNEE ARTHROPLASTY**
ACB	**–**	**ADDUCTOR CANAL BLOCK**
FNB	**–**	**FEMORAL NERVE BLOCK**
LOS	**–**	**LENGTH OF HOSPITAL STAY**
NSAIDS	**–**	**NON- STEROIDAL ANTI INFLAMMATORY DRUGS**
MHz	**–**	**MEGAHERTZ**
IVRA	**–**	**INTRAVENOUS REGIONAL ANAESTHESIA**
VAS	**–**	**VISUAL ANALOG SCORE**
NIBP	**–**	**NON INVASIVE BLOOD PRESSSURE**
SD	**–**	**STANDARD DEVIATION**
t	**–**	**TWO SAMPLE T TEST**
MW	**–**	**MANN WHITNEY U TEST**
F	**–**	**FRIED'SMAN TEST**
PCA	**–**	**PATIENT CONTROLLED ANALGESIA**

ABSTRACT

TITLE: "RANDOMISED CLINICAL TRIAL TO ASSESS THE EFFICACY OF ADDITION OF FEMORAL NERVE BLOCK WITH 0.2% ROPIVACAINE TO EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN RELIEF AFTER TOTAL KNEE ARTHROPLASTY".

Background & Aims

Femoral nerve block is a safe, easy and excellent technique of post-operative analgesia after Total Knee Arthroplasty which became even more safer under Ultrasound guidance. The aim of the study is assess analgesic efficacy between Epidural analgesia alone vs Epidural analgesia and Femoral nerve block after Total Knee Arthroplasty.

SETTING AND DESIGN: A ONE-YEAR RANDOMISED CLINICAL TRIAL.

MATERIALS AND METHODS:

A total of 60 adult patients of either sex, ASA grade I – II- III, scheduled for Total Knee Arthroplasty were enrolled in the study and randomised into two groups. Post operatively, Group EF received 15ml of 0.2% Ropivacaine along with epidural analgesia. Group E received epidural alone. Post operative analgesia up to 24 hours and the rescue analgesics used were recorded.

RESULT:

Combined Epidural analgesia and Femoral nerve block (Group EF) patients showed lower VAS scores, better post operative analgesia and consumed less rescue analgesics when compared to Epidural alone (Group E) patients .

CONCLUSION:

The analgesic efficacy of Combined Epidural analgesia and Femoral Nerve Block was superior than Epidural analgesia alone and also there is lower consumption of rescue analgesics in combined Epidural analgesia and Femoral Nerve Block patients than Epidural analgesia alone.

KEYWORDS: Epidural anaesthesia, Ropivacaine, Femoral nerve block, total knee arthroplasty.

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INTRODUCTION

Total knee Arthroplasty (TKA) is a familiar orthopaedic surgical- procedure and a primary mode of treatment for end-stage arthritic knee disease for the betterment of patient's quality of life and enhance mobility and reduce pain. TKA is linked with moderate to severe pain during the perioperative period which indirectly causes low patient's satisfaction, increase in length of hospital stay (LOS), & functional recovery after the surgery. Proper pain relief protocols are essential during the early postoperative period to enable ambulation, initiation of physiotherapy, and for better patient comfort [1]. A multimodal approach to combat post operative pain after TKA has been commonly utilized and has consisted of combination of oral and intravenous analgesics (NSAIDS and Opioids), which can cause side effects like nausea, vomiting, gastritis, pruritus, headache etc.

Epidural analgesia is widely used alone or in combination with oral or intravenous analgesics to manage post operative pain.

Recently, there has been a growing interest in localized pain management techniques such as peri-articular infiltration, Adductor canal block, Femoral nerve block (FNB)due to their effectiveness in providing analgesia for longer duration.

Continuous Epidural analgesia provided via an epidural catheter though effective in post operative pain management after Total Knee Arthroplasty, many a times requires supplemental NSAIDS or opioids which can be associated with several side effects.

Literature search did not reveal any study comparing Epidural analgesia vs Combined Epidural analgesia with Femoral Nerve Block for post operative pain after Total Knee Arthroplasty.

Here in, we propose to conduct the present study to compare Epidural analgesia and Epidural analgesia with Femoral Nerve Block using relatively newer drug ropivacaine for postoperative pain after Total Knee Arthroplasty.

Our Null hypothesis is that the two methods are equally effective in relieving the post operative pain after Total Knee Arthroplasty.

OBJECTIVE OF THE STUDY

Primary Objective-To assess analgesic efficacy between "Epidural analgesia alone vs Epidural analgesia with Femoral Nerve Block for Total Knee Arthroplasty patients".

Secondary Objective- To assess the total amount of rescue analgesics used for post operative pain for 24hrs.

REVIEW OF LITERATURE

Total knee arthroplasty (TKA) is a common orthopaedic procedure that typically results in moderate to severe postoperative pain. Effective analgesia is crucial not only for patient comfort but also to aid in physiotherapy and rehabilitation, reduce hospital stays, and enhance overall recovery. A multimodal analgesic regimen, incorporating nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and regional anaesthesia, is commonly employed. Epidural analgesia is the predominant regional technique used for pain relief following Total Knee Arthroplasty[2].

Keith R.Reinhardt et.al., Conducted a Randomized Clinical Trial on 102 Patients undergoing Elective Total Knee Arthroplasty to compare "Intra articular analgesia Vs Epidural Analgesia And Femoral Nerve Block(FNB)" after TKA and found that both the techniques are equally effective for pain relief after TKA.[3]

In a study carried out by Petchara Subdarathiti et al., on patients undergoing Total Knee Arthroplasty to asses post operative analgesia and rehabilitation after TKA in patients receiving "Continuous Femoral Nerve Block and Continuous Epidural Infusion of 0.125% Levo Bupivacaine" observed that optimal analgesia with fewer side effect and greater patient satisfaction with improved rehabilitation indices in patients receiving Continuous Femoral Nerve Block[4].

Andrea Casati et al., from a prospective randomised multicentre trial to evaluate pain relief following Total Knee Arthroplasty using "Continuous Epidural infusion of 0.125% Bupivacaine or Intravenous patient – controlled analgesia with morphine" concluded that post operative pain scores were significantly less in Continuous Epidural infusion[5].

In a study done by Myung ku Kim et al., on effectiveness of "Continuous Femoral Nerve Block, Epidural patient- controlled analgesia and Periarticular injection for pain relief in patients undergoing TKA" concluded that Continuous Femoral Nerve Block was more effective analgesic technique, that epidural patient - controlled analgesia or peri articular injection for acute post operative pain control for 24 hrs after total knee arthroplasty [6].

Chang.Kil .Park et.al., from an observational clinical trial to evaluate the minimal effective infusion rate of 0.125% Bupivacaine for continuous Femoral nerve block after Total Knee Arthroplasty concluded that 4ml/hr of 0.125% bupivacaine provided adequate pain relief.[7]

A study done by Georgio Z. Karpetas et al., on three different analgesic techniques "Continuous Epidural analgesia, Continuous Intra-articular infusion analgesia and Continuous Femoral nerve block" in post operative pain management after Total Knee arthroplasty concluded that numerical rating score at rest, at passive and active movement did not show any statistically significant differences among the three groups[8].

Harshil J Gandhi et al., after a randomized clinical trial to compare "Continuous femoral nerve block and continuous epidural infusion using 0.2% ropivacaine for post operative analgesia and knee rehabilitation after TKA" observed both technique are equally effective for post operative analgesia.[9]

In a Study, done by Aya Mahmoud et.al., on "Saphenous nerve block versus Femoral Nerve block" has concluded that in contrast to Femoral nerve block,

Saphenous nerve block is a superior mode of analgesia post- total knee arthroplasty by safeguarding quadriceps motor strength and facilitating prompt mobilization.[10]

Donghai li et al., conducted a study, on "Ultrasound guided Adductor canal block combined with lateral Femoral cutaneous nerve block for postoperative pain following Total Knee Arthroplasty" emphasised that, it provides a significantly better pain control by safeguarding muscle function without impeding functional recovery.[11]

Dauri .M et al. carried out a study, comparing "Epidural, Continuous Femoral block and Intra-articular analgesia for pain management after anterior cruciate ligament reconstruction" concluded that Epidural or Continuous Femoral nerve block provided adequate pain relief than Intra-articular analgesia.[12]

BASIC SCIENCES

Applied Anatomy

An anaesthesiologist requires to have an accurate and in depth knowledge of the anatomy of vertebral column and its contents for a safe and successful administration of epidural anaesthesia, not only in terms of performance but also in terms of spread of drug in epidural space and level of block achieved.

Vertebral column

Main function of vertebral column is to protect the spinal cord. There are 33 vertebrae in vertebral column which includes

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

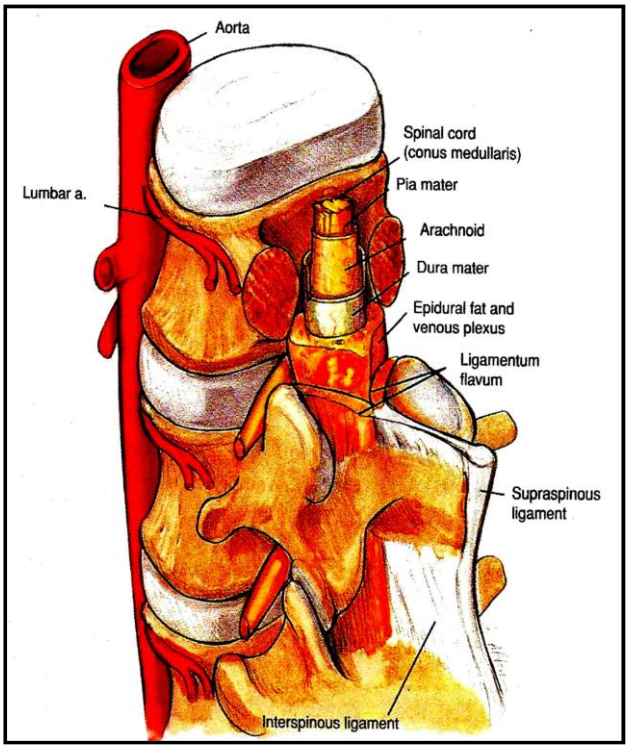
Curves of spine

In adults, curves of vertebral column have significant effect on spread of drugs in subarachnoid space and these curves are:[13]

- Cervical curve - Convexity anterior
- Thoracic curve - Concave anterior
- Lumbar curve - Convexity anteriorly

Cervical (C) five and lumbar (L) five are the highest points of cervical and lumbar curves in supine position and the lowest points of thoracic and sacral are at thoracic (T) five and sacral (S) two respectively.[13]

Figure 1: Vertebral Column



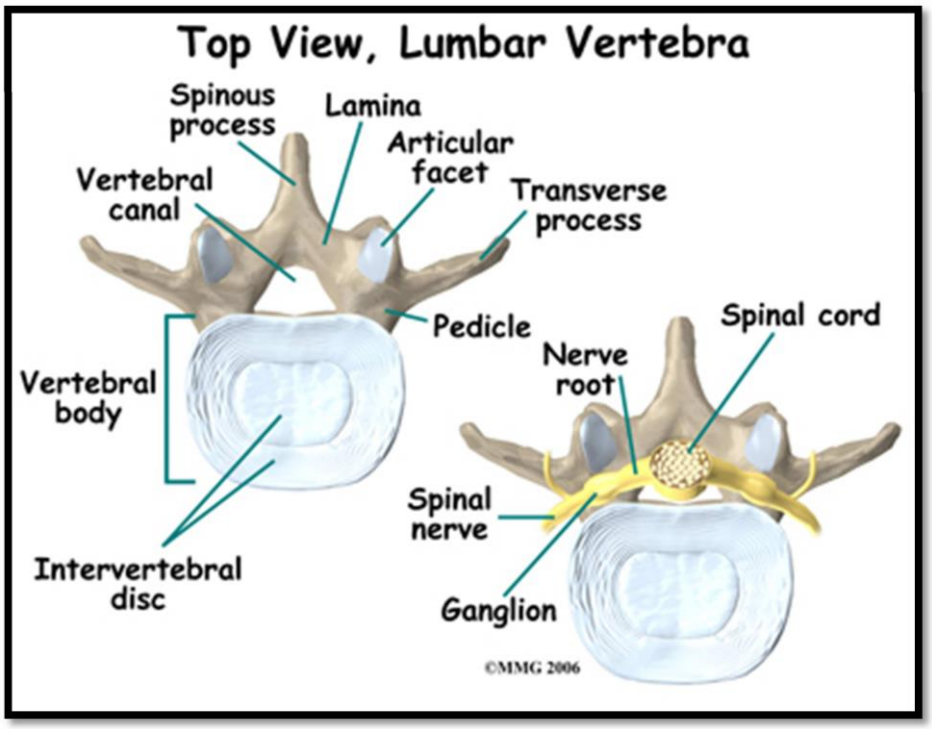
Lumbar vertebrae

A typical lumbar vertebra consists of:

- A kidney shaped body.
- Two pedicles directed backwards from the upper part of the body.
- Two transverse processes
- Two laminae meeting posteriorly and enclosing the triangular vertebral foramen.
- Thick, broad and quadrilateral spinous processes.

- Two upper and lower articular processes which prevent rotation but allow limited flexion and extension between contiguous vertebrae.

Figure 2: Typical lumbar vertebra



Thoracic vertebrae :

- A heart shaped body
- A small costal demi facet on superior border of lateral side of body and a larger demi facet on the inferior surface
- Shallow superior vertebral notches and deeper inferior vertebral notches
- Transverse processes are directed backwards and laterally , carrying a costal facet for articulation with ribs.

Vertebral ligaments

The following overlapping ligaments provide stability to the vertebral column and protect the spinal cord :

Supraspinous ligament: This is a strong fibrous cord which connects apices of spinous processes from sacrum to C_5 where it is continued as the ligamentum nuchae . The width depends upon the width of the spinous process – in lumbar region it might be upto 1 cm wide. In elderly people and manual labourers this ligament calcifies thus making the midline approach difficult.

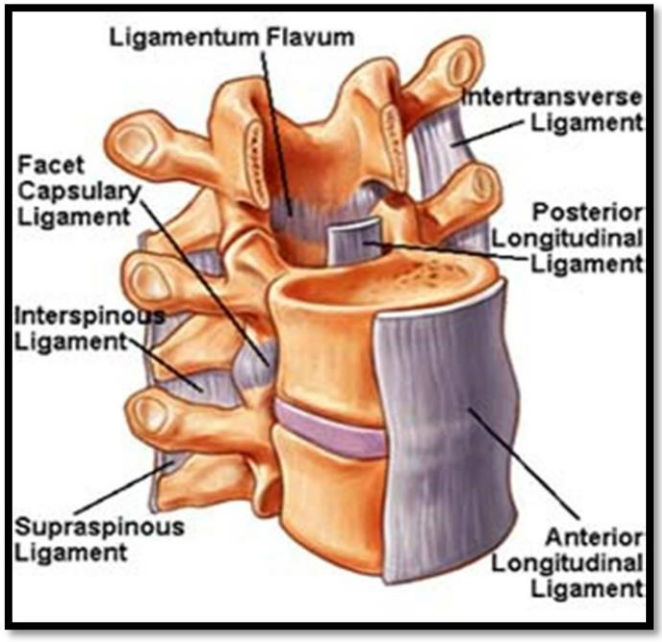
Interspinous ligament: This is a thin membranous ligament running obliquely and connecting spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament. In the lumbar region, this ligament is rectangular in shape leading to the characteristic and identifiable "loss of resistance" feel to air or saline.

Ligamentum flavum: This ligament comprises of yellow elastic fibres and connects adjacent laminae. Laterally, this ligament begins at the root of articular processes and extends posteriorly and medially to the point where laminae join to form spinous process. It provides the classic springy resistance in the lumbar region.

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

For epidural anaesthesia, needle pierces the first three ligaments when midline approach is used, in para median approach only the ligamentum flavum is encountered.

Figure 3 :Vertebral ligaments



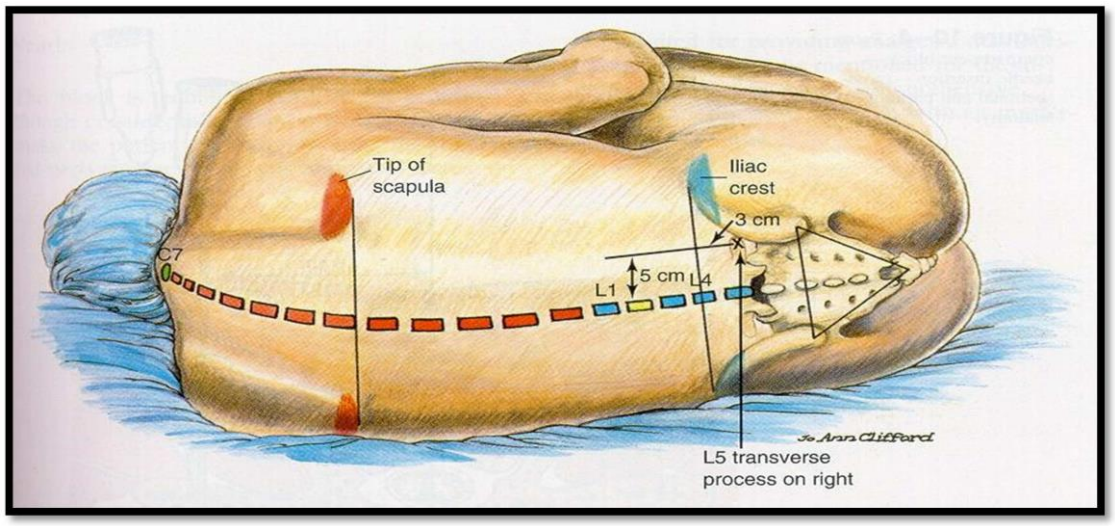
Intervertebral Discs[14]

These are principle connecting link between vertebral bodies. They form about 25% of the length of the spine. They consist of two parts - The outer fibrous part called the *annulus fibrosus* (made up of fibrous tissue), while the *nucleus pulposus* is the softer core. The discs serve as shock absorbers and lend flexibility to the vertebral column.

Topographical Line of Tuffier

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

Figure 4: Topographical line of Tuffier



Vertebral canal:

The vertebral canal is bound by the vertebral bodies and intervertebral discs anteriorly , the laminae , ligamentum flavum and laterally by pedicles and laminae.

The contents of vertebral canal are as follows :

- Spinal cord
- Spinal nerve roots
- Meninges
- Cerebrospinal fluid
- Vessels
- Fat
- Loose areolar tissue

Spinal cord

The average length of the spinal cord in males is 45 centimetres (cms) and in females it is 42 cms. The average weight is approximately 30 gm.

The spinal cord is a continuation of the medulla oblongata below the level of foramen magnum and it tapers off into a conical extremity known as conus medullaris. Filum terminale descends to the back of first segment of coccyx from apex of conus medullaris.

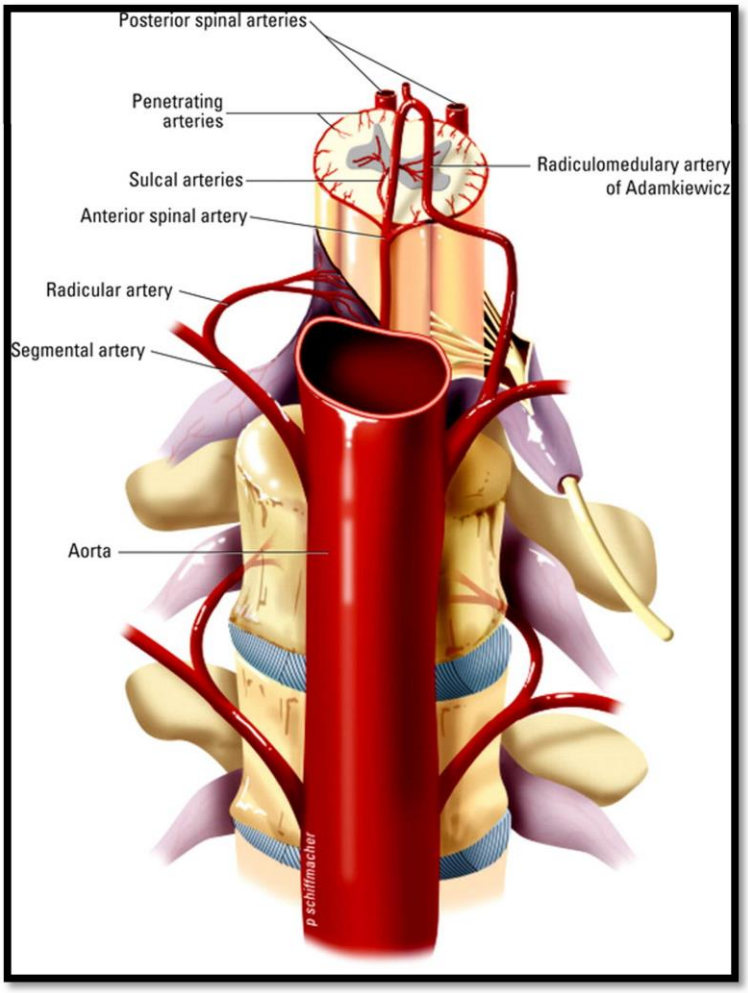
At birth, Spinal cord ends at the level of lower border of lumbar (L) three vertebra and in adults, it is as follows;

- Lower border of L1 - 50%
- Upper border of L2 - 40%
- Upper border of L3 - 3%

From the spinal cord arise 31 pairs of spinal nerves, each made of a ventral and a dorsal root. These anterior and posterior roots after crossing the subarachnoid space, pass through the dura and extradural space independently and unite at the level of intervertebral foramen to form spinal nerve trunks, which further divide into anterior and posterior primary divisions.

The amount of white matter declines progressively from the cervical region down to the lumbar region. The gray matter is greatly increased in the both the lumbar and cervical enlargement.

Figure 5: Blood supply of spinal cord



Blood Supply of Spinal Cord:

The spinal cord receives its blood supply from anterior and posterior spinal arteries. The anterior spinal artery is a single vessel lying in front of the anterior median fissure. It is formed by two small arteries, one given off from each vertebral artery at the level of the foramen magnum. It receives small communications from the intercostal and lumbar arteries; to provide the extra blood supply needed in the cervical, thoracic and lumbar enlargements.

There are two posterior spinal arteries-one on each side. They are derived from the vertebral artery or more often from a primary branch of each vertebral artery. They supply the posterior one-third of the spinal cord. This supply is augmented by spinal branches of vertebral, ascending cervical, posterior intercostals, lumbar and lateral sacral arteries, which pass through the intervertebral foramina.

Venous drainage is through a plexus of anterior and posterior veins in the neck, azygous veins in the thorax, lumbar veins in the abdomen, and lateral sacral veins in the pelvis. There is no anastomosis between the anterior and posterior spinal arteries.

The longest of the feeder arteries is the radicularis magna (artery of Adamkiewicz), which supplies the anterior spinal artery in the area of the lumbar enlargement of the cord. It enters by way of a single intervertebral foramen (78% of the time on the left) between the T8 and L3 foramina.

Meninges

The spinal cord is covered by three membranes from inward to outward, they are the pia mater, the arachnoid mater and the dura mater. The dural sac is the continuation of meningeal layer of the cranial dura mater. It is a circular sac or sleeve surrounding the spinal cord. Above, it is attached firmly to the circumference of the foramen magnum.

Duramater

It is the outermost membrane, the fibres of which run longitudinally. Although continuous, it can be described in two parts: the cranial and the spinal. The cranial

dura consists has two layers, outer endosteal layer, which lines the skull, and an inner meningeal layer, which invests the brain and folds inward to form the falx cerebri and tentorium cerebelli.

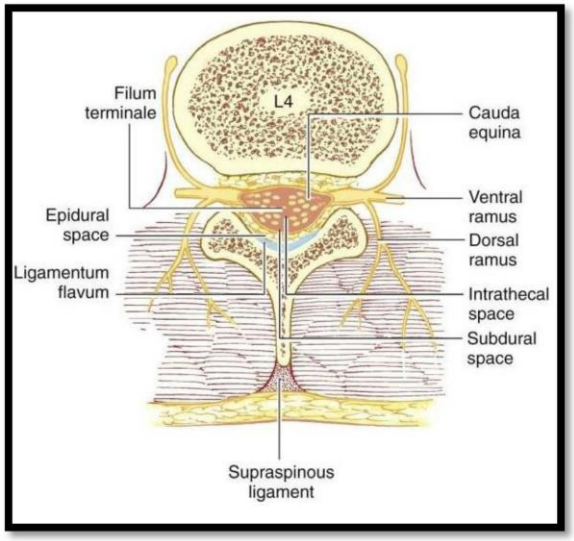
Arachnoid Mater

The arachnoid mater is a delicate non-vascular membrane applied closely to the dura mater. The lower extent of dural sac is as follows;

Below this the dura continues as the filum terminale. The subarachnoid space is the space between the arachnoid and pia mater. This space is occupied by the cranial and spinal nerves and by the cobweb trabeculae. The space is annular in the cranial and thoracic vertebrae and is about three mm deep. Below the first lumbar vertebrae it is circular in shape.

EPIDURAL SPACE[15]

Figure 6 : Epidural Space



Boundaries of the epidural space

The epidural space is bounded

Superior: by foramen magnum , where periosteal and spinal layers of duramater fuse.

Inferior: by sacroccygeal membrane and sacral hiatus .

Anterior : by the posterior longitudinal ligament, vertebral bodies and discs

Posterior : by ligamentum flavum , periosteum of anterior surface of laminae and connecting ligaments.

Lateral : by periosteum of pedicles and intervertebral foramina.

Rarely, a fold of duramater divides the space into ventral and dorso – medial compartments leading to patchy or unilateral analgesia or missed segments.

Shape and size: These are largely determined by the shape of the lumbar vertebral canal and the position and size of the dural sac within it.

Cervical : 1.5 mm

Upper thoracic : 2.5 – 3 mm

Lower thoracic : 4-5 mm

Lumbar : 5-6 mm

Types of epidural space

The epidural space can be categorized into cervical, thoracic, lumbar and sacral epidural spaces. These spaces can be defined according to their margins. At the cervical epidural space, there is a fusion of the spinal and periosteal layers of dura mater at the foramen magnum to lower margin of the 7th cervical vertebra. While the

thoracic epidural space is formed by the lower margin of C_7 to the upper margin of L_1, the lumbar epidural space is formed by the lower margin of L_1 vertebra to the upper margin of S_1 vertebra. The sacral epidural space is formed by the upper margin of S_1 to sacrococcygeal membrane and sacral hiatus.

Contents of the epidural space :

Contains semi liquid fat , lymphatics , arteries , loose areolar tissue spinal nerve roots and a very rich plexus of veins.

Fat

The epidural space is filled with semi fluid , lobulated fat tissue. Fat cells are also abundant in the dura that forms the sleeves around spinal nerve roots but they are not embedded within the laminae that form the dura mater of the dural sac. The fat in the epidural space buffers the pulsatile movements of the dural sac and protects nerve structure, creates a reservoir of lipophilic substances, and facilitates the movement of the dural sac over the periosteum of the spinal column during flexion and extension. The areolar tissue of this space has a very rich blood supply with small capillaries forming a network in its substance . Drugs stored in fat, inside dural sleeves, could have a greater impact on nerve roots than drugs stored in epidural fat, given that the concentration of fat is proportionally higher inside nerve root sleeves than in the epidural space, and that the distance between nerves and fat is shorter. Similarly, changes in fat content and distribution caused by different pathologies may alter the absorption and distribution of drugs injected in the epidural space. The maximum amount of fat is present posteriorly, where it assumes triangular capsular shapes and is linked to the midline of the ligamentum flavum by a vascular pedicle. Drugs with

high lipid solubility like bupivacaine have a high affinity for fatty tissue and thus remain in epidural fat for a longer time thus leaving a small quantity of the drug to interact with nerve roots at any time. Uptake of local anaesthetic by fat competes with it's vascular and neural uptake .

Lymphatics

The lymphatics of the epidural space are mostly found in the region of the dural roots where they remove foreign materials including microorganisms from the subarachnoid and epidural spaces.

Vertebral venous plexus

The internal vertebral venous plexus consists of four interconnecting longitudinal vessels, two anterior and two posterior. The external vertebral plexus (EVP) in contrast, lies peripheral to the vertebrae and is made of the anterior and posterior external vertebral plexuses.The EVP is situated anterior to the vertebral bodies and in relation to the laminae, spinous processes, transverse processes and articular processes respectively. These veins communicate with the segmental veins of the neck, the intercostal, azygous and lumbar veins. With the veins of bones of the vertebral column, the internal and external vertebral plexuses form Batson's plexus.These veins are predominantly in the antero-lateral part of the epidural space, and ultimately drain into the azygous system of veins. As the whole system is valveless, increased intrathoracic or intra-abdominal pressure (e.g. ascites, pregnancy, tumours etc.) can lead to major congestion and vessel enlargement within the spinal canal. The epidural venous plexus is surrounded by sparse quantity of fat.

The anterior epidural space is entirely occupied by a rich venous plexus (valveless system of veins). The plexus communicates with the intracranial sigmoid sinus, basilar venous sinus, basivertebral vein, occipital vein, and the azygous system. The plexus is linked to the abdominal and thoracic veins by the intervertebral foramina and through this connection transmit intraabdominal and intrathoracic pressure to the epidural space. The venous plexus is also connected to the iliac veins through the sacral venous plexus. Obstruction of the inferior vena cava, advanced pregnancy or intra abdominaltumors can cause distension of the venous plexus leading to an increased risk of being traumatized during needle and/or catheter placement in the epidural space. These veins are more prominent along the lateral wall of the vertebral canal usually they are out of reach of a correctly placed needle by midline approach. The dose and rate of local anaesthetic should also be reduced in any case of increased intraabdominal pressure / inferior vena cava obstruction as the resultant engorgement of the venous plexus would reduce the effective volume of the epidural space. The injected drug may therefore spread rapidly upwards or downwards along the epidural space.

Epidural arteries

The epidural arteries located in the lumbar region of the vertebral column are branches of the ilio-lumbar arteries. These arteries are found in the lateral region of the space and therefore accidental puncture is uncommon by midline approach.

Spinal arteries:

As already discussed, the spinal cord is supplied by one anterior spinal and two posterior spinal arteries. The spinal branches of the subclavian, aortic and iliac

arteries cross the epidural space on the way to sub arachnoid space. The largest of them, the artery of Adamkiewicz supplies the anterior spinal artery at the lumbar level. This artery enters the epidural space between $T_8 - L_3$ levels and any damage to itwoul cause ischaemia of entire lumbar region of the cord. In general, anterior spinal artery is more susceptible due to it being unpaired.

Pharmacokinetics Of Epidural Blockade

Epidural anaesthesia results from the interaction of local anaesthetics with nerve structures located within the epidural space. Local anaesthetics can reach the sites of action along various distribution pathways. Uptake into extraneural tissues like epidural fat and systemic absorption compete with neural tissue distribution thereby affecting the clinical potency and duration of action. Therefore, epidural doses of local anaesthetics are much higher than spinal doses.

Specifically, drugs may

1) Exit the intervertebral foramina to reach the paraspinous muscle space,
2) Drugs may diffuse into epidural fat,
3) Drugs may diffuse into ligaments and finally,
4) Drugs may diffuse across the spinal meninges.

The only mechanism by which drugs redistribute from the epidural space to the spinal cord is diffusion through the spinal meninges and the cellular arachnoid mater is the principal meningeal barrier to diffusion accounting for 95% of the resistance to meningeal permeability.

Meningeal permeability is not the only determinant of a drug spinal cord bioavailability after epidural administration. Drugs can partition into various environments in the epidural space and be unavailable for transfer across the spinal meninges.

Lipid soluble drugs have a tendency to get sequestrated into epidural fatty tissue. The dura mater is an important site of drug clearance especially in humans where dura mater is a highly vascular structure. As lipid soluble molecules traverse capillaries more readily than do more hydrophilic molecules, lipid soluble drugs may be cleared by this mechanism more readily than less lipid soluble drugs.

Meninges contain multiple enzyme systems, which are capable of drug metabolism. In addition, the meninges express enzymes capable of metabolizing neurotransmitters, including epinephrine, norepinephrine, acetylcholine and neuropeptides. After epidural administration, local anaesthetics need to cross the spinal meninges to reach their site of action

Epidurally administered drugs that reach the CSF, also can diffuse back across the meninges into the epidural space, but this happens only when the drug concentration in the epidural space falls below that in the CSF. Diffusion is dependent mainly on the drug's physicochemical properties, particularly, lipid solubility.

Physiological Effects Of Epidural Blockade

The physiological responses to epidural anaesthesia are mainly due to sympathetic blockade accompanied by sensory and motor blockade to various degrees. Some of the most important (but not all) physiological effects of epidural blockade can be discussed in relation to either sympathetic blockade of

vasoconstrictor fibres (below T_4) and/or of cardiac sympathetic fibres. Major sympathetic blockade can be avoided by trying to keep the block level around or below T_{10}. Lower abdominal, urologic, gynaecological and lower limb surgeries can be carried out satisfactorily with acceptable sympathetic blockade.

Zone of differential blockade:

Erlanger and Gasser showed that action of local anaesthetics on nerve fibres is by "differential conduction blockade". The nerve fibres are of three types viz A, B , C

A minimum length of myelinated nerve fibres should come in contact with local anaesthetic for conduction blockade. In myelinated fibres, the blockade occurs at nodes of Ranvier and three consecutive nodes need to be blocked for impulse conduction to be completely interrupted.

All types of nerve fibres are affected by local anaesthetics. but within any one fibre type, there is tendency for small, slower conducting fibers to be more readily blocked than large, fast conducting fibres. Between fibre types however, these rules do not hold good. Myelinated preganglionic B fibres which have a faster conduction time are about three times more sensitive to local anaesthetics than the slower non-myelinated post ganglionic C fibers.

Sensory $A\alpha$ fibres appear to be more sensitive to blockade than motor A_β fibres, although of the same conduction velocity, this may be because sensory fibres conduct at a higher frequency. It has been suggested that this selectivity for sensory fibres exhibited by Bupivacaine and Ropivacaine is a function of frequency dependent block.

Sensory

In intradural block sympathetic fibres are blocked two or three segments higher than sensory fibres. In extradural block, the relationship is complex. Level of sympathetic block is the same as (or lower than) sensory with epidural blockade. Sympathetic block will be greater when more concentrated solutions are used or when adrenaline added, as this has similar effect.

Motor

In intradural block, the difference between sensory and motor block is slight (two segments). In extradural block, the difference in levels is greater, depending on nature of local anaesthetic solution.

Factors Influencing Height And Distribution Of Local Anaesthetic:

Patient characteristics:

- Age: Study done by Bromage shows a correlation between age and dose, an increase in dose from age 4-18 years followed by a gradual decrease from 19 year onwards.
- Height: A simple thumb rule is to use 1ml per segment for height of 150 cm and then add 0.1 ml per segment for each 5 cm over 150 cm.
- Weight: Under normal circumstances, there is not much correlation between spread of analgesia and the weight. However in morbidly obese patients a given dose of local anaesthetics can cause a higher than normal block due to compression of epidural space due to increased intra-abdominal pressure.

- Intra-abdominal pressure: epidural venous engorgement in pregnancy, obesity, tumours can cause a higher blockade with a given dose due to narrower epidural space
- Posture: In sitting position there is slight propensity of the drug to spread caudally and higher doses may be required.
- Gender

Technique of injection:

- Site of injection: Rapid onset and denser blockade is seen when the point of injection was nearer to nerve roots. Lumbar epidural injection has a better cephalad spread than caudal epidurals.
- Direction of bevel
- Rate of injection: A rapid injection of local anaesthetic produces a rapid but incomplete and more extensive block. Injection rate of 0.3 – 0.75 ml/sec results in most reliable block.

Characteristics Of Anaesthetic Solution:

- Amount: Earlier epidural anaesthesia was considered to be equivalent to multiple paravertebral blocks and the tendency was to give a large volume of diluted drug. However studies by Bromage showed that increasing dosage linearly increases the degree of sensory blockade.
- Concentration: An increase in the drug concentration increases the density of motor blockade.
- Density
- Temperature
- Use of adjuvants

Effects Of Epidural Anaesthesia On Various Organ Systems:

Cardiovascular System:

The action of epidural anaesthesia on cardiovascular system depends on the level of block:

1. If the level of block is below T_4 there is dilation of resistance and capacitance vessels due to loss of sympathetic tone. This causes a fall in BP. However if there is a blockade of cardiac efferent sympathetic fibres from T_1 to T_4 there is a loss of chronotropic and inotropic drive resulting in a fall in cardiac output.
2. The activation arterial or Bainbridge reflex causing bradycardia -The lowering of blood pressure in the right atrium consequent to diminished venous return [Bainbridge (1874-1921) effect]
3. The operation of Mary's law causing tachycardia.
4. Depression of vascular smooth muscle and β adrenergic blockade of myocardium with fall in cardiac output.

Block not extending above T4 is not always associated with fall of blood pressure in fit young adults. However, elderly may suffer significant hypotension when moderate volumes are injected into the epidural space.

Slowing heart rate is caused if any of the anterior roots carrying sympathetic cardiac accelerator fibres are blocked (T_1– T_4). Activation of Bainbridge reflex may further contribute to bradycardia which is more frequent than tachycardia.

Theories of causation of fall in blood pressure

1. Diminished cardiac output consequent on reduction of venous return to heart due to failure of peripheral pump – calf muscles.
2. Dilatation of post arteriolar capillaries and small venules due to paralysis of vasoconstrictors, compensatory vasoconstriction takes place in areas not anaesthetized via carotid sinus reflexes. In high spinal blocks, majority of vasoconstrictor fibres including those to arm (T2-T10), are paralyzed, hence low blood pressure.
3. Paralysis of sympathetic nerve supply to heart T_1-T_4. Bradycardia may give rise to fall in cardiac output.
4. Paralysis of sympathetic nerve supply to adrenal glands splanchnic nerves, with consequent catecholamine depletion.
5. Absorption of drug into circulation. Seen more commonly with epidural blockade due to the larger volume of drug used.
6. Pre-existent hypovolemia, if present, may cause precipitous hypotension after central neuraxial blockade. Compression of great vessels within abdomen, by the pregnant uterus, abdominal tumours or abdominal packs may cause severe hypotension in presence of central neural blockade.

Respiratory System:

The phrenic nerve supplying diaphragm arises from the anterior roots of C_3, C_4, C_5 and should not be encroached upon during neuraxial blockade. Lumbar and even mid thoracic epidurals usually do not cause much effects on respiratory system. During epidural anaesthesia, breathing becomes quiet and tranquil. This is not only due to motor blockade, but also to differentiation with reduction of sensory input to respiratory center.

The ventilation perfusion during extradural block is not greatly altered and effects on respiratory functions are relatively small with no effect on FRC or V/Q ratio. The lung volumes and capacities (tidal volume, vital capacity) are basically unchanged during epidural anaesthesia. Abdominal muscle and intercostals muscle paralysis is compensated by diaphragm moving down. The pulmonary gas exchange is preserved.

The patient may stop breathing so that respiratory support by IPPV and, if necessary, the tracheal intubation maybe required. Causes may be:

- Inadequate medullary blood flow due to inadequate cardiac output-a serious situation demanding immediate cardiorespiratory support.
- Massive epidural spread.
- Accidental subdural injection
- Toxic effects of local analgesic drug.
- Injecting narcotic analgesic drugs

Gastrointestinal System:

Pre ganglionic sympathetic fibres from T5 to L1 are inhibitory to gut, there is no effect on oesophagus, the innervations of which is vagus. The small gut is contracted as the sympathetic inhibitory impulses are removed, the vagus being all powerful, Sphincters are relaxed and peristalsis is active although not more frequent. Pressure within the bowel lumen is increased.

Nausea and vomiting due to the hypotension may occur in up to 20% of patients and usually come on in waves-lasting a minute or so and then passing away spontaneously. Stimuli arising in the upper abdomen might not be blocked causing discomfort. Colonic blood supply and oxygen availability are increased, perhaps an important factor in the prevention of anastomotic breakdown following gut resection.

1. Theories of causation of nausea and vomiting:
    a. Hypotension: corrected using fluid boluses and vasopressor drugs
    b. Increased peristalsis
    c. Traction on nerve endings and plexuses, especially via vagus (usually upper abdomen)
    d. Presence of bile in stomach due to relaxation of pyloric and bile-duct sphincters
    e. Narcotic analgesics (premedication)
    f. Psychological factors
    g. Hypoxia

Liver

There are no specific effects of significance. The degree of hypotension that compromises liver function is not known. Liver disease may interfere with the metabolism of local anaesthetic drugs.

Endocrine system

Surgical stress produces a variety of changes in endocrine system and metabolic function. There is an increased catabolism of proteins and oxygen consumption. Increased plasma concentrations of catecholamines, vasopressin, growth hormones, renin, angiotensin, glucose, Anti diuretic hormone (ADH) and Thyroid Stimulating Hormone (TSH) are noted and this is referred to as surgical stress response.

Neuraxial blocks in general suppress the increase of ADH.It also delays adrenal response to trauma, whereas operations under GA cause a rise in steroids.

In any case, either regional or general, there is no difference in the postoperative period once the effects of the block are discontinued. Spinal block suppresses the hyperglycemic response to surgery and stress and so is useful in diabetic patients but this does not extend into postoperative period. The response to insulin is augmented and anaesthetist should be aware of possibility of hypoglycemia.

Epidural block prevents lymphopenia and granulocytosis after operation, thus inhibiting the metabolic endocrine response to surgery and preventing immune depression.

Femoral Nerve

Anatomy-

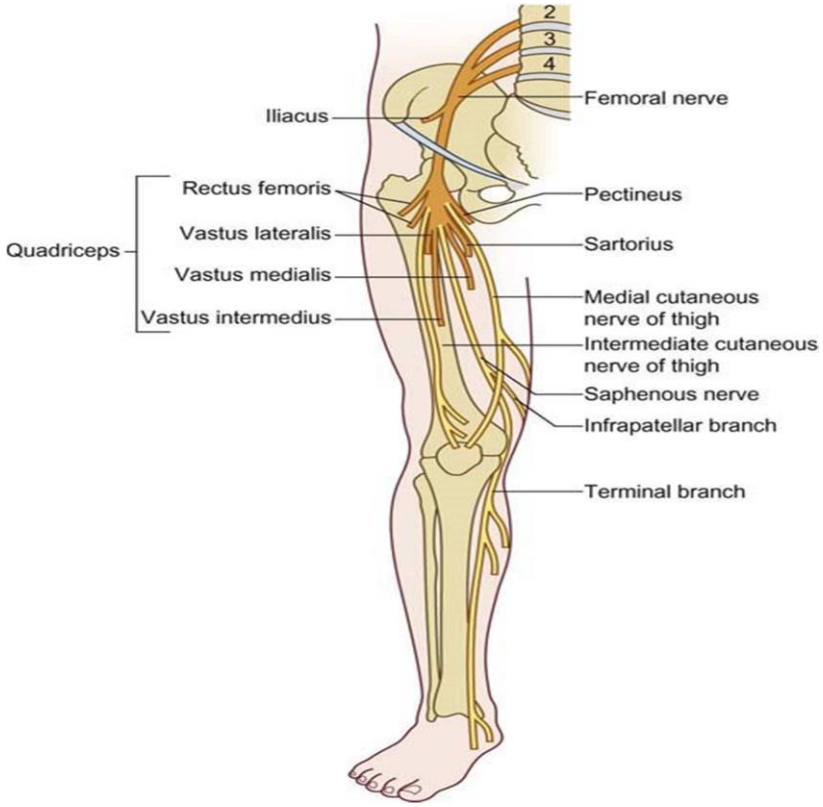
The Femoral nerve is the largest branch of the lumbar plexus. It is formed by the dorsal divisions of the anterior rami of the L2, L3 and L4 spinal nerves.

It emerges from the lateral border of the psoas muscle, approximately at the junction of the middle and lower thirds of that muscle.

Along with its course to the thigh, it remains deep to the fascia iliac . it enters the thigh posterior to the inguinal ligament, where it is positioned immediately lateral and slightly posterior to the femoral artery. At this level, it is situated deep to both fascia Lata and fascia iliaca.

As the nerve passes into the thigh , it divides into anterior and posterior branches . Located above the fascia iliaca ,the anterior branches innervates the sartorius and pectineus muscles and the skin of anterior and medial aspects of thigh.

Figure 7 : Femoral Nerve Block



Indications -

A femoral nerve block is well suited for surgeries on the anterior aspect of the thigh and for superficial surgery on the medial aspect of the leg below the knee.

Examples-

- Repair of quadriceps tendon or quadriceps muscle biopsy
- Long saphenous vein stripping
- Post operative analgesia after femur and knee surgery
- Supplement to sciatic or popliteal block to provide complete anaesthesia of the lower leg and ankle.

Contraindications –

Contraindications for femoral nerve block includes

- Previous ilioinguinal surgery
- Large inguinal lymph nodes or tumor
- Local Infection
- Peritoneal Infection
- Pre-existing femoral neuropathy.

Ultrasonography [16-18]

Ultrasound waves are sound waves with a frequency greater than 20,000Hz.These frequencies are above the audible upper limit of human hearing. Medical ultrasound is the application of this ultrasound waves to visualize the internal organs of our human body. The frequencies used for this purpose, ranges from 3 to 20 MHz. In recent years, ultrasound is widely used in anaesthesia for obtaining vascular access and performing peripheral nerve blocks. Ultrasound guided techniques helps in increasing success rate and reduce its complications.

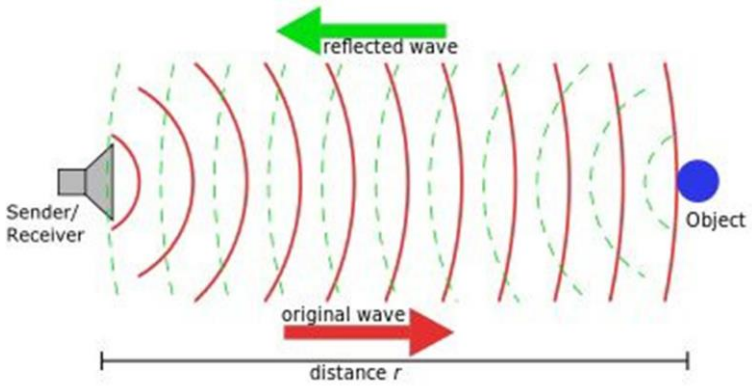
Ultrasound Pulse Generation

The ultrasound transducer contains multiple piezoelectric crystals which are interconnected electronically. When mechanical energy is applied to these crystals and some ceramics, they generate electrical energy. This phenomenon known as the "Piezoelectric Effect" was first described by the Curie brothers in 1880. They also described the "Reverse Piezoelectric effect", wherein application of electricity to these crystals produced vibrations which generate ultrasound waves.

Ultrasound Wavelength and Frequency

The wavelength and frequency are inversely related. High frequency ultrasound waves (10 to 20 MHz) give images with a high axial resolution but are more attenuated as we go deeper. Therefore, these transducers are optimal to image the superficial structures. Low frequency ultrasound waves (2 to 8 MHz) penetrate deeper but provide low axial resolution and are used to image deeper structures.

Figure 8-Principles of Ultrasonography



Ultrasound Tissue Interaction:

As the ultrasound waves travel through tissues, they are partly transmitted to deeper structures, partly reflected back to the transducer as echoes, partly scattered, and partly transformed to heat.

Reflection

For image generation, the echoes returned after hitting a tissue interface is of interest to us. The amount of echo returned after hitting a tissue interface is determined by a tissue property called acoustic impedance. The intensity of a

reflected echo is proportional to the mismatch in acoustic impedances between two mediums.

Refraction

The change in the direction of the ultrasound waves after hitting an interface between two media with different velocities of sound transmission is refraction. This causes artefacts as the returning echoes are incorrectly located.

Scattering

Ultrasound waves which incident on the tissues at right angles are reflected back to the transducer. If the waves are not at right angle, then the returning echoes are scattered in all directions in a non-uniform manner

Absorption

Some of the ultrasound waves are absorbed by the tissue and are converted to heat.

Attenuation

As the ultrasound waves travel through tissue, the returning echoes will become weaker due to absorption, scattering and refraction.

Diffraction

The spreading out of the ultrasound waves as its moves further away from the source is diffraction.

Construction

The ultrasound probe has an array of individual transducers which acts as both a transmitter and a receiver. Each transducer emits a short burst of ultrasound and is quiescent until it detects the echoes returning. This is called “Pulsed Ultrasound”. The speed of ultrasound in our body tissues is fairly constant at a speed of 1540m/s.The time taken for an echo to return is used determine the distancebetween the tissue and the probe.

Across the plane of an image, the ultrasound image is swept to form two dimensional images one line at a time. These lines are then summated to produce a frame. The frames are repeated to produce a real-time image. The brightness of the image depends upon the amplitude of the returning echo from the anatomical interfaces.

Scanning Modes

A-mode (amplitude mode): This displays a single echo signal against time to measure depth.

B-mode (brightness mode): It is a two dimensional image produced using an array of transducers and a series of reflected echoes.

M-mode (motion mode): is a specialized type of B-mode imaging where one particular line is ensonified repeatedly to examine a moving structure plotting out how the structure moves with time.

Ultrasound controls

Gain alters the brightness of the image by amplifying the received signal.

Time-Gain Compensation (TGC) differentially amplifies signals from different depths, allowing equal amplitudes from all depths to be displayed.

Focus adjusts the beam to be at its narrowest at the required depth to image the region of interest. It thereby improves lateral resolution

Depth can be adjusted to have the structure that is being examined to be in the centre of the screen.

Approaches and techniques

There are two basic approaches to ultrasound guidance. With the out-of- plane technique, the needle tip crosses the plane of imaging as an echogenic dot. With the in-plane approach, the entire tip and shaft of the advancing needle are visible.

Out-of-plane:

This technique involves insertion of needle at the midpoint of probe such that the needle cuts across the ultrasonic beam. The image obtained is a cross section of the needle shaft or tip. Path to target is shorter as compared to in-plane technique, but visibility of needle is not optimum, indirect markers like tissue movement or hydrodissection is needed to confirm placement.

Advantages:

1) Most similar to other approaches to regional block (nerve stimulation orpalpation)

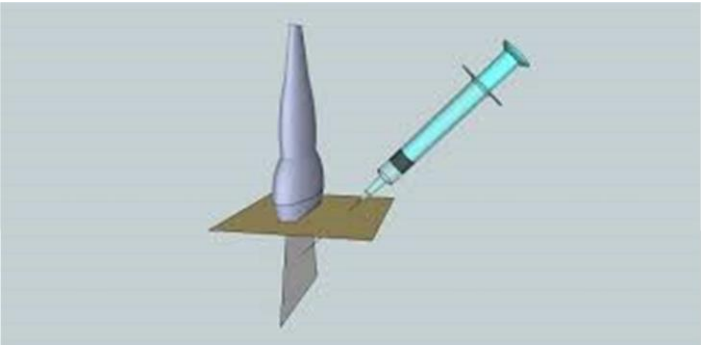
2) Shorter needle path than with in-plane approaches

3) Along the nerve path (catheters)

Disadvantages:

Unimaged needle path, crossing the plane of imaging without recognition.

Figure 9-Out of plane approach



In-plane (IP):

In this technique needle is inserted along the length of ultrasound probe. It aligns the entire length of the beam with the shaft of needle. The image displayed will depict the entire needle shaft and its tip thereby improving the precision of nerve blocks. But the needle visibility depends on angle of insertion and the needle traverses a longer path to reach the target area.

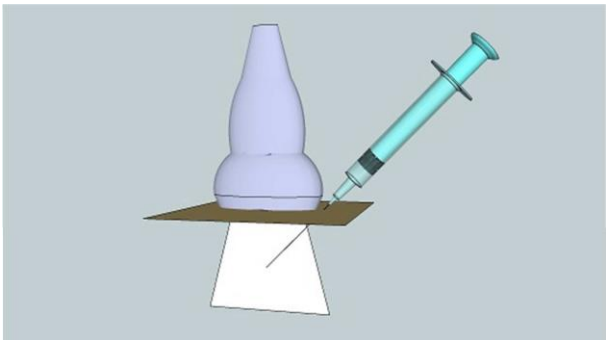
Advantages:

Most direct visualization.

Disadvantages:

1. Partial line-ups (creating a false sense of security when the needle tip is not correctly identified.
2. Some unimaged needle path occurs with IP approach, but typically less than with OOP approach.
3. Longer paths and therefore more structures to cross with the block needle.

Figure 10-Inplane approach of ultrasonography



Ultrasound probes

- Commonly used are three types- Linear high frequency (6 to 12 MHz) probes which has high resolution and lesser penetration and is ideal for visualizing superficial structures.
- Curvilinear low frequency probes (2-5MHz) which has low resolution, higher penetration and is ideal for deeper structures like intraabdominal organs.
- Phased Array Probe also has low frequency (2MHz – 7.5MHz) gives a large depth with a small acoustic window, ideal for chest ultrasound

Figure 11-Ultrasound probes

Imaging

Ultrasound image is produced by echoes received as the Ultrasonic beam interacts with the tissues it travels through. Acoustic impedance of a structure is the function of the elasticity and density of the particular tissue. Materials with higher acoustic impedance transmit sound faster, and do not allow for continued compression by the impending wave. The sound beam is attenuated while traversingvarious tissues within the body. The beam will be scattered somewhat when it encounters varying tissues on the way with different acoustic impedances or it may be reflected back from structures and returns back to the transducer. Refraction and absorption by tissues may also attenuate the waves. Those tissues that reflect the wave are termed echoic and those which do not reflect the wave are termed anechoic. Always use plenty of sterile ultrasound gel to remove the air interface between the skin and probe. Air does not allow the passage of the ultrasound beam even though it has low Acoustic impedance. Bone has high acoustic index so it appears to be white on the ultrasound image as it is hyper reflective to the beam. Blood and other fluids appear to be black on the image since they are anechoicin nature. Soft tissue appears as grey on the sonographic image as they have medium echogenicity.

The nerves appear round or oval in transverse view and are hypo-echoic or they appear as honeycomb structures with septations inside them. Nerves are bordered by a hyper-echoic layer of connective tissue. Blood vessels will appear as circular hypoechoic to anechoiec structures with a well-defined hyper- echoic border which is the vessel wall. Veins are compressible with thinner walls whereas arteries have thicker walls and appear pulsatile in nature. Muscles have fibrous-lamellartexture and appear as heterogeneous or homogeneous hypoechoic structures with hyper-echoic septa in between.

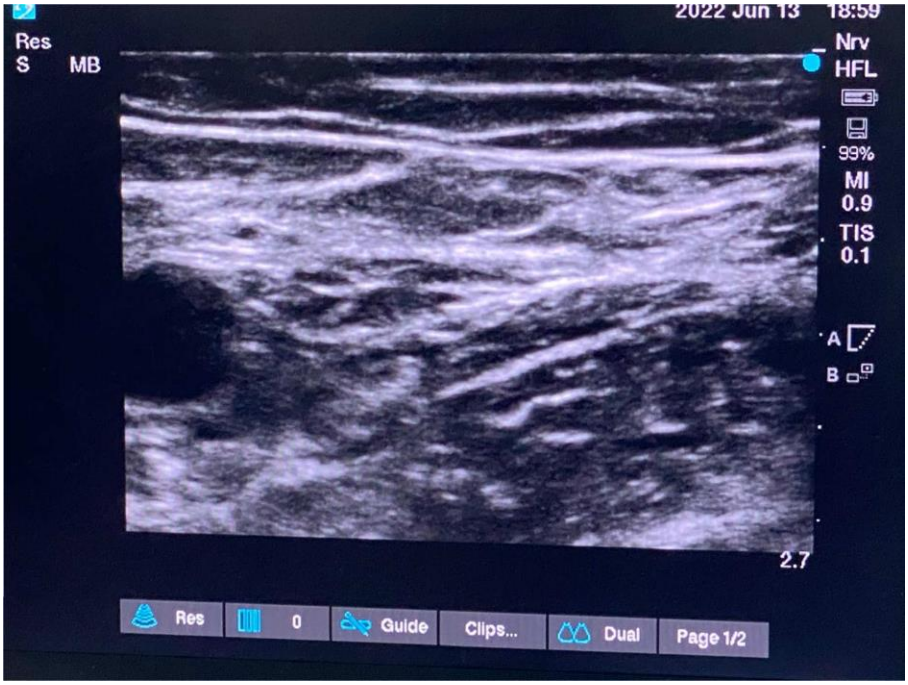
Basic principles of ultrasound guided nerve blocks.

- First involves the identification of anatomical structures like muscles, fascia, blood vessels and bones.
- Visualization of the nerve plexus or the fascial plane where drug should be deposited.
- Should be able to differentiate between normal and altered anatomy of the region scanned.
- Identify the correct plane for needle insertion to avoid trauma to vessels
- Strict aseptic technique
- Real time visualization of needle when it is inserted inside.
- -Once the target is reached, inject a small volume of drug or saline and see the spread and confirm location, else reposition the needle
- Do frequent aspiration during injection of drug to rule out intravascular injection.
- Complete visualization of the spread of total volume of local anaesthetic drug injected.

- Always keep ready all resuscitation equipment, drugs and standard monitoring.

Femoral Nerve Block Under Ultra-Sound Guidance

For FNB, a high-frequency linear ultrasound probe should be placed over the inguinal crease. In cross-section, femoral vessels and femoral nerve were identified. Just lateral to the artery and deep to fascia iliaca, the femoral nerve was located as a spindle-shaped structure with a honeycomb appearance. The 23 G block needle Melsung, inserted using an in-plane technique. After advancing the needle through fascia iliaca, 15 mL of 0.2% ropivacine and injection dexamethasone 4 mg were injected after careful aspiration at the target point. Local drug spread was confirmed around the nerve on the USG screen.



ROPIVACAINE

Introduction

Ropivacaine is a newer, longer acting local anaesthetic agent which belongs to the amino amide group. It was first synthesized by Ekenstam in 1957; however it was first introduced for clinical practice only since 1996. Chemically it belongs to the same group as bupivacaine and mepivacaine (epipecoloxylidide local anaesthetic).

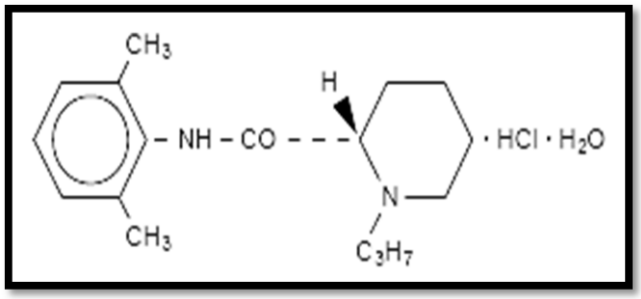
It was found that butyl derivatives of pipecoloxylidides (example bupivacaine) were more cardiotoxic than propyl derivatives, causing a significant number of cardiac arrests.[19]

Thus ropivacaine was developed as a pure S – enantiomeric form of pipecoloxylidides. Though ropivacaine has been available internationally for over three decades, it is a relative new entrant in the Indian market.

It is becoming increasingly popular among anaesthesiologists and has been used extensively in almost all modes of regional anaesthesia: infiltration, peripheral nerve blocks, spinal anaesthesia, epidural anaesthesia as well as caudal epidural blocks in paediatric patients.

Chemical Structure

Figure 12: Chemical structure of ropivacaine



Ropivacaine is an amino amide local anaesthetic agent, chemically described as S-(-)-1-propyl-2',6'-pipecoloxylidide hydrochloride monohydrate. The ***International Union of Pure and Applied Chemistry*** name is (S)-N-(2,6-dimethylphenyl) -1- propylpiperidine-2-carboxamide. It's molecular formula is $C_{17}H_{26}N_2O•HCl•H_2O$ and it has a molecular weight of 328.89.

Ropivacaine is a white crystalline powder. At 25°C ropivacaine hydrochloride has a solubility of 53.8 mg/mL in water and a distribution ratio between n-octanol and phosphate buffer at pH 7.4 of 14:1. The pKa of ropivacaine is 8.07 which is very similar to that of bupivacaine (8.1) .

However, ropivacaine has a much lesser lipid solubility as compared to bupivacaine and mepivacaine. This can be explained on the basis of presence of a propyl (3 Carbon) side chain in ropivacaine as compared to a butyl (4 Carbon) side chain in the other two local anaesthetics. This lower lipid solubility ***Physical Properties*** of ropivacaine has a significant effect on the block characteristics of ropivacaine as discussed ahead.[20]

Mechanism Of Action And Corelation With Structure

Ropivacaine reversibly inhibits the voltage gated sodium channels present on the nerve cell membranes thus preventing the influx of sodium ions into the cells. This:

I. Blocks generation and conductance of nerve impulses.

II. Slows propagation of nerve impulses

III. Reduces the rate of rise of action potential

Almost all local anaesthetic agents block the unmyelinated C and myelinated Aδfibres, which transmit pain impulses, at the same rate.

The rate of blockade of motor fibres (Aα and Aβ), however depends upon the physio chemical properties like pKa and lipid solubility of the individual drug. As ropivacaine is less lipid soluble than bupivacaine, the Aα and Aβ blockade is slower and hence motor blockade is less potent. Studies of lumbar epidural block in humans have confirmed that equal volumes and concentrations of bupivacaine and ropivacaine produce similar degree of sensory block but the motor block produced by ropivacaine is slower in onset, lesser in intensity and shorter in duration.

Clinically the order of blockade of nerve fibres is autonomic, sensory and motor, while the regression of the block occurs in reverse order.

The nerve impulse transmission is lost in the following order:

The order of the loss of nerve function is

1. Pain
2. Temperature
3. Touch
4. Proprioception
5. Skeletal muscle tone.

Pharmacokinetics

Absorption :

The systemic concentration of ropivacaine depends on the total dose and concentration of drug given, the route of administration, the patient's haemodynamic state and the vascularity of the site of administration. When administered in the epidural space, ropivacaine has a biphasic absorption. The half-lives of the two phases (mean$\pm$ SD) are 14$\pm$7 minutes and 4.2 $\pm$0.9 hours respectively.

Distribution :

After intravascular infusion, ropivacaine has a steady state of distribution of 41 ± 7 litres. It is 94% protein bound, mainly to α_1-acid glycoprotein. In case of continuous epidural infusion of ropivacaine the plasma concentration can rise due to increased protein binding and reduced clearance. Ropivacaine can easily cross the placenta.

Metabolism and excretion :

Ropivacaine is extensively metabolized by the liver, predominantly by the cytochrome P_{4501A} mediated aromatic hydroxylation to produce 3 – hydroxyl ropivacaine. After a single IV dose, approximately 37% of the total dose is excreted in the urine as both free and conjugated 3-hydroxy ropivacaine. An additional unquantified amount of 2 – hydroxyl – methyl ropivacaine has also been identified s a metabolite.

Ropivacaine metabolites are mainly excreted via kidney. After i.v. administration 86% of the dose is excreted in urine of which only 1% is in unchanged form. Following IV administration, ropivacaine has a mean ± SD total plasma clearance of 387 ± 107 mL/min, an unbound plasma clearance of 7.2 ± 1.6 L/min and a renal clearance of 1 mL/min. The mean ± SD terminal half life is 1.8 ± 0.7 h and 4.2 ±1.0 h after i.v. and epidural administration respectively.

Pharmacodynamics

Central Nervous System &CardioVascularSystem :

Ropivacaine has a higher threshold for both cardiac as well as neuro toxicity as compared to bupivacaine due to its lower lipid solubility and stereo - selective properties. This holds good for both isomers of ropivacaine which have been shown to be less cardio depressant than respective bupivacaine isomers in animal studies.

CNS toxicity occurs earlier than cardiac toxicity on iv infusion in healthy volunteers.

Potency :

Lipid solubility of a local anaesthetic correlates well with its potency and toxicity. Compounds which are more lipophilic penetrate the nerve cell membrane more readily. Thus, fewer molecules are required to produce the desired conduction blockade.

Others :

Continuous epidural infusion of 0.375 % and 0.188% ropivacaine has been shown to inhibit platelet aggregation in plasma.

Adverse Effects

Excessive plasma levels are due to over dosage, unintentional intravascular injection or slow metabolic degradation. The mean doses at which CNS symptoms of toxicity begin to occur in human beings are 4.3 and 0.6 mcg/mL of total and free plasma concentrations respectively. When prolonged blocks are used the risks of reaching a toxic plasma concentration or inducing local neural injury are increased. Various possible side effects include

a) Injection site pain
b) **Cardiovascular system toxicity:** Vasovagal reaction, syncope, postural hypotension, non-specific ECG abnormalities which include wide QRS complexes, increased conduction time and reduced contractility.
c) **Gastrointestinal system toxicity:** Faecal incontinence, tenesmus, nausea, vomiting.

d) **Central nervous system toxicity:** Tremor, Horner's syndrome, dyskinesia, neuropathy, vertigo, convulsion and coma. Because of depressant effect of ropivacaine on medulla, excitatory stage of CNS might not occur.

e) **Liver and Biliary system toxicity:** Jaundice

f) **Metabolic disorders:** Hypomagnesemia

Advantages Over Other Local Anaesthetics

Ropivacaine produces a more differential blockade allowing better separation between sensory and motor block and is therefore a better choice for use in labour analgesia and post operative pain relief. When compared to bupivacaine it produces less dense motor blockade of shorter duration and hence permits earlier mobilization and discharge thus reducing both morbidity as well as cost of treatment. It has a lower systemic toxicity than bupivacaine and a better, cardio stable profile. Ropivacaine has been developed to offer a safer alternative to bupivacaine while retaining the desirable blocking properties of racemic bupivacaine.

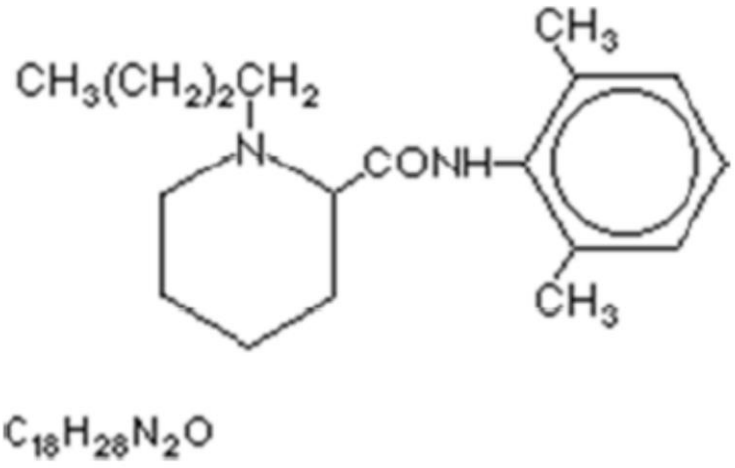
BUPIVACAINE [21-22]

Bupivacaine is an amino amide class of local anaesthetic drug. It was first synthesized by Ekenstam in 1957 and its clinical use was started by LJ Telivuo in 1963. Since then, it has become one of the widely used local anaesthetic agents clinically.

Bupivacaine consists of a tertiary amine attached to a substituted aromatic ring by an amide linkage. The butyl group attached to the piperidine nitrogen makes bupivacaine more lipid soluble and potent. The molecular weight is 288. It is a chiral

drug that exists as two enantiomeric forms – dextrorotary (R-) and levorotary (S-) forms. The pure levorotary form Levobupivacaine produce less cardiotoxicity compared to that of the racemic mixture.

Figure 13- Structure of Bupivacaine



PHARMACODYNAMICS

Bupivacaine permeates the nerve's axon membranes and accumulate within the axoplasm. Binding to sites on voltage-gated Na+ channels prevent opening of the channels by inhibiting theconformational changes that underlie channel activation.

On comparison with lignocaine, it is four times more potent but the onset of action is slower. The duration of action is considerably longer. The sensory blockade caused by bupivacaine is much more than the motor blockade.

PHARMACOKINETICS

It is a weak base with a pKa of 8.1. Bupivacaine is highly protein bound (95%) and most important plasma protein binding site is alpha1 acid glycoprotein. At physiological pH of 7.4, 17% is non-ionised.

The onset and duration of action depend on the dose, concentration, route of administration and vascularity of the site of administration. The volume of distribution is 54 L. The elimination half-life is 210 minutes. The Clearance is 0.32 L/min. Bupivacaine undergoes biotransformation in liver by aromatic hydroxylation, N-dealkylation, amide hydrolysis, and conjugation. The metabolites are excreted viathe kidney. Less than 5% of the drug is excreted unchanged.

Dosage and preparations

Maximum dose of bupivacaine 2-3 mg/kg. Preparations available include 0.25%, 0.5% solutions in 10 ml and 20 ml vials, preservative free 0.5% bupivacaine and 0.75% bupivacaine for intrathecal injections.

Uses

- Peripheral nerve block (0.25-0.5%)
- Epidural Anaesthesia (0.25-0.5%)
- Spinal Anaesthesia (0.5%, 0.75%)
- Caudal Anaesthesia (0.25-0.5%)
- Infiltration Anaesthesia (0.25-0.5%)

Contraindications

- Known hypersensitivity to local anaesthetics
- Intravenous regional anaesthesia (IVRA)

Adverse effects

Local Anaesthesia Systemic Toxicity– Plasma concentration greater than 5mcg/ml due to overdosage, unintentional intravascular injection and slow metabolic degradation causes systemic toxicity.

Central Nervous System Toxicity

Non-specific signs of toxicity are metallic taste, circumoral numbness, diplopia, tinnitus, dizziness. Excitation is characterized by restlessness, anxiety, dizziness, tinnitus, blurred vision or tremors. Then, there is a depression of central nervous system causing drowsiness, unconsciousness and cardiac arrest.

Cardiovascular system effects

Part of the cardiac toxicity that occurs with high plasma concentrations of bupivacaine occurs because of the blockade of cardiac sodium channels. Accidental intravenous injection of bupivacaine causes cardiac dysrhythmias, atrioventricular block, ventricular tachycardia and ventricular fibrillation, bradycardia and asystole.

Pregnancy increases the sensitivity of cardiotoxic effects of bupivacaine.

MATERIALS AND METHODS:

Source of Data:

40-80 years , Of either gender, ASA grade I,II,III scheduled for elective unilateral Total Knee Arthroplasty(TKA) at K.L.E's DR. Prabhakar Kore Charitable Hospital and Medical Research Centre, Nehru Nagar, Belgaum, between March 2023 – Feb 2024.

Study Design: Randomized Clinical Trial

Study Period: ONE YEAR

Sample Size: Based on using mean & standard deviation, the minimum required sample size formula is determined by.

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

Where z α is linked with the level of significance and z β is linked with the power of the test. For 5% level of the significance z α =1.96 and z β =0.84 for 80% power of the test.

Ref: “Epidural analgesia compared with peripheral nerve blockade after Major knee surgery” author- S.J.Fowler .[23]

The parameter considered in the calculation is VAS score.

X_1 = Mean of the 1st group (1.7) , X_2 = Mean of the 2nd group (3.1).

S_1 =standard deviation of the 1st group (1.7) , S_2 = standard deviation of the 2nd group (2.0).

The sample size obtained is 28. To ensure more definitive results the sample size raised to 30.

There will be two groups with 30 each.

Inclusion Criteria:

- Patients American society of anaesthesiologists physical status -I II and III
- Patients aged 40-80 years old of either gender scheduled for unilateral Total Knee Arthroplasty undergoing combined sub arachnoid block and epidural analgesia.
- And patients who have ability to provide written consent for and cooperate with the study.

Exclusion Criteria:

- American society of anaesthesiologist's physical status >3.
- Patients with – Infected TKA, History of stroke, Major neurological defect and any spinal pathology that contraindicates Neuraxial Blockade are not included in study.

Sampling technique:

The study analysis to compare two groups was done as follows. Mean & standard deviation was computed for continuous quantitative variables. Inter-group continuous variables were compared using suitable statistical techniques such as the

un-paired Student's t-test. Within-group comparisons of 2 quantitative variables were analysed using Student's paired t-test.

Presentation of categorical data was done by using rates, ratios, and percentages. Chi-square test or Fisher's exact test was utilized to evaluate the association among the outcome and clinical as well as demographics of patients

Median was utilized to represent discrete variables.

Nonparametric tests were utilized for comparing discrete variables.

Appropriate graphs were utilized to illustrate the comparison

In all tests, a significance level of less than 5% (0.05) was deemed significant.

Ethical Clearance: Before commencing the study, approval was secured from the Institutional Ethical and Research Committee, J N M C, Belagavi.

Informed Consent: Type of research and the intervention being done was explained to all of the patients who met the selection criteria.

Prior to enrollment, handwritten informed consent was obtained from every patient.

Methodology:

Following approval from the ethics committee, obtaining written informed consent from patients, the study enrolled 60 patients scheduled for primary total knee arthroplasty under combined subarachnoid and epidural block. Patients meeting the specified inclusion, exclusion criteria and consenting to participate were included.

By computerized randomization, patients are divided in to 2 groups

GROUP E: Epidural analgesia group**.**

GROUP EF: Combined Epidural and Femoral Nerve block group.

Before the day of surgery, a comprehensive pre-anaesthetic evaluation and standard investigations were conducted. After confirming patient's nil-by-mouth status, intravenous access was secured using 18G intravenous cannula secured and preloading was done with 10ml/kg of crystalloids. The patient was then shifted inside the operating theatre, where standard equipment to monitor vital signs, non- invasive blood pressure., heart rate, ECG & pulse oximeter, were applied.

The patients were randomised in to one of the above two groups .

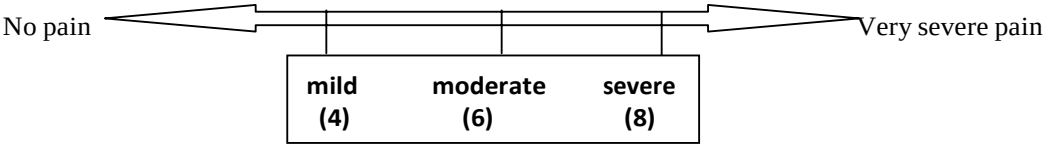
Under strict aseptic precautions, Epidural space identified at L2-L3 intervertebral space using the 18G Tuohy needle with the patient in sitting position, Epidural catheter passed for 5cm into the epidural space and secured with tapes. Following this subarachnoid block was given at L3-L4 intervertebral space using 27G Whitacre needle with 3.2ml of 0.5% bupivacaine (hyperbaric) as a standard volume across all groups and also to achieve a dense sensory block to the level of T10.

Postoperatively the patients were monitored in the post anaesthesia care unit and on returning of motor movement at toes (active toe movements) on the operated site patients in Group E were started on Epidural infusion of (0.1%) bupivacaine at 4ml/hr and patients in Group EF in addition to Epidural infusion of (0.1%) bupivacaine at 4ml/hr had received Femoral Nerve Block just below the inguinal ligament on the operated side using ultrasonography by in plane technique, FNB was achieved with 15ml of (0.2%) ropivacaine .

The patients were monitored for vital parameters heart rate, NIBP, SPO2 and Visual Analog Score.

The Epidural infusion rate is reduced by 1ml/hr if the mean blood pressure <30% of base line and increased by 1ml/hr if the mean blood pressure >30% of the baseline and also if the VISUAL ANALOG SCORE <3 rate epidural infusion is decreased by 0.5ml/hr, maximum up to 4 ml/hr.

In either group, VISUAL ANALOG SCORE.



IF VAS SCORE >/4 then inj. Paracetamol, 20mg/kg, given as rescue analgesic.

If Vas score >4 within 6hrs after giving paracetamol a second rescue analgesic Inj. Diclofenac sodium 1.5mg/ kg was given as intravenous infusion.

The patients were monitored for 24hrs post operatively for VAS scores.

The average pain score over 24hrs and total consumption of rescue analgesics were note

Data analysis table:

	Heart Rate	Blood Pressure	Visual Analog Score	Amount of Rescue Analgesics used	Rate of epidural infusion
0 Min					
15 Mins					
30 Mins					
45 Mins					
60 Mins					
90 Mins					
2 Hrs					
6 Hrs					
12 Hrs					
24 Hrs					

RESULTS:

Data contains measurements on 60 subjects who are divide into 2 groups of 30 subjects each. The following table gives the comparison of demographic details over groups.

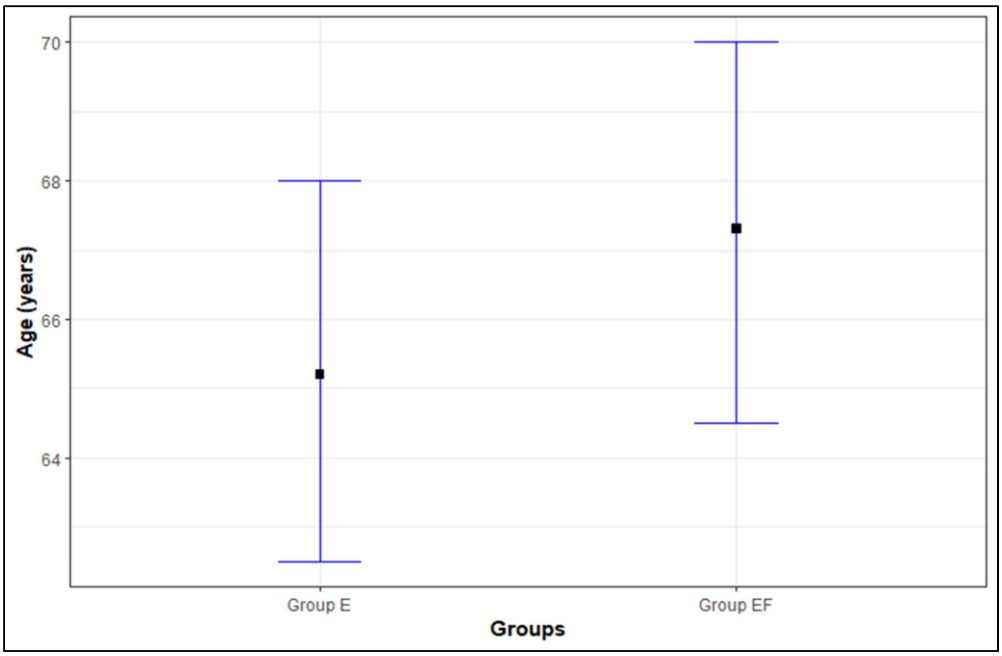
"Table 1: Comparison of demographic details over groups".

Variables	Sub Category	Group E	Group EF	Total	p-value
Age (years)	Mean ± SD	65.24 ± 7.23	67.27 ± 7.4	66.27 ± 7.32	0.2923[t]
	Median (Min, Max)	65 (49, 77)	68.5 (49, 78)	68 (49, 78)	
Sex	Female	20 (66.67%)	22 (73.33%)	42 (70%)	0.5731[C]
	Male	10 (33.33%)	8 (26.67%)	18 (30%)	

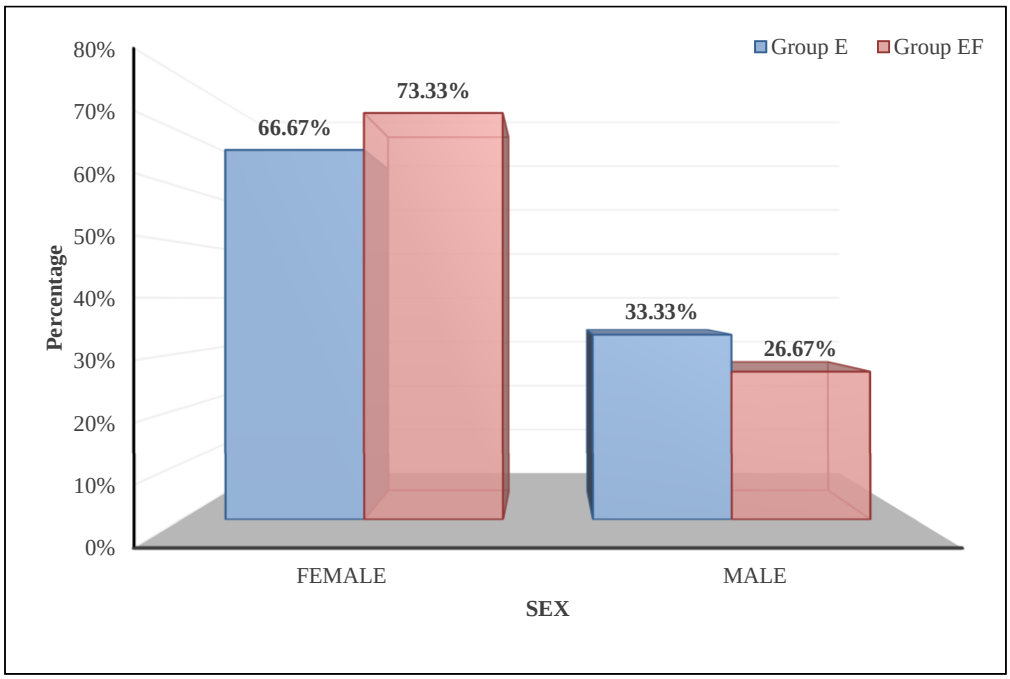
Abbreviation: C – Chi square test, t – Two sample t test.

Group E had a mean age of 65.24 years (SD ± 7.23) with a median of 65 years (range 49 to 77 years), while Group EF had a slightly higher mean age of 67.27 years (SD ± 7.4) and a median of 68.5 years (range 49 to 78 years). From two sample t test, it is observed that, the difference in age between the two groups is not statistically significant (p-value = 0.2923).

Group E had 66.67% females and group EF had 73.33% females. However, from Chi square test, it is observed that, there is no significant difference in the distribution of sex over groups.



Graph 1 "Mean Age Comparision" Over Groups.



Graph 2: Distribution of sex over groups.

The following table gives the comparison of heart rate over time and groups.

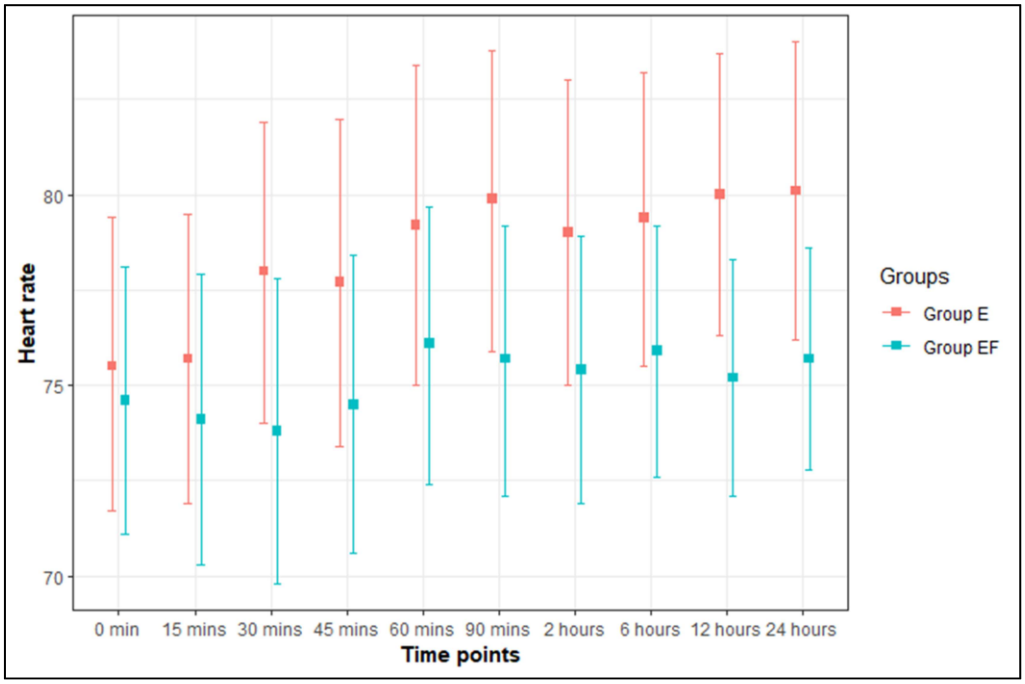
Table 2: Comparison of heart rate over time and groups.

Time points	Group E	Group EF	Total	p-value
0 min	75.53 ± 10.31 73 (60, 98)	74.63 ± 9.35 72 (60, 101)	75.08 ± 9.77 72 (60, 101)	0.9409^{MW}
15 mins	75.73 ± 10.19 73 (58, 98)	74.1 ± 10.2 72 (58, 102)	74.92 ± 10.15 72 (58, 102)	0.5375^{t}
30 mins	77.97 ± 10.62 75.5 (58, 99)	73.8 ± 10.78 70 (58, 100)	75.88 ± 10.82 74 (58, 100)	0.1370^{t}
45 mins	77.7 ± 11.53 79.5 (59, 99)	74.5 ± 10.38 75.5 (54, 98)	76.1 ± 11 76 (54, 99)	0.2634^{t}
60 mins	79.17 ± 11.23 78.5 (54, 96)	76.07 ± 9.75 77.5 (55, 100)	77.62 ± 10.54 78 (54, 100)	0.2582^{t}
90 mins	79.87 ± 10.58 82.5 (56, 92)	75.67 ± 9.53 75 (60, 96)	77.77 ± 10.2 78.5 (56, 96)	0.0780^{MW}
2 hours	79 ± 10.65 80 (54, 94)	75.4 ± 9.45 74 (58, 94)	77.2 ± 10.14 77 (54, 94)	0.1713^{t}
6 hours	79.37 ± 10.26 81 (60, 94)	75.87 ± 8.84 76 (60, 96)	77.62 ± 9.66 78 (60, 96)	0.1623^{t}
12 hours	80 ± 9.86 82 (62, 96)	75.23 ± 8.28 74 (62, 92)	77.62 ± 9.34 77.5 (62, 96)	0.0425^{MW}*
24 hours	80.1 ± 10.49 79.5 (60, 98)	75.7 ± 7.8 77 (63, 96)	77.9 ± 9.43 78 (60, 98)	0.0703^{t}
p-value	**< 0.001^{F}***	0.0024^{F}*	-	-

*Abbreviation: 't – Two sample t test', MW – Mann Whitney U test, F – Friedman's test, * indicates statistical significance.*

At the initial time point (0 minutes), there was no significant difference in heart rate between Group E and Group EF (p-value = 0.9409). As time progressed (15 minutes to 24 hours), similar trends were observed where the differences in heart rate between the two groups were not statistically significant. However, at the 12-hour time point, there was a statistically significant difference, (p-value = 0.0425), indicating that Group E had a higher heart rate compared to Group EF.

Additionally, Friedman's test showed significant differences in heart rate over time within each group ($p < 0.001$ for Group E and $p = 0.0024$ for Group EF). Overall, while heart rate varied over time within each group, significant differences between Group E and Group EF were only observed at the 12-hour time point.



Graph 3: Mean plot of heart rate over time and groups

The following table gives the comparison of SBP over time and groups.

Table 3: Comparison of SBP over time and groups.

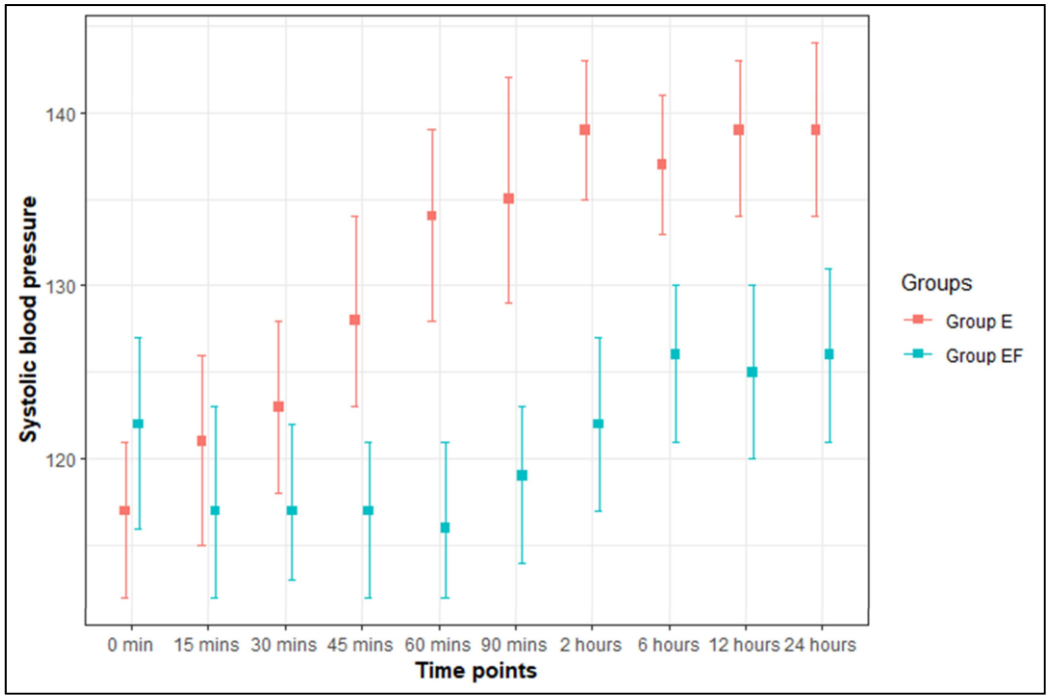
Time points	Group E	Group EF	Total	p-value
0 min	116.57 ± 11.53 110 (100, 150)	121.67 ± 15.55 125 (100, 140)	119.12 ± 13.82 110 (100, 150)	0.2071^{MW}
15 mins	120.67 ± 14.61 120 (100, 140)	117.33 ± 14.61 110 (90, 140)	119 ± 14.58 120 (90, 140)	0.4188^{MW}
30 mins	123.33 ± 13.48 125 (100, 150)	117.33 ± 12.3 110 (100, 140)	120.33 ± 13.14 120 (100, 150)	0.0736^{MW}
45 mins	128.33 ± 15.33 130 (90, 150)	116.67 ± 12.69 110 (100, 150)	122.5 ± 15.14 120 (90, 150)	**0.0017^{MW}***
60 mins	133.67 ± 14.26 140 (100, 150)	116.37 ± 12.27 110 (100, 151)	125.02 ± 15.81 130 (100, 151)	**$< 0.001^{MW}$***
90 mins	135.33 ± 17.17 140 (100, 170)	118.67 ± 12.52 115 (100, 140)	127 ± 17.1 130 (100, 170)	**$< 0.001^{MW}$***
2 hours	138.67 ± 10.42 140 (120, 170)	122 ± 12.15 120 (100, 140)	130.33 ± 14.02 130 (100, 170)	**$< 0.001^{MW}$***
6 hours	137 ± 11.79 140 (110, 150)	125.67 ± 12.23 130 (110, 150)	131.33 ± 13.21 130 (110, 150)	**$< 0.001^{MW}$***
12 hours	138.53 ± 10.81 140 (110, 156)	124.93 ± 13.92 130 (110, 150)	131.73 ± 14.13 130.5 (110, 156)	**$< 0.001^{MW}$***
24 hours	138.83 ± 12.98 140 (100, 160)	126 ± 13.29 130 (110, 150)	132.42 ± 14.54 130 (100, 160)	**$< 0.001^{MW}$***
p-value	**$< 0.001^{F}$***	**$< 0.001^{F}$***		-

*Abbreviation: MW – Mann Whitney U test, F – Friedman's test, * indicates statistical significance.*

At the 0-minute time point , there was no significant difference in SBP between "Group E" and "Group EF" (p-value = 0.2071).

However, as time progressed, significant differences in SBP between the two groups emerged. At the 45-minute time point onwards up to the 24-hour mark, the differences in SBP were statistically significant (p-values < 0.001 for all time points). Group E consistently showed higher SBP compared to Group EF across these time intervals.

Additionally, Friedman's test indicated significant changes in SBP over time within each group (p < 0.001 for both Group E and Group EF), suggesting that SBP varied significantly over the observed time period within each group.



Graph 4: Mean plot of SBP over time and groups.

The following table gives the comparison of DBP over time and groups.

Table 4: Comparison of DBP over time and groups.

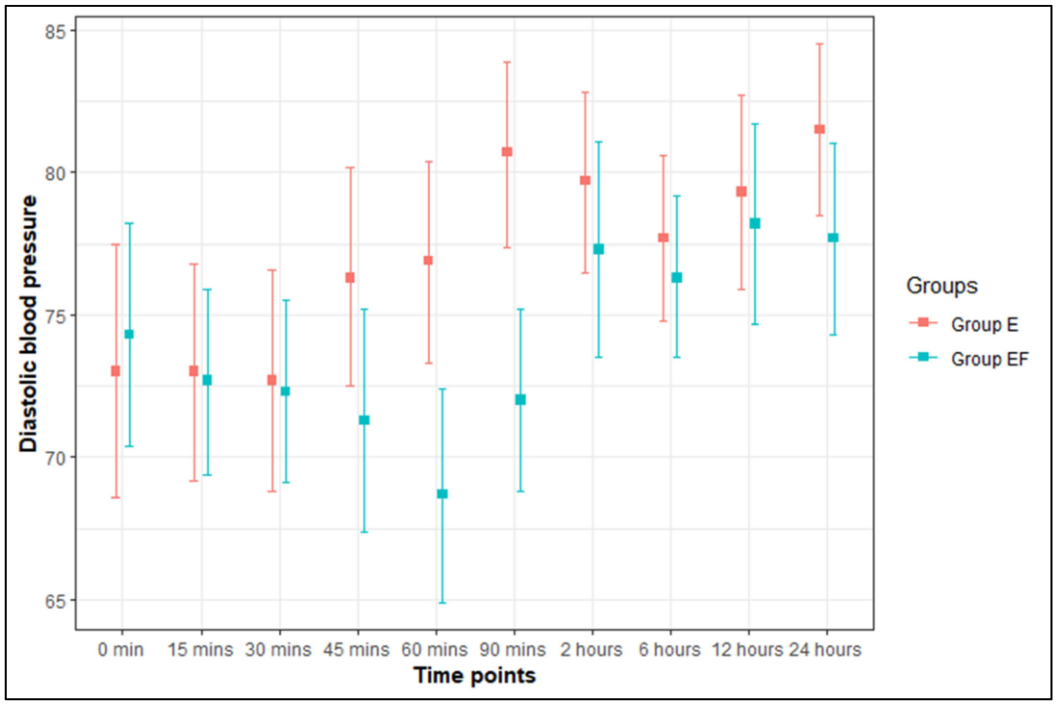
Time points	Group E	Group EF	Total	p-value
0 min	73.03 ± 11.99 70 (50, 100)	74.33 ± 10.4 70 (60, 90)	73.68 ± 11.15 70 (50, 100)	0.5705^{MW}
15 mins	73 ± 10.22 75 (60, 90)	72.67 ± 8.68 70 (60, 90)	72.83 ± 9.4 70 (60, 90)	0.8523^{MW}
30 mins	72.67 ± 10.48 70 (50, 90)	72.33 ± 8.58 70 (60, 90)	72.5 ± 9.5 70 (50, 90)	0.9429^{MW}
45 mins	76.33 ± 10.33 80 (50, 90)	71.33 ± 10.42 70 (50, 90)	73.83 ± 10.59 80 (50, 90)	$0.0482^{MW}*$
60 mins	76.87 ± 9.51 80 (60, 90)	68.67 ± 10.08 70 (50, 90)	72.77 ± 10.56 70 (50, 90)	$0.0027^{MW}*$
90 mins	80.67 ± 8.68 80 (60, 90)	72 ± 8.47 70 (60, 90)	76.33 ± 9.56 80 (60, 90)	**$< 0.001^{MW}*$**
2 hours	79.67 ± 8.5 80 (60, 90)	77.33 ± 10.15 80 (60, 90)	78.5 ± 9.36 80 (60, 90)	0.4023^{MW}
6 hours	77.67 ± 7.74 80 (60, 90)	76.33 ± 7.65 80 (60, 90)	77 ± 7.66 80 (60, 90)	0.4488^{MW}
12 hours	79.33 ± 9.07 80 (60, 90)	78.17 ± 9.33 80 (60, 90)	78.75 ± 9.14 80 (60, 90)	0.6094^{MW}
24 hours	81.5 ± 8 80 (60, 90)	77.67 ± 8.98 80 (60, 90)	79.58 ± 8.65 80 (60, 90)	0.0675^{MW}
p-value	**$< 0.001^{F}*$**	**$< 0.001^{F}*$**	-	-

*Abbreviation: MW – Mann Whitney U test, F – Friedman's test, * indicates statistical significance.*

Initially, at the 0-minute, 15 minute and 30-minute time points, there was no significant difference in DBP between Group E and Group EF.

However, as time progressed, notable differences in DBP between the two groups became evident. From the 45-minute time point onwards up to the 90-minute mark, the differences in DBP were statistically significant (p-values < 0.05 for all time points), indicating that Group E consistently exhibited higher DBP compared to Group EF over these intervals. After that from 2 hours time point up to 24 hours' time point, there was no statistically significant difference in DBP observed between the groups".

Additionally, Friedman's test revealed significant changes in DBP over time within each group (p < 0.001 for both Group E and Group EF), indicating variability in DBP across the observed time period within each grp.



Graph 5: Mean plot of DBP over time and groups.

The following table gives the comparison of VAS over time and groups.

Table 5: Comparison of VAS over time and groups.

Time points	Group E	Group EF	Total	p-value
0 min	0.67 ± 1.09 0 (0, 3)	0.03 ± 0.18 0 (0, 1)	0.35 ± 0.84 0 (0, 3)	0.0047^{MW}*
15 mins	1.33 ± 1.45 1 (0, 4)	0.9 ± 0.96 0.5 (0, 2)	1.12 ± 1.24 0.5 (0, 4)	0.2561^{MW}
30 mins	2.47 ± 1.2 2.5 (0, 5)	1.77 ± 1.1 2 (0, 3)	2.12 ± 1.19 2 (0, 5)	0.0372^{MW}*
45 mins	3.7 ± 1.02 4 (1, 6)	1.9 ± 0.88 2 (0, 4)	2.8 ± 1.31 3 (0, 6)	**< 0.001^{MW}***
60 mins	4.43 ± 0.73 4.5 (3, 6)	2 ± 0.83 2 (1, 4)	3.22 ± 1.45 3 (1, 6)	**< 0.001^{MW}***
90 mins	4.43 ± 0.82 4 (3, 6)	2.03 ± 0.96 2 (1, 4)	3.23 ± 1.5 4 (1, 6)	**< 0.001^{MW}***
2 hours	4.53 ± 0.9 5 (2, 6)	2.2 ± 1.16 2 (1, 5)	3.37 ± 1.56 4 (1, 6)	**< 0.001^{MW}***
6 hours	4.27 ± 0.91 4 (2, 6)	2.43 ± 1.19 2 (0, 5)	3.35 ± 1.4 4 (0, 6)	**< 0.001^{MW}***
12 hours	4.07 ± 0.91 4 (2, 6)	2.53 ± 1.07 2 (1, 5)	3.3 ± 1.25 3 (1, 6)	**< 0.001^{MW}***
24 hours	3.97 ± 1.16 4 (1, 7)	2.23 ± 1.07 2 (0, 5)	3.1 ± 1.41 3 (0, 7)	**< 0.001^{MW}***
p-value	**< 0.001^{F}***	**< 0.001^{F}***	-	-

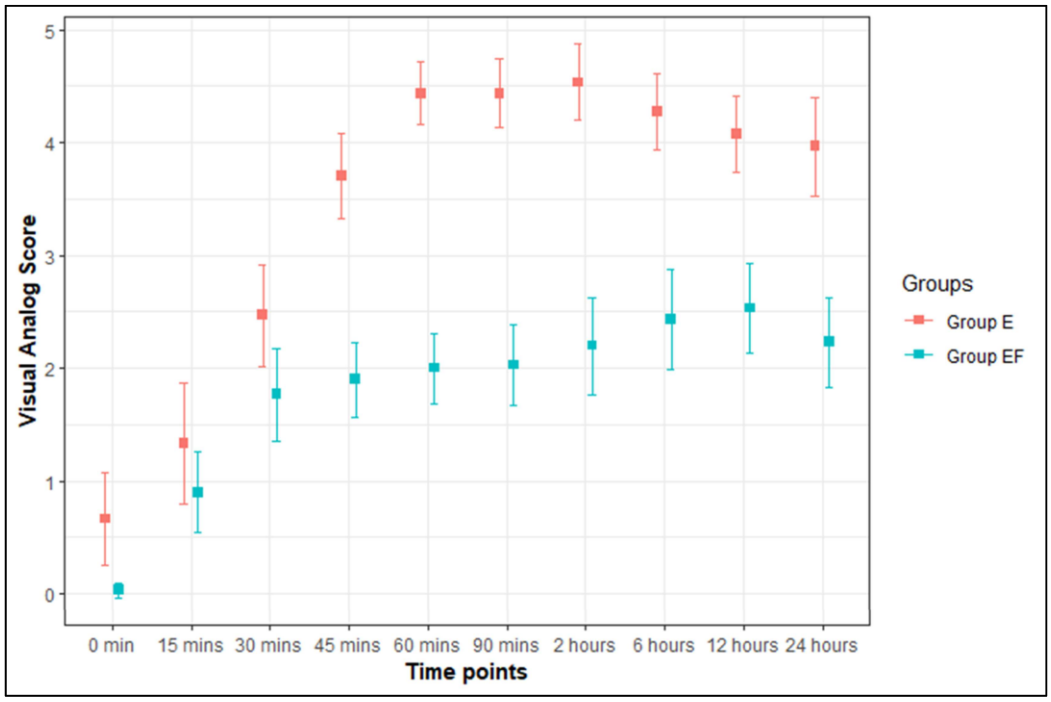
*Abbreviation: MW – Mann Whitney U test, F – Friedman's test, * indicates statistical significance.*

Initially, at the 0-min, there was a significant difference in VAS scores between Group E and Group EF (p-value = 0.0047), indicating that Group E had higher baseline VAS scores compared to Group EF. Group E had higher VAS scores

compared to Group EF in 15 minutes time point. However, this difference wasn't found to be statistically significant.

As time progressed, significant differences in VAS scores between the two groups persisted across all subsequent time points (30 minutes to 24 hours). Group E consistently showed higher VAS scores compared to Group EF, with p-values < 0.05 for each time point, indicating statistically significant differences in pain perception between the groups.

Moreover, Friedman's test demonstrated significant changes in VAS scores over time within each group ($p < 0.001$ for both Group E and Group EF), suggesting that VAS scores varied significantly over the observed time period within each group.



Graph 6: Mean plot of VAS over time and groups.

The following table gives the comparison of Analgesics Used over time and groups.

Table 6: Comparison of Analgesics Used over time and groups.

Time points	Sub Category	Group E	Group EF	Total	p-value
0 min	No	30 (100%)	30 (100%)	60 (100%)	1^{C}
15 mins	No	28 (93.33%)	30 (100%)	58 (96.67%)	0.5047^{MC}
	Yes	2 (6.67%)	0	2 (3.33%)	
30 mins	No	26 (86.67%)	30 (100%)	56 (93.33%)	0.1264^{MC}
	Yes	4 (13.33%)	0	4 (6.67%)	
45 mins	No	19 (63.33%)	30 (100%)	49 (81.67%)	**$< 0.001^{C}$***
	Yes	11 (36.67%)	0	11 (18.33%)	
60 mins	No	17 (56.67%)	30 (100%)	47 (78.33%)	**$< 0.001^{C}$***
	Yes	13 (43.33%)	0	13 (21.67%)	
90 mins	No	28 (93.33%)	29 (96.67%)	57 (95%)	$> 0.9999^{MC}$
	Yes	2 (6.67%)	1 (3.33%)	3 (5%)	
2 hours	No	12 (40%)	28 (93.33%)	40 (66.67%)	**$< 0.001^{C}$***
	Yes	18 (60%)	2 (6.67%)	20 (33.33%)	
6 hours	No	6 (20%)	27 (90%)	33 (55%)	**$< 0.001^{C}$***
	Yes	24 (80%)	3 (10%)	27 (45%)	
12 hours	No	6 (20%)	27 (90%)	33 (55%)	**$< 0.001^{C}$***
	Yes	24 (80%)	3 (10%)	27 (45%)	
24 hours	No	11 (36.67%)	28 (93.33%)	39 (65%)	**$< 0.001^{C}$***
	Yes	19 (63.33%)	2 (6.67%)	21 (35%)	

Initially, at the 0-minute time point, all participants in both Group E and Group EF reported no analgesic use (100% for both groups).

As time progressed, significant differences in analgesic usage between the groups became apparent. At 15-minute, time point and onwards, Group E consistently showed a higher proportion of participants using analgesics compared to Group EF, with statistically significant differences observed at the 45-minute time point and beyond (p-values < 0.001). Specifically, at later time points (2 hours to 24 hours), a larger proportion of participants in Group E used analgesics compared to Group EF, where Group E ranged from 60% to 80% while Group EF ranged from 6.67% to 10% (p-values < 0.001 for all these time points).

The following table gives the comparison of Rate of Epidural Infusion over time and groups.

Table 7: Comparison of Rate of Epidural Infusion over time and groups.

Time points	Sub Category	Group E	Group EF	Total	p-value
0 min	0	16 (53.33%)	11 (36.67%)	27 (45%)	0.1945^{C}
	4	14 (46.67%)	19 (63.33%)	33 (55%)	
15 mins	0	0	4 (13.33%)	4 (6.67%)	0.1264^{MC}
	4	30 (100%)	26 (86.67%)	56 (93.33%)	
30 mins	0	0	1 (3.33%)	1 (1.67%)	$> 0.9999^{MC}$
	4	30 (100%)	29 (96.67%)	59 (98.33%)	
45 mins	0	0	1 (3.33%)	1 (1.67%)	$> 0.9999^{MC}$
	4	30 (100%)	29 (96.67%)	59 (98.33%)	
60 mins	4	30 (100%)	30 (100%)	60 (100%)	1^{C}
90 mins	4	30 (100%)	30 (100%)	60 (100%)	1^{C}
2 hours	4	30 (100%)	30 (100%)	60 (100%)	1^{C}
6 hours	4	30 (100%)	30 (100%)	60 (100%)	1^{C}
12 hours	4	30 (100%)	30 (100%)	60 (100%)	1^{C}
24 hours	4	30 (100%)	30 (100%)	60 (100%)	1^{C}

Initially, at the 0-mins, 15 mins, 30 mins and 45 mins time points, there was no statistically significant difference in the rate of epidural infusion between Group E and Group EF.

From the 60 minutes time point and onwards through all subsequent time points (60 minutes to 24 hours), all participants in both Group E and Group EF received epidural infusion at rate 4 (100% at rate 4 for both groups) suggesting that the rate of epidural infusion was consistent.

DISCUSSION

Total knee arthroplasty typically results in postoperative pain, with around 30% experiencing moderate pain and 60% experiencing severe pain. Our study aims, to evaluate the most effective method of postoperative analgesia within the initial 24 hours to enhance early patient ambulation and rehabilitation. Effective postoperative analgesia also diminishes the risk of chronic post-surgical pain, which is closely linked to the severity of acute postoperative pain.

Our study is a randomised clinical trial conducted at Department of Anaesthesiology, KLE, Dr Prabhakar kore hospital between Jan 2023 to March 2024. The study was conducted on 60 volunteers between aged 40-80 years posted for Unilateral Total knee arthroplasty. The volunteers were enrolled and randomly distributed into two groups of 30 each with help of a computer-generated randomised table. Group E included individuals who received epidural analgesia alone with 0.1%bupivacaine infusion at the rate of 4ml/hr and Group EF included individuals who received femoral nerve block with 15ml of 0.2% ropivacaine along with Epidural analgesia.

Among the 60 individuals enrolled, Group E had 66.67% females and Group EF had 73.3% females. Group EF had a higher mean age of 67.27 years (SD ± 7.4) and Group E had mean age of 65.24 years (SD ± 7.23) and it was observed that difference in age between two groups is not statistically significant (p value = 0.2923).

At the initial time point (0 minutes), there was no significant difference in heart rate between Group E and Group EF (p-value = 0.9409). As time progressed (15

minutes to 24 hours), similar trends were observed where the differences in heart rate between the two groups were not statistically significant. However, at the 12-hour time point, there was a statistically significant difference (p-value = 0.0425), indicating that Group E had a higher heart rate compared to Group EF.

In a previous study conducted by Suma Vishwanatha et al to compare "Continuous Femoral Nerve block vs Epidural analgesia for post operative pain relief in patients undergoing knee surgery" observed that the heart rate in the group were comparable over the period of 72 hours.[24]

In our study, we observed not much difference in systolic diastolic blood pressures in both the groups during initial hours with p value (0.2071), but as the time progressed, from 45 minute time onwards there was statistically significant increase in systolic and diastolic blood pressures in Group E compared to Group EF at all intervals up to 24 hours.

The results observed in our study are not consistent with the previous study conducted by Kavita M et al., to compare "Ultrasound guided lumbar paravertebral block and lumbar epidural block with ropivacaine for post operative pain relief, in patients undergoing total hip replacement" observed that, mean arterial pressure were comparable between both the groups at the baseline and significantly dropped in lumbar epidural group at 30 mins after surgery.[25]

In another study done by Angelik. P et al., to compare "Intra venous PCA and Epidural analgesia for pain relief after total hip arthroplasty" observed that, mean arterial pressure was higher in Intra venous PCA group than in epidural group at 24-hour mark. [26]

In another study done by Keith et al., to compare "Intra-articular analgesia vs Epidural plus Femoral nerve block for patients undergoing knee arthroplasty" observed, no statistically significant differences in post operative blood pressures between 2 groups.[3]

In our study, we observed that at 0-minute time point, there was a significant difference in VAS scores between Group E and Group EF (p-value = 0.0047), indicating that Group E had higher baseline VAS scores compared to Group EF. Group E had higher VAS scores compared to Group EF in 15 minutes time point. However, this difference wasn't found to be statistically significant.

As time progressed, significant differences in VAS scores between the two groups persisted across all subsequent time points (30 minutes to 24 hours). Group E consistently showed higher VAS scores compared to Group EF, with p-values < 0.05 for each time point, indicating statistically significant differences in pain perception between the groups.

Our study is in line with other study conducted by Davies A F et al., to compare "Epidural infusion and Combined Femoral/ sciatic nerve blocks for perioperative analgesia after Total Knee Arthroplasty" observed lower vas scores in combined femoral/ sciatic nerve block when compared to epidural group.[27]

In another study, done by Zeki et al., to compare efficiency of "Continuous Femoral Nerve block using concentrations of Bupivacaine 0.25%,0.125% and no block for recovery of patients after primary Total Knee Arthroplasty" observed significantly higher pain scores in no block group compared with 0.25% bupivacaine and 0.125% bupivacaine infusion for continuous femoral nerve block.[28]

In another study, done by Khalid A et al., to compare "Adductor canal blockade versus Continuous epidural analgesia after total knee joint replacement" observed greater VAS scores in Continuous epidural group when compared to Adductor canal Block group at different time intervals for the first 48 hours after surgery.[1]

In another study, conducted by Remon N et al., to compare between "Continuous epidural analgesia , Ultrasound guided Continuous Femoral nerve block and Ultrasound guided Adductor canal block for postoperative pain management after Total Knee Replacement" had observed lower vas scores in Continuous Adductor canal block when compared to Continuous Femoral nerve block with 0.125%bupivacaine up to 48 hours.[29]

In the recovery process after total knee arthroplasty, in our study Paracetamol and diclofenac were used as rescue analgesics if patients VAS scores were more than 3 after the surgery.

In our study, At 0-minute time point, all participants in both Group E and Group EF reported no analgesic use (100% for both groups).

As time progressed, significant differences in analgesic usage between the groups became apparent. At the 15-minute time point and onwards, Group E consistently showed a higher proportion of participants using analgesics compared to Group EF, with statistically significant differences observed at the 45-minute time point and beyond (p-values < 0.001). Specifically, at later time points (2 hours to 24 hours), a larger proportion of participants in Group E used analgesics compared to

Group EF, where Group E ranged from 60% to 80% while Group EF ranged from 6.67% to 10% (p-values < 0.001 for all these time points).

Our study results were consistent with a study done by Khalid et al to compare "Adductor canal blockade versus Continuous epidural analgesia in patients after Total Knee Arthroplasty" had observed significantly higher number of patients in Combined spinal epidural group required more IV analgesic when compared to Adductor canal group.[1]

In a study done by Zeki et al., to compare "Continuous Femoral nerve block using concentrations of bupivacaine 0.25%,0.125% and no block for recovery of patients after primary total knee arthroplasty" observed significantly less opioid consumption with 0.125% bupivacaine infusion compared to 0.25% bupivacaine infusion for continuous femoral nerve block.[28]

In another study, conducted by Remon N et al., to compare "Continuous epidural analgesia , Ultrasound guided Continuous Femoral nerve block and Ultrasound guided Adductor canal block for postoperative pain management after total knee replacement" had observed lower opioid consumption used as recue analgesic in Continuous epidural infusion group compared to Continuous Femoral nerve block and Continuous Adductor canal block group with 0.125% bupivacaine up to 48 hours which is not in line with our inference.[29]

23 studies were analysed by James.P et al to compare "Femoral Nerve block with Epidural & Intra venous patient control analgesia after Total Knee Arthroplasty" observed reduced opioid usage in femoral nerve block when compared to intravenous patient controlled analgesia.[30]

LIMITATIONS

The limitations in our study includes-

1. Our study did not include continuous femoral nerve block which provides more prolonged and efficient analgesia compared to single shot femoral nerve block.
2. Another limitation of our study is quadriceps muscle strength is not assessed which might affect patient early ambulation and rehabilitation.

CONCLUSION-

The analgesic efficacy of Combined Epidural and Femoral nerve block was superior and effective than Epidural analgesia alone and also there is lower consumption of rescue analgesics in of Combined Epidural and Femoral nerve block (Group EF) than Epidural analgesia (Group E).

SUMMARY

60 cases of American society of Anaesthesiologists physical status I,II &III who were posted for Total knee arthroplasty were divided randomly into Group EF (Combined Epidural and Femoral Nerve Block) and Group E(Epidural analgesia alone), by computerised randomisation method. Both groups underwent a Combined spinal epidural anaesthesia , post operatively Group EF received femoral nerve block with 15ml of 0.2% ropivacaine under ultrasound guidance and group E received epidural analgesia alone

Following parameters were seen in present study-

- Haemodynamic – Heart rate , Blood Pressure
- Post operative Vas scores up to 24 hours
- Rescue analgesics used by each group
- Rate of epidural infusion

In present study the observations are as follows-

- Heart rate and blood pressure were lower in Group EF when compared to Group E.
- Combined Epidural and Femoral Nerve Block had provided better post operative analgesia compared to Epidural analgesia alone . The amount of rescue analgesics used were higher in Group E than Group EF.
- Altogether, Combined Epidural and Femoral Nerve Block provided superior and effective analgesia in patients undergoing Total Knee Arthroplasty.

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ANNEXURE I -

INFORMED CONSENT FORM

"RANDOMISED CLINICAL TRIAL TO ASSESS THE EFFICACY OF ADDITION OF FEMORAL NERVE BLOCK WITH 0.2% ROPIVACAINE TO EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN RELIEF AFTER TOTAL KNEE ARTHROPLASTY".

Objective To assess analgesic efficacy between epidural analgesia alone vs epidural analgesia and femoral nerve block for total knee arthroplasty patients.

Introduction: Total knee Arthroplasty is a common elective orthopedic procedure for the treatment of end-stage arthritic knee cases to improve the patient's pain, mobility, and quality of life. Total knee Arthroplasty is associated with considerable pain during the early postoperative period which can significantly affect the patient's satisfaction, length of hospital stay (LOS), And functional recovery after the surgery. Therefore, adequate and immediate pain relief is essential especially in the early postoperative period to enable ambulation, initiation of physiotherapy, and the prevention of other postoperative complications [1].A multimodal approach to combat post operative pain after Total knee Arthroplasty has been commonly utilized and has consisted of a combination of oral and intravenous analgesics both NSAIDS and Opioids. Some patients experience several side effects due to these drugs including nausea, vomiting, gastritis, pruritus, headache etc.

Epidural analgesia is widely used alone or in combination with oral or intravenous analgesics to manage post operative pain.

Recently interest in localized additional pain management methods like femoral nerve block has been increasing owing to their ability to ameliorate pain with few adverse effects

Continuous Epidural analgesia provided via an epidural catheter though effective in post operative pain management after Total knee Arthroplasty, many a times requires supplemental NSAIDS or opioids which may lead to adverse effects.

Literature search did not reveal any study comparing Epidural analgesia vs Combined Epidural analgesia with femoral nerve block for post operative pain relief after Total knee Arthroplasty.

Hence, we propose to conduct the present study to compare epidural analgesia and epidural analgesia with femoral nerve block using a relatively newer drug ropivacaine for postoperative pain after Total knee Arthroplasty.

Our Null hypothesis is that the two methods are equally effective in relieving the post operative pain after total knee arthroplasty.

Explanation of procedure: If u Agree to enroll in my study, I will ask you Present, past and family history. Then, you will be clinically examined in detail. You will be allowed into one of the two groups randomly using computer generated software. Group EF-will undergo Epidural analgesia and Femoral nerve block. Group E will undergo Epidural analgesia alone.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the.

Possible benefits from participating in the study: There will be be better post operative analgesia and pain relief.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study **"RANDOMISED CLINICAL TRIAL TO ASSESS THE EFFICACY OF ADDITION OF FEMORAL NERVE BLOCK WITH 0.2% ROPIVACAINE TO EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN RELIEF AFTER TOTAL KNEE ARTHROPLASTY".** My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE - II - PROFORMA

"RANDOMISED CLINICAL TRIAL TO ASSESS THE EFFICACY OF ADDITION OF FEMORAL NERVE BLOCK WITH 0.2% ROPIVACAINE TO EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN RELIEF AFTER TOTAL KNEE ARTHROPLASTY".

Name:

Age:

Gender:

Weight:

Height :

Date of Examination:

Address:

Occupation :

Pre examination evaluation:

Past History:

- HTN DM IHD Arrhythmia Valvular heart diseases .
- H/o previous surgery/(s):

General physical examination:

Weight (Kg) : Temperature (^{o}F) :

Pallor :

Cyanosis : Pedal edema :

Clubbing :

PR : BP :

RR:

Systemic examination:

RS: CNS:

CVS : GIT:

Preoperative physical status ASA Grade I II III IV V

Methodology:

After institutional ethical committee approval and obtaining return inform consent a total number of 60 patients will be included in the study. After thorough pre anesthetic assessment and necessary investigations patient aged 40-80 years of either gender with ASA I-III scheduled for primary total knee Arthroplasty under combined sub arachnoid and epidural block is included in the study. Patients with revision or infected total knee arthroplasty, peripheral neuropathy, allergy to local anesthetics and contraindications for regional anesthesia will be excluded from the study.

The patients will be randomized into 2 groups

Group E: Epidural analgesia group

Group EF: combined epidural analgesia and femoral nerve block group

All the patients will be kept nil by mouth 8 hours before surgery In the pre anesthetic room, vital parameters such as heart rate, Blood pressure will be recorded, an 18G intravenous cannula secured and preloading will be done with 10ml/kg of crystalloids. Patients will be shifted to operating theatre and basic monitors ECG,NIBP,SPO2 probe will be attached and under strict aseptic precautions Epidural space identified at L2-L3 intervertebral space using the 18G Tuohy needle with the patient in sitting position, Epidural catheter will be passed for 5cm into the epidural space and secured with tapes .Following this subarachnoid block will be given at L3-L4 intervertebral space using 27G Whitacre needle with 3.2ml of 0,5% bupivacaine(hyperbaric) as a standard volume across all groups and also to achieve a dense sensory block to the level of T10. Postoperatively the patients will be monitored in the post anesthesia care unit and on returning of motor movement at toes (active toe movements) on the operated site patients in Group E will be started on Epidural infusion of 0.1% bupivacaine at 4ml/hr and patients in Group EF in addition to Epidural infusion of 0.1% bupivacaine at 4ml/hr. will receive FEMORAL NERVE BLOCK just below the inguinal ligament on the operated side using ultrasonography by in plane technique, Femoral nerve block will be achieved with 15ml of 0.2% ropivacaine .

The patients will be monitored for vital parameters heart rate, NIBP, SPO2 and VISUAL ANALOG SCORE.

The Epidural infusion rate is reduced by 1ml/hr, if the mean blood pressure <30% of base line and increased by 1ml/hr, if the mean blood pressure >30% of the baseline and also if the VISUAL ANALOG SCORE <3 rate epidural infusion is decreased by 0.5ml/hr.

In either groups,

VISUAL ANALOG SCORE-

- 0- NO PAIN
- 1-4-mild pain
- 4-7- moderate pain
- 8-10- severe pain
- 10- worst pain

IF VAS SCORE >/4 then inj. paracetamol 20mg/kg is given as rescue analgesic.

If Vas score >4 within 6hrs after giving paracetamol a second rescue analgesic Inj Diclofenac sodium 1.5mg/kg is given as intravenous infusion.

The patients will be monitored for 24hrs post operatively for VAS scores.

The average pain score over 24hrs and total consumption of rescue analgesics will be noted.

In Post Operative period

Parameters to be noted:

	Heart Rate	Blood Pressure	Visual Analog Score	Amount of Rescue Analgesics used	Rate of epidural infusion
0 Minute					
15 Minutes					
30 Minutes					
45 Minutes					
60 Minutes					
90 Minutes					
2 Hours					
6 Hours					
12 Hours					
24 Hours					

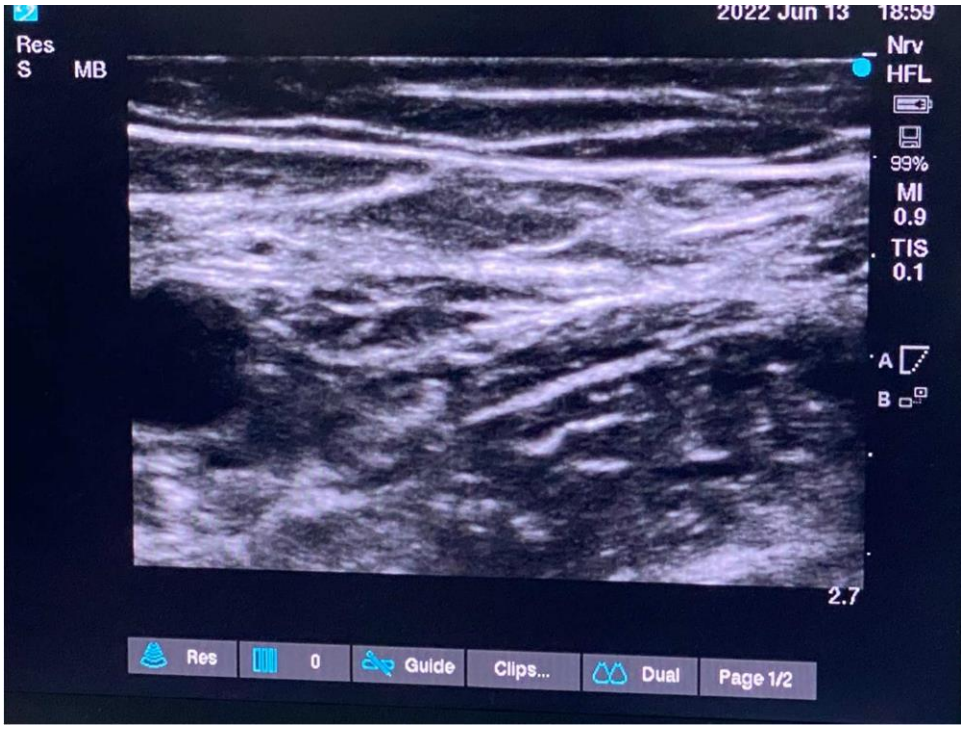
Name and Signature of Investigator: Name and Signature of Anesthesiologist:

Name and Signature of Witness:

ANNEXURE – III- PHOTOGRAPHS

PHOTOGRAPH 1: USG machine with probe

PHOTOGRAPH 2: Linear ultrasound probe

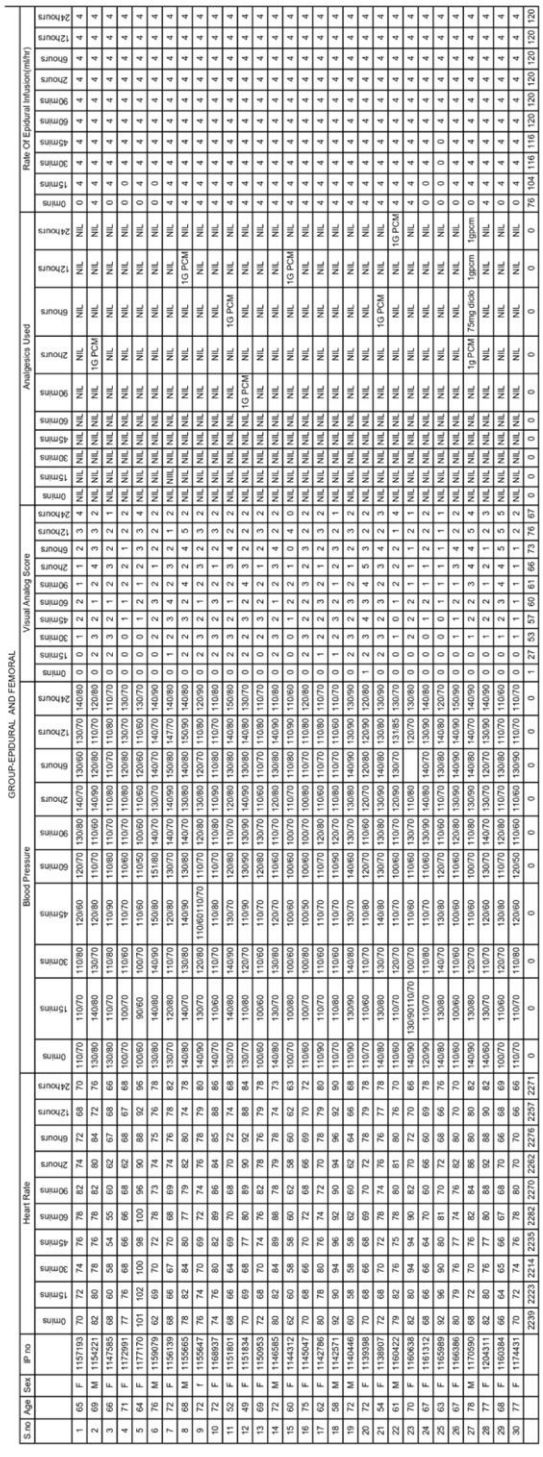


PHOTOGRAPH 3: Femoral Nerve Block

PHOTOGRAPH 4 : Femoral Nerve Block Procedure

ANNEXURE – IV

MASTER CHART:



GROUP-EPIDURAL AND FEMORAL

S.no	Age	Sex	IP no	Heart Rate								Blood Pressure								Visual Analog Score								Analgesics Used								Rate Of Epidural Infusion(ml/hr)							
				0mins	15mins	30mins	45mins	60mins	90mins	2hours	24hours	0mins	15mins	30mins	45mins	60mins	90mins	2hours	24hours	0mins	15mins	30mins	45mins	60mins	90mins	2hours	24hours	0mins	15mins	30mins	45mins	60mins	90mins	2hours	24hours	0mins	15mins	30mins	45mins	60mins	90mins	2hours	24hours
1	65	F	1157193	70	72	74	76	78	82	74	72	68	110/70	110/70	110/80	120/60	120/70	130/80	140/70	130/70	140/90	0	0	1	2	1	2	3	4	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
2	69	M	1154221	82	80	78	76	78	82	80	84	72	76	130/80	140/80	120/80	110/70	130/80	140/90	120/80	110/70	120/80	0	2	3	2	1	2	4	3	2	NIL	NIL	NIL	NIL	1G PCM	NIL	NIL	NIL	4	4	4	4	4	4	4
3	66	F	1147585	68	60	58	54	55	60	62	67	68	66	130/80	110/70	110/90	110/80	110/70	110/80	110/70	110/70	130/70	0	2	3	2	1	2	3	2	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
4	71	F	1172991	77	76	68	66	66	68	62	68	67	68	110/70	100/70	110/80	110/70	110/80	120/80	130/70	130/70	130/70	0	0	0	1	1	2	2	1	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
5	64	F	1177170	101	102	100	98	100	96	90	88	92	95	100/60	90/60	100/70	110/60	110/60	120/60	110/60	130/70	130/70	0	0	0	1	2	1	2	3	4	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
6	76	M	1159079	62	69	70	72	78	73	74	75	76	78	130/80	140/80	140/90	150/90	150/80	140/70	130/70	140/70	140/70	0	0	0	2	3	2	1	2	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
7	72	F	1156139	68	66	67	70	68	69	74	76	78	82	130/70	120/80	110/70	120/80	130/70	140/90	150/80	147/70	140/80	0	1	2	3	4	2	3	2	1	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
8	68	M	1155665	78	82	84	80	77	79	82	80	78	74	140/80	140/70	130/80	140/90	130/80	140/70	130/80	140/80	150/90	0	2	3	2	1	2	3	2	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	1G PCM	4	4	4	4	4	4	4	4
9	72	T	1155647	76	74	70	69	72	74	76	78	79	80	140/90	130/70	120/80	110/60/110/70	110/70	120/80	130/80	120/70	110/80	0	2	3	2	1	2	3	2	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
10	72	F	1168937	74	76	80	82	89	86	84	85	88	86	140/70	110/60	110/70	110/80	110/70	110/80	110/90	110/70	110/80	0	2	3	2	1	2	3	2	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
11	52	F	1151801	68	66	64	69	70	68	70	72	74	68	130/70	140/80	140/90	130/70	120/80	110/70	120/80	130/80	140/80	0	2	3	2	1	2	3	4	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	1G PCM	4	4	4	4	4	4	4	4
12	49	F	1151834	70	69	68	77	80	89	90	92	88	84	130/70	110/80	120/70	110/90	130/90	130/90	140/90	130/80	140/80	0	2	3	2	4	3	2	2	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
13	69	F	1150953	72	68	70	74	76	82	78	76	79	78	100/60	10/60	110/60	110/70	120/80	130/70	110/60	110/70	110/80	0	0	2	3	2	1	2	3	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
14	72	M	1146585	80	82	84	89	88	78	79	78	74	73	140/80	130/70	130/80	120/70	110/60	110/70	120/80	130/80	140/90	0	2	3	2	1	2	3	4	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
15	60	F	1144312	62	60	58	56	60	62	58	60	62	63	100/70	100/80	100/80	100/60	100/60	100/70	110/70	110/80	110/90	0	0	0	1	2	1	0	4	0	NIL	NIL	NIL	NIL	NIL	NIL	NIL	1G PCM	4	4	4	4	4	4	4	4
16	75	F	1145047	70	68	66	70	72	68	66	69	70	72	110/60	100/70	100/80	100/50	100/60	100/70	100/80	110/70	110/80	0	2	3	2	3	2	2	2	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
17	62	F	1142786	80	78	80	76	74	72	70	78	79	80	110/60	110/70	110/70	110/70	110/70	120/80	110/60	110/70	110/80	0	1	2	3	2	1	2	3	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
18	58	M	1142571	82	90	94	96	82	90	94	96	92	90	110/70	110/80	110/70	110/90	120/70	130/80	140/90	139/90	150/90	0	2	3	2	1	2	3	2	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
19	72	M	1140446	60	58	58	58	62	60	62	64	66	68	110/90	130/90	140/80	130/70	140/80	130/70	140/90	140/90	150/90	0	3	2	3	2	1	2	3	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
20	72	F	1139598	70	68	66	68	69	70	72	78	79	78	110/70	110/60	110/80	110/70	120/70	120/80	110/60	120/70	120/80	1	2	3	4	5	3	2	2	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
21	54	F	1138907	72	68	70	72	76	74	76	76	77	78	140/80	130/80	130/70	140/80	130/80	130/90	130/90	140/80	130/80	0	2	3	2	3	4	2	3	4	NIL	NIL	NIL	NIL	NIL	NIL	NIL	1G PCM	4	4	4	4	4	4	4	4
22	61	M	1160422	79	82	76	75	78	80	81	80	76	76	110/60	110/70	120/70	110/70	110/60	110/70	120/90	130/70	131/85	0	0	1	0	1	2	2	1	4	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
23	70	F	1160638	82	80	94	94	90	82	70	72	68	66	140/90	130/70/110/70	100/70	110/60	110/60	130/70	110/80	120/70	130/80	0	0	2	1	2	1	1	2	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	4	4	4	4	4	4	4	4
24	67	F	1161312	68	66	66	64	70	60	66	60	69	78	120/90	110/70	110/80	110/70	110/60	130/90	140/80	140/70	130/90	140/80	0	0	1	2	1	1	2	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	0	4	4	4	4	4	4
25	63	F	1165989	92	96	90	80	81	70	72	68	66	76	140/80	130/80	140/70	130/80	120/70	110/60	110/70	130/80	140/80	120/70	0	0	0	1	1	1	1	1	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	0	0	4	4	4	4	4
26	67	F	1166386	80	79	76	77	74	76	82	80	70	70	110/60	100/60	110/60	100/60	110/60	120/80	130/90	140/90	150/90	0	0	1	1	2	1	3	4	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
27	78	M	1170590	68	72	70	76	82	84	86	80	80	82	140/90	130/80	120/70	110/60	100/70	110/80	130/90	140/80	140/70	140/90	0	0	1	2	2	3	4	5	NIL	NIL	NIL	NIL	NIL	NIL	NIL	1g PCM	0	4	4	4	4	4	4	4
28	77	F	1204311	82	80	76	77	80	88	92	88	90	90	140/60	130/70	110/70	120/60	130/70	140/70	130/70	120/70	130/90	140/90	0	0	1	2	1	2	3	4	NIL	NIL	NIL	NIL	NIL	NIL	NIL	75mg diclo	1gpcm	4	4	4	4	4	4	4
29	68	F	1160384	66	64	65	66	67	68	70	66	68	69	100/70	110/60	120/70	130/80	110/70	120/80	130/80	110/70	110/60	0	0	1	2	3	4	4	5	5	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
30	77	F	1174431	70	72	74	76	78	80	70	70	66	66	110/70	110/70	110/80	120/60	120/50	110/60	110/60	130/90	110/70	110/70	0	0	1	1	1	1	1	2	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	0	4	4	4	4	4	4	4
			2239	2223	2214	2235	2282	2270	2262	2276	2257	2271	0	0	0	0	0	0	0	0	0	1	27	53	57	60	61	66	73	76	67	0	0	0	0	0	0	0	0	76	104	116	120	120	120	120

GROUP-EPIDURAL ONLY

S.no	Age	Sex	IP no	Heart Rate 0mins	15mins	30mins	45mins	60mins	90mins	2hours	6hours	12hours	24hours
1	74	F	1172011	66	64	68	69	72	74	70	68	66	68
2	57	F	1178065	69	72	74	66	68	67	66	69	70	70
3	59	M	1142205	88	89	94	92	88	86	79	82	83	84
4	64	F	1188429	68	70	66	69	82	84	74	76	75	88
5	77	F	1184881	60	58	62	60	54	56	54	60	62	60
6	51	M	1188354	74	70	78	80	76	70	82	84	84	80
7	68	F	1188359	69	70	74	66	60	62	64	60	63	64
8	64	F	1189940	92	98	99	96	94	92	90	88	84	89
9	68	F	1196196	72	70	74	68	79	84	88	80	89	74
10	66	F	1196738	78	82	86	80	92	90	86	88	82	78
11	60	F	1183523	98	92	94	90	90	92	94	92	88	80
12	54	F	1188879	84	82	80	70	74	70	68	69	82	82
13	68	M	1189211	69	70	66	62	64	66	72	80	70	70
14	62	M	1190472	60	62	58	59	66	70	66	62	68	66
15	Nil	M	1192017	66	68	70	66	78	79	70	68	69	70
16	71	F	1194173	66	69	70	74	66	74	80	88	82	79
17	62	F	1164865	66	64	66	68	66	66	64	65	66	69
18	75	M	1140856	74	76	82	83	86	89	92	94	96	98
19	69	F	1142470	88	92	94	96	92	90	88	92	89	92
20	70	M	1161800	86	88	90	99	86	82	84	89	90	96
21	65	F	1195138	69	74	78	80	77	92	90	86	88	90
22	63	F	1196694	79	78	83	85	90	85	80	82	80	77
23	70	M	1204356	89	88	92	94	96	92	80	77	80	76
24	49	F	1204593	88	87	89	90	94	92	93	90	96	97
25	64	M	10014132	66	69	72	70	75	74	77	75	74	73
26	75	M	10015370	78	74	76	75	74	77	73	80	81	82
27	68	F	10007611	82	80	75	80	86	90	91	92	93	94
28	77	F	1204866	70	72	74	80	78	76	77	75	74	79
29	62	F	1204897	86	80	83	85	90	92	94	85	87	86
30	60	F	1144547	66	64	72	79	82	83	84	85	89	92
				2266	2272	2339	2331	2375	2396	2370	2381	2400	2403

S.no	Blood Pressure 0mins	15mins	30mins	45mins	60mins	90mins	2hours	6hours	12hours	24hours
1	110/70	130/80	120/70	110/50	140/60	130/70	140/80	150/90	156/80	140/90
2	110/60	100/70	100/50	120/70	110/80	110/90	130/90	140/80	150/80	140/80
3	130/90	140/80	120/70	110/80	120/70	130/80	140/70	150/80	150/90	140/90
4	110/70	140/80	120/90	130/70	140/80	150/90	130/80	150/70	150/90	150/90
5	110/80	130/90	140/90	150/90	140/90	140/90	130/90	140/80	140/90	140/80
6	130/70	120/60	110/70	120/80	130/80	140/80	130/80	140/80	140/80	150/80
7	110/70	100/80	120/70	110/80	140/80	130/90	140/90	120/80	130/90	130/90
8	100/70	110/60	100/60	90/60	100/60	100/70	130/80	120/70	130/60	110/60
9	110/50	120/60	130/90	130/90	130/70	120/90	130/90	140/80	130/80	130/80
10	110/70	100/60	110/70	120/80	130/70	110/60	120/70	130/80	140/80	140/80
11	110/60	100/60	110/70	100/60	100/70	110/80	130/90	110/70	110/80	100/60
12	100/70	100/70	110/60	120/90	140/80	140/80	150/70	140/80	150/70	140/90
13	110/60	120/70	130/90	140/90	150/80	140/80	140/80	140/90	130/90	140/90
14	110/70	130/70	130/80	140/90	140/90	140/90	150/80	150/80	140/90	140/90
15	130/90	140/90	130/90	140/80	110/70	110/60	140/90	130/80	120/70	150/80
16	110/60	100/60	130/70	140/70	120/60	110/80	120/80	110/60	120/70	130/80
17	130/90	140/80	150/70	140/80	130/90	140/80	150/70	130/80	140/80	140/80
18	110/70	110/60	100/60	110/70	140/80	130/90	140/80	150/80	140/90	150/80
19	110/70	120/80	130/80	150/80	150/76	140/70	130/80	120/90	140/80	150/80
20	130/99	120/80	140/70	150/80	150/80	170/90	150/60	140/70	150/80	155/75
21	110/70	100/60	110/70	120/80	140/90	160/90	150/90	140/90	150/90	160/90
22	120/70	130/80	120/70	140/80	140/90	130/80	140/70	140/60	130/70	130/80
23	110/70	120/80	130/70	140/70	130/80	150/80	140/80	130/80	140/80	130/80
24	110/60	120/70	110/60	130/80	150/90	140/80	150/70	140/70	130/60	130/80
25	130/70	140/80	130/70	140/80	130/70	150/70	140/80	150/70	130/80	140/90
26	117/72	130/80	120/90	130/80	140/90	150/90	140/70	130/80	140/90	130/80
27	130/90	130/80	140/70	140/60	140/70	140/80	140/90	140/80	150/70	130/80
28	110/70	110/60	130/70	120/80	150/70	160/80	170/80	150/80	140/70	140/70
29	150/100	140/90	140/70	140/60	150/70	140/80	140/90	150/70	140/80	150/90
30	130/80	130/70	140/70	130/80	130/70	150/80	130/70	140/80	150/70	160/80
	0	0	0	0	0	0	0	0	0	0

S.no	Visual Analog Score 0mins	15mins	30mins	45mins	60mins	90mins	2hours	6hours	12hours	24hours
1	0	0	2	4	4	4	5	5	5	5
2	0	0	1	3	4	3	5	5	5	5
3	0	3	4	5	5	4	4	3	4	3
4	0	2	2	3	5	5	4	4	5	3
5	0	2	3	4	5	5	4	2	2	1
6	0	0	2	1	4	4	5	4	3	4
7	0	0	1	3	4	4	3	2	2	3
8	0	0	1	3	5	5	5	4	4	4
9	0	0	2	3	5	3	4	5	4	3
10	0	0	1	3	4	4	4	5	4	3
11	0	0	2	4	3	4	4	5	4	3
12	0	0	1	3	5	5	6	5	5	4
13	0	3	4	3	4	3	2	4	5	5
14	0	2	2	3	5	5	4	4	3	3
15	0	0	2	4	5	4	5	5	4	5
16	0	2	3	5	5	4	3	4	4	4
17	2	2	3	4	5	5	6	4	4	4
18	0	0	0	2	4	4	5	5	4	3
19	0	0	1	5	6	6	5	5	4	5
20	0	0	4	4	5	5	4	5	4	4
21	0	0	3	4	4	5	5	4	5	5
22	2	3	3	4	4	4	5	4	3	3
23	1	2	3	3	4	4	5	4	3	4
24	3	4	4	5	5	6	4	4	5	4
25	3	4	5	6	3	4	5	5	6	6
26	2	3	3	4	4	5	4	5	4	4
27	2	2	3	4	4	4	5	4	4	4
28	3	3	4	5	5	5	6	4	4	5
29	2	3	3	4	3	4	5	3	4	3
30	0	0	2	3	5	6	5	6	5	7
	20	40	74	111	133	133	136	128	122	119

S.no	Analgesics Used 0mins	15mins	30mins	45mins	60mins	90mins	2hours	6hours	12hours	24hours
1	NIL	NIL	NIL	1GPCM	NIL	NIL	75MG DICLO	NIL	1GPCM	1GPCM
2	NIL	NIL	NIL	NIL	1G Pcm	Nil	75mg Diclo	75mg Diclo	1gpcm	1gpcm
3	NIL	NIL	1GPCM	NIL	NIL	NIL	1GPCM	NIL	1GPCM	NIL
4	NIL	NIL	NIL	NIL	1gPcm	NIL	NIL	1G Pcm	NIL	NIL
5	NIL	NIL	NIL	1GPCM	NIL	NIL	75MG DICLO	NIL	1GPCM	NIL
6	NIL	NIL	NIL	NIL	1G Pcm	NIL	75mg dICLO	1G Pcm	NIL	1gpcm
7	NIL	NIL	NIL	NIL	1G PCM	NIL	NIL	NIL	NIL	NIL
8	NIL	NIL	NIL	NIL	1g Pcm	NIL	75 Mg diclo	1g Pcm	1g Pcm	1g Pcm
9	Nil	Nil	Nil	Nil	1g Pcm	Nil	1g Pcm	75 mg Diclo	1g Pcm	Nil
10	Nil	NIL	NIL	Nil	1g Pcm	Nil	Nil	75mg diclo	1g Pcm	Nil
11	NIL	NIL	NIL	1g Pcm	Nil	Nil	1g Pcm	75mg diclo	1g pcm	Nil
12	NIL	NIL	NIL	NIL	1g pcm	Nil	75mg Diclo	75 mg diclo	1gPcm	1g Pcm
13	NIL	Nil	1g Pcm	Nil	Nil	Nil	Nil	1g PCM	75Mg Diclo	1g Pcm
14	NIL	NIL	NIL	NIL	1g Pcm	Nil	NIL	1gpcm	NIL	NIL
15	NIL	NIL	NIL	NIL	1gpcm	NIL	NIL	75mg Diclo	1GPCM	1g Pcm
16	Nil	NIL	NIL	1g Pcm	Nil	Nil	Nil	1g PCM	1g Pcm	1g Pcm
17	NIL	NIL	NIL	1GPCM	NIL	NIL	75MG Diclo	1g PCm	1GPCM	1g Pcm
18	NIL	NIL	NIL	NIL	1g PCM	NIL	NIL	75Mg Diclo	1g Pcm	Nil
19	NIL	NIL	NIL	1g Pcm	Nil	Nil	75 Mg Diclo	75 Mg Diclo	1g Pcm	1g Pcm
20	Nil	Nil	1g Pcm	Nil	Nil	Nil	Nil	75mg Diclo	1g	1g Pcm
21	NIL	NIL	NIL	1g Pcm	Nil	75Mg Diclo	Nil	1g Pcm	1g Pcm	1g Pcm
22	NIL	NIL	NIL	1GPCM	NIL	NIL	75MG DICLO	1G PCM	NIL	NIL
23	NIL	NIL	NIL	NIL	1G Pcm	Nil	75mg Diclo	1g pcm	Nil	1g Pcm
24	Nil	1g Pcm	Nil	Nil	Nil	75mg diclo	NiL	1G pcm	75mg diclo	1gpcm
25	Nil	1g Pcm	Nil	Nil	Nil	Nil	75Mg Diclo	Nil	1g Pcm	1g Pcm
26	Nil	Nil	Nil	1g Pcm	Nil	Nil	Nil	75 mg diclo	1g pcm	1g pcm
27	Nil	Nil	Nil	1g Pcm	Nil	Nil	75mg Diclo	1g Pcm	1g Pcm	1g pcm
28	Nil	Nil	1g Pcm	Nil	Nil	Nil	75mg Diclo	1g Pcm	1g Pcm	1g Pcm
29	Nil	Nil	Nil	1g Pcm	Nil	Nil	75MG DICLO	Nil	1g Pcm	Nil
30	Nil	Nil	Nil	Nil	1g Pcm	Nil	75MG DICLO	75mg diclo	1g Pcm	1g Pcm
	0	0	0	0	0	0	0	0	0	0

S.no	Rate Of Epidural Infusion 0mins	15mins	30mins	45mins	60mins	90mins	2hours	6hours	12hours	24hours
1	0	4	4	4	4	4	4	4	4	4
2	0	4	4	4	4	4	4	4	4	4
3	0	4	4	4	4	4	4	4	4	4
4	0	4	4	4	4	4	4	4	4	4
5	0	4	4	4	4	4	4	4	4	4
6	0	4	4	4	4	4	4	4	4	4
7	0	4	4	4	4	4	4	4	4	4
8	0	4	4	4	4	4	4	4	4	4
9	0	4	4	4	4	4	4	4	4	4
10	0	4	4	4	4	4	4	4	4	4
11	0	4	4	4	4	4	4	4	4	4
12	0	4	4	4	4	4	4	4	4	4
13	0	4	4	4	4	4	4	4	4	4
14	4	4	4	4	4	4	4	4	4	4
15	0	4	4	4	4	4	4	4	4	4
16	4	4	4	4	4	4	4	4	4	4
17	4	4	4	4	4	4	4	4	4	4
18	4	4	4	4	4	4	4	4	4	4
19	4	4	4	4	4	4	4	4	4	4
20	0	4	4	4	4	4	4	4	4	4
21	0	4	4	4	4	4	4	4	4	4
22	4	4	4	4	4	4	4	4	4	4
23	4	4	4	4	4	4	4	4	4	4
24	4	4	4	4	4	4	4	4	4	4
25	4	4	4	4	4	4	4	4	4	4
26	4	4	4	4	4	4	4	4	4	4
27	4	4	4	4	4	4	4	4	4	4
28	4	4	4	4	4	4	4	4	4	4
29	4	4	4	4	4	4	4	4	4	4
30	4	4	4	4	4	4	4	4	4	4
	56	120	120	120	120	120	120	120	120	120

ANNEXURE – V - KEY TO MASTER CHART

ASA	-	American society of Anaesthesiologists (Grades I – II)
ml	-	Milli litre
mg	-	Milli gram
g	-	Gram
min	-	Minutes
hrs	-	Hours
VAS	-	Visual Analog Score
PCM	-	Paracetamol
Diclo	-	Diclofenac