SYNERGISTIC EFFECT BETWEEN DEXMEDETOMIDINE AND

EPIDURAL ROPIVACAINE 0.75% FOR ELECTIVE

ORTHOPEDIC PROCEDURES

Dissertation submitted

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CERTIFICATE

This is to certify that this dissertation titled "synergistic effect between dexmedetomidine and epidural ropivacaine 0.75% for orthopedic procedures" has been prepared by Dr.J.RAJARAM under my supervision in the Department of Anesthesiology, Government Kilpauk Medical College, Chennai during the academic period 2009-2011 and is being submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the University regulation for the award of Degree of Doctor of Medicine (M.D Anesthesiology) and his dissertation is a bonafide work.

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DECLARATION

I, Dr.J.Rajaram, solemnly declare that the dissertation , "SYNERGISTIC EFFECT BETWEEN DEXMEDETOMIDINE AND EPIDURAL ROPIVACAINE 0.75% FOR ELECTIVE ORTHOPEDIC PROCEDURES" is a bonafide work done by me in the Department of Anesthesiology and Critical care, Government Kilpauk Medical College ,Chennai under the guidance of Prof.Dr.P.S.Shanmugam, M.D.,D.A., Professor and HOD, Department of Anesthesiology, Government Kilpauk Medical College, Chennai.

Place: Chennai   Signature

Date: (J. RAJARAM)

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I also thank all my colleague Postgraduates for supporting me throughout the study.

I also thank the theatre personnel for their co-operation and assistance. I also thank my family members for their constant encouragement and help throughout the study.

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CONTENTS

INTRODUCTION

Epidural blockade is one of the most useful and versatile procedure in modern anesthesiology. It is unique in that in can be placed virtually at any level of spinal spine, allowing more flexibility in clinical practice. It is more versatile than spinal anesthesia, giving the anesthetist the opportunity for providing continuous surgical analgesia and anesthesia. It can also be utilized for post operative pain control and more rapid recovery from surgery.

Epidural anesthesia can reduce the adverse physiologic responses to surgery such as autonomic hyperactivity, cardiovascular stress, increased metabolic rate, pulmonary dysfunction and immune system dysfunction. Epidural anesthesia also reduces the incidence of hyper coaguability, deep vein thrombosis (DVT), pulmonary embolism (PE) and also decreases intraoperative blood loss. Epidural anesthesia reduces venous blood pressure (measured in the operative wound), and this is the significant factor in determining surgical bleeding.

Orthopedic anesthesia is a challenge for every anesthetist and most of the procedures are well suited for regional anesthetic techniques. Postoperative pain management, a significant problem after orthopedic procedures; with regional anesthetic techniques, leads to superior pain relief. In addition, severe

acute pain after orthopedic surgery can develop into a chronic pain syndrome, which may be ameliorated by aggressive perioperative analgesia. Regional anesthesia avoids manipulation of the airway, and conscious patients can aid in the safest and most comfortable positioning for surgery. The special advantage of epidural adjuvant was the synergistic effect that they exhibit with local anesthetics, which allowed a marked decrease in the dose of both drugs to achieve the same level of analgesia.

AIM OF STUDY

The aim of this study is to evaluate and compare the clinical effects of added dexmedetomidine to epidural ropivacaine 0.75% for lower limb orthopedic procedures.

EPIDURAL ANESTHESIA

HISTORY:

In 1885 Leonard Corning first performed epidural anesthesia with cocaine for relief of pain in an extremity. But it was apparently accidental.

Two French physicians, Jean-Anthanase Sicard and Ferdinand Cathelin have been credited with the intentional administration of caudal epidural anesthesia in 1901. They found that injecting a dilute solution of cocaine through sacral hiatus can provide effective treatment for sciatic pain and suggested the technique for surgical procedures.

In 1921, Fidel Pages (1886-1923), a Spanish military surgeon, devised a technique to introduce epidural procaine at all levels of the neuraxis. His method was to use a blunt needle and then feel and hear entry of the needle through the ligamentum flavum.

Achille Mario Dogliotti (1897-1966) described epidural injections of local anesthetics in 1931, apparently without previous knowledge of the work of Pages. Dogliotti performed extensive studies to determine the spread of solutions within the epidural and paravertebral space after injection. An important innovation was Dogliotti's method of identification of the epidural

space, with the use of continuous pressure on the plunger of a saline-filled syringe as the needle is advanced through the ligamentous structures and sudden loss of resistance when epidural space is entered.

Gutierrez of Argentina developed the "hanging drop" sign, which is still used to identify the epidural space.

In 1936 Charles B. Odom of New Orleans introduced the concept of a test dose to detect intrathecal injection in lumbar epidural anesthesia.

Edward B. Tuohy (1908-1959) used a ureteral catheter threaded through a large Huber-tipped spinal needle to provide continuous spinal anesthesia.

In 1947, Manuel Martinez Curbelo of Havana, Cuba, used the Tuohy needle and a small ureteral catheter to provide continuous lumbar epidural analgesia.

Philip R. Bromage and John J. Bonica performed several studies on epidural dose-response relationships and the hemodynamic changes that followed initiation of the block.

Combining spinal with epidural anesthesia (CSE) began shortly after epidural anesthesia was reintroduced by Dogliotti.

In 1939, Dr. A. L. Soresi presented a paper in which he and his colleagues provided a combination of spinal and epidural anesthesia safely to over 200 patients.

In 1979, a Swedish physician named Curelaru was the first to describe a combined technique using separate intervertebral injections.

Then in 1982, Coates from England and Mumtaz from Sweden published reports of the popular needle-through-needle approach.

DEFINITION

A regional anesthesia may be considered as a reversible form of anesthesia of an anatomic part produced by the application of a chemical capable of blocking conduction in nerve tissue associated with that part without damaging the tissue permanently.

Epidural anesthesia (peridural or extradural) is anesthesia obtained by blocking spinal nerves in the epidural space as the nerves emerge from the dura and then pass into the intervertebral foramina.

ANATOMY:

EPIDURAL SPACE:
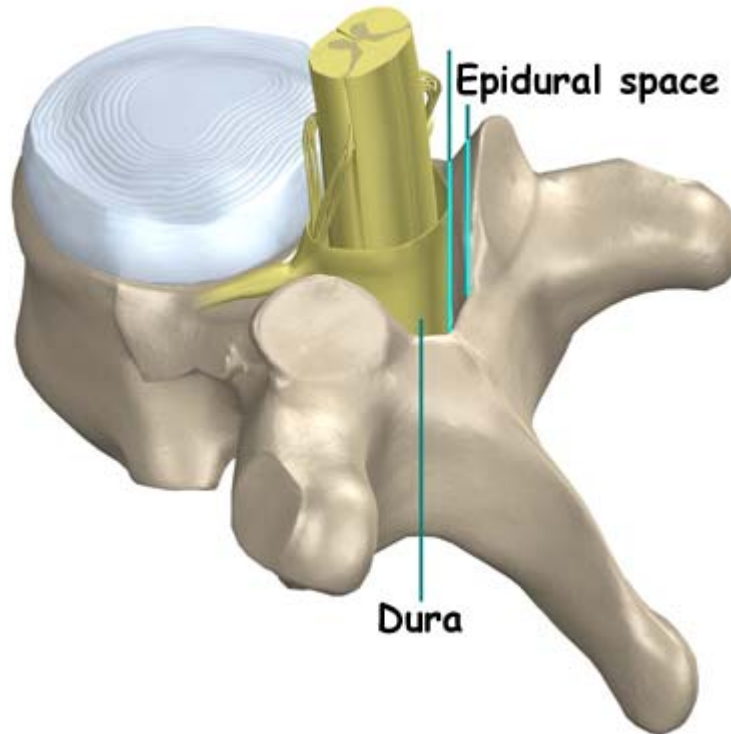
The epidural space is smaller than the subarachnoid space, extends from foramen magnum to the sacral hiatus, and surrounds the dura mater anteriorly, laterally, and posteriorly .At the level of foramen magnum, the periosteal layer of the spinal vertebral canal fuses with the dural layers of the skull. The lower limit is the sacrococcygeal membrane. The epidural space is bounded anteriorly by the posterior longitudinal ligaments, laterally by the pedicles and intervertebral foramina, and posteriorly by the ligamentum flavum. Contents of

the epidural space include the nerve roots that traverse it from foramina to peripheral locations, as well as fat, areolar tissue, lymphatics, and blood vessels, including the well-organized Batson venous plexus. The volume of fat is greater in obese individuals and less in elderly, which explains the age related changes in epidural dose requirements.

Batson's venous plexus is continuous with the iliac vessels in the pelvis and the azygos system in the abdominal and thoracic body walls and has no valves. Off-midline needle insertion more commonly result in blood vessel puncture due to engorged epidural veins converging into the intervertebral foramina.
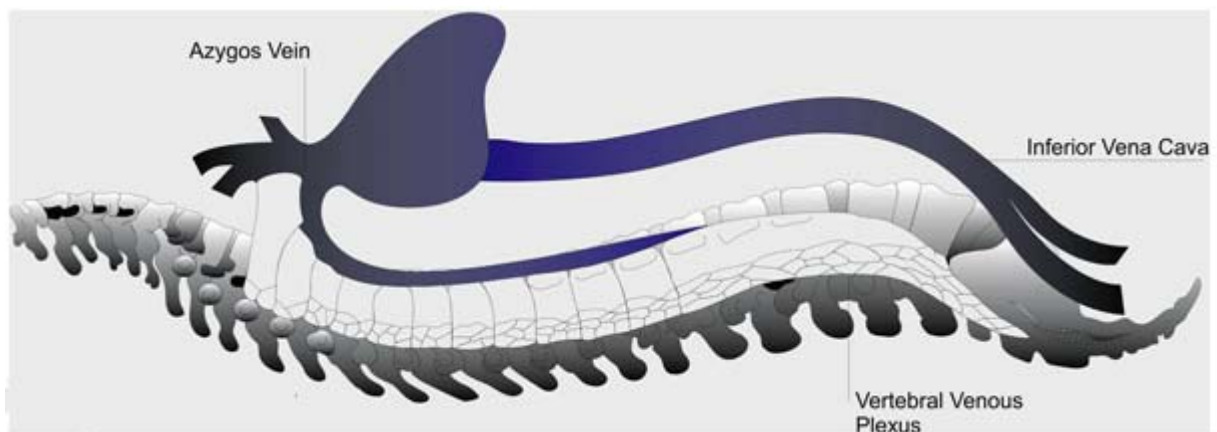
To reach the epidural space in a midline sagittal plane, skin and subcutaneous tissues, supraspinous ligaments, interspinous ligaments and ligamentum flavum are penetrated. Vertebral column provides anatomic factors important in inserting the epidural needle, in cervical and lumbar areas the spinal processes are more horizontal while in the thoracic region they are oblique. The existence of a dorsomedian connection between the dura and the ligamentum flavum is of help in explaining some of the results occurring during the performing of clinical epidural anesthesia.

Surface Anatomy, Structures Superficial to the Epidural Space:

The safest point of entry into the epidural space is below the level of the spinal cord. In adults, this corresponds to the lower border of the L1 vertebrae, and in children, at the lower border of the L3 vertebrae. Epidural insertion in adults is commonly introduced at either the L3-4 interspinous space or one higher, L2-3. A line drawn between the superior aspect of the iliac crests crosses either the spinous process of L4 or the L4-5 interspace. The interspinous space above this point (L3-4 interspinous space) or one higher (L2-3) can safely be chosen for needle entry into the epidural space of adults.

Distance from Skin to Epidural Space:

The epidural space width is 5-6mm in the lumbar region and the thickness of the dura is 0.66-0.33mm. The distance from skin to epidural space is 4cm for 50% of patients and 4 to 6cm for 80% of patients. Maximum depth occurs in between L_3 & L_4 spines, probably related to lumbar lordosis.

VERTEBRAL COLUMN:

GENERAL APPEARANCE

The vertebral column consists of 7 cervical, 12 thoracic, and 5 lumbar vertebrae. At the caudal end, the 5 sacral vertebrae are fused to form the sacrum, and the 4 coccygeal vertebrae are fused to form the coccyx . The primary functions of the vertebral column are to maintain erect posture, to encase and protect the spinal cord, and to provide attachment sites for the muscles responsible for movements of the head and trunk.

STRUCTURE OF VERTEBRAE

Each vertebra is composed of a vertebral body and a bony arch. The arch consists of two anterior pedicles and two posterior laminae. The transverse processes are located at the junction of the pedicles and lamina, and the spinous process is located at the junction of the laminae. The spinous processes vary in their angulation in the cervical, thoracic, and lumbar regions. The spinous processes are almost horizontal in the cervical, lower thoracic, and lumbar regions, but become significantly more sharply angled in the midthoracic region. The greatest degree of angulation is found between the T3 and T7 vertebrae, making insertion of an epidural needle in the midline more difficult.

JOINTS OF THE VERTEBRAL COLUMN

The vertebrae articulate at the intervertebral and facet joints. The intervertebral joints are located between adjacent vertebral bodies. They maintain the strength of attachment between vertebrae. The facet joints form between articular processes. The facet joints are heavily innervated by the medial branch of the dorsal ramus of the spinal nerves. This innervation serves to direct contraction of muscle that moves the vertebral column.

LIGAMENTS

The vertebrae are joined together by a series of ligaments and disks. Anteriorly, the vertebral bodies are separated by the intervertebral disks. The ligament connecting them runs from the base of the skull to the sacrum and is called the anterior longitudinal ligament. The posterior surface of the vertebral bodies is connected by the posterior longitudinal ligament, which also forms the anterior wall of the vertebral canal. The other ligaments of importance:

- Intertransverse ligaments: connects transverse processes

- Supraspinous ligaments: attaches to the apices of the spinous processes, extends from sacrum to skull where it becomes the ligamentum nuchae

- Interspinous ligaments: connects spinous processes

- Ligamentum flavum: thick, elastic ligament, connects the laminae, composed of a right and left ligament that joins in the middle forming an acute angle; narrows toward the articular processes
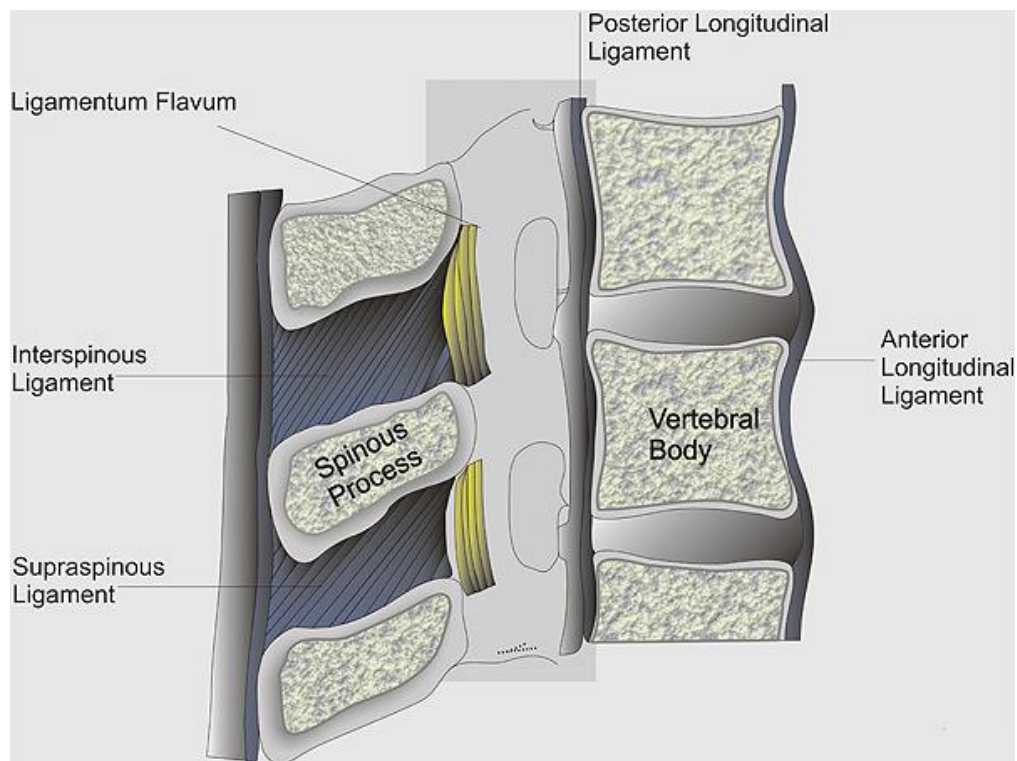
SPINAL CORD/SPINAL CANAL

The spinal canal is formed by adjacent vertebral foramina. The canal provides support and protection to the spinal cord and its nerve roots. The spinal cord extends from the foramen magnum to the L1-2 vertebral level in adults, and L3 vertebral level in children before becoming the conus medullaris.

From the spinal cord extends a series of dorsal and ventral roots that converge to form mixed spinal nerves. The mixed nerves contains motor, sensory, and in many cases, autonomic fibers. There are eight cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal pairs of spinal nerves. The roots inferior to the conus medullaris become the cauda equina before exiting through the lumbar and sacral foramina. After the spinal nerves leave the spinal canal through the intervertebral foramina, they divide into the anterior and posterior primary rami. The posterior primary rami innervate the skin and muscles of the back. The anterior rami supply the rest of the trunk and the limbs. Each spinal nerve supplies a specific region of skin referred to as a dermatome.

Preganglionic fibers of the sympathetic nervous system originate from the spinal cord from T1 to L2. They travel with spinal nerves to form the sympathetic chain. This chain extends the entire length of the spinal column on the anterolateral aspects of the vertebral bodies. The chain gives rise to the stellate ganglion, splanchnic nerves, and the celiac plexus.
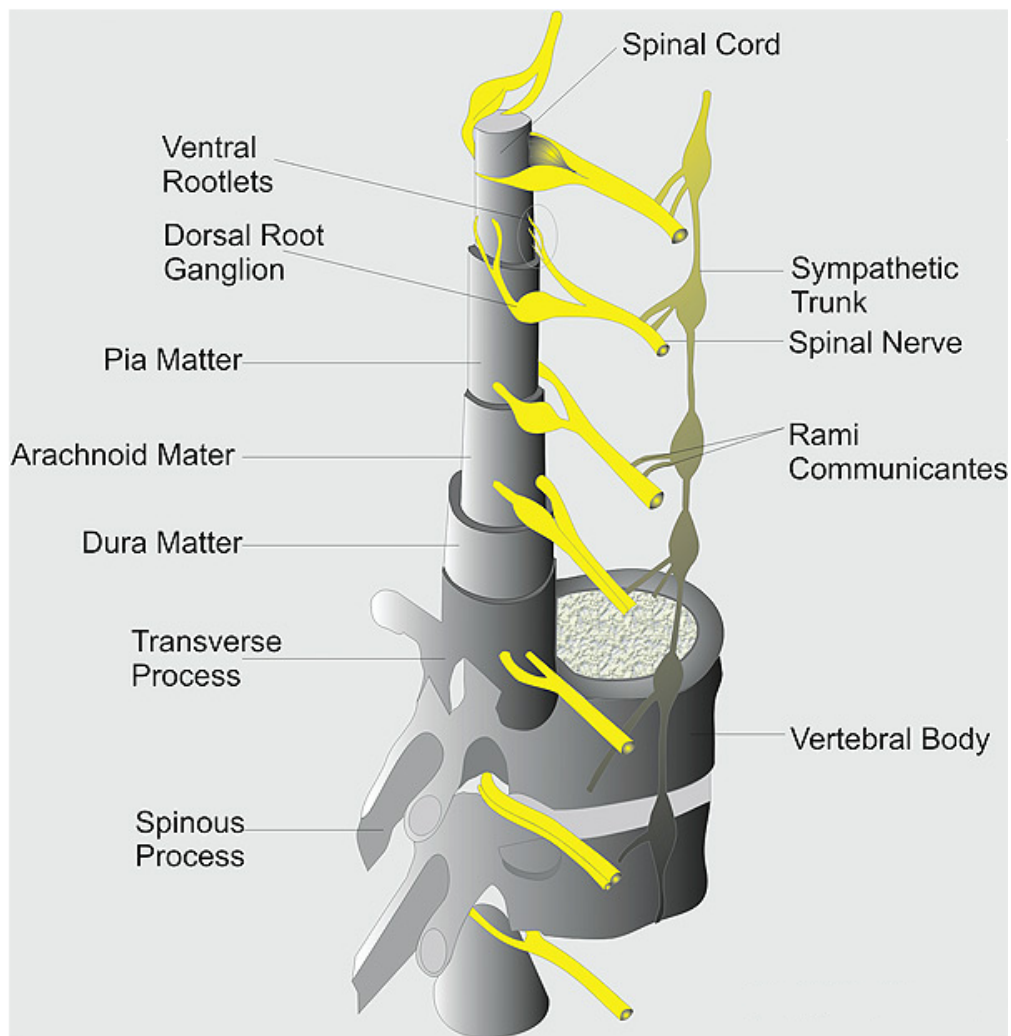
MENINGES/MENINGEAL SPACES

Surrounding the spinal cord and its roots are three layers of membranes. The innermost layer is called the pia mater, which attaches intimately to the surface of the spinal cord and roots of the spinal nerves. As the roots of the spinal nerves extend distally, the pia mater transforms into the second layer called the arachnoid. The arachnoid detaches from the roots and reflects back across the pia, enclosing the spinal cord within a cavity called the subarachnoid space. The space is filled with cerebrospinal fluid and transmits blood vessels to and from the spinal cord. Superficial to the arachnoid is the thick dura mater. The space between the arachnoid and dura is called the subdural space. Because the arachnoid is pushed against the dura mater by the pressure of the CSF, the subdural space is negligible. It contains a small amount of serous fluid which allows the dura and arachnoid to move over each other.

EPIDURAL PHYSIOLOGIC CONSIDERATIONS

A negative epidural pressure was described in 1928 by Heldt and Moloney.In lower lumbar region it amounts to 0.5cmH2O, in upper lumbar region 1cmH2O and 2cmH2O in thoracic region.

1. Cone theory: The needle introduced into the epidural space depresses the dura, creating a large epidural space an artifact caused by indentation of dura by advancing needle which creates negative pressure.

2. Transmission theory: Negative pressure in the epidural space is caused by transmission of intrapleural negative pressure through the intervertebral foramina to epidural space.

SITE OF ACTION

The site of action of local anesthetic agents in epidural include

1. On the nerves as they traverse the epidural space.

2. On the nerves as they pass out through intervertebral foramina,where spinal nerves lose their protective dural sheaths.

3. On the nerves in the subarachnoid space-the agent having reached this area by diffusion through the dura.

FATE OF EPIDURAL AGENTS (VASCULAR ABSORBTION PHARMACOKINETIC):

Bromage has summarized the fate of epidural local anesthetic agents

1. Leakage by vascular absorbtion

2. Leakage through interverbral foramina

3. Diffusion through dural root sleeves

4. Diffusion through dura mater into CSF

FACTORS DETERMINING SPREAD OF EPIDURAL ANESTHESIA:

1. Volume of anesthetic solution-The dose of local anesthetics necessary for analgesia or anesthesia is a function of the concentration of the solution and the volume injected. Volume is the variable that affects the degree of distribution of the block. Guideline for dosing an epidural in adults is 1–2 mL per segment to be blocked.

2. Age factor-Spread increases with age due to the fact that escape from epidural space is less due to intervertebral foramina being more fixed and epidural vessels less penetrable. Decrease in epidural space adipose tissue with age may dominate the age-related changes in epidural dose requirements.

3. Height factor-segment volume should be modified according to patient height. Up to 150cm 1.0ml/segment and increase 0.1ml/segment anesthetic solution for each 5cm as suggested by Bromage

4. Selection of interspace-Next to volume of anesthetic solution, selection of interspace is the single most important factor in assuring adequate analgesia. The epidural blockade is most effective when the block or the catheter is inserted in a location that corresponds to the dermatomes covered by the surgical incision. The most rapid onset and the densest block occur at the site of injection.

DETECTION OF EPIDURAL SPACE:

1. Hanging drop sign(Gutierrez sign)-A small drop of sterile water is placed at the hub of needle,when the needle advanced through the ligamentum flavum this drop is sucked into the epidural space.

2. Loss of resistance technique-sudden loss of pressure exerted on the plunger of a syringe filled with air,saline or water as the needle advanced through the ligamentum flavum was used to identify epidural space.

3. whoosh test- The "Whoosh" test involves injecting air through the needle while an assistant simultaneously listen with a stethoscope over the thoracolumbar spine in the midline. If injection of air is heard with the stethoscope (a positive whoosh test) then the needle was deemed to be correctly located in the epidural space. Saline is used instead of air in modified"Swoosh" test.

4. Lund sign-As the epidural space is entered , there is a sudden loss of resistance and saline is injected into the epidural space and the patient may experience burning pain.

5. Bonniot's phenomenon-On entering epidural space with a bare needle,an audible hiss may be noticed,signifying that air is sucked into epidural space.

6. Mostert reported a reverse phenomenon.when a syringe filled with equal parts of air and saline is injected into epidural space ,the syringe is quickly reversed, there will occur an outward reflux of froth.

7. Bidigital pressure test(BiP Test): BiP Test is that when pressure is applied to the tissues ,this compresses them, increasing their density and thus increasing resistance to the needle.

8. Free dripping saline: The infusion set was prepared with saline and connected to the hub of an epidural needle. Free dripping of saline was regarded as a sign that the needle tip had entered the epidural space.

9. Queckenstedt-test- new method to confirm epidural puncture by assessing indirect changes in epidural pressure using the Queckenstedt-test procedure, which increases subarachnoid pressure by compressing the internal jugular veins .

CLINICAL CONSIDERATION OF EPIDURAL:

INDICATIONS	CONTRAINDICATIONS
Poor risk patients	Severe hemorrhage or shock
Cardiac disease	Uncooperative or apprehensive patients
Pulmonary disease	Previous laminectomy
Metabolic disturbances	Coagulation defects: patients on anticoagulants or hemophiliacs
When spinal anesthesia is contraindicated	Local inflammation
When general anesthesia is contraindicated	Increased intracranial pressure
Obstetric anesthesia	Allergy to local anesthetics

ADVANTAGES	DISADVANTAGES
The area of anesthesia is well defined	Technical difficulty resulting from the need for accurate placement of needle.
The duration of anesthesia is longer than spinal	Incomplete muscle relaxation.
The more severe disturbances of spinal naesthesia (headaches, meningitis, arachnoiditis) are minimized.	Need for large volumes of fluid and hence large quantities of drug to achieve anesthesia .
GI complaints are minimal. Nausea and vomiting are minimal.	Danger of entering subarachnoid space.
Catheterization incidence is small; urinary retention average 1.5%.	Bleeding in epidural space by catheter injuring venous plexus
	Spotty segmental block not infrequent
	Occasional back pain.

EPIDURAL ADJUVANTS:

Many classes of drugs have been used in epidural as adjuvants, which includes opioids, α-adrenergic agonists, anticholinesterases, ketamine and midazolam.

α-adrenergic agonists used in neuraxial anesthesia along with local anesthetics has many advantages which includes,

1. Prolongs and intensifies the effects of epidural local anesthetics without increasing the degree of hypotension for epidural anesthesia and analgesia

2. Produces analgesia without motor impairment and prolongs the duration of the local anesthetic analgesic effect

3. Modulates the immune stress response to surgery

4. May reduce cytokine response, therefore further reducing pain sensitivity

PHYSIOLOGIC EFFECTS OF EPIDURAL BLOCKADE

The primary site of action of local anesthetic solutions injected into the epidural space is the spinal nerve roots. The segmental nerve roots in the thoracic and lumbar regions are mixed nerves, containing somatic sensory, motor, and autonomic nerve fibers. Sensory blockade interrupts the transmission of both somatic and visceral painful stimuli, whereas motor blockade provides muscle relaxation with a varying degree of sympathetic blockade. The injection site for epidural anesthesia should be close to the nerve roots of interest in order to obtain the best results with minimal amount of local anesthetic and decreased risk of side effects from systemic absorption of the local anesthetic.

Differential nerve block, an important concept for epidural anesthesia, refers to the phenomenon in which nerve fibers with different functions demonstrate a varying sensitivity to the effects of local anesthetics. Sympathetic fibers are usually blocked first followed by pain/temperature, then proprioception, followed by motor blockade. After an epidural block, sympathetic blockade (temperature) may vary from zero to four segments higher than the sensory block level (pain/light touch), which is two segments higher than motor blockade. Regression of the block occurs in reverse order.

The physiologic effects of epidural blockade on organ systems depends on the spinal level and the number of spinal segments blocked. In general, high thoracic epidural blocks and extensive epidural blocks are associated with more profound sympathetic block, resulting in a more profound physiologic effect in the cardiovascular system.

CARDIOVASCULAR SYSTEM:

BLOCK BELOW T4

The effect of epidural anesthesia on the cardiovascular system depends on the level and the degree of sympathetic blockade. The sympathectomy that accompanies the techniques depends on the height of the block, with the sympathectomy typically described as extending for two to six dermatomes above the sensory level with spinal anesthesia and at the same level with epidural anesthesia. Vasomotor tone is maintained by sympathetic fibers from T5 to L1 that innervate vascular smooth muscle. Blockade of these fibers cause venodilation with venous pooling as well as arterial vasodilation with decreased systemic vascular resistance. The venous pooling leads to a marked decrease in venous return, right atrial pressure, and subsequently, cardiac output. The decrease in venous return can then lead to an increase in cardiac

vagal tone,especially for blocks near the T5 level. Clinically, the patient can be hypotensive withouta change or a decrease in heart rate.

The compensatory mechanism for the decrease in mean arterial pressure is a reflex increase in vasoconstriction above the level of the block as well as a release in catecholamines from the adrenal medulla.

BLOCK ABOVE T4

The cardiovascular effects of a block above T4 are the result of a high sympathetic block. The cardiac sympathetic fibers arise from T1 to T4, and when blocked, profound hypotension (the result of a decrease in cardiac contractility) and bradycardia can occur. In addition to the cardiac effects, a high level of sympathetic blockade causes:

- Increased central venous pressure without an increase in stroke volume
- Vasoconstriction in the head, neck, and upper limbs
- Splanchnic nerve blockade with blockade of medullary secretion of catecholamines
- Blockade of vasoconstrictive effect on the capacitance vessels of the lower limbs

RESPIRATORY SYSTEM:

Lung volumes (tidal volume, vital capacity), resting minute ventilation, and dead space are basically unchanged even with a higher thoracic epidural. Even with abdominal or intercostal muscle paralysis by a high thoracic block, major alteration in pulmonary function is not seen.

There is concern regarding the use of epidural blockade in patients with severe chronic lung disease patients dependent on accessory muscle function to maintain adequate ventilation, because paralysis of respiratory muscles and changes in bronchial tone from epidural analgesia can occur. Thoracic epidural analgesia with 0.25% bupivacaine did not adversely affect ventilator mechanics, breathing pattern, gas exchange, and inspiratory muscle force generation even in COPD patients.Respiratory arrest in epidural blockade is from the sympathetic block, leading to decreased cardiac output with subsequent reduced blood flow to the brain.

GASTROINTESTINAL SYSTEM:

The gastrointestinal effects of epidural anesthesia are largely the result of blockade of the sympathetic splanchnic fibers from the T5 through L1 level. Unopposed vagal dominance leads to an increase in secretions; peristalsis; and a small, contracted gut. Postoperatively, gastrointestinal motility returns more quickly when epidural analgesia with a local anesthetic is instituted. Segmental sympatholysis creating an increase of sympathetic activity in segments below the block leads to impaired splanchnic blood flow. Nausea is a related to increased gastric peristalsis secondary to unopposed vagal activity. It can be prevented by promptly treating hypotension with a fluid bolus, ephedrine. Atropine has been shown to be an effective treatment for nausea associated with a high thoracic block.

RENAL/GENITOURINARY SYSTEM:

Since renal blood flow is maintained through autoregulation, an epidural has very little effect on renal function. Neuraxial blockade at the lumbar level has been postulated to impair control of bladder function secondarily to blockage of the S2 to S4 segments. Urinary retention may occur until the block wears off. If a continuous epidural is used, then urinary catheterization may be necessary.

NEUROENDOCRINE SYSTEM:

Increased protein catabolism and oxygen consumption are common. Increased plasma concentrations of catecholamines, vasopressin, growth hormone, renin, angiotensin, cortisol, glucose, antidiuretic hormone, and thyroid-stimulating hormone have been documented and referred to as the surgical stress response. Intraoperative manifestations of the response is demonstrated as hypertension, tachycardia, hyperglycemia, suppressed immune function, and altered renal function. Afferent sensory information from the surgical site is thought to play a pivotal role in the response.The response can be completely abolished by an appropriate level of sensory blockade produced by regional anesthesia. The inhibitory effect is greatest with lower abdominal and lower extremity surgery and slightly less effective in upper abdominal and thoracic surgery, probably because the epidural cannot completely block all nociceptive afferent pathways.

The most critical effect of neuroendocrine activation in the perioperative period is the increase in plasma norepinephrine, which peaks about 18 h after the surgical stimulus is initiated. The increase in plasma norepinephrine is associated with activation of nitric oxide in the endothelium of patients with atherosclerotic disease, producing paradoxic vasospasm. Thus, in patients with

significant atherosclerotic disease, the combination of paradoxic vasospasm and the hypercoagulable state may be the reason underlying the cardioprotective effects of thoracic epidural anesthesia and analgesia in patients with cardiac disease.

PHARMACOLOGY OF EPIDURAL BLOCKADE

The principal site of action of local anesthetics after epidural injection is thought to be the spinal nerve roots, the spinal cord, and possibly the brain. Nerve fibers with different features and function display varying sensitivity to local anesthetic blockade. Sympathetic fibers (thin, myelinated when entering the sympathetic trunk) tend to be blocked with the lowest concentration of drug, followed by pain, touch, and finally motor fibers.

NERVE IMPULSE PHYSIOLOGY

Nerve conduction involves the propagation of an electrical impulse created by the rapid movement of ions across the nerve cell membrane, creating an action potential. The principal ions involved in generating the action potential are sodium and potassium. The concentration of sodium is high extracellularly and low intracellularly. The opposite is true of potassium (high intracellularly, low extracellularly).

At rest, the cell is more permeable to the positively charged cation potassium. The leakage of a positively charged ion leaves the inside of the cell more negative than the outside of the cell, creating a negative resting membrane potential of -60 to -70 mV. The sodium–potassium pump actively

transports sodium ions out of the cell and potassium into the cell to maintain the gradient at the resting level.

Once chemical, mechanical, or electrical excitation occurs, an impulse is conducted along the nerve axon, causing depolarization of the nerve cell membrane. If the depolarization exceeds the threshold level (membrane potential of–60 mV), ion channels in the cell membranes open, allowing a sudden influx of sodium. The rapid influx of positively charged sodium ions causes depolarization of the cell. The influx of positively charged ions alters the membrane potential to become positive (above +30 mV). When the membrane potential exceeds approximately −30 mV, the sodium channels close, abating the influx of sodium into the cell. Depolarization generates a current that causes further depolarization of adjacent segments of the nerve, allowing the action potential to spread along the entire length of the nerve. The cell attempts to return to its resting potential with the efflux of potassium, thereby making the membrane potential less positive (repolarization). Baseline concentration gradients are eventually reestablished by the sodium–potassium–ATP-ase pump.

The rapid influx of sodium that leads to depolarization of the nerve occurs through specific channels in the cell membrane. The sodium channel is

a path that changes the nerve from nonconductive to conductive of an action potential (referred to as gated channels). If the change in conductance is created by electrical changes, the channel is called a voltage-gated channel. The voltage-gated sodium channel in the nerve is considered to be the site of action for local anesthetics.

ACTION OF LOCAL ANESTHETICS

Local anesthetic binds to sodium channels, primarily in the inactivated state, preventing further channel activation. Sodium ion movement into the cell is prevented, effectively blocking the development of the action potential. The resulting resting membrane potential is unaffected by further nerve stimulation, referred to as membrane stabilization of local anesthetics.

MECHANISM OF ACTION OF LOCAL ANESTHETICS IN NEURAL BLOCKADE:

Within the dorsal horn, local anesthetics can block both sodium and potassium ion channels in the dorsal horn neurons, inhibiting the generation and propagation of pain signals (nociceptive electrical activity). Motor blockade occurs from a similar action on the ventral horn neurons. Blockade of calcium ion channels in the spinal cord leads to resistance of electrical

stimulation from nociceptive afferent nerves, creating an intense analgesic action seen in centrally administered local anesthetics.

In addition to ion channel alterations in the central neuraxis, epidurally administered local anesthetics indirectly inhibit the release of substance P and other neurotransmitters involved in pain signal processing. Substance P is involved in pain transmission from the presynaptic terminals of dorsal root ganglionic cells. The putative effects of centrally administered local anesthetics on substance P and these other transmitters is linked to the presynaptic blockade of the voltage-gated calcium channel. When calcium entry is blocked at the presynaptic level, release of these neurotransmitters (glutamate, substance P, calcitonin gene-related peptide [CGRP], neurokini-1 and -2 [NK1, NK2]) at the presynaptic level does not occur. Therefore, epidurally administered local anesthetics can indirectly inhibit pain signal transmission.

ROPIVACAINE PHARMACOLOGY:

Ropivacaine is a long acting ,enantiomerically pure (S-enantiomer) amide local anesthetic. It is the propyl analogue of bupivacaine with high pKa and low lipid solubility.

PHARMACOKINETICS:

The pKa is 8.07, protein binding is 90-94%, while its partition coefficient is 147 and molecular weight is 328.89.this agent is 30% more potent than bupivacaine and CC:CNS ratio is 5:1

PHARMACODYNAMICS:

Ropivacaine has significantly better sensory-motor differentiation due to lower lipid solubility and so blocks nerve fibres involved in pain transmission (A delta and C fibres) to a greater degree than those controlling motor function (A beta fibres). Its onset time and duration are comparable to bupivacaine but with less cardiotoxicity due to the fact that it dissociates from sodium channels more rapidly and produces less accumulation of sodium channel.ropivacaine has mild intrinsic vasoconstricing properties, so it is unsuitable for infiltration in tissues without collateral blood supply and is the reason for longer cutaneous anesthesia.

STRUCTURAL FORMULA OF ROPIVACAINE:
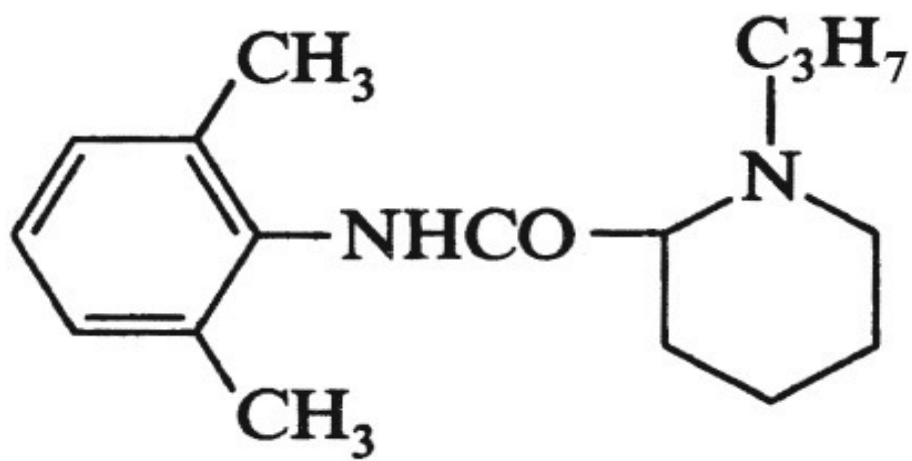
DEXMETOMIDINE:

HISTORY

The α_2-adrenergic agonists provide sedation, anxiolysis, hypnosis, analgesia, and sympatholysis. Dexmedetomidine is a more selective α_2 agonist with a 1600 greater selectivity for the α_2 receptor compared with the α_1 receptor.

PHYSICOCHEMICAL CHARACTERISTICS

Dexmedetomidine is the d-enantiomer of medetomidine, a substance that has been used for sedation and analgesia in veterinary medicine for many years. It shows a high ratio of specificity for the α_2 receptor (α_2/α_1 1600:1) compared with clonidine (α_2/α_1 200:1), making it a complete α_2 agonist. Dexmedetomidine belongs to the imidazole subclass of α_2 receptor agonists, similar to clonidine.

STRUCTURAL FORMULA OF DEXMEDETOMIDINE:
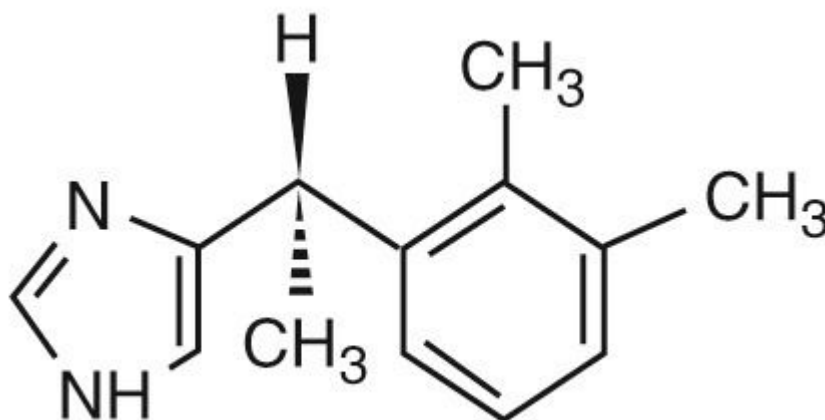
METABOLISM AND PHARMACOKINETICS

Dexmedetomidine is rapidly distributed and extensively metabolized in the liver and excreted in urine and feces. Dexmedetomidine is 94% protein bound, and its concentration ratio between whole blood and plasma is 0.66 and displays nonlinear pharmacokinetics.. These pharmacokinetic parameters apparently are unaltered by age or weight or renal failure, but clearance is a function of height. The elimination half-life of dexmedetomidine is 2 to 3 hours.

PHARMACOLOGY

Dexmedetomidine is a nonselective α_2 agonist. Alpha$_2$ adrenoreceptors are membrane-spanning G proteins. Intracellular pathways include inhibition of adenylate cyclase and modulation of ion channels. These receptors are involved in the sympatholysis, sedation, and antinociception effects of α_2 adrenoreceptors.

EFFECTS ON THE CENTRAL NERVOUS SYSTEM

The α_2 agonists produce their sedative-hypnotic effect by an action on α_2 receptors in the locus caeruleus and an analgesic action at α_2 receptors within the locus caeruleus and within the spinal cord. Despite sound levels of sedation

with dexmedetomidine, there is limited respiratory depression, providing wide safety margins. The α2 agonists have the advantage that their effects are readily reversible by α2-adrenergic antagonists (e.g., atipamezole).Dexmedetomidine reduced the intracerebral catecholamine outflow during injury and resulted in less neural tissue damage with better neurologic outcome.

EFFECTS ON THE RESPIRATORY SYSTEM

Dexmedetomidine at concentrations producing significant sedation reduces minute ventilation, but retains the slope of the ventilatory response to increasing carbon dioxide. Dexmedetomidine also exhibited a hypercarbic arousal phenomenon, which has been described during normal sleep and is a safety feature.

EFFECTS ON THE CARDIOVASCULAR SYSTEM

The basic effects of $α_2$ agonists on the cardiovascular system are decreased heart rate; decreased systemic vascular resistance; and indirectly decreased myocardial contractility, cardiac output, and systemic blood pressure. Infusion of dexmedetomidine also has been shown to result in a compensated reduction in systemic sympathetic tone without changes in baroreflex sensitivity.

INTRODUCTION TO CLINICAL STUDY

The α_2-adrenergic agonists provide sedation, anxiolysis, hypnosis, analgesia, and sympatholysis. Dexmedetomidine shows a high ratio of specificity for the α_2 receptor (α_2/α_1-1600:1) compared with clonidine (α_2/α_1-200:1), making it a complete α_2 agonist [27].

Alpha$_2$ agonists do have an analgesic effect when injected via the intrathecal or epidural route [4,5,6]. Intrathecally injected dexmedetomidine in sheep reduces blood pressure in 1 minute. When dexmedetomidine is injected into the epidural space, it rapidly diffuses into the CSF (in one study, 22% of the injected dose was identified in the CSF). The effects on blood pressure are slower in onset with an epidural injection than with an intrathecal administration. Epidural effects are seen in 5 to 20 minutes. The primary site of analgesic action is thought to be the spinal cord [5,6].

In humans, dexmedetomidine was first administered epidurally in 1997, combined with lidocaine 1.5 % in patients undergoing hysterectomy, prolonging postoperative analgesia [6]. Based on studies with clonidine [7.8], we evaluated the synergism of dexmedetomidine with ropivacaine during epidural administration, in improving the characteristics of anesthesia. The aim of this study was to evaluate the clinical effects of Dexmedetomidine added to ropivacaine on the characteristics of epidural anesthesia.

METHODOLOGY

After approval of the study protocol by the Ethics committe and obtaining informed consent. It was a comparative, double blind, randomized, controlled study and distribution by means of a draw with a sealed envelope.

INCLUSION CRITERIA	EXCLUSION CRITERIA
□ ASA I & II	□ ALLERGY TO LOCAL ANESTHETICS
□ BOTH SEXES	□ NM DISEASES
□ AGE BETWEEN 18-70 yrs	□ USING α_2 ANTAGONISTS
□ ELECTIVE ORTHOPEDIC PROCEDURE	□ WEIGHT MORE THAN 120 kg
□ UNDER EPIDURAL ANESTHESIA	
□ WITHOUT COMORBID ILLNESS	

Patients were admitted to the hospital, after a period of absolute fasting at least 8 hours, without administering premedication. venipuncture was performed with an 18G catheter for administration of Ringer's lactate, 8 ml.kg^{-1}. h^{-1}. Monitoring consists of, Pulse oximetry (SpO$_2$), NIBP,ECG. persons not directly involved in the anesthetic prepared dexmedetomidine or sodium chloride 0.9%, 1 ml syringe . Epidural puncture was performed with a 18G Tuohy needle, through the lumbar epidural space, with patients in sitting position, through loss of resistance technique.Patients were sedated on demand basis with pentazocine or midazolam.

All patients received an epidural:

Control Group (n = 20): 1 ml of sodium chloride 0.9 % (placebo); Dexmedetomidine group (n = 20): 1 $\mu g.kg^{-1}$ + dexmedetomidine solution of sodium chloride 0.9 %, so that the volume was completed in 1 ml syringe. Immediately after the injection of the study drug, all patients were administered 20 ml of 0.75% (150 mg), the rate of 1 ml every three seconds.

After the surgery, patients were referred to the recovery room, where they remained for a period, until there was complete recovery of sensory and motor block.All were monitored with Pulse oximetry (SpO_2), NIBP,ECG.Patients who complained of pain were given rescue post-operative analgesia with 10ml of 0.2% Ropivacaine through epidural route.

DEFINITION OF VARIABLES:

SENSORY BLOCK ONSET TIME

Time interval between end of anesthetic injection and appearance of cutaneous analgesia in dermatomes T-12, T-10, T-8, T-6

DURATION OF MOTOR BLOCK

Administration of anesthetic and attainment of grade 0 in Bromage motor scale

DURATION OF ANALGESIA

Administration of anesthetic and disappearance of cutaneous level at each dermatomal level

POST-OP ANALGESIA DURATION

Administration of anesthetic and time of analgesic usage in PACU

SUPPLEMENTAL SEDATION

If patient felt pain or uncomfortable , with pentazocine 0.3mg/kg and or midazolam 0.02mg I.V

If there were hypotension, (measured as systolic blood pressure less than 30 % of its initial value or below 90 mmHg) during anesthesia, it was treated

with administration of ephedrine, 6 to 12 mg and increased administration of intravenous fluids.

Bradycardia(heart rate<45) were treated with atropine, 0.6 mg , and administration of oxygen via face mask (4 l.min^{-1}), if SpO$_2$ was < 94%.

STATISTICAL ANALYSIS:

It's a double blind randomized controlled clinical study

Variables were analysed with Student't' test, Chi Square test

Variables like age, sex, weight, height were compared using Levene's test for equality of variance

Sample size obtained according to previous background study

'p' value less than 0.05 was taken as significant

RESULTS

One patient in the control group excluded for failure of epidural and need for general anesthesia.

There was no significant difference between groups in distributions of age, weight, height and sex, type of surgery or duration of surgery.

VARIABLES		CONTROL	DEX
Age		42.25	39.1
Sex	Female	3	4
	Male	17	16
Height (cm)		169.4	163.2
Weight (kg)		69.95	66.75
Level Of Epidural	L1-L2	2	2
	L2-L3	10	10
	L3-L4	8	8
Cathetar Length (cm)		6.5	6.85
Surgery	IM / IL Nailing	10	9
	Illizarao ring fixation	4	2
	DHS	2	5
	TKR	1	1
	THR	1	0
	DCS	0	1
	Encirclage / TBW L Patella	1	0
	Plate & Screw fixation	0	2
	Hemiarthroplasty	1	0
ASA	I	12	15
	II	8	5
DURATION OF SURGERY (mins)		158.3	177

Regarding block onset time (time to attain analgesia at T12,T10,T8,T6), dex group has slightly shortented onset time with less significance when compared to control group(13.90mins vs 12.45mins) p<0.08

Bar Chart
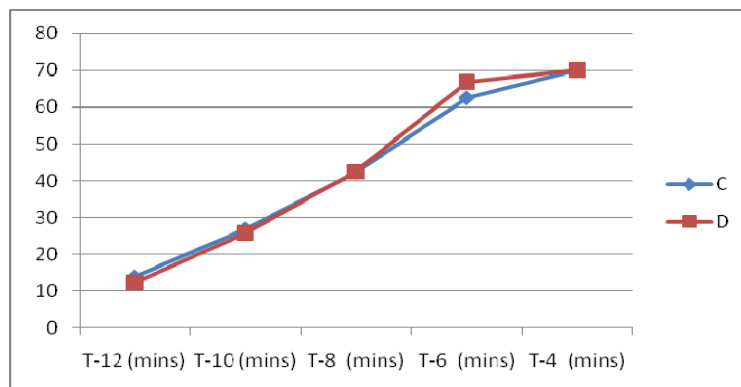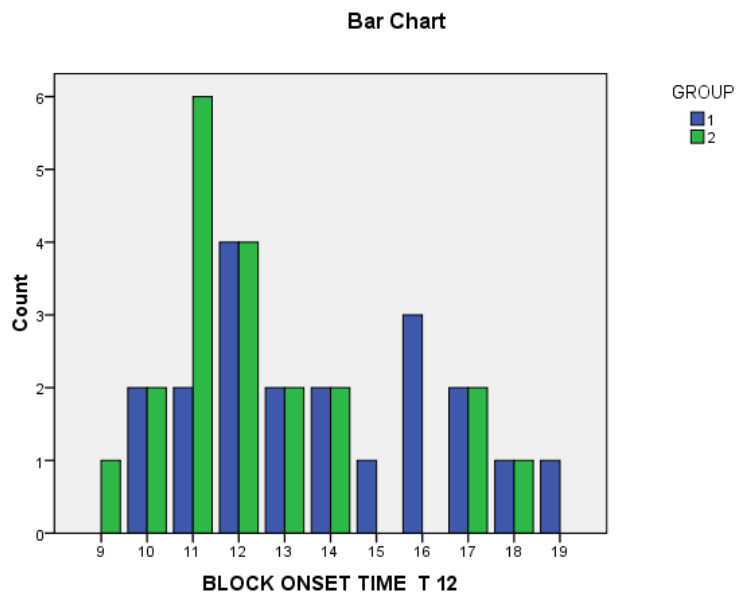
Regarding the upper level of analgesia, examined after an hour after epidural, all patients did attain T6 level without any significance between groups
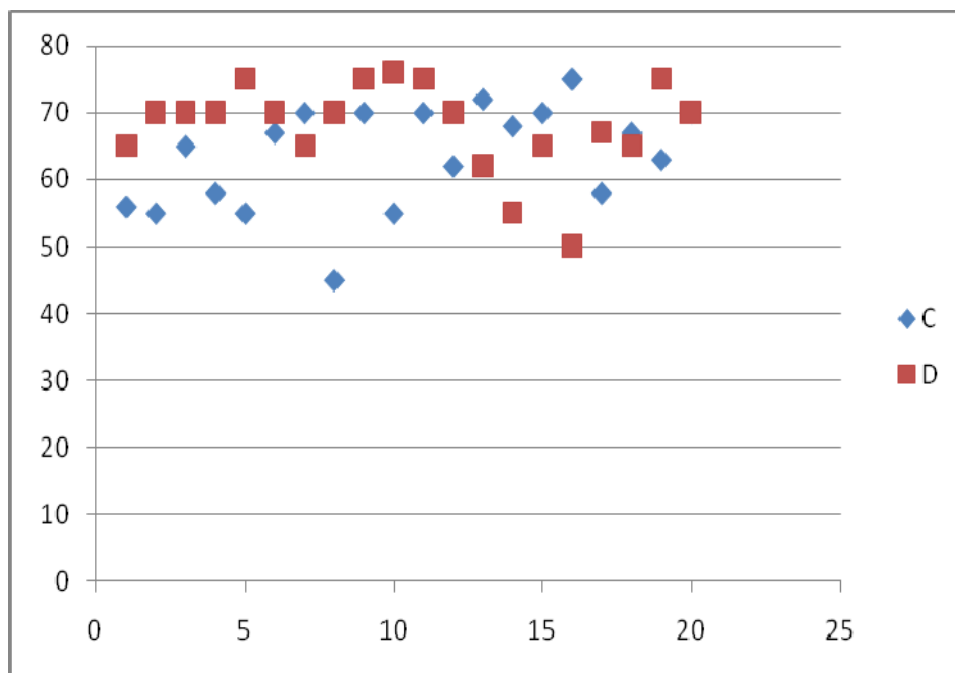
Regarding the duration of analgesia, the group receiving dexmedetomidine had significantly higher compared to the control group. In dex group it is 304.25mins compared to 236.35 in control group (p<0.02) and two segment regression time was prolonged in dex group.

Independent Samples Test

			t-test for Equality of Means	
		Df	Sig. (2-tailed)	Mean Difference
ANALGESIA DURATION MINUTES	Equal variances assumed	38	.000	-67.900
	Equal variances not assumed	37.821	.000	-67.900

		Levene's Test for Equality of Variances		t-test for Equality of Means
		F	Sig.	T
REGRESSION TIME T6-T10 MINUTES	Equal variances assumed	1.614	.212	-12.787
	Equal variances not assumed			-12.787
REGRESSION TIME T10-12 MINUTES	Equal variances assumed	4.076	.051	-.394
	Equal variances not assumed			-.394

Regarding motor block duration, dex group showed significant prolongation in duration(248mins) when compared to control group (204.65mins), level of significance p<0.04, slightly increased intensity of blockade assessed by Bromage motor scale was observed with dex group, but without much significance p<0.37.

Bar Chart
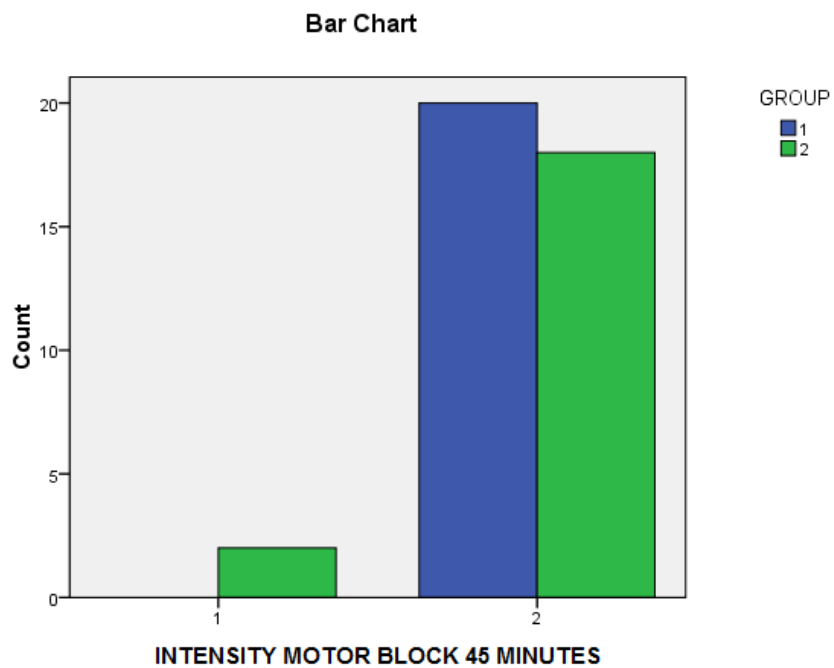
The duration of postoperative analgesia was significantly different between groups (p < 0.001) , and the dexmedetomidine group had a duration of analgesia which is 60% more than control group. Values in minutes as an average were 496.95mins for dex group when compared to 309mins in control group.

Independent Samples Test

		t-test for Equality of Means		
		Df	Sig. (2-tailed)	Mean Difference
POST OF ANALGESIS IN MINUTES.	Equal variances assumed	38	.000	-187.450
	Equal variances not assumed	32.091	.000	-187.450
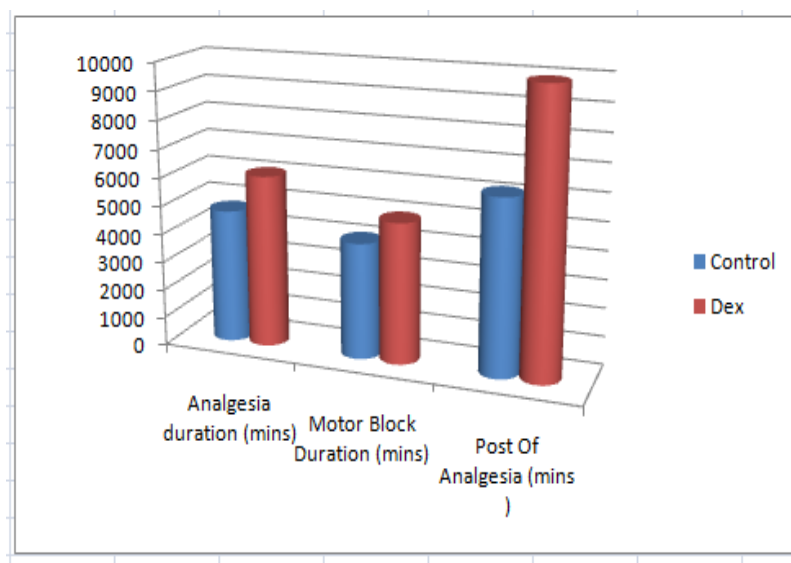
The occurrence of hypotension and the need for vasopressors in the intra-and postoperatively was similar between groups , with no significant difference p>0.13.Both groups showed excellent hemodynamic stability with less incidence of hypotension or bradycardia.The need for sedation was decreased in dex group when compared to control groups.
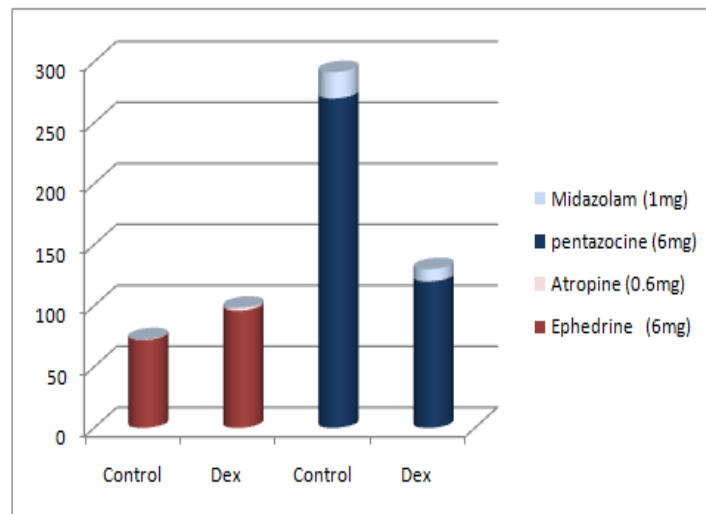
DISCUSSION

In this study, the effect of added dexmedetomidine to epidural ropivacaine was evaluated. The results showed duration of analgesia, motor block duration and post-operative analgesia were significantly increased and there is clear synergism between dexmedetomidine and ropivacaine when administered epidurally.

Previous studies evaluated the effect of α_2 agonist added with various local anesthetics.This study conducted based on previous studies with epidural clonidine[8,10,11],which prolongs post operative analgesia[12,14,15].

Dexmedetomidine is a nonselective α_2 agonist. Three subtypes of α_2 adrenoreceptors have been described in humans: α_{2A}, α_{2B}, and $\alpha_{2C.}$[27,30].The α_{2A} adrenoreceptors are primarily distributed in the periphery, whereas α_{2B} and α_{2C} are in the brain and spinal cord. Postsynaptic located α_2 adrenoreceptors in peripheral blood vessels produce vasoconstriction, whereas presynaptic α_2 adrenoreceptors inhibit the release of norepinephrine, potentially attenuating the vasoconstriction. The overall response to α_2 adrenoreceptors agonists is related to the stimulation of α_2 adrenoreceptors located in the CNS and spinal

cord. These receptors are involved in the sympatholysis, sedation, and antinociception effects of α_2 adrenoreceptors.

Ropivacaine is a long acting amide local anesthetics and 'S' isomer of the propyl analogue of mepivacaine and bupivacaine. It has similar properties to bupivacaine , but with better cadiotoxicity profile because it dissociates from Na+channels more rapidly and produces less accumulation of Na+channel block.Significantly better sensory-motor differentiation,due to lower lipid solubility than bupivacaine Has mild intrinsic vasoconstricting properties and so unsuitable for infiltration in tissues without collateral blood supply and is the reason for longer cutaneous anesthesia.Ropivacaine pKa is 8.07, Protein binding is 94%, Partition co-efficient is 11, CC:CNS ratio is 5:1, Potency 4.

Dexmedetomidine is an agonist of α_2 adrenergic receptor − agonist where ratio among $\alpha_2 : \alpha_1$ is 1600:1.Dex epidural effect is dose dependent and superior than I.V due to its high affinity for α_2 adrenergic receptors in spinal cord. After epidural administration of Dex, it is rapidly detected in CSF within five mins, however only 22% is absorbed into intra thecal space [19,31,33]. Its anti-nociceptive effect is dose dependent and is related to affinity of located α_2 adrenergic receptors in spinal cord and higher lipid solubility and penetration of meninges[5,20].Prolonged analgesic action of local anesthetics in epidural

space is due to reduced systemic absorbtion caused by local vasoconstriction mediated by α_{2C} adrenergic receptors in smooth muscle of epidural venous plexus[11,21,27].

The α_2 agonists produce their sedative-hypnotic effect by an action on α_2 receptors in the locus caeruleus and an analgesic action at α_2 receptors within the locus caeruleus and within the spinal cord [28, 33, 34]. During epidural administration cephalad spread of the drug into meninges may be responsible for sedation [16,22].The α_2 agonists act through the endogenous sleep-promoting pathways to exert their sedative effect . Dexmedetomidine produces a decrease in activity of the projections of the locus caeruleus to the ventrolateral preoptic nucleus. This increases GABAergic and galanin release in the tuberomammillary nucleus, producing a decrease in histamine release in cortical and subcortical projections.

Dexmedetomidine at concentrations producing significant sedation reduces minute ventilation, but retains the slope of the ventilatory response to increasing carbon dioxide. Dexmedetomidine also exhibited a hypercarbic arousal phenomenon, which has been described during normal sleep and is a safety feature. IV or inhaled dexmedetomidine has been implicated in blocking histamine-induced bronchoconstriction in dogs [22].

Another advantage is that their effects are easily reversible with alpha-2-adrenergic agonists such as atipamazole (with an affinity for the receptors of 60:1, compared to dexmedetomidine), which is the dependent dose, it rapidly reverses the sedation and cardiovascular effects at doses from 15 to 150 micg/kg[29].

The basic effects of α_2 agonists on the cardiovascular system are decreased heart rate; decreased systemic vascular resistance; and indirectly decreased myocardial contractility, cardiac output, and systemic blood pressure.Bradycardia and hypotension with administration of dexmedetomidine is dose dependent and occurs in epidural if level is higher [19,21,22,24]. Shivering incidence may be reduced with α_2 agonists due to central inhibition of thermoregulatory centre [23,25,26]

CONCLUSION

We conclude that dexmedetomidine at a dose of 1 µg.kg-1 acts synergistically with ropivacaine 0.75% in epidural anesthesia. The drug increases the duration of analgesia, motor block duration, prolongs the duration of postoperative analgesia and decreases sedative usage and shivering episodes.

REVIEW OF LITERATURE

1. Fukushima K, Nishime Y, Mori K, Kaneko I, Fukushima Y.- The pioneering use of dexmedetomidine epidurally in humans occurred in 1997, in which dexmedetomidine at a dose of 2 µg.kg-1 was combined with lidocaine 1.5% in total dose of 225 mg in patients anesthetized with isoflurane and underwent hysterectomy. The authors found that the duration of postoperative analgesia was doubled by dexmedetomidine, compared with only the administration of epidural lidocaine

2. Aantaa R, Jaakola ML, Kallio A, Kanto J. et al suggested that alpha 2-Adrenergic agonists have been shown to reduce anesthetic requirements of other anesthetics and concluded that with the high dose of dexmedetomidine, the MAC of isoflurane was 47% less than that without dexmedetomidine.

3. Lima OS, Neto DSC, Araujo GS Jr, Benevides AM et al In a comparative study, administration of clonidine, 150 micrograms, or dexmedetomidine, 100 micrograms, associated with ropivacaine 1% in total dose of 200 mg, resulted in no significant difference in onset time of sensory block10.Moreover, it was found, with the administration of dexmedetomidine, a significant increase of the duration of analgesic

block in dermatomes T10 and T12. There was also enhancement of the intensity of motor block and duration of this blockage caused by dexmedetomidine. Similar to the increased length of anesthesia, dexmedetomidine also promoted a significant increase of the duration of postoperative analgesia.

4. Silva et al. In 2002, also found post-operative analgesic action of dexmedetomidine in additional fixed dose of 100 mg when administered in combination with bupivacaine 0.5% in patients undergoing hysterectomy under epidural anesthesia.

5. Maroof et al. Studying patients undergoing orthopedic surgical procedures, found a higher incidence of bradycardia associated when dexmedetomidine, 2 μg.kg-1, 0.5% bupivacaine epidural anesthesia compared with the separate administration of bupivacaine. However, no significant difference in blood pressure was observed.they suggested that dexmedetomidine at a dose of 2 μg.kg-1 plus bupivacaine 0.5% epidural anesthesia significantly reduced the incidence of shivering, an effect that is mainly due to central inhibition of thermoregulatory control .

6. Ala-Kokko TI, Pienimaki P, Lampel And Hollmen AI, Pelkonen O, Vahakangas K.et al in their study, "Transfer of clonidine and dexmedetomidine across the isolated perfused human

placenta",suggested that enhanced analgesic potency of dexmedetomidine compared with clonidine, when injected epidurally, due not only to its greater selectivity for alpha 2 receptors , but probably also to higher lipid solubility and penetration into the meninges.

7. Eisenach JC, Shafer SL, Bucklin BA, Jackson C, Kallio A. et al in their animal study, "Pharmacokinetics and pharmacodynamics of intraspinal dexmedetomidine in sheep", suggested that in sheep, after the epidural administration of dexmedetomidine it is rapidly detected in the cerebrospinal fluid, reaching maximum concentration after five minutes. Only 22% of the injected dose was identified in the CSF ,and concluded that primary spinal site of action for decreased blood pressure after intraspinal dexmedetomidine injection.

STATISTICS

AGE:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
AGE	1	20	42.25	14.145	3.163
	2	20	39.10	14.836	3.317

HEIGHT & WEIGHT:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
WEIGHT	1	20	69.95	7.944	1.776
	2	20	66.75	7.181	1.606
HEIGHT	1	20	169.35	6.761	1.512
	2	20	163.15	9.161	2.048

]

DURATION OF SURGERY:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
DURATION OF SURGERY IN MINUTES	1	20	158.25	22.553	5.043
	2	20	177.00	29.037	6.493

CATHETAR LENGTH IN EPIDURAL SPACE:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
CATHETAR LENGTH IN CENTIMETERS	1	20	6.50	.827	.185
	2	20	6.85	.813	.182

BLOCK ONSET TIME:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
BLOCK ONSET TIME T 12	1	20	13.90	2.713	.607
	2	20	12.45	2.460	.550
BLOCK ONSET TIME T10	1	20	26.85	4.522	1.011
	2	20	25.90	3.932	.879
BLOCK ONSET TIME T8	1	20	42.30	5.352	1.197
	2	20	42.45	4.673	1.045
BLOCK ONSET TIME T6	1	20	62.40	7.632	1.707
	2	20	66.65	7.534	1.685
BLOCK ONSET TIME T4	1	2	70.00	.000[a]	.000
	2	2	70.00	.000[a]	.000

A. t cannot be computed because the standard deviations of both groups are 0.

REGRESSION TIME:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
REGRESSION TIME T6-T10 MINUTES	1	20	115.55	12.361	2.764
	2	20	177.30	17.708	3.960
REGRESSION TIME T10-12 MINUTES	1	20	57.25	11.516	2.575
	2	20	58.45	7.244	1.620

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means
		F	Sig.	T
REGRESSION TIME T6-T10 MINUTES	Equal variances assumed	1.614	.212	-12.787
	Equal variances not assumed			-12.787
REGRESSION TIME T10-12 MINUTES	Equal variances assumed	4.076	.051	-.394
	Equal variances not assumed			-.394

Independent Samples Test

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
REGRESSION TIME T6-T10 MINUTES	Equal variances assumed	38	.000	-61.750
	Equal variances not assumed	33.962	.000	-61.750
REGRESSION TIME T10-12 MINUTES	Equal variances assumed	38	.695	-1.200
	Equal variances not assumed	32.000	.696	-1.200

Independent Samples Test

		t-test for Equality of Means		
			95% Confidence Interval of the Difference	
		Std. Error Difference	Lower	Upper
REGRESSION TIME T6-T10 MINUTES	Equal variances assumed	4.829	-71.526	-51.974
	Equal variances not assumed	4.829	-71.564	-51.936
REGRESSION TIME T10-12 MINUTES	Equal variances assumed	3.042	-7.358	4.958
	Equal variances not assumed	3.042	-7.397	4.997

ANALGESIA DURATION:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
ANALGESIA DURATION MINUTES	1	20	236.35	20.704	4.630
	2	20	304.25	19.325	4.321

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means
		F	Sig.	T
ANALGESIA DURATION MINUTES	Equal variances assumed	.426	.518	-10.722
	Equal variances not assumed			-10.722

Independent Samples Test

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
ANALGESIA DURATION MINUTES	Equal variances assumed	38	.000	-67.900
	Equal variances not assumed	37.821	.000	-67.900

MOTOR BLOCK DURATION:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
MOTOR BLOCK DURATION IN MINUTES	1	20	204.65	13.922	3.113
	2	20	248.00	28.442	6.360

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means
		F	Sig.	T
MOTOR BLOCK DURATION IN MINUTES	Equal variances assumed	14.025	.001	-6.122
	Equal variances not assumed			-6.122

Independent Samples Test

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
MOTOR BLOCK DURATION IN MINUTES	Equal variances assumed	38	.000	-43.350
	Equal variances not assumed	27.610	.000	-43.350

INTRA OP HEMODYNAMICS:

PULSE RATE INTRA-OP:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
INTRA OP HEMODYNAMICS-PR-1 MINUTES	1	20	87.85	12.609	2.819
	2	20	83.60	12.015	2.687
INTRA OP HEMODYNAMICS-PR-5 MINUTES	1	20	86.65	13.132	2.936
	2	20	81.60	13.438	3.005
INTRA OP HEMODYNAMICS-PR-15 MINUTES	1	20	86.60	14.558	3.255
	2	20	81.60	14.140	3.162
INTRA OP HEMODYNAMICS-PR-30 MINUTES	1	20	88.20	17.225	3.852
	2	20	80.90	14.101	3.153

SYSTOLIC BP INTRA-OP:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
INTRA OP HEMODYNAMIC SYSTOLIC BP 1 MINUTES	1	20	131.15	12.525	2.801
	2	20	125.50	10.501	2.348
INTRA OP HEMODYNAMIC SYSTOLIC BP 5 MINUTES	1	20	126.95	12.951	2.896
	2	20	122.25	9.267	2.072
INTRA OP HEMODYNAMIC SYSTOLIC BP 15 MINUTES	1	20	125.50	16.340	3.654
	2	20	116.65	13.172	2.945
INTRA OP HEMODYNAMIC SYSTOLIC BP 30 MINUTES	1	20	119.80	16.932	3.786
	2	20	111.40	15.736	3.519
INTRA OP HEMODYNAMIC SYSTOLIC BP 60 MINUTES	1	20	120.60	14.773	3.303
	2	20	112.00	13.219	2.956

Group Statistics

DIASTOLIC BP INTRA-OP:

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
INTRA OP HEMODYNAMIC DIASTOLIC BP 1 MINUTES	1	20	83.00	7.384	1.651
	2	20	81.50	6.708	1.500
INTRA OP HEMODYNAMIC DIASTOLIC BP 5 MINUTES	1	20	83.00	7.384	1.651
	2	20	81.50	6.708	1.500
INTRA OP HEMODYNAMIC DIASTOLIC BP 15 MINUTES	1	20	81.55	8.095	1.810
	2	20	77.55	8.959	2.003
INTRA OP HEMODYNAMIC DIASTOLIC BP 30 MINUTES	1	20	80.60	10.763	2.407
	2	20	72.50	18.749	4.192

POST OP ANALGESISA DURATION:

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
POST OP ANALGESIS IN MINUTES.	1	20	309.00	22.880	5.116
	2	20	496.45	36.200	8.095

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means
		F	Sig.	t
POST OP ANALGESIS IN MINUTES.	Equal variances assumed	4.085	.050	-19.575
	Equal variances not assumed			-19.575

Independent Samples Test

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
POST OP ANALGESIS IN MINUTES.	Equal variances assumed	38	.000	-187.450
	Equal variances not assumed	32.091	.000	-187.450

INTENSITY OF MOTOR BLOCK:

INTENSITY MOTOR BLOCK 45 MINUTES * GROUP

			GROUP		
			1	2	Total
INTENSITY MOTOR BLOCK 45 MINUTES	1	Count	0	2	2
		% within GROUP	.0%	10.0%	5.0%
	2	Count	20	18	38
		% within GROUP	100.0%	90.0%	95.0%
	Total	Count	20	20	40
		% within GROUP	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.105[a]	1	.147		
Continuity Correction[b]	.526	1	.468		
Likelihood Ratio	2.878	1	.090		
Fisher's Exact Test				.487	.244
Linear-by-Linear Association	2.053	1	.152		
N of Valid Cases	40				

A. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.00.

B. Computed only for a 2x2 table

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PROFORMA

NAME: AGE/SEX: IP NO.:

DATE: Wt.:   Ht.:   GROUP:

DIAGNOSIS:

SURGERY:

BRIEF HISTORY:

COEXISTING ILLNESS:

EXAMINATION:

    PR: CVS:

    BP: RS:

    RR: AIRWAY:

INVESTIGATIONS:

    Hb: BLOOD UREA:

    URINE ALB: BLOOD SUGAR:

    URINE SUGAR: Sr. CREATININE:

    X-RAY CHEST: Sr. ELECTROLYTES:

    ECG:

ANESTHESIA DETAILS:

    PREMEDICATION:

    GROUP:

    LEVEL OF EPIDURAL:

    CATHETAR LENGTH IN EPIDURAL SPACE:

    NO. OF ATTEMPTS:

    DRUG DETAILS:

    DURATION OF SURGERY:

PARAMETERS OBSERVED

BLOCK ONSET TIME: T-12   T10   T8   T6

UPPER LEVEL OF ANALGESIA&TIME:

INTENSITY OF MOTOR BLOCK: GRADE   0   1   2   3

ANALGESIC & MOTOR BLOCK DURATION:

SENSORY SCORE: 0   1   2

SEDATION SCORE:

HEMO DYNAMICS:

PARAMETERS	1 min	5 mins	15 mins	30 mins	1 Hr	2 Hrs	3 Hrs
PR							
BP							
SpO_2							

DURATION OF POST OP ANALGESIA:

Master Chart (Control Group)

SI No.	Group	Name	Date	Age	Sex	Weight (kg)	Height (cm)	Surgery	ASA	DURATION OF SURGERY (mins)	Level Of Epidural	Cathetar Length (cm)	T-12 (mins)
1	C	Sathish	12-5-2010	28	M	60	165	Encirclage / TBW L Patella	I	120	L3-L4	6	11
2	C	Joseph	12-5-2010	26	M	62	167	IM / IL Nailing	I	195	L2-L3	6	16
3	C	Chandran	13-5-2010	35	M	75	180	IM / IL Nailing	I	180	L3-L4	8	18
4	C	Rahim	13-5-2010	34	M	80	174	IM / IL Nailing	I	150	L3-L4	7	12
5	C	Anandhan	26-5-2010	32	M	80	174	Illizarao ring fixation	I	120	L2-L3	7	12
6	C	Udhayakumar	24-5-2010	21	M	68	170	IM / IL Nailing	I	180	L1-L2	8	13
7	C	Pachiyappam	24-5-2010	55	M	60	170	Illizarao ring fixation	II	150	L3-L4	7	13
8	C	Devi	2-6-2010	55	F	60	170	IM Nailing	II	150	L2-L3	5	10
9	C	Damodharan	2-6-2010	55	M	73	175	IM Nailing	II	180	L2-L3	6	19
10	C	Srivasan	10-6-2010	49	M	76	160	IM Nailing	II	150	L2-L3	6	10
11	C	Brimadhanadan	16-6-2010	38	M	80	165	IM Nailing	I	150	L2-L3	6	14
12	C	Sekar	16-6-2010	48	M	85	175	Hemiarthroplasty	I	120	L2-L3	6	12
13	C	Subramani	21-6-2010	70	M	65	172	THR	II	150	L2-L3	6	12
14	C	Karupusami	21-6-2010	52	M	73	174	Illizarao ring fixation	II	150	L2-L3	6	14
15	C	Radha	3-5-2010	38	F	65	159	IM Nailing	I	150	L3-L4	6	15
16	C	Ramesh	3-5-2010	23	M	65	179	IM Nailing	I	180	L3-L4	7	17
17	C	Radhika	5-5-2010	32	F	58	153	DHS	I	180	L2-L3	7	17
18	C	Ravi	19-5-2010	48	M	72	165	DHS	II	180	L1-L2	8	16
19	C	Anbu Selvam	23-6-2010	38	M	70	170	Illizarao ring fixation	I	180	L3-L4	6	11
20	C	Arumugam	20-5-2010	68	M	72	170	TKR	II	150	L3-L4	6	16

Block Onset Time (Control Group)				Regression Time		Analgesia duration (mins)	Motor Block Duration (mins)	Intensity of motor block					
T-10 (mins)	T-8 (mins)	T-6 (mins)	T-4 (mins)	T-6 to T-10 (mins)	T-10 to T-12 (mins)			45mins	120mins	180mins	240mins	1 mins	5 mins
34	48	56		106	46	208	210	2	3	1	1	75	70
33	42	55		104	46	205	195	2	3	1	0	95	90
29	45	65		112	52	229	190	2	3	1	0	89	85
22	42	58		118	76	252	195	2	3	1	1	70	65
23	38	55		126	76	257	205	2	3	2	1	80	85
29	41	67		125	80	272	210	2	3	2	1	85	89
32	42	55	70	98	56	224	225	2	3	2	1	86	86
20	34	45		102	64	211	215	2	3	2	1	86	90
22	40	70		133	53	256	220	2	3	2	1	86	90
22	36	55		120	56	231	205	2	3	2	1	60	55
32	55	70		125	72	267	210	2	3	2	1	86	82
20	34	62		117	63	242	200	2	2	1	1	77	72
23	40	72		106	46	224	205	2	3	2	0	86	88
28	42	68		136	55	259	245	2	3	2	1	82	84
28	48	62	70	131	51	252	195	2	3	2	1	92	94
29	44	75		96	46	217	195	2	3	1	1	110	102
24	39	58		125	43	226	201	2	3	2	1	106	98
30	48	67		120	64	251	190	2	3	1	1	102	98
26	39	63		113	55	231	190	2	2	2	1	98	102
31	49	70		98	45	213	192	2	3	2	0	106	108

	Intra op Hemodynamics (pulse rate per min) (Control Group)								Intra op Hemodynamics (systolic BP in					
15 mins	30 mins	60 mins	120 mins	150 mins	180 mins	210 mins	240 mins	1 mins	5 mins	15 mins	30 mins	60 mins	120 mins
76	80	70	72	0	0	0	0	135	130	125	120	113	120
94	95	110	90	88	90	0	0	110	110	110	090	091	096
88	90	86	88	86	92	0	0	130	130	135	130	120	110
65	67	69	70	72	74	0	0	110	100	102	090	112	110
90	90	90	86	0	0	0	0	130	122	130	132	136	126
95	90	82	88	90	86	0	0	129	130	120	132	120	120
90	96	98	86	90	0	0	0	110	110	090	086	100	102
76	78	76	86	82	0	0	0	130	136	128	130	140	130
76	78	76	86	82	84	0	0	130	136	128	130	140	130
56	56	65	68	62	0	0	0	130	127	126	120	120	110
84	80	84	82	88	0	0	0	140	144	136	140	142	146
68	62	66	72	0	0	0	0	130	120	124	110	114	110
88	90	92	94	86	0	0	0	140	120	110	116	120	120
80	76	78	80	82	0	0	0	130	120	110	112	116	120
86	82	78	76	72	0	0	0	160	150	140	144	130	126
108	120	118	113	114	108	0	0	139	138	140	138	130	136
96	110	108	107	112	118	0	0	140	138	130	126	132	112
108	112	116	114	108	106	0	0	130	128	128	128	132	114
112	114	121	112	108	111	0	0	120	110	168	102	096	106
96	98	102	92	94	0	0	0	150	140	130	120	108	112

150 mins	180 mins	210 mins	240 mins	1 mins	5 mins	15 mins	30 mins	60 mins	120 mins	150 mins	180 mins	210 mins	240 mins	Intra OP Drugs
		(Control Group)						Intra op Hemodynamics (diastolic BP in mmhg)						
000	000	000	000	80	80	80	90	70	70	00	00	00	00	---
092	100	000	000	80	80	80	50	52	54	56	70	00	00	Inj. Ephedrine-18mg/inj.midazolam 1.5mg/inj pentazocine 30mg
122	122	000	000	80	80	85	90	70	80	72	70	00	00	inj.pentazocine 30mg/inj midazolam 1mg
122	110	000	000	70	70	76	70	72	72	72	72	00	00	Inj. Ephedrine 12mg/inj pentazocine 15mg/inj.midazolam 1mg
000	000	000	000	70	70	90	90	90	92	00	00	00	00	Inj.pentazocine 15mg/inj.midazolam 1mg
130	122	000	000	80	80	70	82	80	88	84	80	00	00	inj.petazocine 15mg/inj.midazolam 1mg
112	000	000	000	80	80	60	64	70	76	82	00	00	00	Inj. Ephedrine 12mg/inj.pentazocine 30mg
122	000	000	000	80	80	80	82	90	80	84	00	00	00	inj.pentazocine 15mg/inj.midazolam 1mg
122	124	000	000	80	80	80	82	90	80	84	86	00	00	Ephedrine 6mg/inj midazolam 1mg/inj.pentazocine15mg
116	000	000	000	80	80	80	70	76	82	84	00	00	00	Inj. Atropine 0.6mg/inj.pentazocine 15mg/inj.midazolam 1mg
132	000	000	000	90	90	90	90	94	94	88	00	00	00	inj midazolam 2mg/inj.pentazocine 15mg
000	000	000	000	80	80	76	80	86	72	00	00	00	00	inj.midazolam 2mg
124	000	000	000	80	80	80	88	76	74	72	00	00	00	inj.midazolam 2mg
122	000	000	000	80	80	80	88	78	76	80	00	00	00	inj.midazolam 2mg
130	000	000	000	98	98	84	86	80	84	90	00	00	00	inj.pentazocine 15mg/inj.midazolam 1mg
130	126	000	000	96	96	90	90	80	84	80	80	00	00	---
120	122	000	000	90	90	92	86	88	78	70	88	00	00	inj.pentazocine 15mg/inj.midazolam 1mg
126	122	000	000	90	90	94	86	88	80	78	88	00	00	inj.pentazocine15mg/inj.midazolam 1mg
110	116	000	000	86	86	76	78	70	70	76	70	00	00	Ephedrine 12mg/inj.pentazocine 15mg/inj.midazolam 1mg
120	000	000	000	90	90	88	70	70	74	78	00	00	00	Ephedrine 12mg/inj.pentazocine 30mg/inj.midazolam 1mg

intra op drugs (Control Group)				
Ephedrine (6mg)	Atropine (0.6mg)	pentazocine (6mg)	Midazolam (1mg)	Post Of Analgesia (mins)
0	0	0	0	290
3	0	5	1.5	280
0	0	5	1	315
2	0	2.5	1	330
0	0	2.5	1	335
0	0	2.5	1	310
2	0	5	0	320
0	0	2.5	1	295
1	0	2.5	1	315
0	1	2.5	1	325
0	0	2.5	2	296
0	0	0	2	311
0	0	0	2	293
0	0	0	2	350
0	0	2.5	1	278
0	0	0	0	274
0	0	2.5	1	330
0	0	2.5	1	281
2	0	2.5	1	305
2	0	2.5	1	347