

**“STUDY TO EVALUATE USEFULNESS OF MAGNESIUM  
SULPHATE AND DEXMEDETOMIDINE AS ADJUVANT TO  
BUPIVACAINE FOR LOWER LIMB AND ABDOMINAL  
SURGERIES UNDER EPIDURAL ANAESTHESIA”**

By

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**DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF  
HIGHER EDUCATION AND RESEARCH CENTER, KOLAR, KARNATAKA**

*In partial fulfillment of the requirements for the degree of*

**DOCTOR OF MEDICINE**

**IN**

**ANAESTHESIOLOGY**

**Under the Guidance of**

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**APRIL 2021**

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## **ABSTRACT**

### **STUDY TO EVALUATE USEFULNESS OF MAGNESIUM SULPHATE AND DEXMEDETOMIDINE AS ADJUVANT TO BUPIVACAINE FOR LOWER LIMB AND ABDOMINAL SURGERIES UNDER EPIDURAL ANAESTHESIA BACKGROUND AND OBJECTIVES:**

#### **BACKGROUND AND OBJECTIVE:**

Central neuraxial blockade not only provides us good anaesthetic and surgical conditions but it has also advantages over general anaesthesia. To compare the onset time of motor blockade and sensory blockade and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability, and adverse effects if any and number of rescue analgesia in the first 24 hours after surgery.

#### **MATERIALS AND METHODS:**

After ethical committee clearance and patient consent, the study was been conducted on 90 patients aged 18 to 65 years belonging to ASA- I and II undergoing lower limb and also lower abdominal surgeries, which were randomly divided into 3 groups. GROUP A (control group) received epidural bupivacaine 0.5% (17 ml) + 1ml 0.9% normal saline. GROUP B received epidural Bupivacaine 0.5% (17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

GROUP C received epidural Bupivacaine 0.5% (17 ml) + 1ml 50mg magnesium sulphate. Exclusion criteria include patients with bradyarrhythmias, cerebrovascular diseases, neurodegenerative diseases, renal and hepatic diseases, uncontrolled hypertension, bronchial asthma, ischemic heart disease, drug and alcohol abuse and uncontrolled diabetes mellitus.

Qualitative data were represented as proportions and bar charts. Quantitative data were represented as mean, standard deviation. Test of significance was the ANOVA and chi-square test. P value <0.05 statistically significant.

**RESULTS:**

Group B has rapid onset of action and better hemodynamic stability, where as Group C has better postoperative analgesia with no complications.

**KEY WORDS:** Epidural anaesthesia, bupivacaine, dexmedetomidine, magnesium sulphate.

## **ABBREVIATIONS**

HR	Heart rate
Bpm	Beats per minute
PR	Pulse rate
SBP	Systolic blood pressure
DSP	Diastolic blood pressure
MAP	Mean arterial blood pressure
NIBP	Non invasive blood pressure
ECG	Electrocardiogram
SPO2	Peripheral capillary oxygen saturation
CVS	Cardiovascular system
PA	Per abdomen
RS	Respiratory system
CNS	Central nervous system
VAS	Visual analogue scale
IV	Intravenous
NS	Normal saline
RL	Ringer lactate
MgSO <sub>4</sub>	Magnesium sulphate
ICU	Intensive care unit
NMDA	N-methyl-D aspartate

IT	Intrathecal
CBC	Complete blood count
HB	Haemoglobin
BT	Bleeding time
CT	Clotting time
WBC	White blood count
RFT	Renal function test
mcg	microgram
Hrs	Hours
mins	Minutes
FDA	Food and drug administration
ETCO2	End tidal carbon dioxide
mmhg	Millimetre of mercury
Kg	Kilogram
cm	Centimetre
SD	Standard deviation
ml	Millilitre
g	Gram
No of	Number of

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## **INTRODUCTION**

Many lower limb and abdominal surgical procedures are commonly done under neuraxial block, either spinal or epidural anaesthesia. Central neuraxial blockade not only provides us good anaesthetic and surgical conditions but it has also advantages over general anaesthesia. Advantages include less airway related and pulmonary complications that include reduced chances of pulmonary aspiration and decreased stress response<sup>1</sup>

Epidural anaesthesia is widely used and a standard technique which is practiced in many surgical procedures. There are various advantages of epidural anaesthesia over spinal anaesthesia that includes slow onset of hypotension, level of blockade and duration of blockade can be extended and mostly used to provide post operative analgesia through catheter. The most dreaded complication of spinal anaesthesia that is postdural puncture headache can be avoided in epidural anaesthesia.

Most common local anaesthetic used in epidural is Bupivacaine. Various drugs have been added as adjuvant to bupivacaine to prolong duration of anaesthesia and analgesia and also it reduces dose dependent side effects. When adjuvants added in neuraxial anaesthesia it should provide stable hemodynamics, better perioperative sedation, and has the ability to provide peri and post operative analgesia. These adjuvants include opioids, midazolam and ketamine.<sup>1</sup> Opioids have many acute side effects like nausea, vomiting, pruritis, respiratory depression, urinary retention and somnolence.

$\alpha$ -2agonists cause sedation, analgesia, anxiolysis, hypnosis and sympatholysis.<sup>2</sup> They are administered through various routes which include epidural anaesthesia. Dexmedetomidine a well known alpha 2 agonist, 8 times potent than clonidine when added as an adjuvant to bupivacaine administered via epidural route produces synergistic anti nociceptive effect and also prolongs the duration of blockade and analgesia.<sup>3</sup>

Magnesium which is a major cation and 4<sup>th</sup> most abundant mineral in the body produces anti nociceptive effects, due to antagonism of calcium and NMDA receptors. This blocks calcium influx and thus reduces acetylcholine release in neuromuscular junctions. NMDA receptors after nociceptive stimuli are involved in pain processing by central sensitization, magnesium prevents this sensitization. Epidural magnesium prolongs duration of analgesia and is a rapid onset of surgical anaesthetic without increasing side effects.<sup>14</sup>

Majority of magnesium use has been in obstetric anaesthesia, but by understanding its pain physiology and action over NMDA receptors it's been widely used as secondary analgesics and adjuvants in neuraxial blockade.<sup>5</sup>

Hence we intend to study the efficacy of dexmedetomidine, an  $\alpha$ -2agonist and magnesium sulphate as adjuvants to bupivacaine in epidural anaesthesia.

## **AIMS AND OBJECTIVES**

To administer epidural bupivacaine with normal saline, epidural bupivacaine with dexmedetomidine, epidural bupivacaine with magnesium sulphate each in 30 patients undergoing lower limb and lower abdominal surgeries and document the time of onset and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability and adverse events if any.

To compare the time for motor blockade, sensory blockade and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability, adverse effects if any and number of rescue analgesia in the first 24hours after surgery.

## **ANATOMY OF EPIDURAL SPACE**

Brainstem continues proximally as spinal cord and distally terminates in conus medullaris as filum terminale (fibrous extension) and conus medullaris (neural extension). Spinal cord ends at L1 in adults and L3 in children. Spinal cord is covered by the pia mater, the arachnoid mater, the dura mater. Cerebrospinal fluid (CSF) occupies the subarachnoid space.

Piamater is the highly vascularised structure which closely covers the brain and spinal cord. 500ml of CSF is being produced per day by choroid plexus. Arachnoid mater is a non-vascularised and delicate structure and acts as a barrier for drugs crossing into and out of CSF. Dura mater is the outermost layer which extends from foramen magnum and sacral hiatus and the surrounding dura is the epidural space.<sup>6</sup>

Boundaries of epidural space are

**Anteriorly** - Posterior Longitudinal ligaments.

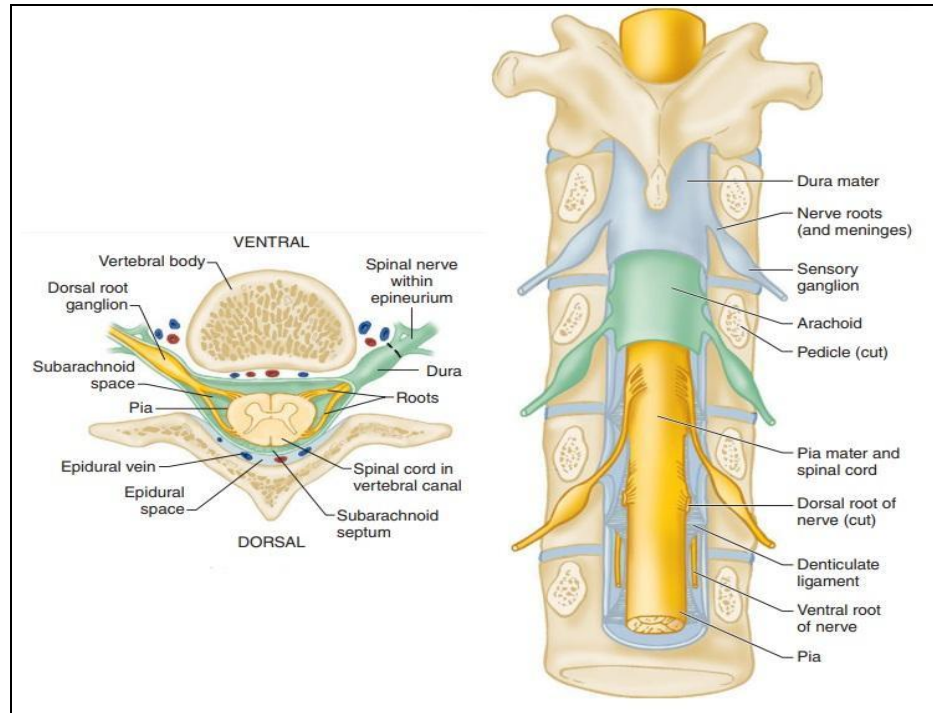
**Laterally** - Pedicles of vertebrae and intervertebral foramina.

**Posteriorly** - Anterior surface of vertebral body and Ligamentum Flavum.

**Above** - Foramen Magnum, periosteal and spinal layers of dura fuse together.

**Below** - Sacrococcygeal Membrane.<sup>6</sup>





**FIG 1: SHOWING BOUNDARIES AND CONTENTS OF EPIDURAL SPACE**

Contents of epidural space are

- ✓ Nerve roots
- ✓ Fat
- ✓ Areolar tissue
- ✓ Lymphatics,

Blood vessels including the well-organized Batson's plexus of veins.

Ligamentum Flavum (yellow ligament) is present posterior to epidural space that extends from foramen magnum to sacral hiatus which is thin over cervical region and thickest over lumbar region. Blood supply to the spinal cord is from; One Anterior Spinal artery (originating from the vertebral artery), Two Posterior Spinal arteries (originating from the inferior cerebellar artery), and Segmental spinal arteries (originating from the intercostal and lumbar arteries).

### **Venous drainage**

- Three Anterior Spinal veins
- Three Posterior Spinal veins

Finally communicating with the segmental anterior and posterior radicular veins and then into the internal vertebral plexus in the medial and lateral components of the epidural space. No veins are present in the posterior epidural space except for those present caudal to the L5-S1 disk.<sup>7</sup>

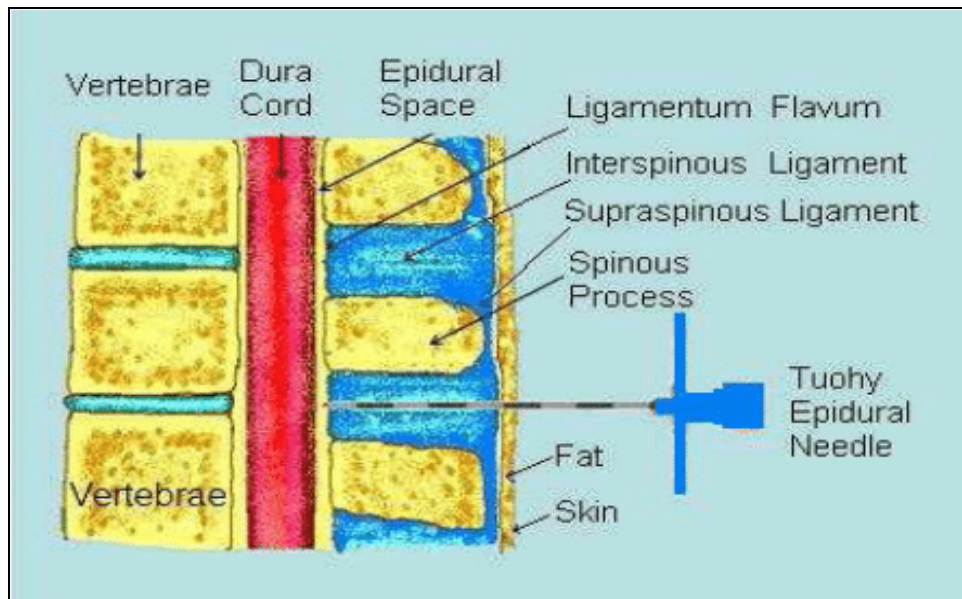
### **MECHANISM OF ACTION OF EPIDURAL ANAESTHESIA:**

Local anaesthetic binds to the nerve tissue which disrupts nerve transmission and results in neural blockade. Spinal nerve roots and the dorsal root ganglia are the main sites of action.

The rate of speed of neural blockade depends

- ✓ Size.
- ✓ Surface area.
- ✓ Degree of Nerve fibre myelination.

Studies show that S1 and L5 posterior roots are larger and most resistant to blockade in epidural anaesthesia.



**FIG 2: LAYERS FROM SKIN TO EPIDURAL SPACE**

**Order of blockade: <sup>8</sup>**

Small **preganglionic sympathetic fibers (B fibres)**, 1 to 3  $\mu\text{m}$ , minimally myelinated)

- most sensitive to local anaesthetic blockade.

**Sensory C fibres** (0.3 to 1  $\mu$ , unmyelinated), which conduct cold temperature sensation.

A-delta fibres (1 to 4  $\mu$ , myelinated), which conduct pinprick sensation.

A-beta fibres (5 to 12  $\mu$ , myelinated), A-gamma fibres (4-8  $\mu$ , myelinated) which conduct Joint afferents, pressure and touch sensation last sensory fibres to be blocked.

·Larger A-alpha motor fibres (12 to 20  $\mu\text{m}$ , myelinated) are more resistant than any fibres.

**Regression of blockade:**

Motor function – Touch – Pinprick - Cold sensation.

**INDICATIONS:**

- For procedures that involve the lower extremities, perineum, or lower abdomen.
- For postoperative analgesia in acute and also chronic pain like malignancies
- In labour and delivery – labour analgesia/ walking epidurals.
- In patients with pre-existing respiratory disease undergoing abdominal surgery.

**CONTRAINDICATIONS:****ABSOLUTE:**

- Patient refusal
- Localized sepsis.
- A patient's inability to maintain stillness during needle puncture, which can expose the neural structures to traumatic injury.
- Raised intracranial pressure – Brain stem herniation.

**RELATIVE:****Neurological:**

- Myelopathy or Peripheral Neuropathy.
- Spinal Stenosis.
- Spine Surgery.
- Multiple Sclerosis – Increased sensitivity to LA – prolonged sensory and motor blockade.
- Spina Bifida.

**Cardiac conditions:**

- Aortic Stenosis or Fixed Cardiac Output.
- Hypovolemia

**Haematological:**

- Thromboprophylaxis.
- Inherited Coagulopathy - Hemophilia, Von Willebrand disease, or Idiopathic Thrombocytopenic Purpura.

**Infection:**

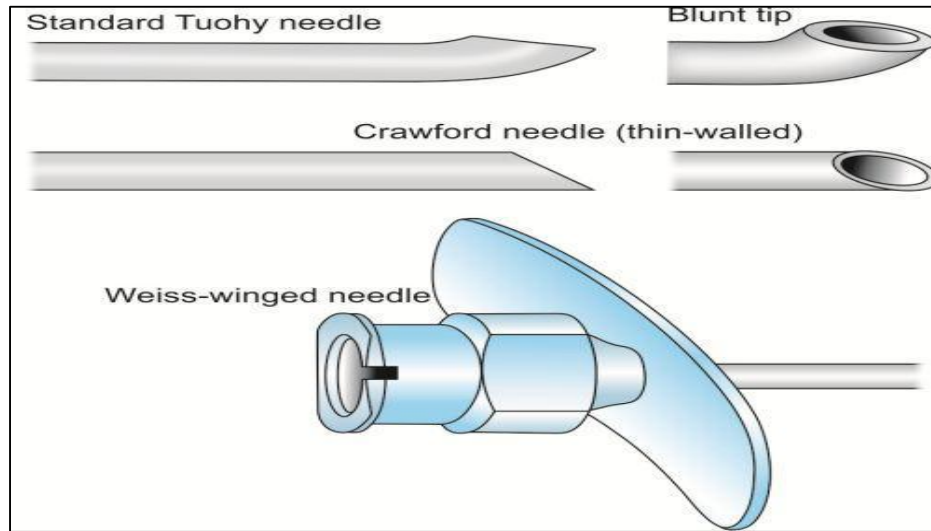
- Systemic infection and Meningitis.<sup>9</sup>

**EPIDURAL TECHNIQUE:****Preparation:**

Written informed consent to be taken from the patient, on day of surgery vitals to be checked and wide bore cannula secured and extent of surgical field is known for securing epidural catheter at the appropriate level. The procedure done at full sterile condition as a catheter is left in situ.

**Epidural needles/ Catheters:**

A wide variety of epidural needles are used for epidural anaesthesia. Tuohy needles are most common, needles are 16 to 18 g in size and have a 15- to 30-degree curved, blunt “*Huber*” tip - to both reduce the risk of accidental dural puncture and guide the catheter cephalad. The needle shaft is marked in 1-cm intervals so depth of insertion can be identified. The catheter is flexible, calibrated, durable, radiopaque plastic with either a single end hole or multiple side orifices near the tip.<sup>10</sup>



**FIG 3: TYPES OF EPIDURAL NEEDLE**

#### **IDENTIFICATION OF EPIDURAL SPACE:**

1. The Hanging Drop Sign of Gutierrez
2. Loss of Resistance Test of Sicard and Forestier and Of Dogliotti

#### **Position:**

Sitting and lateral decubitus position.

#### **Important surface landmark:**

- Intercristal line (corresponding to L4-L5 interspace),
- Inferior angle of the scapula ( T7 vertebral body),
- Root of scapular spine (T3),
- Vertebra prominence (C7).

**Approach:**

- Midline.
- Paramedian.
- Modified Paramedian (Taylor approach).
- Caudal.<sup>11</sup>

**Epidural test dose:**

Before activating epidural anaesthesia or analgesia, always epidural test dose to be given to rule out intravascular or intrathecal placement.

3 ml of lignocaine 1.5% with epinephrine (1 in 2 lakhs dilution) of 5µg/ ml of Adrenaline in per ml of LA is given as test dose. An increase in systolic blood pressure more than 15 mm Hg or an increase in heart rate more than 10 beats/min ascertained intravascular placement of epidural catheter.<sup>12</sup>

**COMPLICATIONS:****1. Neurologic:**

- Paraplegia
- Cauda Equina Syndrome
- Epidural Haematoma
- Nerve Injury
- Post Dural Puncture Headache (PDPH)
- Transient Neurological Symptoms

## **2. Cardiovascular:**

- Hypotension
- Bradycardia
- Cardiac arrest

## **3. Respiratory:**

Respiratory depression – Neuraxial opioids – dose dependent.

Early – occurs in the first 30 min – with lipophilic drugs.

Late - > 2 hrs after drug administration – Fentanyl, Sufentanil.

## **4. Infections:**

- Bacterial meningitis – Streptococcus viridans.
- Epidural abscess.

## **5. Backache.**

## **6. Nausea and Vomiting.**

## **7. Urinary Retention.**

## **8. Pruritis.**

## **9. Shivering.**

## **Complications specific to epidural anaesthesia:**

- Intravascular injection.
- Intrathecal injection<sup>8</sup>



## PHARMACOLOGY OF BUPIVACAINE

### PHARMACOLOGY

#### BUPIVACAINE :<sup>13,14</sup>

Bupivacaine which is an amide local anaesthetic first used by L J Telivuo in 1963.

#### Chemical structure :

Bupivacaine HCL (1-butyl-2', 6' pipecoloxylidide hydrochloride) is along actingamide local anaesthetic, first synthesized in 1957 by Ekernstam.

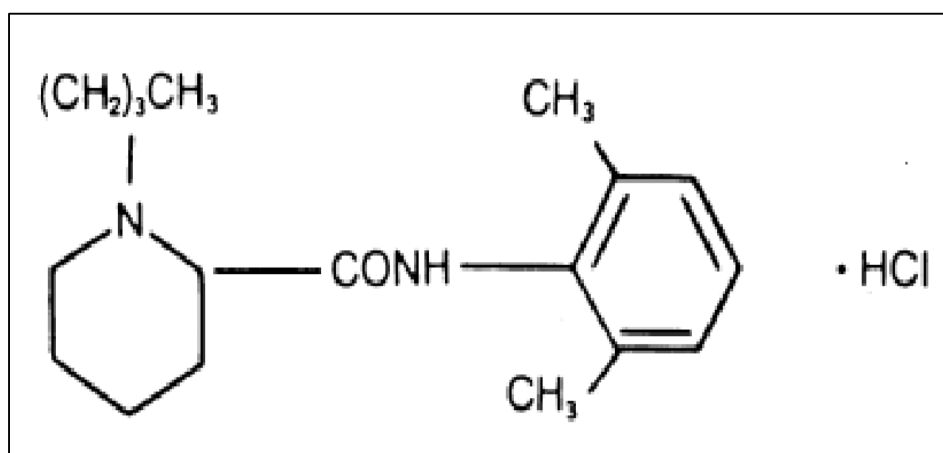


FIG 4: CHEMICAL STRUCTURE OF BUPIVACAINE

#### Mechanism of action:

Acts by binding to an intracellular portion of sodium channels that blocks sodium influx into nerve cells which prevents depolarization. It inhibits NMDA receptor transmission in the dorsal horn of the spinal cord.

**Dose of Bupivacaine:** 2-3mg/kg

**Onset of action:** 5 to 7 minutes

**Duration of action:** 4 to 6 hours

**Pharmacokinetics:**

- ✓Molecular weight (base) – 288 daltons.
- ✓Pka - 8.1.
- ✓Bound in plasma - 95%.
- ✓Volume of distribution - 0.9 - 0.4 litres/kg.
- ✓Clearance - 7.1-2.8 ml/min/kg.
- ✓Lipid solubility - 2.4-1.2 hours.
- ✓Peak time - 0.17-0.5 hour.
- ✓Peak concentration - 0.8microgram/ml.
- ✓Toxic plasma concentration - >1.5microgram /ml.
- ✓Plasma protein binding site - alpha1 acid glycoprotein.
- ✓Enzymatic degradation occurs in liver
- ✓Excretion through kidney

**Clinical Uses:**

- ✓Central neuraxial blockade (intrathecal, epidural, caudal)
- ✓For peripheral nerve blocks and infiltration analgesia.

**Toxicity:**

Toxicity can happen because of accidental intravascular injection or systemic absorption that may depend on the dose administered, presence of adrenaline (adrenaline in solution decreases the systemic absorption by one third), property of the drug and vascularity of the tissue.

**Various toxic features are:**

- Mild systemic symptoms are circumoral numbness, auditory changes like tinnitus, agitation.
  - Central nervous system toxic effects like CNS depression, seizures, coma and respiratory arrest.
  - Cardiovascular system toxic features are tachycardia, bradycardia, hypotension or hypertension, ventricular arrhythmias and cardiac arrest.
- Bupivacaine is more cardio toxic.

**Treatment for toxic doses of Bupivacaine:**

- Airway management.
- Seizure suppression – Thiopentone/ Benzodiazepines /neuromuscular blocking agents.
- Cardiac arrest – ACLS
- Use small initial doses of epinephrine (10–100 mg boluses), Vasopressin is not recommended. Avoid calcium channel blockers, beta adrenergic blockers, and Local anaesthetics (lidocaine, procaine).
- Ventricular arrhythmias – Amiodarone.

Lipid emulsion therapy - at first signs of LAST, 1.5 ml/ kg bolus of 20% lipid emulsion. Infusion at 0.25 ml/kg/min for at least 10 min after return of circulatory stability, second bolus increasing infusion to 0.50 ml/ kg if circulatory stability is not attained. Upper limit of lipid emulsion for the first 30min is 10 ml /kg.

Cardiopulmonary bypass if lipid emulsion treatment fails.

## PHARMACOLOGY OF DEXMEDETOMIDINE

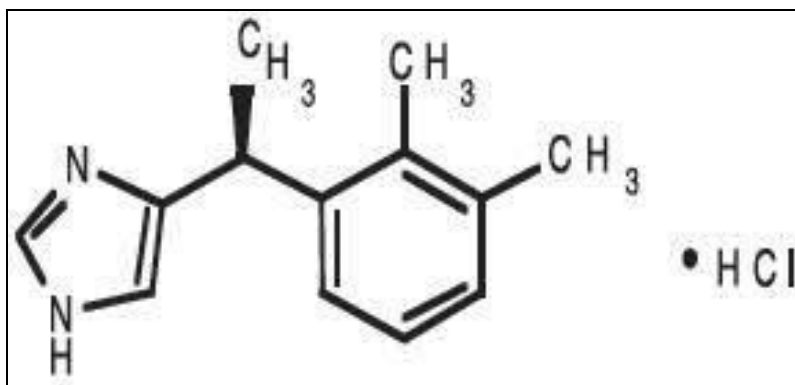
### DEXMEDETOMIDINE :<sup>15,16,17,18</sup>

Dexmedetomidine is a highly selective and specific alpha 2 adrenergic agonist.

#### Chemical formula:

Dexmedetomidine chemical formula (+) 4-(S)-[1-(2,3-dimethylphenyl)-1H-imidazole monohydrochloride.

#### Molecular formula: C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>·2HCl



**FIG 5: CHEMICAL STRUCTURE OF DEXMEDETOMIDINE**

#### Mechanism of action:

Dexmedetomidine is a centrally acting alpha 2 adreno receptor agonist that activates G proteins in the brainstem which inhibits norepinephrine release thus has sedative and anaesthetic properties.

**Pharmacokinetics:**

- ✓ Molecular weight : 236.7
- ✓ pKa : 7.1
- ✓ pH : 4.5 to 7
- ✓ Solution is preservative free and has no additives.
- ✓ % protein binding : 94%
- ✓ Total body clearance : 39l/hr
- ✓ Peak plasma concentration : 0.3-1.5ng/ml
- ✓ Distribution half life : 6minutes
- ✓ Elimination half life : 2hours
- ✓ Volume of distribution : 118 litres
- ✓ Rapidly distributed in highly vascular organs such as lung, heart and brain then skeletal muscle and then fat compartment
- ✓  $t^{1/2}$  - 2 hours
- ✓ Metabolised in liver
- ✓ Renal excretion

**Pharmacodynamics:**

- **Cardiovascular system:**

It reduces heart rate, systemic vascular resistance and myocardial contractility, cardiac output and systemic blood pressure.

- **Central nervous system :**

It reduces cerebral blood flow, alpha a2 receptors are responsible for sedation, anxiolysis and sympatholysis. It also produces analgesic effect

- **Autonomic nervous system :**

It blocks the sympathetic stress response to surgical stimulation.

- **Respiratory system :**

It produces analgesia without respiratory depression.

**Clinical uses:**

- It is used as analgesic in regional and general anaesthesia
- It provides anxiolysis and sedation
- It is used in sedating intubated cases in an intensive care setting
- Also used for sedation of non-intubated cases during surgical procedure without respiratory depression.

**Drug interaction:**

Doesn't interact with other anaesthetic agents, it reduces the dose of other analgesic agents.

**Adverse effects:**

- ✓ Hypotension
- ✓ Hypertension
- ✓ Bradycardia
- ✓ Nausea
- ✓ Atrial fibrillation
- ✓ Dry mouth

**Contra indication:**

- ✓ Patients with heart block
- ✓ Patients with bradyarrhythmias
- ✓ Hypotension
- ✓ History of allergy to dexmedetomidine

**Antagonist of dexmedetomidine:**

Atipamezole, a highly selective  $\alpha_2$  antagonist is effective, at a dose of 50mcg/kg, given intramuscularly.

## ***PHARMACOLOGY OF MAGNESIUM SULPHATE***

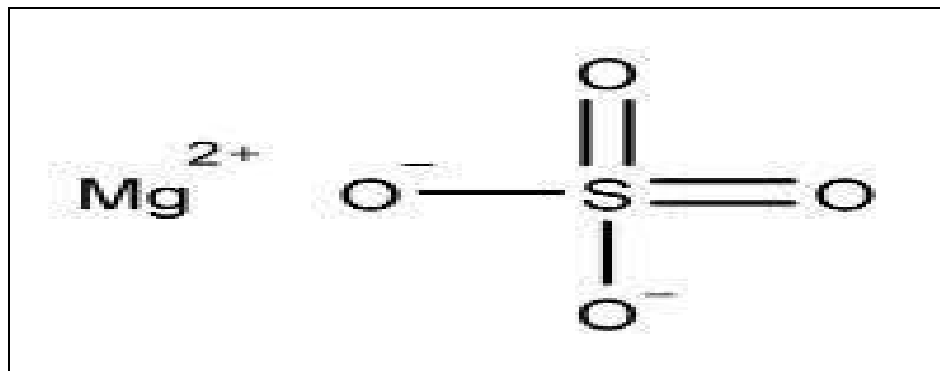
### **MAGNESIUM SULPHATE :**<sup>19,320,21,22,23</sup>

- Used as an anaesthetic induction agent
- Used in surgery for pheochromocytoma
- Used in cardiac rhythm disorders as it acts as an membrane stabilizing agent
- During ischaemia it provides cellular protection and it also improves myocardial contractility. Magnesium is the 4<sup>th</sup> common cation in the body and second most common intracellular cation.

#### **Chemical formula:**

Chemical formula of magnesium sulphate is  $\text{MgSO}_4$

Molecular formula:  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$



**FIG 6: CHEMICAL STRUCTURE OF MAGNESIUM**



## **SULPHATE**

### **Mechanism of action:**

It acts as calcium antagonist and inhibits vasoconstriction, it blocks NMDA receptors and decreases intracellular calcium and also inhibits Ryanodine receptors decreasing muscle contraction.

### **Pharmacokinetics:**

- Molecular weight : 246.48
- pH : 6
- Solution has no bacteriostatic, antimicrobial agents and preservative free.
- Protein binding : 25-30%
- Total body clearance : 1.21 l/hr
- Half life :43.2hours
- Absorbed in Gastrointestinal tract
- Renal excretion
- Normal plasma magnesium level ranges from 1.2 to 2 mEq/L

### **Pharmacodynamics:**

- **Cardiovascular system :**

It inhibits calcium uptake and influences myocardial contractility

- **Respiratory system :**

Magnesium acts as bronchodilator

- **Musculoskeletal :**

Magnesium decreases the effect of acetylcholine and increases the threshold of axonal excitation. Hypomagnesemia induces neuromuscular hyperexcitability, while hypermagnesemia causes neuromuscular weakness.

- **Central nervous system :**

Reduces excitability of nerves, acts as an anticonvulsant, inhibits NMDA receptor and thus acts as an analgesic

- **Genitourinary system :**

Acts as a tocolytic and has mild diuretic property

- **Hematologic system :**

Reduces platelet activity

**Clinical uses:**

- It has tocolytic property and also has hypotensive action in preeclampsia by maintaining uterine blood flow and fetal oxygenation
- It has bronchodilator action
- Used in perioperative analgesic adjuvant
- Used in chronic pain states as it blocks NMDA receptors

**Drug interactions:**

- Dose of barbiturates, opioids, general anaesthetics and other CNS depressants should be titrated as magnesium also has central depressant effects
- Excessive neuromuscular blockade happens if dose of neuromuscular agent is not reduced in patients receiving parenteral magnesium
- Magnesium given along with cardiac glycosides can result in heart block

**Adverse effects:**

- Magnesium intoxication that includes hypotension, depressed reflexes, flushing, sweating, flaccid paralysis, hypothermia, circulatory collapse, cardiac and CNS depression that leads to respiratory paralysis.
- Hypocalcemia

**Contra indication:**

- ✓ Patients with skeletal muscle disorder
- ✓ Hypocalcemia
- ✓ Decreased renal function
- ✓ Myasthenia gravis

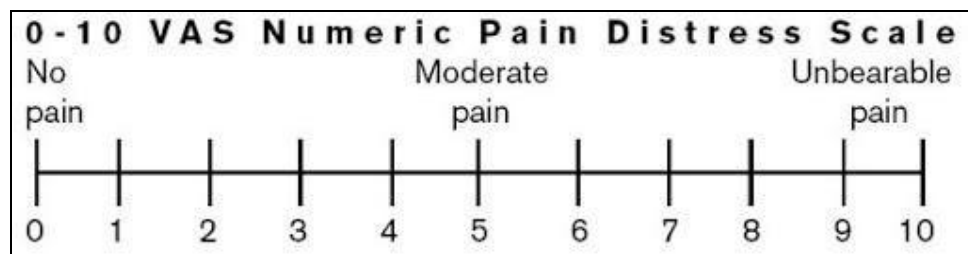
<b>Plasma concentration of magnesium sulphate (mEq/L)</b>	<b>Effect</b>
1.2 - 2	Normal
4 - 8	Therapeutic
5- 10	ECG changes (prolonged PR interval, widened QRS complex)
>10	Muscle weakness; deep tendon reflexes are lost
>15	SA/AV node block; respiratory paralysis
>20	Cardiac arrest

#### **Antagonist:**

Calcium gluconate (10ml of 10% solution over 10minutes) given intravenously.

#### **ASSESSMENT OF PAIN**

Pain is a highly subjective expression and affects many aspects of life. Hence measuring it is an important task for a physician. Many validated scales are available. It cannot be stressed more that the patient's self report should be accepted and acted upon. In rare cases, there may be an exaggeration by the patient, so the physician must exert vigilance. Because pain is dynamic, it should be reassessed regularly and adjustments to therapy made as appropriate. Unidimensional self report scales are a very simple, useful, valid method to assess pain. A visual analogue scale (VAS) consists of a 10 cm line, which has no pain in the beginning and worst pain in the end.<sup>24</sup>



## **REVIEW OF LITERATURE :**

**Aantaa R, Kanto J et al in 1990** designed a study by infusing dexmedetomidine before induction for minor gynaecological surgeries to evaluate the dose reduction of anaesthetic agent. It was found that dexmedetomidine reduced the induction dose and also post operative recovery was good by assessing visual analogue scale.<sup>25</sup>

**Koinig H, Wallner T et al in 1998** carried a study in 46 patients undergoing arthroscopic knee surgery with total intravenous anaesthesia, in this study patient received intravenous magnesium sulphate preoperatively and intraoperatively to assess intraoperative and postoperative analgesic requirement comparing patient who received magnesium sulphate and patient who dint receive magnesium sulphate, it was found that patient who received magnesium reported reduced analgesic requirement.<sup>26</sup>

**Kamibayashi T, Maze M in 2000** stated in their study that dexmedetomidine, more potent alpha 2 agonist can also be used as a single sedative agent or as adjunct that reduces the patient requirement for other additional agents for sedation and analgesics and also reduces the requirement of anaesthetics.<sup>1</sup>

**Kroin JS, McCarthy RJ et al in 2000** found in their study on rats that magnesium potentiates analgesic action of opioid when added intrathecally along with opioids and they have concluded that magnesium can be an useful adjunct when used in neuraxial anaesthesia, they have also mentioned in their study that magnesium delays onset of tolerance.<sup>27</sup>

**Li X, Eisenach J in 2001** stated in their study that alpha 2 adrenergic agonist given intrathecally or epidural produces antinociceptive effect and also alters spinal neurotransmission by reducing excitatory neurotransmitter releasing from peripheral afferents thus can be used in acute and chronic neuropathic pain.<sup>28</sup>

**Buvanendran A, McCarthy RJ et al in 2002** conducted a prospective randomised study, where it was identified that magnesium added intrathecally along with fentanyl potentiates the analgesic action of opioids in patients during caesarean section. The study included 52 patients where it got divided into two groups. One group received intrathecal bupivacaine with fentanyl alone and other group received intrathecal bupivacaine with fentanyl and magnesium sulphate, it was concluded that magnesium along with fentanyl given intrathecally prolongs the analgesic action of opioid.<sup>29</sup>

**Ozalevli M, Cetin TO, Unlugenc H, Guler T, in 2005** conducted a study in 102 patients by adding magnesium intrathecally along with bupivacaine fentanyl to know its onset of motor and sensory block along with analgesic effect, conclusion was made that, in patients undergoing lower extremity surgery, magnesium sulphate was added intrathecally(50 mg) to spinal anaesthesia induced by Bupivacaine and Fentanyl significantly delayed the onset of both sensory and motor blockade, but also prolonged the period of anaesthesia without additional side-effects.<sup>30</sup>

**Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD in 2006** prospective, double-blind study - 60 patients undergoing transurethral resection of prostate or bladder tumor, under spinal anesthesia were selected and comparison between clonidine and dexmedetomidine along with bupivacaine given intrathecally done. The onset times to reach peak sensory and motor levels, and the sensory and motor regression times, were recorded. Hemodynamic changes and the level of

sedation were also recorded. The study concludes that Dexmedetomidine, clonidine, when added to intrathecal bupivacaine, produces prolonged in the duration of the motor and sensory block with better hemodynamic stability.<sup>31</sup>

**Arcioni R, Palmisani S, Tigano S et al in 2007** studied whether supplementation of spinal anaesthesia when combined intrathecally and also epidurally infused magnesium reduced patients post operative requirement of analgesia in 120 patients in orthopedic surgery, it was concluded that supplementation of spinal anaesthesia with combined intrathecal and also epidural magnesium sulphate significantly reduces patients post operative analgesic requirements.<sup>32</sup>

**Bilir S. Gulec A. Erkan A. Ozcelik. in 2007** they conducted a study on fifty patients who underwent hip surgery to receive either fentanyl or fentanyl plus magnesium sulphate for 24 hours for epidural analgesia. Ventilatory frequency, heart rate, blood pressure, assessing pain using a visual analogue scale (VAS), sedation scores and fentanyl consumption were recorded in the postoperative period. They found there was no significant difference between groups in time and also the first analgesic requirement. The groups were similar with respect to haemodynamic and respiratory variables, sedation, pruritis, and nausea. It has been concluded that co-administration of magnesium for postoperative analgesia results in a reduction of fentanyl requirement.<sup>33</sup>

**El-Hennawy AM, Abd-Elwahab AM et al in 2009** compared the analgesic effects and side effects of dexmedetomidine and clonidine added with caudal bupivacaine in paediatric patients undergoing lower abdominal surgeries of 60 patients. Hemodynamic variables, end tidal sevoflurane and emergence time were monitored. Post-operative analgesia, use of analgesics and side effects assessed during the postoperative in the first 24hours. Thus it was concluded that addition of



dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia in children undergoing lower abdominal surgeries with no significant advantage of dexmedetomidine over clonidine and without increase in incidence of side effects.<sup>34</sup>

**Ghatak T, Chandra G, Malik A, Singh D, Bhatia VK in 2010.** They did prospective randomised double-blind study to establish the effect of adding magnesium or clonidine, as adjuvant, to epidural bupivacaine in lower abdominal and lower limb surgeries. A total of 90 ASA grade I and II patients posted for lower abdominal and lower limb surgeries were enrolled to receive either magnesium sulphate or clonidine along with epidural bupivacaine for surgical anaesthesia. The study concludes that magnesium sulphate is a predictable and safe adjunct to epidural bupivacaine for rapid onset of anaesthesia & clonidine for prolonged duration of anaesthesia with sedation.<sup>35</sup>

**Sukhminder Jit Singh Bajwa, Sukhwinder Kaur Bajwa, Jasbir Kaur in 2011,** Dexmedetomidine and clonidine added with epidural anaesthesia: A comparative evaluation. A randomized study was carried out which included 50 adult female patients between age of 44 and 65 years of ASA I/II grade who undergone vaginal hysterectomies. Onset of analgesia, sensory and motor block levels, sedation, duration of analgesia and also side effects were observed. Dexmedetomidine is a better neuraxial adjuvant compared to clonidine.<sup>36</sup>

**Jain d, Khan RM et al in 2011** evaluate the perioperative effect of epidural dexmedetomidine, in conjunction with intrathecal bupivacaine in 60 patients posted for lower limb orthopedic surgeries and it was concluded that addition of dexmedetomidine epidurally prolongs the duration of analgesia and decreases the number of rescue analgesics in patients posted for lower limb orthopedic surgery.<sup>37</sup>

**Sukhminder Jit Singh Bajwa, Vikramjit Arora, Jasbir Kaur in 2011** evaluated the efficacy of dexmedetomidine and fentanyl for analgesia in lower limb orthopedic surgeries. This study was done in 100 patients and authors concluded that dexmedetomidine is a better adjuvant than fentanyl as it provides comparable stable hemodynamics , early onset and establishment of sensory anesthesia, prolongs post op analgesia, lower consumption of LA for epidural analgesia and provides better sedation levels<sup>38</sup>

**Abir Hassan Aly Knadil et al in 2012** evaluated the analgesic efficacy of magnesium sulphate when added to epidural bupivacaine in patients undergoing surgery in the lower limb. 60 patients posted for lower limb orthopedic surgery were studied. VAS was significantly less in the magnesium group intra operatively and post operatively with reduced rescue analgesics and reduction on PCEA fentanyl consumption. Thus it was concluded that magnesium added epidurally provides better intraoperative analgesia, without increasing the incidence of side effects compared to bupivacaine alone.<sup>39</sup>

**Sonali Banwait, Sujata Sharma and Rajesh Sood in 2012** evaluated the efficacy of single bolus administration of magnesium epidurally as an adjuvant to epidural fentanyl for postoperative analgesia in 60 patients posted for total hip replacement under combined spinal epidural anaesthesia. The results of the investigations showed that a single bolus of epidural magnesium as an adjuvant to fentanyl for post operative analgesic requirement results in prolonged duration of analgesia as compared to epidural fentanyl alone. Concomitant administration of magnesium reduces the requirement for breakthrough analgesics with no increased incidence of side effects.<sup>40</sup>

**Shahi V, Verma AK, Agarwal A, Singh CS in 2014** conducted a prospective randomized study of comparing dexmedetomidine and magnesium sulfate along with epidural bupivacaine in 120 patients to determine the motor and sensory onset of action and duration of analgesia post operatively, they have concluded that dexmedetomidine group showed rapid onset of action and prolonged duration of action with better post operative analgesia when compared to magnesium sulphate group.<sup>41</sup>

**Mohammad W, Mir SA, Mohammad K, Sofi K. in 2015** Compared postoperative pain relief in patients undergoing an elective thoracotomy with thoracic epidural analgesia using single shot magnesium and clonidine as adjuvant to bupivacaine. In a randomized prospective study, 60 patients of American Society of Anesthesiologists physical status I-III of either sex, between 20 and 60 years undergoing elective unilateral thoracotomy, were allocated to three equal groups of 20 patients. They concluded that thoracic epidural analgesia using bupivacaine with clonidine is an efficient therapeutic modality for post-thoracotomy pain. Magnesium as an adjuvant provided quality postoperative analgesia decreasing the need for postoperative rescue analgesia and incidence of postoperative shivering without causing sedation<sup>42</sup>

**Goyal V, Kubre J, Radhakrishnan K. in 2016** conducted study in 100 pediatric population using using dexmedetomidine as adjuvant in caudal anaesthesia with bupivacaine and concluded that it increases the duration of caudal anaesthesia and improves the hemodynamic stability in babies undergoing infraumbilical surgeries.<sup>43</sup>

**Sayed JA, Kamel EZ et al in 2018** conducted a study in 120 pediatric cases to evaluate the usefulness of adding dexmedetomidine and magnesium sulphate together as adjuvant in caudal anesthesia and they have concluded in their study that when

both dexmedetomidine and magnesium sulphate is added together in caudal anaesthesia it prolongs the time of first analgesic requirement.<sup>44</sup>

**Yan MJ, Wang T et al in 2019** evaluated a study to compare dexmedetomidine and sufentanil along with ropivacaine for epidural analgesia after thoracotomy. This was a double blinded prospective study that was conducted in 120 patients who underwent lung lobectomy. The study concludes that dexmedetomidine, superior than sufentanil in providing postoperative analgesia, as it also possess sedative property with very few side effects.<sup>45</sup>

**Yehia MF, Ahmad AEA et al in 2019** conducted a study in 60 patients undergoing total knee replacement comparing magnesium sulphate and dexmedetomidine as adjuvant to epidural bupivacaine to assess postoperative analgesic requirement and concluded that both magnesium and dexmedetomidine are considered as safe adjuvant to epidural bupivacaine, with dexmedetomidine has superior analgesic property along with sedation.<sup>46</sup>

**LiL, FangM, WangC, et al in 2020** concludes that when epidural bupivacaine given along with magnesium sulphate than given alone provides better analgesic property and also reduces number of rescue analgesia.<sup>47</sup>

## **METHODOLOGY**

### **METHODS AND MATERIALS :**

#### **Source of data:**

90 patients undergoing lower abdominal and lower limb surgeries at R. L. Jalappa Hospital and Research Centre, Tamaka , Kolar, from January 2019 to June 2020 were included in the study.

#### **Method of collection of data:**

#### **Inclusion criteria:**

- Patients belonging to
- ASA Grade I and II
- Both genders
- Age group between 18 to 60 years

#### **Exclusion criteria:**

Patients suffering from

- ☐ Cardiovascular disease: chronic hypertension, advanced heart block, severe ventricular dysfunction
- ☐ Hypovolemia
- ☐ Bradycardia
- ☐ Hepatic impairment
- ☐ Diabetes mellitus
- ☐ Pregnancy and lactating mothers
- ☐ Patients who are on sedatives and hypnotics.
- ☐ Patients with known allergy to dexmedetomidine
- ☐ Patients refusal.

## **SAMPLING PROCEDURE:**

➤ All patients were evaluated one day prior to surgery, during pre operative evaluation and informed consent was taken.

➤ The ethical committee approval was taken to conduct the study.

The following investigations were done pre operatively

- ☐ Complete haemogram.
- ☐ Bleeding time and clotting time.
- ☐ Random blood sugar.
- ☐ Blood urea and serum creatinine.
- ☐ Serum electrolytes.
- ☐ Urine analysis for sugar, albumin and microscopy.
- ☐ ECG and chest x-ray.
- ☐ No special investigations were required.

➤ An elaborated clinical examination was conducted and necessary investigations sent and reviewed before surgery.

➤ Airway assessment was done using the Mallampati score. Spine examination done and spine deformities were ruled out

➤ Fasting of 6 hours was ensured and were premedicated with Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg and the drugs were repeated 2 hours before the surgery. Patients were randomly allocated into three groups of 30 each. Randomization done by computer generated table.

➤ Patients were segregated into three groups of 30 patients each

**GROUP A** (control group) received epidural bupivacaine 0.5%(17 ml) + 1ml 0.9% normal saline.

**GROUP B** received epidural Bupivacaine 0.5%(17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

**GROUP C** received epidural Bupivacaine 0.5%(17 ml) + 1ml 50mg magnesium sulphate.

➤ After securing a venous access using a 18G cannula, the patient was preloaded with Ringer's Lactate infusion at a rate of 5ml/kg/hr.

➤ On arrival to the operation room, baseline HR, NIBP, ECG, SPO2 were recorded and monitoring were started.

➤ All patients received a standard epidural block under full aseptic conditions in sitting position. Skin was infiltrated with 1% lidocaine (2ml) by a 26G hypodermic needle. Epidural space was identified at L2-3 or L3-4 interspace using a loss of resistance technique via a midline approach with an 18G Touhy's needle. The epidural catheter was then advanced 3 to 5cm cephalad into the epidural space. After the procedure, the patient was turned supine slowly .

➤ Correct placement of the catheter was verified by a test dose of 3ml lidocaine 2% with adrenaline (1:2,00,000) after confirming negative backflow of blood and CSF. The patients were then given epidural medications accordingly to the allocated groups. All study drugs were diluted to 1ml in 0.9% normal saline. Thus the total volume of the epidural anesthesia was 18ml in all the groups. The time of drug injection was noted and recorded as 0.

Following parameters of blockade characteristics and hemodynamic parameters were noted:

**I. SENSORY BLOCKADE:**

- a. Onset of sensory blockade
- b. Time to achieve T6 sensory level
- c. Quality and extent of sensory blockade

**II. MOTOR BLOCKADE**

- a. Onset of motor blockade
- b. Quality of motor blockade

**III. TWO SEGMENT REGRESSION**

**IV. TIME FOR FIRST EPIDURAL TOP UP**

**V. HEMODYNAMIC STABILITY**

**VI. SIDE EFFECTS AND COMPLICATIONS**

- Sensory blocks were assessed bilaterally by loss of pin prick sensation with short hypodermic 22G needle in mid clavicular line. Motor blocks were assessed by Modified Bromage scale.

**MODIFIED BROMAGE SCALE:**

- 1- Free movement of legs and feet, with ability to raise extended leg.
- 2- Inability to raise extended legs and knee flexion is decreased, but full flexion of feet and ankles is present.
- 3- Inability to raise leg or flex knees, flexion of ankle and feet present.
- 4- Inability to raise leg, flex knee or ankle or move toes.



**Onset of sensory blockade:**

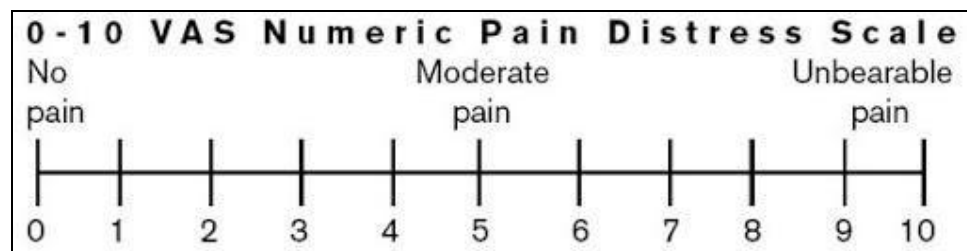
This was subjectively assessed by complaint of sensation of tingling or warmth in the patient's limbs. It was confirmed by loss of pin prick sensation at L1. Measured from the time of injection of the drug to loss of pin prick at L1 noted in minutes.

**Time to achieve T6 sensory level:**

It was taken as the time when drugs administered to attain T6 sensory level were noted in minutes.

**Quality and extent of sensory block:**

The maximum level of sensory blockade was noted. The quality of sensory blocks were assessed by standard 10 point visual analogue scale. The patients were asked to evaluate their pain on standard 10 point visual analogue pain scale (VAS 0 = no pain, VAS 10 = worst possible pain)



VAS was assessed every 10minutes. In the event of pain, (VAS > 4), intraoperatively a bolus of epidural bupivacaine 0.25%(6ml) was administered, post operatively a bolus of epidural bupivacaine 0.125%(8ml) was administered.

**Onset of motor blockade:**

It was subjectively assessed by the feeling of heaviness of leg and confirmed by modified bromage scale score of 1. Measured from the time of injection of the drug to modified bromage score of 1

**Quality of motor blockade:**

Quality of motor block was assessed by using modified bromage scale. The maximum score achieved was noted.

**Two segment regression:**

The time for regression of the sensory level by two dermatomes was recorded. It was noted in minutes.

**Time for first epidural top-up:**

Time for the first epidural top up dose was recorded. In the event of pain, when VAS > 4, bolus of epidural top up was given and it is noted down in minutes.

**Hemodynamic stability:**

Monitoring consisted of heart rate, non-invasive arterial blood pressure, SpO<sub>2</sub> at the interval of 5minutes for the first 30minutes and 20minutes interval thereafter.

Hypotension- defined as systolic BP < 90mmHg or >30% decrease in baseline values. It was treated with rapid infusion of intravenous ringer lactate 250ml and 6mg of intravenous mephentermine if there was no response to intravenous fluid administration.

Bradycardia was defined as heart rate < 60/min or >30% decrease in baseline value. Bradycardia treated with injection atropine 0.6mg intravenously.

Respiratory depression- defined as fall in respiratory rate <10breaths/min or fall of peripheral oxygen saturation <90%, treated with oxygen supplementation of 5lit/min by face mask.

Intravenous fluids were administered in the form of ringer lactate solution in calculated doses depending on the patient's body weight and further adjusted as per blood loss during the surgery. Colloid and blood was administered as per the loss and requirement.

### **Side effects and complications:**

Occurrence of any adverse events (intra operatively or post operatively) was recorded such as hypotension, bradycardia, nausea vomiting, shivering. The total duration of the surgery was recorded. Patients were followed up for 48hours and the epidural catheter was removed after 48hours.

### **STATISTICAL ANALYSIS:**

Study design : Randomised double blind study.

Data was entered in Ms Excel, MS word and analyzed using SPSS 22 version software.

Qualitative data was presented in the form of proportions and bar charts was used to represent graphically. Quantitative data was presented as mean, standard deviation. The one-way analysis of variance (ANOVA) was employed to determine whether there were any statistically significant differences between the means of three or more independent (unrelated) groups. P value <0.05 was been considered as statistically significant.

**FORMULA:**

$$n = \frac{2Sp^2 [S_{1-\alpha/2} + S_{1-\beta}]^2}{\mu^2 d}$$

$$S_p^2 = \frac{S_1^2 + S_2^2}{2}$$

$S_1^2$  = standard deviation in first group

$S_2^2$  = standard deviation in second group

$\mu^2$  = mean difference between sample

$\alpha$  = significance level

$1-\beta$  = power

Sample size of study were based on time to acquire T10 by Vaibhav Shahi et al in a comparative study of magnesium sulfate vs dexmedetomidine as an adjuvant to epidural bupivacaine observed a variance estimate of four with 95% confidence interval with 80% power with equal allocation to detect a difference of 10% time in achieving T8 blockade, the required sample size per group was 30.<sup>41</sup>

## **RESULTS:**

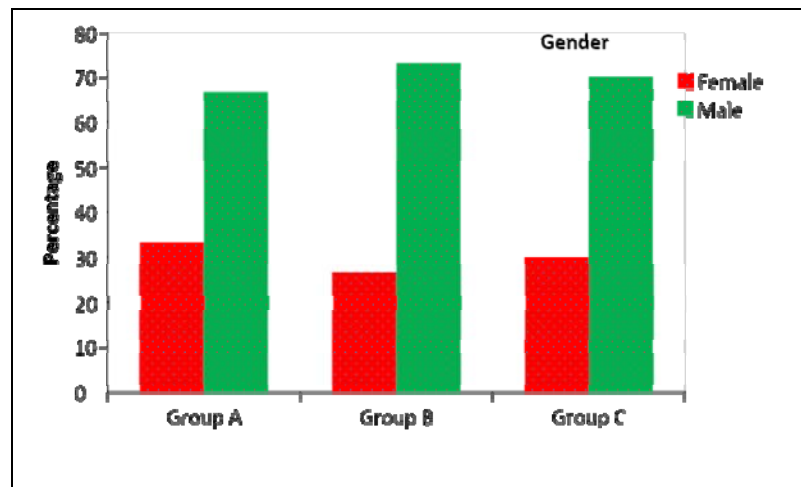
**TABLE NO 1 :**

### **GENDER DISTRIBUTION OF SUBJECTS BETWEEN THREE**

#### **GROUPS:**

Gender	Group A	Group B	Group C	Total
Female	10(33.3%)	8(26.7%)	9(30%)	27(30%)
Male	20(66.7%)	22(73.3%)	21(70%)	63(70%)
Total	30(100%)	30(100%)	30(100%)	90(100%)

In this study 27% were female and 63% were male and there was no significant difference in gender between three groups ( $P=0.853$ ), chi square test was used.



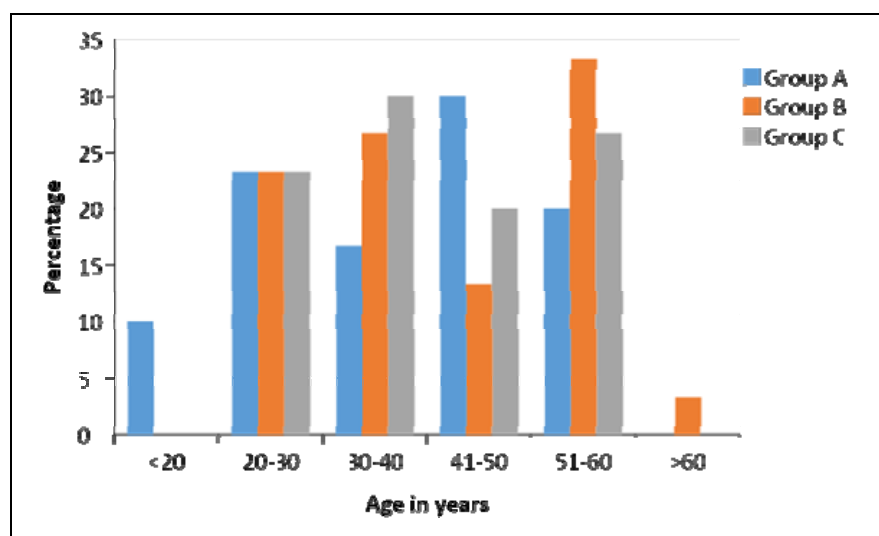
**FIGURE NO 7: BAR DIAGRAM SHOWS GENDER DISTRIBUTION  
BETWEEN THREE GROUPS**

**TABLE NO 2:**

**AGE DISTRIBUTION OF PATIENTS BETWEEN THREE GROUPS**

Age in years	Group A	Group B	Group C	Total
<20	3(10%)	0(0%)	0(0%)	3(3.3%)
20-30	7(23.3%)	7(23.3%)	7(23.3%)	21(23.3%)
30-40	5(16.7%)	8(26.7%)	9(30%)	22(24.4%)
41-50	9(30%)	4(13.3%)	6(20%)	19(21.1%)
51-60	6(20%)	10(33.3%)	8(26.7%)	24(26.7%)
>60	0(0%)	1(3.3%)	0(0%)	1(1.1%)
Total	30(100%)	30(100%)	30(100%)	90(100%)
Mean±SD	39.13±13.31	42.82±13.48	41.67±12.54	41.20±13.06

There were no significant difference in mean age groups with P value 0.543



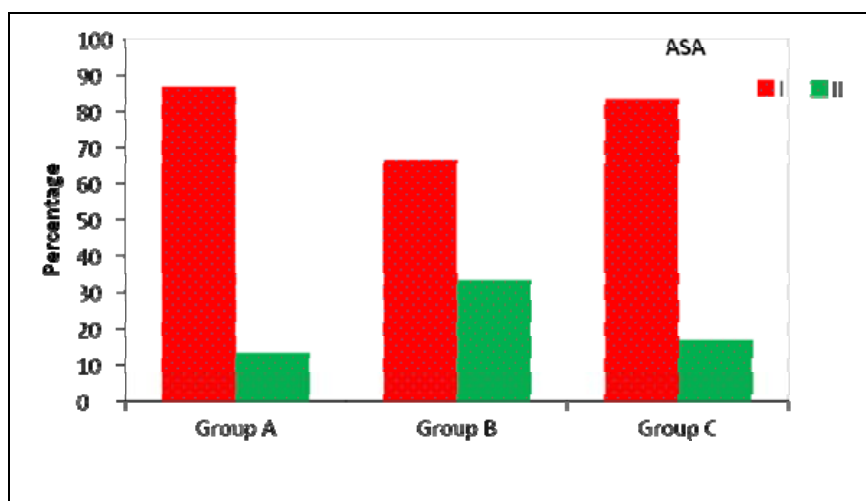
**FIGURE NO 8 : BAR DIAGRAM SHOWING AGE DISTRIBUTION  
BETWEEN THREE GROUP**

**TABLE NO 3:**

**ASA GRADE DISTRIBUTION IN THREE GROUPS**

ASA	Group A	Group B	Group C	Total
I	26(86.7%)	20(66.7%)	25(83.3%)	71(78.9%)
II	4(13.3%)	10(33.3%)	5(16.7%)	19(21.1%)
Total	30(100%)	30(100%)	30(100%)	90(100%)

In this study 71% belongs to ASA I and 19% belongs to ASA II. There was no significant difference in ASA grading with P value of 0.126%



**FIGURE NO 9: BAR DIAGRAM SHOWING ASA GRADE DISTRIBUTION  
IN THREE GROUPS:**

**TABLE NO 4:****HEART RATE (bpm) COMPARISON BETWEEN THREE GROUPS:**

PR (BPM)	Group A	Group B	Group C	Total	P value
PRE-OPERATIVE VITALS	83.83±8.07	81.7±11.02	79.4±9.15	81.64±9.56	0.201
0	86.43±8.98	81.57±9.96	79.47±8.96	82.49±9.66	0.015*
3	85.1±9.33	77.37±8.61	76.77±7.24	79.74±9.18	<0.001**
5	83.3±8.98	74.2±8.51	74.77±7.48	77.42±9.25	<0.001**
10	83.33±10.09	68.9±7.49	74.13±8.64	75.46±10.57	<0.001**
20	83.2±9.52	67.73±8.18	75.53±8.44	75.49±10.72	<0.001**
30	83.97±9.96	64.87±8.25	76.17±8.78	75±11.91	<0.001**
40	83.63±9.34	63.03±7.69	77.33±9.83	74.67±12.42	<0.001**
50	84.4±10.11	63.6±7.43	77.93±9.54	75.31±12.54	<0.001**
60	88.14±11.98	64.24±6.2	77.19±15.61	77.11±15.39	<0.001**
90	97.91±10.83	63.33±4.45	75.63±13.15	77.41±17.65	<0.001**
120	101.17±10.3	63.5±4.32	86±7.21	83.07±18.93	<0.001**

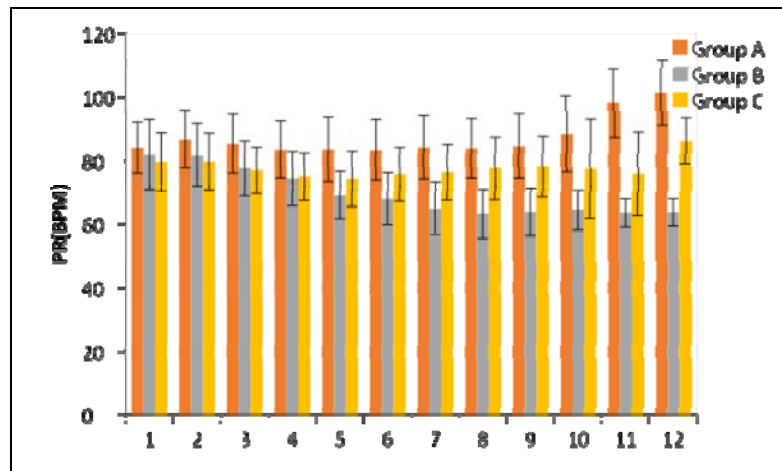
Baseline HR (bpm) were comparable in three groups, which were 86.43±8.98, 81.57±9.96 and 79.47±8.96 in group A, group B and group C respectively

In group A there were no significant difference in PR, even after 30 minutes of epidural bupivacaine it remained at 83.97±9.96 and there was increased PR seen after 1hour of epidural bupivacaine with normal saline, it was 101.17±10.3 after 120min of epidural.



In group B after 10minutes of epidural bupivacaine with dexmedetomidine PR dropped to  $64.87 \pm 8.25$  and it remained on the lower side all though the procedure without tremendous increase in PR. It was  $63.5 \pm 4.32$  even after 120 minutes of epidural.

In group C, PR remained the same all through the procedure, after 30minutes of epidural bupivacaine with magnesium sulphate it was  $75 \pm 11.91$  and it was  $86 \pm 7.21$  after 120minutes of epidural.



**FIGURE NO 10: BAR DIAGRAM SHOWING COMPARISON OF HEART RATE IN THREE GROUPS**

**TABLE NO 5:****SYSTOLIC BLOOD PRESSURE- COMPARISON IN ALL THREE GROUPS**

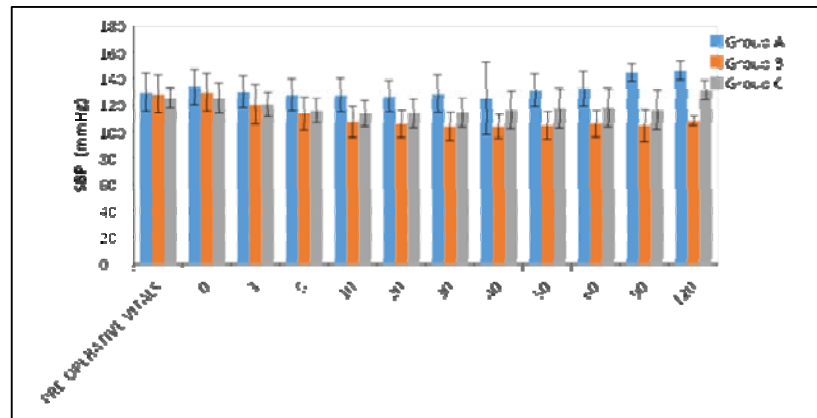
<b>SBP (mmHg)</b>	<b>Group A</b>	<b>Group B</b>	<b>Group C</b>	<b>Total</b>	<b>P value</b>
PRE- OPERATIVE VITALS	129.67±14.23	128.33±14.13	125.33±7.31	127.78±12.32	0.382
0	133.63±13.16	129.6±14.11	125.13±11.26	129.46±13.22	0.043*
3	130.03±11.67	120.37±14.82	120.57±9.32	123.66±12.84	0.003**
5	127.7±11.88	113.63±12.52	116±9.28	119.11±12.78	<0.001**
10	127.57±12.57	107.3±11.88	113.63±9.66	116.17±14.15	<0.001**
20	126.63±11.7	105.7±10.39	113.87±10.91	115.4±13.91	<0.001**
30	128.53±14.05	103.9±10.7	114.37±10.98	115.6±15.62	<0.001**
40	124.97±27.39	103.83±9.07	116.53±14.32	115.11±20.36	<0.001**
50	131.3±12.17	104.67±10.45	117.53±14.81	117.83±16.58	<0.001**
60	132.5±13.07	105.81±10.06	117.96±14.48	119.27±16.75	<0.001**
90	144.42±6.56	104.44±12.14	116.5±14.93	120.44±20.95	<0.001**
120	146±7.27	108±3.46	131.33±7.09	127.87±18.52	<0.001**

Baseline SBP in all the three groups were 133.63±13.16, 129.6±14.11 and 125.13±11.26 in group A, group B and group C respectively.

In group A there were fall in SBP only after 40minutes of epidural which was 124.97±27.39 and was gradually increasing as the time proceeded, it was 146±7.27 after 120 minutes of epidural.

In group B there was a significant fall in SBP after 10minutes of epidural which was 107.3±11.88 and it remained on the lower side all through the procedure , it was 108±3.46 after 120 minutes of epidural.

In group C there was fall in BP after 10minutes of epidural but it was not significant when compared to group B which was  $115.6 \pm 15.62$ , and there was no much change thereafter, it was  $127.87 \pm 18.52$  after 120minutes of epidural



**FIGURE NO 11: BAR DIAGRAM SHOWING COMPARISON OF SBP IN ALL THREE GROUPS**

**TABLE NO 6:****DIASTOLIC BLOOD PRESSURE- COMPARISON IN ALL THREE GROUPS**

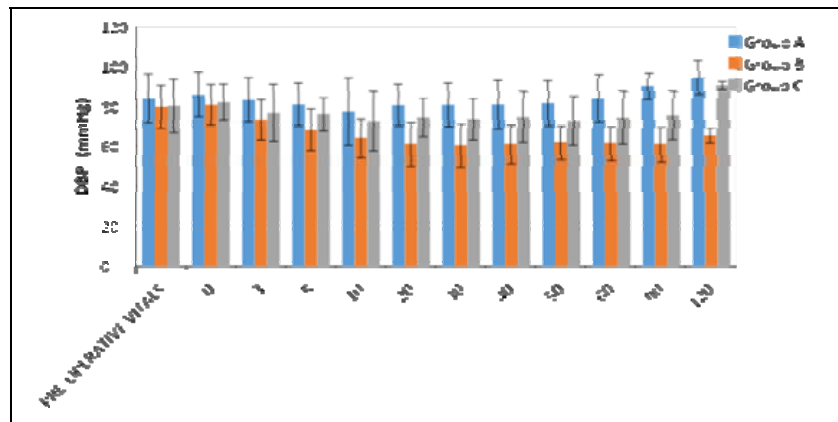
<b>DBP (mm Hg)</b>	<b>Group A</b>	<b>Group B</b>	<b>Group C</b>	<b>Total</b>	<b>P value</b>
PRE- OPERATIVE VITALS	84.10±12.35	79.9±10.82	80.33±13.51	81.44±12.29	0.350
0	86.13±11.21	80.97±10.13	82.30±9.07	83.13±10.29	0.130
3	83.53±11.10	73.30±10.33	76.77±14.47	77.87±12.71	0.005**
5	81.13±10.8	68.17±10.59	76.17±8.49	75.16±11.26	< 0.001**
10	77.40±17.10	64.20±9.46	72.57±15.2	71.39±15.16	0.002**
20	80.80±10.5	61.03±10.95	74.57±9.87	72.13±13.25	<0.001**
30	80.87±11.05	60.47±10.87	73.60±10.60	71.64±13.68	<0.001**
40	81.07±12.31	61.10±9.51	74.73±12.93	72.3±14.27	<0.001**
50	81.70±11.44	61.97±8.20	72.87±12.49	72.18±13.46	<0.001**
60	84.21±11.94	61.54±8.18	74.42±13.42	73.79±14.67	<0.001**
90	90.31±6.55	61.00±8.53	75.50±12.34	74.84±15.50	<0.001**
120	94.67±8.41	65.33±3.88	90.67±2.08	82.13±15.33	<0.001**

Baseline DBP in all three groups were  $86.13 \pm 11.21$ ,  $80.97 \pm 10.13$  and  $82.30 \pm 9.07$  in group A, group B and group C respectively.

In group A there was no much in fall in DBP after 40minutes of epidural it was  $81.07 \pm 12.31$  and it remained the same all throughout the procedure and started increasing as time proceeded, it was  $94.67 \pm 8.41$  after 120minutes of epidural.

In group B there was a significant reduction in DBP after 20minutes of epidural it was  $61.03 \pm 10.95$  and it was on the lower side thereafter, it was  $65.33 \pm 3.88$  after 120minutes of epidural.

In group C there was no much reduction in DBP, it was  $73.60 \pm 10.60$  after 30minutes of epidural and there was no much change thereafter. It was  $90.67 \pm 2.08$  after 120minutes of epidural.



**FIGURE NO 12: BAR DIAGRAM SHOWING COMPARISON OF DBP IN ALL THREE GROUPS**

**TABLE NO 7:MEAN ARTERIAL BLOOD PRESSURE- COMPARISON IN  
ALL THREE GROUPS**

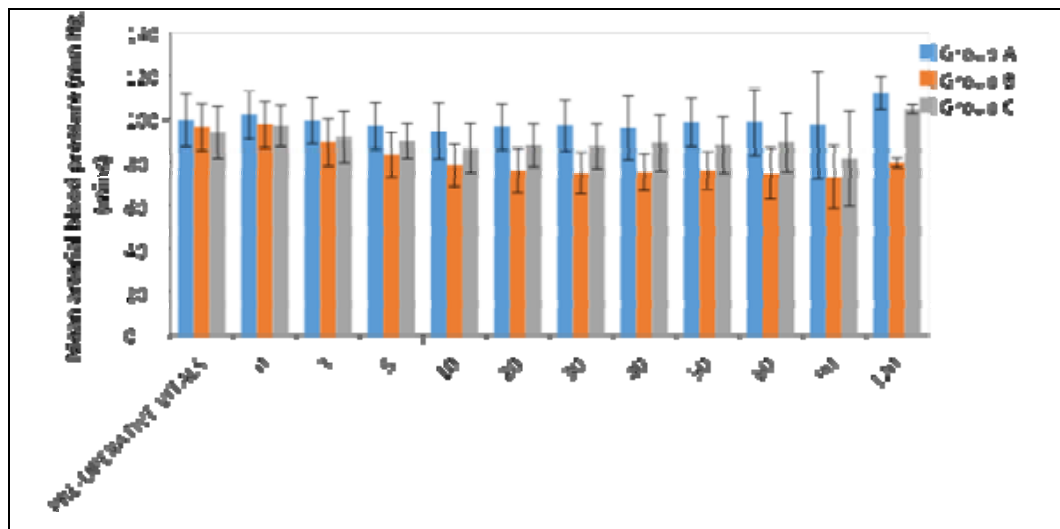
<b>Mean arterial blood pressure (mm Hg) (mins)</b>	<b>Group A</b>	<b>Group B</b>	<b>Group C</b>	<b>Total</b>	<b>P value</b>
PRE- OPERATIVE VITALS	99.29±12.27	96.04±10.76	93.56±12.03	96.30±11.81	0.170
0	101.90±11.3 5	97.17±10.66	96.60±9.51	98.56±10.69	0.108
3	98.97±10.72	88.93±10.83	91.43±11.89	93.11±11.84	0.002**
5	96.60±10.69	83.37±10.30	89.53±7.99	89.83±11.05	<0.001**
10	94.20±12.93	78.47±9.52	86.27±11.29	86.31±12.93	0.002**
20	96.20±10.47	76.03±10.18	87.63±9.80	86.62±13.03	<0.001**
30	96.77±11.74	74.93±9.51	87.17±10.21	86.29±13.75	<0.001**
40	95.70±14.79	75.37±8.40	88.67±12.85	86.58±14.83	<0.001**
50	98.20±11.22	76.10±8.52	87.73±12.95	87.34±14.2	<0.001**
60	98.40±15.56	74.78±11.77	88.92±13.49	87.75±16.81	<0.001**
90	97.07±24.61	73.00±14.47	81.50±21.92	83.55±22.49	0.010**
120	111.83±7.65	79.67±2.16	104.33±2.08	97.47±16.05	<0.001**

Baseline mean arterial blood pressure in all three groups were 101.90±11.35, 97.17±10.66 and 96.60±9.51 in group A, group B and group C respectively.

In group A MAP remains constant and there is no much fall in MAP, it was  $95.70 \pm 14.79$  after 40minutes of epidural, and it was  $111.83 \pm 7.65$  after 120minutes of epidural.

In group B significant reduction of MAP is seen after 30minutes of epidural and it was  $74.93 \pm 9.51$ , it was stable all through the procedure and it was  $79.67 \pm 2.16$  after 120minutes of epidural

In group C MAP remains constant without increase or decrease from its basal value, it was  $79.67 \pm 2.16$  after 30minutes of epidural, and it was  $104.33 \pm 2.08$  after 120minutes of epidural.

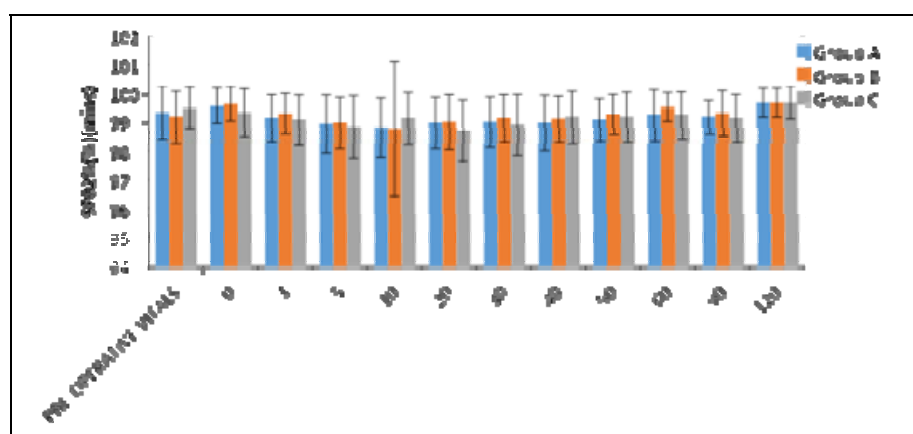


**FIGURE NO 13 : BAR DIAGRAM SHOWING COMPARISON ON MAP  
IN ALL THREE GROUPS.**

**TABLE NO 8:****COMPARISON OF SPO2 IN ALL THREE GROUPS**

SPO2(%) (mins)	Group A	Group B	Group C	Total	P value
PRE-OPERATIVE VITALS	99.33±0.92	99.17±0.91	99.50±0.73	99.33±0.87	0.329
0	99.57±0.63	99.63±0.61	99.33±0.84	99.51±0.71	0.227
3	99.13±0.82	99.3±0.7	99.07±0.87	99.17±0.8	0.510
5	98.93±1.01	98.97±0.89	98.83±1.09	98.91±0.99	0.866
10	98.8±1.03	98.77±2.34	99.13±0.9	98.9±1.56	0.607
20	98.97±0.89	99.00±0.95	98.7±1.06	98.89±0.97	0.423
30	99.00±0.87	99.13±0.82	98.9±1.06	99.01±0.92	0.619
40	98.97±0.96	99.10±0.80	99.17±0.91	99.08±0.89	0.680
50	99.07±0.74	99.27±0.69	99.17±0.87	99.17±0.77	0.607
60	99.23±0.9	99.52±0.51	99.23±0.82	99.33±0.77	0.284
90	99.17±0.58	99.31±0.79	99.13±0.83	99.22±0.72	0.801
120	99.67±0.52	99.67±0.52	99.67±0.58	99.67±0.49	1.000

There was no significant change in saturation in all three groups.



**FIGURE NO 14 : BAR DIAGRAM SHOWING COMPARISON OF SPO2 IN ALL THREE GROUPS.**



**TABLE NO 9 :SHOWING COMPARISON OF VARIOUS VARIABLES IN  
ALL THREE GROUPS**

<b>variables</b>	<b>Group A</b>	<b>Group B</b>	<b>Group C</b>	<b>Total</b>	<b>P value</b>
Weight (kg)	62.8±10.21	69.07±9.19	63.17±9.06	65.01±9.83	0.020*
Onset of Sensory Block	14.12±6.18	4.63±1.22	5.75±1.71	8.17±5.65	<0.001**
Onset of Motor Block	17.17±2.01	7.02±1.70	8.10±2.05	10.76±4.96	<0.001**
Time to achieve T6level	13.22±1.43	4.73±1.32	5.82±1.72	7.92±4.07	<0.001**
Duration of Surgery	85.50±21.24	85.43±21.29	74.33±21.51	81.76±21.76	0.071+
Time for Two segment regression	86.77±3.60	106.4±8.01	102.7±8.05	98.62±10.94	<0.001**
Recovery from Motor block	97.77±5.03	121.6±8.42	119.87±10.01	113.08±13.53	<0.001**
Time to first Analgesic request	1.90±0.28	3.18±0.83	4.08±0.95	3.06±1.16	<0.001**

Time taken for sensory block in group A was  $14.12 \pm 6.18$ , in group B it was  $4.63 \pm 1.22$  and in group C it was  $5.75 \pm 1.71$ , which signifies that time for onset of sensory block was seen early in group B.

Time for complete motor blockade in group A was  $17.17 \pm 2.01$ , in group B it was  $7.02 \pm 1.70$  and in group C it was  $8.10 \pm 2.05$ , which signifies that early onset of motor blockade was seen in group B.

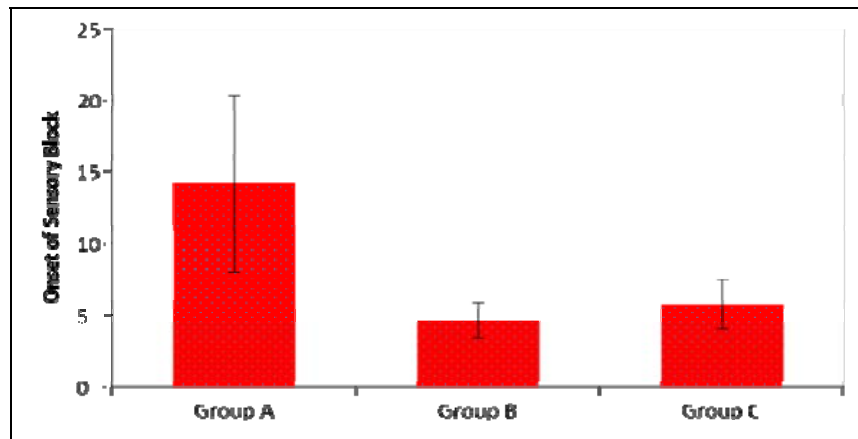
Time taken to achieve T6 level in group A was  $13.22 \pm 1.43$ , in group B it was  $4.73 \pm 1.32$  and in group C it was  $5.82 \pm 1.72$ , which imparts that time to achieve T6 level was seen early in group B.

Time for two segment regression in group A was  $86.77 \pm 3.60$ , it was  $106.4 \pm 8.01$  in group B and it was  $102.7 \pm 8.05$  in group C, which signifies that early two segment regression seen in group A, where as longer time for two segment regression was seen in group B.

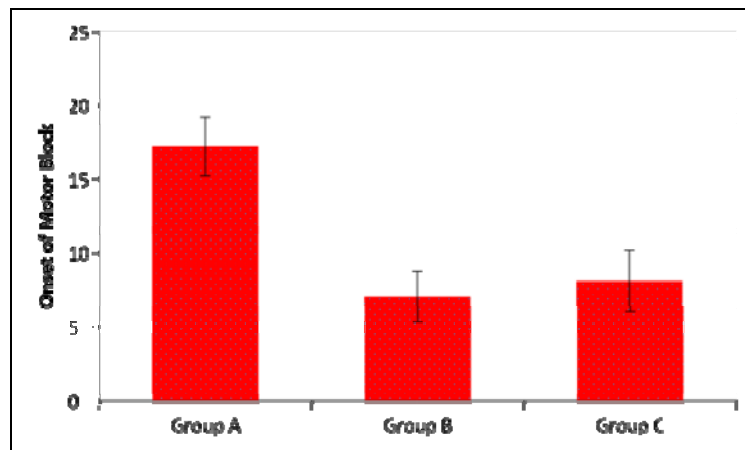
Time for recovery from motor blockade in group A was  $102.7 \pm 8.05$ , in group B it was  $121.6 \pm 8.42$  and in group C it was  $119.87 \pm 10.01$  which signifies that time for regression of motor blockade is longer in group B when compared to other two groups.

Time taken for first analgesic request in group A was  $1.90 \pm 0.28$  hours, in group B it was  $3.18 \pm 0.83$  hours and in group C it was  $4.08 \pm 0.95$  hours, which signifies that analgesics during post operative period was better with group C, that is magnesium sulphate.

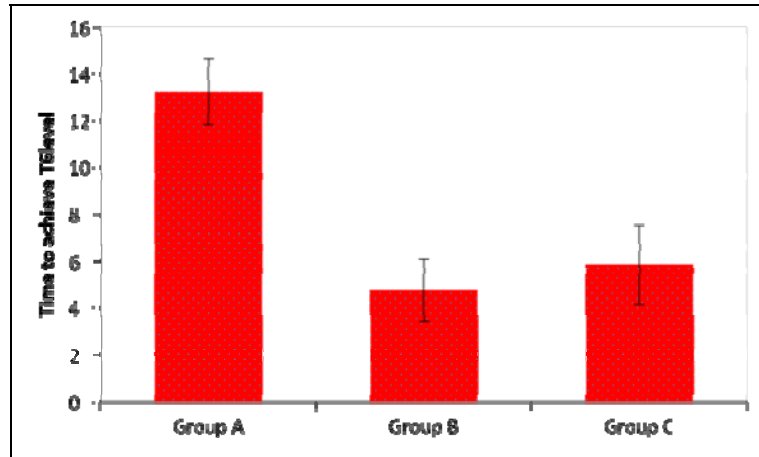
Average time taken for surgeries in group A was  $85.50 \pm 21.24$ , in group B was  $85.43 \pm 21.29$  and in group C it was  $74.33 \pm 21.51$ .



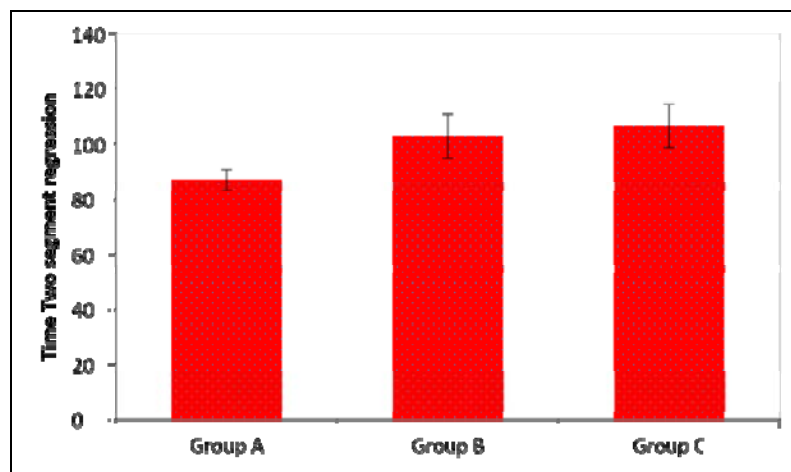
**FIGURE NO 15: BAR DIAGRAM SHOWING DURATION OF THE ONSET OF SENSORY BLOCK IN THREE GROUPS**



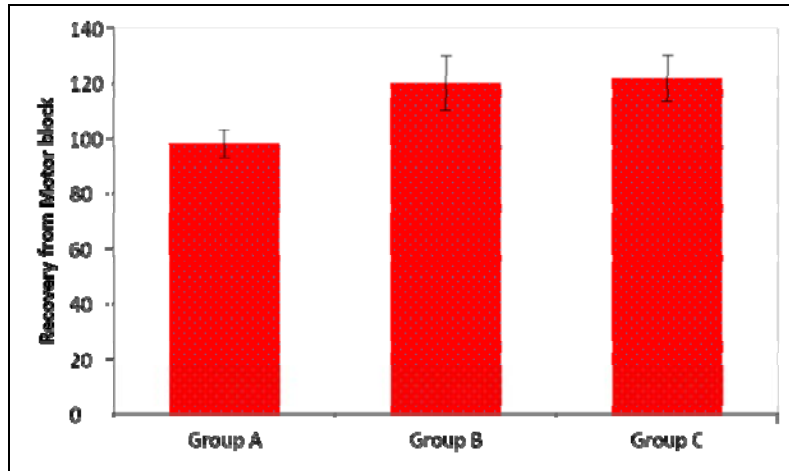
**FIGURE NO 16: BAR DIAGRAM SHOWING THE DURATION OF ONSET OF MOTOR BLOCKADE IN THREE GROUPS**



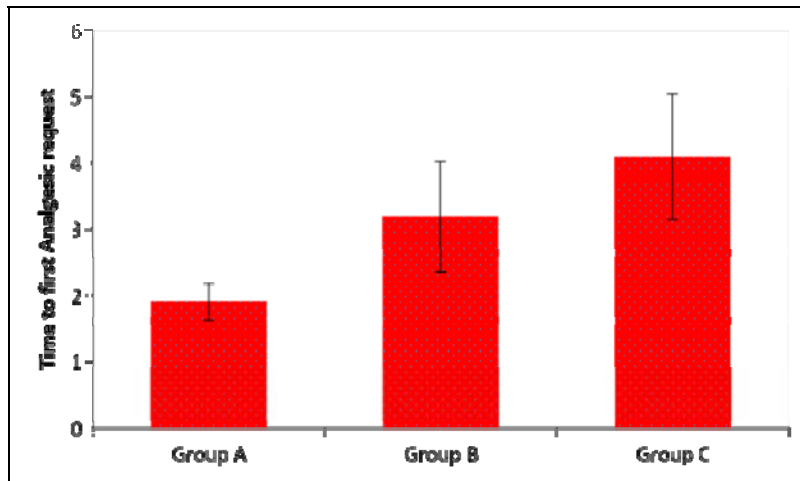
**FIGURE NO 17: BAR DIAGRAM SHOWS THE DURATION OF TIME TO ACHIEVE T6 LEVEL IN THREE GROUPS**



**FIGURE NO 18: BAR DIAGRAM SHOWS THE TIME FOR TWO SEGMENT REGRESSION IN THREE GROUPS**



**FIGURE NO 19: BAR DIAGRAM SHOWS THE TIME FOR RECOVERY FROM MOTOR BLOCKADE IN ALL THREE GROUPS**



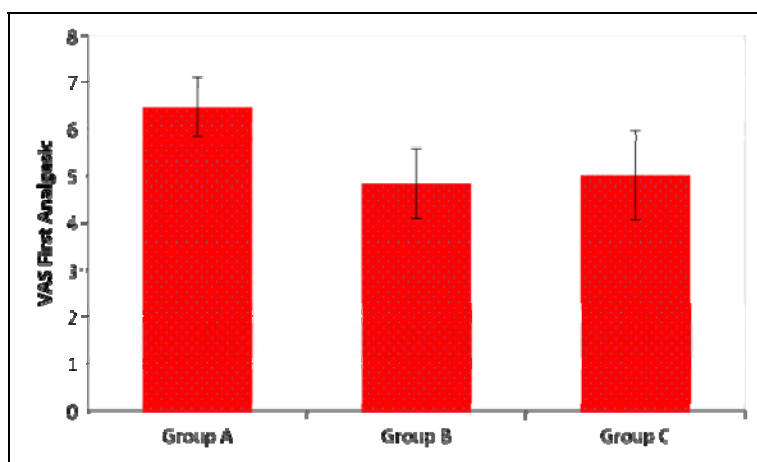
**FIGURE NO 20: BAR DIAGRAM SHOWS THE TIME FOR FIRST ANALGESIC REQUIREMENT IN ALL THREE GROUPS**

**TABLE NO 10:**

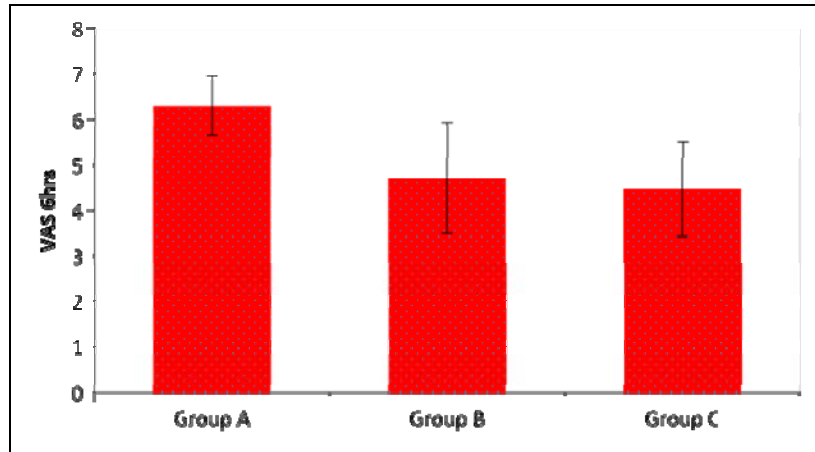
**VAS SCORE IN THREE GROUPS**

variables	Group A	Group B	Group C	Total	P value
VAS First Analgesic	6.47± 0.63	4.83± 0.75	5.00± 0.95	5.43±1.07	<0.001**
VAS 6hrs	6.30±0.65	4.70±1.21	4.47±1.04	5.16±1.28	<0.001**
VAS 12hrs	6.30±0.75	4.77±1.5	4.23±1.19	5.10±1.47	<0.001**
VAS 24hrs	6.13±0.57	4.93±1.31	4.03±1.19	5.03±1.37	<0.001**

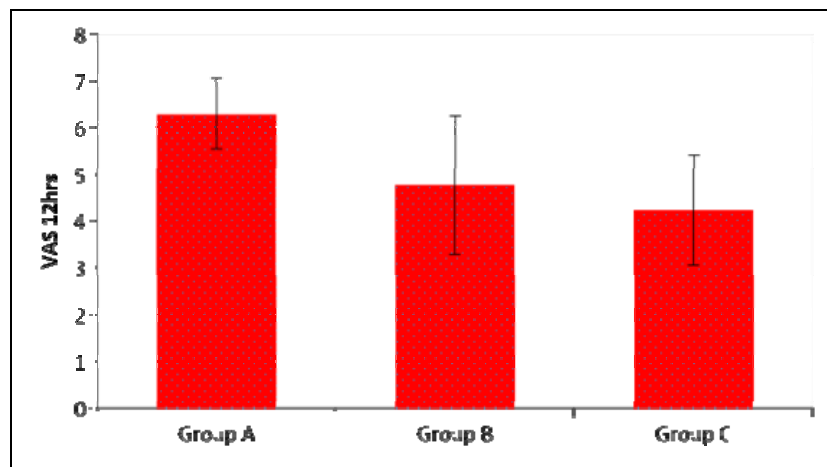
VAS score in all three groups postoperatively in 24hours shown, where it was less in group C after 6hours post operatively, which signifies that post operative analgesic effect is better with group C.



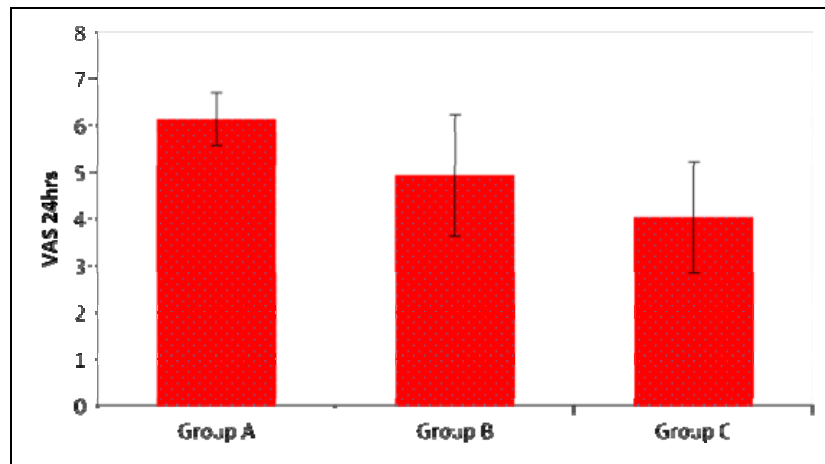
**FIGURE NO 21: BAR DIAGRAM SHOWING VAS SCORE DURING THEIR FIRST ANALGESIC REQUEST IN ALL THREE GROUPS**



**FIGURE NO 22: BAR DIAGRAM SHOWING VAS SCORE AFTER 6 HOURS POST OPERATIVELY IN ALL THREE GROUPS**



**FIGURE NO 23: BAR DIAGRAM SHOWING VAS SCORE AFTER 12 HOURS POST OPERATIVELY IN ALL THREE GROUPS**



**FIGURE NO 24: BAR DIAGRAM SHOWING VAS SCORE AFTER 24 HOURS POST OPERATIVELY IN ALL THREE GROUPS**

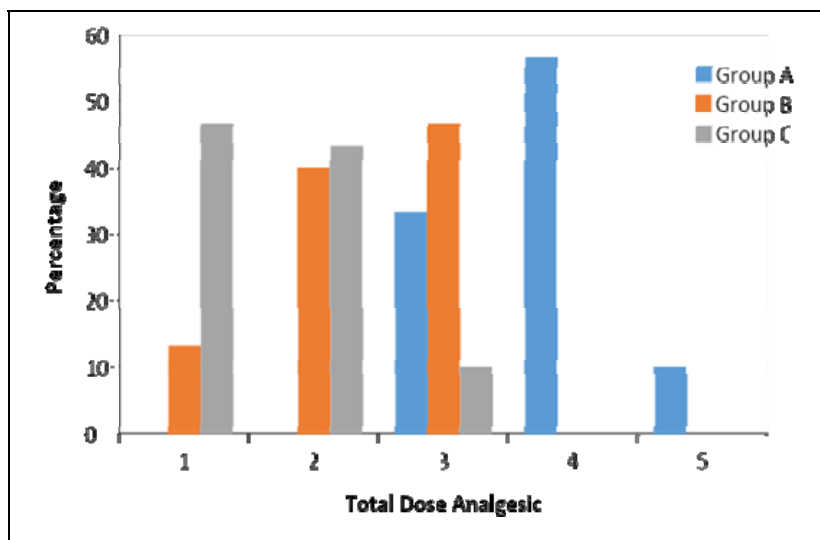


**TABLE NO 11:**

**TABLE SHOWING TOTAL ANALGESIC REQUIREMENT IN 24 HOURS POST OPERATIVELY**

Total Dose Analgesic	Group A	Group B	Group C	Total
1	0(0%)	4(13.3%)	14(46.7%)	18(20%)
2	0(0%)	12(40%)	13(43.3%)	25(27.8%)
3	10(33.3%)	14(46.7%)	3(10%)	27(30%)
4	17(56.7%)	0(0%)	0(0%)	17(18.9%)
5	3(10%)	0(0%)	0(0%)	3(3.3%)
<b>Total</b>	<b>30(100%)</b>	<b>30(100%)</b>	<b>30(100%)</b>	<b>90(100%)</b>

The table shows the no. of analgesic requests in all three groups which was maximum in group A and minimum in group C, which indicates that group C had better analgesic effect. In group A 10 required 3 doses of top up requirement in 24hours, 17 required 4 doses of top ups. In group C only 3 required 3 doses of top ups, 14 required only one dose and 13 required 2 doses.

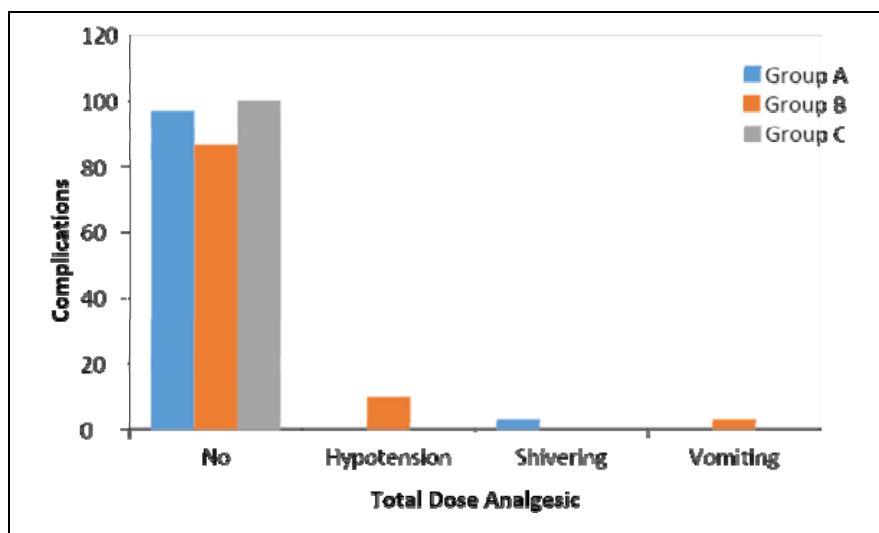


**FIGURE NO 25: BAR DIAGRAM SHOWING TOTAL DOSE OF ANALGESIC REQUEST IN 24 HOURS POST OPERATIVELY IN THREE GROUPS**

**TABLE NO 12:**  
**COMPLICATIONS AND SIDE EFFECTS**

Complications	Group A	Group B	Group C	Total
No	29(96.7%)	26(86.7%)	30(100%)	85(94.4%)
Hypotension	0(0%)	3(10%)	0(0%)	3(3.3%)
Shivering	1(3.3%)	0(0%)	0(0%)	1(1.1%)
Vomiting	0(0%)	1(3.3%)	0(0%)	1(1.1%)
Total	30(100%)	30(100%)	30(100%)	90(100%)

This table shows the complication in three group's intra operatively and post operative period of first 24hours, where 3 in group B had hypotension and one had vomit. 1 had shivering in group A and no complication was seen in group C.



**FIGURE NO 26: BAR DIAGRAM SHOWING COMPLICATION IN ALL THREE GROUPS**

***Significant figures***

- + Suggestive significance (P value:  $0.05 < P < 0.10$ )
- \* Moderately significant (P value:  $0.01 < P \leq 0.05$ )
- \*\* Strongly significant (P value:  $P \leq 0.01$ )

## **DISCUSSION**

Central neuraxial blockade is standard and widely practiced technique popular in many surgical procedures. Bupivacaine is commonly used local anaesthetic drug both in intrathecal and epidural anaesthesia. A variety of drugs been used to potentiate the effect and quality of analgesia of bupivacaine during neuraxial blockade. Epidural opioids, midazolam and ketamine have all been used for this purpose<sup>48,49</sup>. The use of opioid drug associated with the occurrence of undesirable side effects such as pruritus, nausea, vomiting, respiratory depression, urinary retention and somnolence. So the search for an effective analgesic with no or low incidence of side effects is continuing. Various options including alpha 2 agonists are extensively being evaluated as an alternative.

The pharmacological properties of alpha 2 agonist have been largely studied and been employed clinically to achieve desired effects in regional anaesthesia. Epidural administration of these drugs is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis<sup>50</sup>. Introduction of dexmedetomidine, a newer prototype of alpha 2 agonist has widened the scope in regional anaesthesia. It was introduced in clinical practice in 1999<sup>51</sup>. Epidural bupivacaine in a dose of 2mcg/kg given along with intrathecal bupivacaine causes significant prolongation in the duration of analgesia. The number of administered rescue analgesic doses are significantly less in patients receiving epidural dexmedetomidine. The faster onset of action of local anaesthetics, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia in the postoperative period, dose sparing action of local anaesthetics and stable cardiorespiratory parameters make alpha 2 agonist an effective adjuvant in regional anaesthesia<sup>2</sup>.

Parenteral magnesium, used for many years as an antiarrhythmic agent and for prophylaxis in seizures in pre eclampsia. Noxious stimulation leads to release of neurotransmitters, which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors<sup>52</sup>. NMDA receptor signalling may be important in determining the duration of acute pain<sup>53</sup>. Magnesium blocks calcium influx and non competitively antagonizes NMDA receptor channels<sup>54</sup>. Magnesium can prevent the induction of central sensitization at the spinal action by blocking NMDA receptors in a voltage dependent manner. With same mechanism of action when small doses of magnesium was added to local anaesthetics for spinal anaesthesia the duration of action of spinal anaesthesia was prolonged and analgesic requirement postoperatively was reduced and side effects of high doses of local anesthetics and opioids were reduced<sup>55</sup>.

This was double blinded randomized control prospective study carried out at R.L.Jalappa Hospital and Research, Tamaka, Kolar, from Jan 2019 to June 2020. Ninety patients of age group 18 – 65 years with ASA grade I, II of either sex undergoing lower abdominal and lower limb surgeries under epidural anaesthesia and fulfilling the inclusion criteria were segregated into three groups based on computer generated randomisation as follows

**GROUP A** (control group) received epidural bupivacaine 0.5 %( 17 ml) + 1ml 0.9% normal saline.

**GROUP B** received epidural Bupivacaine 0.5 %( 17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

**GROUP C** received epidural Bupivacaine 0.5 %( 17 ml) + 1ml 50mg magnesium sulphate.

Baseline HR, NIBP, ECG, SPO<sub>2</sub> were recorded. Following parameters of blockade characteristics and hemodynamic parameters were noted.

**I. SENSORY BLOCKADE:**

- i) Onset of sensory blockade
- ii) Time to achieve T<sub>6</sub> level
- iii) Quality and extent of sensory blockade

**II. MOTOR BLOCKADE:**

- i) Onset of motor blockade
- ii) Quality of motor blockade

**III. Two segment regression**

**IV. Time for first epidural top up**

**V. Hemodynamic stability**

**VI. Side effects and complications**

**Demographic data:**

The demographic parameters of age, sex were comparable between three groups. The demographic profile in the study were comparable to similar other studies and did not show any significant differences on statistical comparison.

**Duration of surgery:**

Mean duration of surgery in group A was  $85.50 \pm 21.24$ , in group B was  $85.43 \pm 21.29$  and in group C it was  $74.33 \pm 21.51$  and it was not clinically significant.

**Onset of sensory blockade:**

Mean time taken for sensory blockade in group A was  $14.12 \pm 6.18$  and in group B it was  $4.63 \pm 1.22$  and in group C it was  $5.75 \pm 1.71$ . Time to achieve T6 level in group A was  $13.22 \pm 1.43$ , in group B it was  $4.73 \pm 1.32$  and in group C it was  $5.82 \pm 1.72$ . Time for two segment regression in group A was  $86.77 \pm 3.60$ , in group B it was  $106.4 \pm 8.01$  and in group C was  $102.7 \pm 8.05$ , which shows that group B has better onset of sensory blockade when compared to other three groups.

**Onset of motor blockade**

The mean time taken to achieve motor block in group A was  $17.17 \pm 2.01$ , in group B it was  $7.02 \pm 1.70$  and in group C it was  $8.10 \pm 2.05$ . And the time for recovery from motor blockade in group A was  $97.77 \pm 5.03$  and in group B was  $121.6 \pm 8.42$  and in group C was  $119.87 \pm 10.01$ . This shows that Group B has faster onset of motor blockade when compare to other two groups

**Time for first epidural to up and total number of rescue analgesia**

The mean time to first analgesic request in group A was  $1.90 \pm 0.28$  hours and in group B was  $3.18 \pm 0.83$  hours and in group C it was  $4.08 \pm 0.95$  hours. VAS score at 6 and 24 hours in group A was  $6.30 \pm 0.65$  and  $6.13 \pm 0.57$  respectively, in group B was  $4.70 \pm 1.21$  and  $4.93 \pm 1.31$  respectively, in group C it was  $4.47 \pm 1.04$  and  $4.03 \pm 1.19$  respectively. The number of rescue analgesics in group A, 10 required 3 doses of top up requirement in 24hours, 17 required 4 doses of top ups. In group B 4 required single dose, 12 required two doses and 14 required 3doses. In group C only 3 required 3 doses of top ups, 14 required only one dose and 13 required 2 doses. This shows group C has better post operative analgesic effect when compared to other two groups.

**Hemodynamic stability:**

Baseline HR (bpm) were compared in three groups, which were  $86.43 \pm 8.98$ ,  $81.57 \pm 9.96$  and  $79.47 \pm 8.96$  in group A, group B and group C respectively.

In group A there were no significant difference in PR, even after 30 minutes of epidural bupivacaine it remained at  $83.97 \pm 9.96$  and there was increased PR seen after 1 hour of epidural bupivacaine with normal saline, it was  $101.17 \pm 10.3$  after 120min of epidural.

In group B after 10minutes of epidural bupivacaine with dexmedetomidine PR dropped to  $64.87 \pm 8.25$  and it remained on lower side all though the procedure without tremendous increase in PR. It was  $63.5 \pm 4.32$  even after 120minutes of epidural

In group C, PR remained the same all through the procedure, after 30minutes of epidural bupivacaine with magnesium sulphate it was  $75 \pm 11.91$  and it was  $86 \pm 7.21$  after 120minutes of epidural.

Baseline SBP in all the three groups were  $133.63 \pm 13.16$ ,  $129.6 \pm 14.11$  and  $125.13 \pm 11.26$  in group A, group B and group C respectively.

In group A there was fall in SBP only after 40minutes of epidural which was  $124.97 \pm 27.39$  and was gradually increasing as the time proceeded, it was  $146 \pm 7.27$  after 120 minutes of epidural.

In group B there was significant fall in SBP after 10minutes of epidural which was  $107.3 \pm 11.88$  and it remained on lower side all through the procedure , it was  $108 \pm 3.46$  after 120 minutes of epidural.

In group C there was fall in blood pressure after 10minutes of epidural but it was not significant when compared to group B which was  $115.6 \pm 15.62$ , and there was no much change thereafter, it was  $127.87 \pm 18.52$  after 120minutes of epidural.

Baseline DBP in all three groups were  $86.13 \pm 11.21$ ,  $80.97 \pm 10.13$  and  $82.30 \pm 9.07$  in group A, group B and group C respectively.

In group A there were no much in fall in DBP after 40minutes of epidural it was  $81.07 \pm 12.31$  and it remained the same all throughout the procedure and started increasing as time proceeded, it was  $94.67 \pm 8.41$  after 120minutes of epidural.

In group B there were a significant reduction in DBP after 20minutes of epidural it was  $61.03 \pm 10.95$  and it was on the lower side thereafter, it was  $65.33 \pm 3.88$  after 120minutes of epidural.

In group C there were no much reduction in DBP, it was  $73.60 \pm 10.60$  after 30minutes of epidural and there was no much change thereafter. It was  $90.67 \pm 2.08$  after 120minutes of epidural.

Baseline MAP in all three groups were  $101.90 \pm 11.35$ ,  $97.17 \pm 10.66$  and  $96.60 \pm 9.51$  in group A, group B and group C respectively.

In group A MAP remains constant and there is no much fall in MAP, it was  $95.70 \pm 14.79$  after 40minutes of epidural, and it was  $111.83 \pm 7.65$  after 120minutes of epidural.

In group B significant reduction of MAP was seen after 30minutes of epidural and it was  $74.93 \pm 9.51$ , it was stable all through the procedure and it was  $79.67 \pm 2.16$  after 120minutes of epidural.

In group C MAP remains constant without increase or decrease from its basal value, it was  $79.67 \pm 2.16$  after 30minutes of epidural, and it was  $104.33 \pm 2.08$  after 120minutes of epidural.



By this data it was concluded that group B has better hemodynamic stability when compared to other two groups.

**Complications and side effects:**

Complications in three groups intra operatively and post operative period in the first 24hrs were noted, 3 in group B had hypotension and one had vomit. 1 had shivering in group A and no complication was seen in group C.

To conclude when epidural dexmedetomidine when added as adjuvant to bupivacaine has fast onset of motor and sensory blockade and better hemodynamic stability. Magnesium has good postoperative analgesic property with no side effects when added as adjuvant to epidural bupivacaine not associated with any complications.

## **CONCLUSION**

From our study we conclude that when dexmedetomidine added as an adjuvant to epidural bupivacaine it provides fast onset of motor and sensory blockade with better hemodynamic stability. And magnesium when added as adjuvant to epidural bupivacaine it provides better post operative analgesics not associated with any complications.

## **SUMMARY**

It was a double blinded randomized control prospective study carried out at R.L.Jalappa Hospital and Research, Tamaka, Kolar, from Jan 2019 to June 2020. Ninety patients of age group 18 – 65 years with ASA grade I, II of either sex undergoing lower abdominal and lower limb surgeries under epidural anaesthesia and fulfilling the inclusion criteria were segregated into three groups based on computer generated randomisation as follows

**GROUP A** (control group) received epidural bupivacaine 0.5 %( 17 ml) + 1ml 0.9% normal saline.

**GROUP B** received epidural Bupivacaine 0.5 %( 17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

**GROUP C** received epidural Bupivacaine 0.5 %( 17 ml) + 1ml 50mg magnesium sulphate.

Baseline HR, NIBP, ECG, SPO2 were recorded. Following parameters of blockade characteristics and hemodynamic parameters were noted

### **I .SENSORY BLOCKADE:**

- i) Onset of sensory blockade
- ii) Time to achieve T6 level
- iii) Quality and extent of sensory blockade

### **II .MOTOR BLOCKADE:**

- i) Onset of motor blockade
- ii) Quality of motor blockade

### **III. Two segment regression**

### **IV .Time for first epidural top up**

### **V .Hemodynamic stability**

### **VI .Side effects and complications**

In the study, three groups were comparable with respect to age, sex, and ASA physical status grading and showed no statistical differences.

There was a significant difference in mean heart rate between three groups at any intervals.

There was a significant difference in mean systolic blood pressure, diastolic blood pressure, and mean arterial pressure among three groups at any intervals.

There was a significant difference in onset of motor and sensory blockade and also post operative analgesics among three groups.

We conclude that when dexmedetomidine added as an adjuvant to epidural bupivacaine it provides fast onset of motor and sensory blockade with better hemodynamic stability. And magnesium when added as adjuvant to epidural bupivacaine it provides better post operative analgesia not associated with any complications.

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## **ANNEXURES**

### **ANNEXURE - I**

#### **PROFORMA**

INVESTIGATORS: Dr. Manjula Devi S & Dr. Ravi M, Professor & HOD

DIAGNOSIS:

PROCEDURE:

Name: Age :

Sex : Weight:

Hospital No: ASA Grade:

#### **PRE-ANAESTHETIC EVALUATION:**

##### **General examination:**

PR: BP:

Pallor/Icterus/Clubbing/Cyanosis/Lymphadenopathy/Edema:

##### **Systemic examination:**

Respiratory system -

Cardiovascular system -

Central nervous system -

Per abdomen -

##### **Investigations:**

Haemoglobin -

Total leukocyte count -

Platelet count -

Blood grouping -

Blood urea -

Serum creatinine -

Serum sodium -

Serum potassium -

Bleeding time -

Clotting time -

HIV -

HBsAg -

**Groups:**

GROUP A (control group) will receive epidural bupivacaine 0.5 % ( 17 ml) + 1ml 0.9% normal saline.

GROUP B will receive epidural Bupivacaine 0.5 % ( 17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

GROUP C will receive epidural Bupivacaine 0.5 % ( 17 ml) + 1ml 50mg magnesium sulphate.

**Baselines:**

- Heart rate -
- Systolic blood pressure -
- Diastolic blood pressure -
- Mean arterial pressure -
- Oxygen saturation-

**Regional anaesthesia:**

Procedure -

Posture -

Space -

Drug -

Level of blockade -

**INTRAOPERATIVE VITALS**

	0 MIN	3	5	10	20	30	40	50	60	90	120
PR											
NIBP											
SPO <sub>2</sub>											

Total duration of surgery:

Duration of sensory regression by two segments:

Recovery from motor block:

Time of first analgesia request:

Total analgesic use in 24hours:

**VAS - VISUAL ANALOGUE SCALE (for pain)**

0 - No pain

1-3 - mild pain

4-6 - moderate pain

7-10 - severe pain

TIME	VAS (FOR PAIN)
First analgesia request	
6 <sup>th</sup> hour	
12 <sup>th</sup> hour	
18 <sup>th</sup> hour	
24 <sup>th</sup> hour	

**Any significant side effects**

- 1) Hypotension-
- 2) Bradycardia-
- 3) Vomiting-
- 4) Shivering-
- 5) Pruritis-
- 6) Others

**ANNEXURE - II**  
**PATIENT INFORMATION SHEET**

**Title of the study: STUDY TO EVALUATE USEFULNESS OF  
MAGNESIUM SULPHATE AND DEXMEDETOMIDINE AS ADJUVANT TO  
BUPIVACAINE FOR LOWER LIMB AND ABDOMINAL SURGERIES  
UNDER EPIDURAL ANAESTHESIA**

The main objective of the study is to compare the efficacy of magnesium sulphate and dexmedetomidine as an adjuvant to bupivacaine for lower limb and lower abdominal surgeries under epidural anaesthesia.

**Purpose of the research:** Opioids, midazolam, ketamine are used as adjuvant to bupivacaine in lower abdominal and lower limb surgeries which may cause various side effects like nausea, vomiting, pruritis, respiratory depression, urinary retention in order to avoid these side effects, I use and compare the efficacy dexmedetomidine and magnesium sulphate as an adjuvant to bupivacaine under epidural anaesthesia. Magnesium sulphate added as an adjuvant to bupivacaine shortens the onset of sensory and motor blockade and helps in prolonging post operative analgesia without any significant side effects.

Dexmedetomidine added as adjuvant significantly produces increased duration of motor and sensory blockade, it also reduces number of rescue analgesia with better hemodynamic stability.

**Procedures and Protocol:**

This is a randomized double blind prospective study. 90 patients undergoing lower abdominal and lower limb surgeries at R. L. Jalappa Hospital and Research Centre, Tamaka , Kolar, during the period from January 2019 to June 2020 will be included in the study.

After obtaining informed consent, 90 patients will be randomly divided into 3 groups of 30 each. Randomization will be done by computer generated table.

GROUP A (control group) will receive epidural bupivacaine 0.5 %( 17 ml) + 1ml 0.9% normal saline.

GROUP B will receive epidural Bupivacaine 0.5 %( 17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

GROUP C will receive epidural Bupivacaine 0.5 %( 17 ml) + 1ml 50mg magnesium sulphate.

**Reimbursements:** You will not be given money or gifts to take part in this research.

**Confidentiality:** We will not be sharing the identity of the participant. The information we collect from you will be kept confidential and only researchers involved in this project will have access to it.

**Right to Refuse or Withdrawal:** You do not have to take part in this research if you do not wish to do so and you can refuse to participate.

**Whom to Contact:** If you have any questions you may ask us now or later, even after the study has started, you may contact the following person:



**For more information:**

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**ANNEXURE - III**  
**INFORMED CONSENT FORM**

**Name of the institution:** SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH.

**Title of the project:** STUDY TO EVALUATE USEFULNESS OF MAGNESIUM SULPHATE AND DEXMEDETOMIDINE AS ADJUVANT TO BUPIVACAINE FOR LOWER LIMB AND ABDOMINAL SURGERIES UNDER EPIDURAL ANAESTHESIA

**Name of the principal investigator:** Dr. Manjula Devi S

**Name of the guide:** Dr. Ravi M

**Name of the co guide:** Dr Dinesh K

**Name of the subject/participant:**

I, \_\_\_\_\_ aged \_\_\_\_\_, after being explained in my own vernacular language about the purpose of the study and the risks and complications of the procedure, hereby give my valid written informed consent without any force or prejudice for taking magnesium sulphate, dexmedetomidine as adjuvant to bupivacaine in epidural anaesthesia for the purpose of prolonging anaesthetic and analgesic effect. The nature and risks involved have been explained to me to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question

that I have asked, have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research. I hereby give consent to provide my history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc to the doctor / institute etc. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc responsible for any untoward consequences during the procedure / study. A copy of this Informed Consent Form and Patient Information Sheet has been provided to the participant.

\_\_\_\_\_  
(Signature & Name of Pt. Attendant)  
(Relation with patient)

\_\_\_\_\_  
(Signature & Name of Pt)

DATE:

Investigator signature

## KEY TO MASTER CHART

M	: Male
F	: Female
Kgs	: Kilogram
ASA PS	: American Society of Anaesthesiologists physical Status
HR	: Heart rate
SBP	: Systolic blood pressure
DBP	: Diastolic blood pressure
MAP	: Mean arterial pressure
mmHg	: Millimetre of mercury
SPO2	: Peripheral capillary oxygen saturation
VAS	: Visual analogue scale
Mins	: Minutes
Secs	: Seconds
L	: Left
R	: Right
ORIF	: Open reduction with internal fixation
#	: Fracture
IT	: Intertrochanteric
IMIL	: Intramedullary Interlocking
NVD	: Neuro vascular deficit
DNVD	: Distal neuro vascular deficit
AUB	: Abnormal uterine bleeding

## MASTER CHART

[illegible]

MASTER CHART

55	B	850504	M	55	Closed # of tibia middle one third	CRIF with IMIL nailing	I	78	6	8	6	70	94	106	3	4	4	3	3	1	94	130	100	110	100	92	91	86	88	87	88	73	76	72			132	129	113	114	106	109	100	98	99			92	88	76	72	71	74	68	61				105	102	88	86	83	86	79	73	33			99	100	98	99	100	97	98	99	100			no	
56	B	852198	M	60	R neck of femur #	R bipolar hemiarthroplasty	II	61	4.5	7	4.5	120	106	126	3	6	5	6	6	3	86	140	100	113	99	84	81	76	71	72	73	68	65	61	62	60	138	127	113	102	106	101	118	109	112	107	106	99	84	82	75	74	68	64	62	68	64	69	112	98	92	84	85	79	82	78	83	78	81	100	99	98	99	98	99	98	100	99	99	99	no	
57	B	837573	M	20	Acute appendicitis	Open appendectomy	I	54	3.5	5	3.5	70	102	125	3	5	4	5	6	3	73	110	70	83.3	100	73	69	64	63	61	62	60	59	58			112	106	95	94	93	85	84	82	95			72	69	52	44	42	49	41	44	49			85	81	66	61	59	61	55	57	64			100	100	100	100	100	100	100	100			Hypotension		
58	B	834974	F	53	Incisional hernia	Mesh repair	II	83	6	9	6	90	96	114	2.5	4	3	4	4	2	72	130	90	103	100	72	75	78	63	69	64	60	62	62	66		135	124	119	112	119	111	112	107	108	116		92	84	65	60	67	61	79	63	61	68		106	97	83	77	84	78	90	78	77	84		100	100	99	99	99	99	99	99	99	99	no		
59	B	759471	M	48	R inguinal hernia	R Hernioplasty	I	86	3.5	5.5	3.5	90	111	131	2.5	6	7	6	6	3	79	130	100	110	100	78	74	71	65	69	62	61	63	61	62		130	128	114	103	104	98	102	97	96	94		92	87	82	75	62	53	52	58	51	50		105	101	93	84	76	68	69	71	66	65		100	99	99	98	98	100	100	100	100		no		
60	B	983021	M	59	R inguinal hernia	R Hernioplasty	II	74	5.5	7	5.5	75	92	111	5.5	4	3	3	3	1	82	120	60	80	100	83	85	87	77	79	72	75	77	79		120	114	100	98	109	100	102	104	106		60	65	52	58	62	65	66	64	68		80	81	68	71	78	77	78	77	81		100	100	99	100	100	100	100	100	99		vomiting						
61	C	815680	M	21	Acute appendicitis	Open appendectomy	I	58	3.5	4.5	3.5	65	108	122	2.5	6	5	6	6	3	79	120	90	100	100	78	74	76	79	74	73	76	70	18		128	118	106	102	98	92	94	97	98		87	75	62	60	56	52	51	50	54		101	89	77	74	70	65	65	66	69		99	99	98	98	100	100	100	100	100		no						
62	C	827924	M	30	R sided varicocele	Varicocelectomy	I	62	8	7	9	60	97	115	4.5	5	4	5	5	2	69	100	60	73.3	100	68	64	69	71	72	76	68	73	72		108	109	112	106	102	112	114	118	119		64	61	68	64	68	71	72	78	81		79	77	83	78	79	85	86	91	94		100	100	100	100	98	98	98	99	100		no						
63	C	828519	M	60	Varicose vein of R lower limb	varicoseveiny procedure with stripping	II	58	4.5	6	4.5	90	103	132	3	6	6	5	5	2	83	120	90	100	100	83	79	74	75	71	78	81	85	86	88		128	115	112	104	101	98	99	102	100	101		85	79	74	72	68	61	58	57	54	59		99	91	87	83	79	73	72	72	69	73		100	100	98	100	100	99	100	100	100	100		no	
64	C	828738	M	38	Incisional hernia	Mesh repair	I	66	6.5	8.5	6.5	78	94	113	5.5	4	4	3	3	1	74	120	70	86.7	100	78	74	72	70	78	76	75	72	73		121	129	120	114	116	117	112	118	121		82	84	78	74	76	72	79	81	82		95	99	92	87	89	87	90	93	95		99	100	100	100	98	100	100	100	100		no						
65	C	814340	M	37	R inguinal hernia	R Hernioplasty	I	74	3.5	6	3.5	70	109	122	3.5	6	6	5	5	3	85	120	90	100	100	88	86	72	70	85	82	81	80	86		123	114	112	105	112	119	124	118	117		82	76	74	70	64	61	74	72	71		96	89	87	82	80	80	91	87	86		100	100	100	100	99	99	100	100	100		no						
66	C	841492	M	30	Acute appendicitis	Open appendectomy	I	58	6	8	6	50	95	109	4.5	4	4	3	3	1	85	120	90	100	100	86	83	81	78	76	75	71	80		128	126	119	114	121	123	127	129		88	85	84	86	85	84	87	82		101	99	96	95	97	97	100	98		99	99	98	99	100	100	100	100		no											
67	C	840445	M	58	Non healing ulcer with osteomyelitis of first, second, third, and 4th toes	Transmetatarsal amputation	II	52	4	6	4	80	105	132	2.5	6	5	5	5	2	89	130	90	103	100	88	78	74	71	82	84	88	89	91		133	120	121	117	113	119	125	128	138		88	85	74	74	76	81	79	84	87		103	97	90	88	88	94	94	99	104		100	99	98	98	98	99	100	100		no							
68	C	814408	F	36	Umbilical hernia	Hernioplasty	I	64	4	8	4	62	118	134	3	6	6	5	4	2	75	120	80	93.3	100	75	74	76	74	78	86	87	83	81		125	117	112	108	116	119	127	135	136		82	78	71	72	74	72	80	81	85		96	91	85	84	88	88	96	99	102		100	99	100	100	99	98	99	100	98		no						
69	C	834059	M	22	Bilateral psoas abscess	Incision and drainage	I	57	6	9	6	90	101	116	4.5	4	3	3	3	2	89	120	90	100	100	87	84	80	75	71	74	76	75	78	82		122	118	115	124	123	125	128	127	123	124		87	84	86	82	81	78	75	81	83	80		99	95	96	96	95	94	93	96	96	95		100	99	100	100	100	100	100	100	100	100		no	
70	C	835077	M	33	Acute appendicitis	Open appendectomy	I	52	4	6	4	60	114	127	3	6	5	6	6	2	76	120	60	80	100	74	71	78	79	81	84	83	84	88		128	114	112	103	118	124	129	127	122		82	75	72	73	64	71	78	74	74	73		97	88	85	83	82	89	95	92	90	49		100	100	99	99	99	99	99	99	99		no				
71	C	756943	F	60	Post hartmanns procedure end colostomy	Revision stoma	II	46	3.5	7	4.5	45	118	136	3	6	6	5	5	2	70	130	80	96.7	100	72	77	74	76	74	78	84	81		134	121	114	128	123	121	135	138		84	74	76	85	88	82	82	84		101	90	89	99	100	95	100	102		100	100	100	100	100	100	100		no												
72	C	833771	M	38	R Periarethral abscess	Incision and drainage	I	78	7	10	7	50	104	115	5.5	4	3	3	3	1	78	110	70	83.3	100	75	74	73	71	75	76	78	79		111	118	115	112	118	120	127	125		72	70	75	74	76	72	78	72		85	86	88	87	90	88	94	90		100	99	99	99	98	100	100	100		no											
73	C	822754	M	60	Wet gangrene over R leg	R above knee amputation	I	52	4	7	4	90	114	128	3.5	6	6	6	5	2	84	130	100	110	100	84	81	74	72	71	64	85	86	81	80		134	128	114	105	102	98	99	95	102	98		88	91	85	74	71	65	62	64	67	60		110	103	95	84	81	76	74	74	79	73		99	98	100	99	99	99	99	99	99	100	100		no
74	C	438976	M	29	Healing ulcer over L leg	Split skin grafting	I	74	6	8	6	60	97	113	4	5	3	3	3	1	84	130	90	103	99	84	86	87	82	84	81	85	78	86		132	129	127	126	124	120	128	131	129		84	81	74	7	79	71	72	75	74		100	97	92	47	94	87	91	94	92		98	99	99	97	97	97	98	98	99		no						
75	C	392406	F	45	UMbical hernia	Mesh repair	I	61	5	8	5	70	117	123	3	6	5	5	5	2	74	110	90	96.7	98	76	75	71	76	87	84	86	82	83		112	114	108	102	97	99	95	94	92		78	76	72	64	61	58	54	52	50		89	89	84	77	73	72	68	66	64		99	98	97	98	99	98	99	99	99		no						
76	C	820913	F	46	Recurrent appendicitis	Open appendectomy	I	67	8	10	8	50	92	109	3.5	6	4	3	3	1	60	100	50	66.7	97	60	62	59	51	54	55	58	56		102	103	98	96	97	99	94	98		62	58	54	52	57	59	53	52		75	73	69	67	70	72	67	67		100	100	100	99	99	99	99	99	99		no										
77	C	803591	F	48	AUB-F	Total Abdominal hysterectomy	I	65	6	9	6	60	101	118	4	5	4	3	3	1	76	130	90	103	100	78	75	72	74	79	76	71	72	75																																																