DISSERTATION ON THE EFFECT OF COMBINED SPINAL AND EPIDURAL MAGNESIUM ON ANALGESIC REQUIREMENTS OF PATIENTS UNDERGOING LOWER LIMB ORTHOPEDIC SURGERIES

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MARCH 2010

CERTIFICATE

This is to certify that this dissertation entitled dissertation on **"THE EFFECT OF COMBINED SPINAL AND EPIDURAL MAGNESIUM ON THE ANALGESIC REQUIREMENTS OF PATIENTS UNDERGOING LOWER LIMB ORTHOPEDIC SURGERIES"** is the bonafide original work of **Dr.A.SENTHIL KUMAR**, in partial fulfillment of the requirement for MD Anaesthesiology examination of the Tamilnadu Dr. MGR Medical University to be held in March 2010.

Prof. Dr.S. CHITRA, MD., Pathology
DEAN
Govt. Stanley Medical College
Chennai-600 001.

Prof.Dr.R. Subramaniya Bharathiyar, MD, DA.,
Head of the department
Department of Anaesthesiology,
Govt. Stanley medical college and
Hospital, Chennai-600 001.

DECLARATION

I, **Dr.A.SENTHIL KUMAR**, solemnly declare that dissertation titled, Dissertation on **"THE EFFECT OF COMBINED SPINAL AND EPIDURAL MAGNESIUM ON ANALGESIC REQUIREMENTS OF PATIENTS UNDERGOING LOWER LIMB ORTHOPEDIC SURGERIES"** is the bonafide work done by me at Govt. Stanley medical college and hospital during the period May 2009 to August 2009 under the expert guidance and supervision of **Prof.Dr.R.Subramaniya Bharathiyar, MD, DA.,** the dissertation is submitted to the Tamilnadu Dr. MGR Medical university towards partial fulfillment of requirement for the award of MD Degree in anaesthesiology.

Place : Chennai

Date : **Dr. A . SENTHIL KUMAR**

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CONTENTS

INTRODUCTION

Regional anaesthesia is a safe, inexpensive technique with the advantage of prolonged postoperative pain relief. Effective treatment of postoperative pain blunts autonomic, somatic, and endocrine responses. It has become a common practice to use a polypharmacological approach for the treatment of postoperative pain, because no drug has yet been identified that specifically inhibits nociception without associated side effects.[1]

Magnesium is the fourth most plentiful cation in the body. It has anti-nociceptive effects in animal and human models of pain.[2,3] These effects are primarily based on the regulation of calcium influx into the cell, that is natural physiological calcium antagonism and antagonism of N-methyl-D-aspartate receptor.[1] It has been reported that intrathecal magnesium enhances opioid anti-nociception in an acute incisional model.[3] These effects have prompted the investigation of magnesium as an adjuvant for postoperative analgesia. There are studies concerning different routes of magnesium administration such as i.v or intrathecally or epidurally that improve anaesthetic and analgesic quality.[1 4-6]

This study is designed to assess the effectiveness of using intrathecal and epidural magnesium (Mg) in reducing intra and post operative analgesic requirements and to compare the quality of analgesia of intrathecal bupivacaine-fentanyl-magnesium mixture with intrathecal bupivacaine-fentanyl mixture.

AIMS AND OBJECTIVES

1. To assess the effectiveness of using intrathecal and epidural magnesium (Mg) in reducing intra and post operative analgesic requirements.

2. To compare the quality of analgesia of intrathecal bupivacaine-fentanyl-magnesium mixture with intrathecal bupivacaine-fentanyl mixture.

3. To evaluate the hemodynamic response of intrathecal and epidural magnesium.

PHYSIOLOGY OF PAIN

DEFINITION OF PAIN

The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.”

PHYSIOLOGY OF PAIN

Nociception is conveyed from the periphery to the brain at three levels: the peripheral nociceptor, the spinal cord, and the supra-spinal (brain) levels[7].

There are two types of pain- Physiological and Pathological.

I . PHYSIOLOGICAL PAIN :is produced by stimulation of high threshold thermo/mechanical nociceptors, which transmit via fast conducting myelinated A- delta fibres. These enter the dorsal horn of the spinal cord and synapse at laminae I and V.

II . PATHOLOGICAL PAIN: originates from stimulation of the high threshold polymodal nociceptors (free endings) present in all tissues.

The nociceptors respond to mechanical, chemical and thermal stimuli and are transmitted via slow conducting unmyelinated C fibres. These synapse at laminae II and III (substantia gelatinosa) of the dorsal horn. The second order neurons are either nociceptive specific (substantia gelatinosa) or wide dynamic range (WDR) neurons (in laminae V and VI) that respond to a wide range of noxious and non-noxious input. Both pathways ascend up the spinal cord via the spinothalamic tracts to the thalamus, which synapse and project on to the somatosensory cortex. Inhibitory inter-neurons in the substantia gelatinosa prevent activation of the dorsal root ganglia. Interneurons can be activated by A- beta and inhibited by A- beta and C fibre activity. Pain can be gated-out by stimulating the large A beta fibres in the painful area. This is the working mechanism behind transcutaneous electrical nerve stimulation. The descending inhibition pathways originate at the level of the cortex and thalamus, and descend via the brainstem (periaqueductal grey) and the dorsal columns to terminate at the dorsal horn of the spinal cord. Neurotransmitters noradrenaline, serotonin (5-HT) and the endogenous opioids are released to provide antinociception.

EFFECTS OF POSTOPERATIVE PAIN

POST OPERATIVE PAIN

Effects of postoperative pain:

Postoperative pain can affect all organ systems and includes

Cardiovascular - increased myocardial oxygen consumption and ischemia.

Respiratory - reduced cough, atelectasis, sputum retention and hypoxemia

Gastrointestinal - delayed gastric emptying, reduced gut motility and constipation.

Genitourinary - urinary retention.

Neuroendocrine - hyperglycemia, protein catabolism and sodium retention.

Musculoskeletal - reduced mobility, pressure sores and increased risk of deep vein thrombosis.

Psychological - anxiety and fatigue.

ROLE OF EPIDURAL ANALGESIA

Benefits of epidural analgesia

Use of postoperative epidural anaesthesia and analgesia especially with a local anaesthetic – based analgesic solution can attenuate the pathophysiologic response to surgery and may be associated with a reduction in mortality and morbidity compared with analgesia with systemic opioids.

Rodgers et al[8] demonstrated through a meta-analysis of randomized data that perioperative use of neuraxial anaesthesia and analgesia versus general anaesthesia and systemic opioids reduced overall mortality by approximately 30%. Use of epidural analgesia can decrease the incidence of postoperative gastrointestinal, pulmonary and cardiac complications.

Christopherson et al[9] demonstrated that use of intra operative regional anaesthesia reduced hypercoagulable – related events (eg. Deep vein thrombosis, pulmonary embolism, vascular graft failure).

POSTOPERATIVE ANALGESIA IN ORTHOPAEDICS

Postoperative pain is of major concern after orthopaedic lower limb surgery. Moderate to severe at rest, it is exacerbated on movement and particularly after hip and knee surgery and by severe reflex muscular spasm. This not only causes patient discomfort but also compromise the early physical therapy, the most influential factor on rapid postoperative rehabilitation and ambulation.

Postoperative pain relief can be achieved by a number of techniques such as intravenous patient controlled analgesia (PCA) or epidural analgesia. Effective analgesia with epidural or peripheral block reduces narcotic requirements, provides better analgesia, reduces catabolism and results in improved rates of rehabilitation after orthopaedic lower limb surgeries.

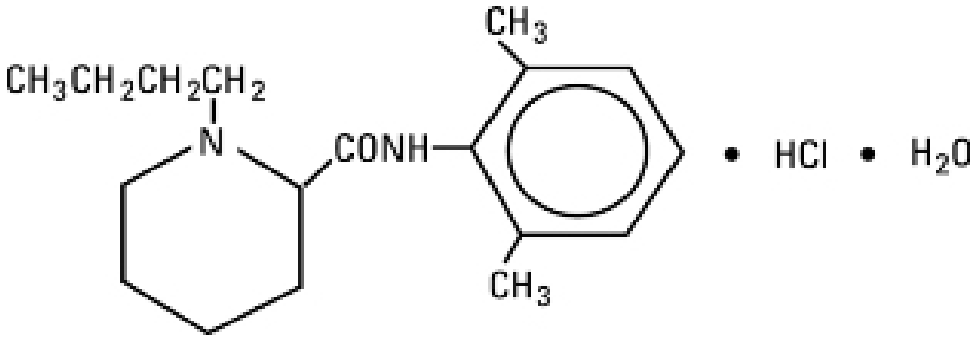
The benefits of effective postoperative analgesia in orthopeadic surgeries was made evident by the fact that it facilitates early ambulation which is beneficial in the prophylaxis of deep vein thrombosis, which is a common problem encountered in orthopaedics[10]. Postoperative modalities like pneumatic compression boots, foot pumps, foot exercises, aspirin and low dose warfarin(started the day after surgery) can be safely used in conjunction with epidural anaesthesia to reduce the incidence of deep vein thrombosis.

BUPIVACAINE

Bupivacaine was introduced by Boaf Ekenstam in 1963.

Chemical structure: bupivacaine hydrochloride is 2-piperidenecarboxamide 1-butyl-N-(2,6 dimethylphenyl) monochloride, a monohydrate is a white crystalline powder that is freely soluble in 95% ethanol, soluble in water and slightly soluble in chloroform or acetone.

It has the following structural formula:



Bupivacaine is related chemically and pharmacologically to the amide group of local anaesthetics. It is structural homologue of mepivacaine.

Presentation: bupivacaine hydrochloride is available in sterile isotonic solution with or without epinephrine 1:2,00,000 for injection. It is available in 0.25%,0.5%,0.75% concentration containing 2.5mg/dl,

5mg/dl, 7.5mg/dl of bupivacaine hydrochloride respectively and sodium chloride, sodium hydroxide ± hydrochloric acid for pH adjustment. Methylparaben 1mg/ml added as preservative. 0.5%(hyperbaric) solution contain 80mg/ml of glucose(with a specific gravity of 1.026)-for intrathecal use.

Mechanism of action:

Local anaesthetics diffuse in their nonionized form through neural sheaths and the axonal membrane to the internal surface of the cell membrane sodium ion channels where they combine with hydrogen ions to form a cationic species which enters the internal opening of the sodium ion channel and combines with a receptor. This produces blockade of the sodium ion channels thereby decreasing sodium conductance and preventing depolarization of the cell membrane.

Pharmacological action:

a) Central nervous system (CNS) : the principle effect of bupivacaine is reversible neural blockade, this leads to a characteristically biphasic effect on the CNS.

- Initially excitation: light headness, dizziness, visual and auditory disturbances and seizures occurs due to blockade of inhibitory pathways in cortex.

- With increasing doses: CNS depression occurs due to depression of both facilitatory and inhibitory pathways leading to drowsiness, disorientation and coma.

- Local anaesthetic agents block neuromuscular transmission when administered intra-arterially(formation of neurotransmitter, receptor and local anaesthetic complex which has negligible conductance).

b) Cardiovascular system(CVS): it binds specifically to myocardial proteins. In toxic concentrations,the drug decreases the peripheral vascular resistance and myocardial contractility producing hypotension and possibly cardiovascular collapse.

Routes of administration: topical, infiltration, intrathecal, epidural

Dose: 2mg/kg

Pharmacokinetics:

Absorption : The absorption of local anaesthetic agent is related to

1. The site of injection (intercostals> epidural> brachial plexus> subcutaneous)

2. The dose linear relationship exists between the total dose and the peak blood concentration achieved.

Distribution: 95% protein bound in plasma. The volume of distribution is 47-103 litres.

Metabolism: occurs in liver by N-dealkylation primarily to pipcolyloxylidine. N-desbutyl bupivacaine and 4-hyroxy bupivacaine are also formed.

Excretion : 5% of the dose is excreted in the urine as pipcolyloxylidine. 16% is excreted unchanged .The clearance is 0.47 l/min and the elimination half life (after intravenous administration) is 0.31-0.61 hours.

Pharmacodynamics: pKa of bupivacaine is 8.1, Heptane: Buffer partition coefficient is 27.5

The onset and duration of conduction blockade is related to the pKa, lipid solubility and the extent of protein binding of the drug.

- A low pKa and high lipid solubility are associated with a rapid onset time

- High degree of protein binding is associated with a long duration of action.

Toxicity /side effects:

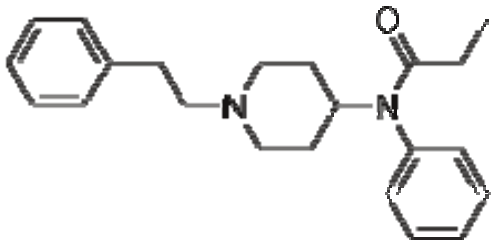
i. Allergic reactions to amide type local anaesthetics- extremely rare.
ii. Intravascular injection can cause refractory cardiac depression .

FENTANYL

Fentanyl was first synthesized by Dr. Paul Janssen in 1960.

Fentanyl is a synthetic opiod which is primarily a μ receptor agonist. It is approximately 50 – 80 times more potent than morphine with 100 μg of fentanyl approximately equivalent to 10 mg of morphine and 75 mg of pethidine in analgesic activity.

Structure :



Fentanyl is a piperidine derivative. The systematic name is N-phenyl-N- (1-phenythyl-4-piperidinyl)propanamide. Molecular formula is $C_{22}H_{28}N_2O$. molecular weight is 336.471 gm/mol.

Preparation :

Injection – clear colourless solution containing 50 μg /ml

Transdermal patches

Lozenges

Buccal tablets

Mechanism of action :

Fentanyl is a highly selective μ receptor agonist involved specifically in mediation of pain. It appears to act by increasing intracellular calcium concentration which in turn increases potassium conductance and hyperpolarisation of excitable cell membranes. The decrease in membrane excitability decreases both pre- and post synaptic responses.

Pharmacological actions :

Cardiovascular system : The most significant cardiovascular effect is bradycardia. Fentanyl obtunds the cardiovascular responses to laryngoscopy and intubation. Cardiac output, mean arterial pressure, pulmonary and systemic vascular resistance and pulmonary capillary wedge pressure are unaffected.

Respiratory system : Fentanyl is a potent respiratory depressant causing a decrease in both respiratory rate and tidal volume. It also diminishes respiratory drive to hypoxia and hypercapnia. Chest wall rigidity may occur.

Central nervous system : Fentanyl is 50-80 times more potent than morphine as an analgesic. It has little hypnotic and sedative activity. Miosis is produced by stimulation of Edinger-Westphal nucleus.

Gastrointestinal system : Fentanyl decreases gastrointestinal motility and decreases gastric acid secretion. It increases common bile duct pressure by causing spasm of sphincter of Oddi.

Pharmacokinetics :

Absorption : Fentanyl is absorbed when administered orally. Oral bioavailability is 33%. Transdermal route has 92% bioavailability. Fentanyl when given through buccal route has 50% bioavailability.

Distribution : Fentanyl is 80 -85% protein bound in plasma with volume of distribution of 0.88-4.41 l/kg. Fentanyl is more lipid soluble than morphine and thus crosses blood brain barrier easily. It thus has more rapid onset of action than morphine.

Metabolism : Fentanyl is primarily metabolized in liver by Cytochrome P-450 3A4 by N-dealkylation and hydrolysis.

Excretion : The metabolites of fentanyl are excreted by kidneys. 10% of unchanged drug is excreted by kidneys. The elimination half life is 1.5 to 6 hrs.

Side effects / toxicity : Nausea and vomiting are the most common side effects. Wooden chest syndrome may occur in some patients. At higher doses respiratory depression may occur.

Uses :

1. To provide analgesia component of general anaesthesia.
2. Used along with benzodiazepine to produce procedural sedation for endoscopy, cardiac catheterization.
3. As an adjuvant in spinal and epidural anaesthesia.
4. In cancer therapy and chronic pain management.

MAGNESIUM

Magnesium was discovered in 1755 by Sir Humpry Davy.

Magnesium is the fourth plentiful cation in the body and second most abundant intracellular cation after potassium. It is a cofactor in hundreds of enzymatic reactions.

Magnesium is a natural calcium antagonist.

Normal physiology :

Magnesium is a bivalent cation with atomic weight of 24.312. Human body contains one mole (24 gms) of magnesium of which 60% is present in bones, 20% is in muscles, 20% is in soft tissues. Only 1% of total body magnesium is present extracellularly.

Intracellular magnesium exists largely (90%) in bound form in ATP molecules of cytoskeleton (nucleus, mitochondria & reticulum). Only a small portion (5 – 14%) remains as ionized form within the cell.

Properties of Magnesium :

1. Magnesium intervenes in the activation of Ca ATPase & Na-K ATPase involved in transmembrane ion exchange. It acts as a stabilizer of cell membrane and intracytoplasmic charges.

2. Magnesium has antagonist action on L type calcium channels. It inhibits Ca inflows into the cell and outflow of Ca from sarcoplasmic reticulum.

3. Magnesium has antagonist effect on N-methyl D-aspartate receptors in nervous system.

4. Intracellular ionized magnesium is involved in phosphorylation & is necessary for activation of hundreds of enzymatic reactions concerning ATP.

Normal serum concentration :

1.6 to 2.6 mEq /L

Pharmacological Effects :

Cardiovascular system : Magnesium causes vasodilatation and may cause hypotension at high doses. It slows the rate of SA node impulse formation and prolongs SA node conduction time, the PR interval and AV nodal effective refractory period. Magnesium attenuates both vasoconstrictor and arrythmogenic actions of adrenaline.

Respiratory system : Magnesium is an effective bronchodilator and attenuates hypoxic pulmonary vasoconstriction.

Central nervous system : Magnesium is a CNS depressant and exhibits anticonvulsant properties. High concentrations inhibit catecholamine release from adrenergic nerve terminals and adrenal medulla.

Gastrointestinal system : Magnesium sulphate acts as osmotic laxative when administered orally.

Genito urinary system : Magnesium has renal vasodilator and diuretic effect.

Toxicity / side effects :

Minor side effects include warmth, flushing, nausea, headache and dizziness. Dose related side effects include somnolence, areflexia, AV and intraventricular conduction disorders, progressive muscle weakness, and cardiac arrest.

Uses :

1. Replacement therapy for hypomagnesemia.
2. Magnesium sulfate is the first-line antiarrhythmic agent for torsades de pointes in cardiac arrest under the 2005 ECC guidelines and for managing quinidine-induced arrhythmias.
3. To treat eclampsia and premature labour in pregnant women.

4. As a bronchodilator after beta-agonist and anticholinergic agents have been tried, e.g. in severe exacerbations of asthma.
5. In surgery for pheochromocytoma and cardiac surgery.
6. During anaesthetic induction to blunt intubation response.
7. Adjuvant in intraoperative analgesia.
8. Oral magnesium sulphate is used as saline laxative.

REVIEW OF LITERATURE

1. Role of magnesium sulfate in postoperative analgesia

Tramer MR et al in 1996 conducted one of the earliest studies to demonstrate the anti nociceptive characteristics of magnesium. METHOD : In a randomized double – blind study, they included 42 ASA I and II patients undergoing abdominal hysterectomy. Study group received 15 ml of 20% magnesium before start of surgery and an infusion of 2.5 ml/hr for next 20 hrs. Control group received same amount of normal saline . Maximum expiratory flow (peak flow), pain at rest and during peak flow and discomfort were evaluated up to the 48th postoperative hour and 1 week and 1 month after surgery. Insomnia was evaluated after the first and second postoperative nights. CONCLUSION: They concluded that the perioperative application of magnesium sulphate is associated with smaller analgesic requirement, less discomfort, and a better quality of sleep in the postoperative period but not with adverse effects. (Anaesthesiology;1996:84(2) 340-7).

2. Magnesium sulphate reduces intra- and postoperative analgesic requirements

Koinig H, Wallner T, Marhofer P, Andel H, Hörauf K, Mayer N in 1998 performed a randomized double blind study in 46 ASA I and II

patients undergoing knee arthroscopy under total iv anaesthesia. METHOD : The patients received either magnesium sulfate 50 mg/kg preoperatively and 8 mg/kg/hr intraoperatively or the same volume of isotonic sodium chloride solution. i.v. anaesthesia was performed with propofol (2 mg/kg for induction, 6-8 mg/kg/hr for maintenance), fentanyl (3 µg/kg for induction), and vecuronium (0.1 mg/kg for intubation). Intraoperative pain was defined as an increase of mean arterial blood pressure and heart rate of more than 20% from baseline values after the induction of anesthesia and was treated with bolus fentanyl (1-2 µg/kg). Postoperative analgesia was achieved with fentanyl (0.5 µg/kg) and evaluated using the pain visual analog scale for 4 hr. CONCLUSION : They concluded that, in a clinical setting with almost identical levels of surgical stimulation, i.v. magnesium sulfate administration reduces intraoperative and postoperative analgesic requirements. (Anesth Analg 1998;87(1):206-10).

3. A comparative study with oral nifedipine, intravenous nimodipine and magnesium sulfate in postoperative analgesia

Zarauza R et al in 2000 tested the ability of two L-type calcium channel blockers (nifedipine and nimodipine) and the N-methyl D-aspartate natural antagonist magnesium to decrease morphine requirements and pain in the postoperative period in 92 patients

undergoing elective colorectal surgery. METHOD : In a randomized, double-blinded study, patients were assigned to one of four groups. The control group received placebo. The nifedipine group received 60 mg of oral nifedipine. The magnesium group received an initial dose of 30 mg/kg followed by 10 mg/kg/hr of magnesium sulphate over 20 h. The nimodipine group received 30 microg /kg/hr of nimodipine over 20 h. Postoperative morphine consumption was assessed for 48 h. Pain at rest and pain on movement were assessed up to the fifth day postsurgery. CONCLUSION: They concluded the perioperative application of oral nifedipine, IV nimodipine, or IV magnesium sulfate failed to decrease postoperative morphine requirements after colorectal surgery. (Anaesth Analg 2000;91(4):938-43).

4. Magnesium infusion reduces perioperative pain

Kara H, Sahin N, Ulusan V, Aydogdu T in 2002 conducted a study to determine whether perioperative infusion of magnesium would reduce postoperative pain and anxiety. METHOD: Twenty-four patients, undergoing elective hysterectomy, received a bolus of 30 mg/kg magnesium sulphate or the same volume of isotonic sodium chloride solution intravenously before the start of surgery and 0.5 g/hr infusion for the next 20 hr. Intraoperative and postoperative analgesia were achieved with fentanyl and morphine respectively. Patients were

evaluated pre- and postoperatively for anxiety. CONCLUSION: Continuous magnesium infusion, including the pre-, intra-, and postoperative periods reduces analgesic requirements and reduces the anxiety of the patients. (Eur J Anaesthesiol. 2002 Jan;19(1):52-6).

5. Intrathecal versus intravenous fentanyl for supplementation of subarachnoid block during cesarean delivery

Sahar and Marie et al in 2002 conducted a randomized study in 48 healthy parturient patients undergoing elective cesarean section. One group received 12 mg of hyperbaric bupivacaine plus 12.5 µg of fentanyl intrathecally. Another group received 12 mg of hyperbaric bupivacaine intrathecally and 12.5 µg of fentanyl intravenously immediately after spinal. They found that additional intravenous fentanyl was needed in IV fentanyl group and incidence of hypotension and use of ephedrine was more in IV fentanyl group. The time to the first request for postoperative analgesia was significantly longer in the intrathecal fentanyl group than in the IV fentanyl group. They concluded that supplementation of spinal bupivacaine anesthesia for cesarean delivery with intrathecal fentanyl provides a better quality of anesthesia and is associated with a decreased incidence of side effects as compared with supplementation with the same dose of IV fentanyl (Anesth Analg 2002;95:209-213)

6. Intrathecal Magnesium Prolongs Fentanyl Analgesia

Asokumar Buvanendran et al in 2002 were one of the first to administer magnesium intrathecally in humans. They conducted a prospective randomized controlled trial in 52 healthy parturient mothers requiring labour analgesia. METHOD: Patients were randomized to receive either intrathecal fentanyl 25 µg plus saline or fentanyl 25 µg plus magnesium sulfate 50 mg as part of a combined spinal-epidural technique. The duration of analgesia of the intrathecal drug combination was defined by the time of patient request for additional analgesia. RESULT: There was significant prolongation in the median duration of analgesia in the magnesium plus fentanyl group compared with the fentanyl alone group. CONCLUSION: They concluded that intrathecal magnesium prolongs spinal opioid analgesia in humans and suggest that the availability of an intrathecal *N*-methyl-D-aspartate antagonist could be of clinical importance for pain management. (Anaesth Analg 2002;95:661-666).

7. Effect of intraoperative magnesium infusion on perioperative analgesia in open cholecystectomy

Bhatia A et al in 2004 conducted a prospective, double-blinded, randomized study in 50 ASA physical status I and II patients scheduled for elective open cholecystectomy with general anesthesia. METHOD:

patients were randomly allocated to receive MgSO4 or saline intravenously. Patients in the magnesium group received 50% MgSO4 (50 mg/kg) in 100 mL saline and those in the control group received an equal volume of saline i.v. during the preoperative period followed by 50 ml/hr infusion of either MgSO4 (15 mg/kg/hr) or saline until the end of surgery. Morphine requirement, pain during rest and on coughing, discomfort, and insomnia were assessed during the postoperative period for 24 hours. CONCLUSION: They concluded the study by saying administration of intraoperative MgSO4 resulted in better pain relief and comfort in the first postoperative hour, but it did not significantly decrease the postoperative morphine requirement. Magnesium sulphate resulted in better sleep quality during the postoperative period, without any significant adverse effects. (J Clin Anesth. 2004 Jun;16(4):262-5).

8. The effect of adding intrathecal magnesium sulphate to morphine for postoperative analgesia after caesarean section

Khemakhem K et al in 2006 conducted a prospective, randomized, double blind, controlled study to know the effect of intrathecal magnesium sulphate, morphine and their association in postoperative analgesia. METHOD: 97 ASA I and II parturients undergoing cesarean section are randomly allocated to 3 groups to receive 0.1 mg of morphine or 100 mg of magnesium or both.

Postoperative analgesia with the visual analogic score (VAS), analgesic requirement, and side effects were recorded. CONCLUSION: The addition of intrathecal magnesium sulphate 100 mg to morphine improved quality and duration of the postoperative analgesia with a better maternal satisfaction without additional side effects. (Euro J Anaes 2006 jun; 23: 183-4).

9. Role of magnesium as adjuvant to ropivacaine in caudal anaesthesia in children

H.Birbicer and D.Avlan et al in 2006 conducted a randomized trial in which 60 ASA I and II patients in age group of 2 – 10 years coming for lower abdominal and penoscrotal surgeries were included. METHOD : After general anaesthesia induction, caudal block given with 0.25% ropivacaine in volume of 0.5 ml/kg in one group and 0.25% ropivacaine with 50 mg magnesium as same volume in second group. Postoperative analgesia levels recorded at 15 min and 1, 2, 3, 4, 6 h by using Paediatric Objective Pain Scale (POPS) and The Children's Hospital of Eastern Ontoria Pain Scale (CHEOPS). Postoperative motor blocks were evaluated with Modified Bromage Motor Block Scale. CONCLUSION : They concluded that addition of magnesium as an adjuvant agent to local anaesthetics for caudal analgesia has no effect on postoperative pain and analgesic need. (Pediatric surgery international 2006;1779:195-198).

10. Epidural magnesium reduces postoperative analgesic requirements after hip surgery

A.Bilir and A.Ozcelik et al in 2007 conducted a randomized double blind study in 50 patients undergoing elective hip surgery. METHOD : Patients were enrolled to receive either fentanyl or fentanyl plus magnesium for 24 hours for epidural analgesia. All patients were equipped with PCEA device and initial setting of a demand bolus dose of fentanyl 25 µg. Patients in magnesium group received magnesium sulphate epidurally as an initial bolus dose of 50 mg and continuous infusion of 100 mg/day. Ventilatory frequency, heart rate, blood pressure, pain assessment using visual analogue scale , sedation scores and fentanyl consumption were recorded in postop period. CONCLUSION : They concluded that co-administration of magnesium for postoperative epidural analgesia results in a reduction of fentanyl consumption without any side effects. (BJA 2007 ;1093: 294-299).

11. Combined intrathecal and epidural magnesium sulphate supplementation of spinal anaesthesia to reduce post-operative analgesia requirements

R.Arcioni et al in 2007 conducted a prospective , randomized, double blind, controlled study in 120 ASA I and II patients coming for lower limb orthopedic surgery. METHOD : Patients were randomly

divide into 4 groups assigned to receive intrathecal magnesium sulphate, epidural magnesium sulphate, combined intrathecal and epidural magnesium sulphate or spinal anaesthesia alone. Post-operative morphine consumption was assessed in all patients using PCA. CONCLUSION : In patients undergoing orthopedic surgery, supplementation of spinal anaesthesia with combined intrathecal and epidural magnesium significantly reduces the post-operative analgesic requirements. (Acta Anaes Scand. 2007 ; 51(4): 482-489).

12. Pre-incisional epidural magnesium provides pre-emptive and preventive analgesia in patients undergoing abdominal hysterectomy

S.Farouk et al in 2008 conducted a prospective randomized, double-blind study designed to evaluate the pre-emptive and preventive analgesic efficacy of adding magnesium to a multimodal regimen of patient-controlled epidural analgesia (PCEA) in patients undergoing abdominal hysterectomy. CONCLUSION: Continuous epidural magnesium started before anaesthesia provided pre-emptive, preventive analgesia, and an analgesic-sparing effect that improved postoperative analgesia without increasing the incidence of side-effects. (BJA 2008 101(5): 694-699).

13. Analgesic requirements for patients undergoing lower extremity orthopedic surgery - the effect of combined spinal and epidural magnesium

H.El-Kerdawy et al in 2008 conducted a randomized control study on 80 ASA I and ASA II patients coming for elective orthopedic lower limb surgery. METHOD : Patients were randomly allocated into two groups , control group received intrathecal 10 mg of 0.5% bupivacaine(2 ml) plus 25 µg of Fentanyl (0.5 ml), plus 0.9% NaCl solution (1 ml) and an epidural infusion of 0.9% NaCl at a rate of 5 ml/hr. The Magnesium Group: patients received intrathecal 10 mg of Bupivacaine 0.5% (2 ml), plus 25 µg of Fentanyl (0.5 ml), plus 50 mg of 5% Mg (1 ml) and an epidural infusion of 2% Mg at a rate of 100 mg/hr (5 ml/hr). RESULTS: Intrathecal Mg prolonged fentanyl analgesia as indicated by increased duration of anesthesia in the Mg group, and thus improving the quality of spinal anesthesia. The effectiveness of the postoperative analgesia was confirmed by markedly lower perioperative analgesic requirements (38.3 % less than the Control group), the patient's low VAS score, the longer time for the patients first requirement of post-operative analgesia in the Mg group. CONCLUSION: They concluded, for lower extremity orthopedic procedure, supplementation of spinal anesthesia with combined intrathecally injected and epidurally infused Mg, considerably

reduced the perioperative analgesic requirements without any side effects. (Middle East J Anaes 2008 Jun;19(5):1013-25).

14. Comparison of intrathecal magnesium, fentanyl, or placebo combined with bupivacaine 0.5% for parturients undergoing elective cesarean delivery

Unlugenc and Ozalevli et al in march 2009 conducted a prospective, randomized, double-blind study to investigate the sensory, motor, and analgesic block characteristics of intrathecal magnesium 50 mg compared with fentanyl 25 µg and saline when added to 0.5% bupivacaine. METHOD : 90 ASA I and II healthy parturients undergoing elective cesarean section were included in the study. Onset and duration of sensory and motor block, maximal sensory block height, the time to reach the maximal dermatomal level of sensory block, and the duration of spinal anesthesia were rocorded. CONCLUSION : They concluded that in patients undergoing cesarean section with spinal anesthesia, the addition of magnesium sulfate (50 mg) intrathecally to 10 mg of spinal bupivacaine (0.5%) did not shorten the onset time of sensory and motor blockade or prolong the duration of spinal anesthesia, as seen with fentanyl. (Acta Anaes Scand 2009: 53 : 346-353).

MATERIALS AND METHODS

Patient selection:

The study population consist of 40 ASA I & ASA II patients in the age group of 18 years to 65 years admitted to undergo elective orthopaedic lower limb surgeries at Govt. Stanley Hospital, Chennai during the period of May 2009 to August 2009. After getting approval from the institutional ethical committee and after obtaining written informed consent from each patient ,the study was conducted.

Inclusion criteria:

1. Age Group 18 – 65 years
2. ASA I and ASA II
3. Elective orthopaedic lower limb surgeries
4. Duration of Surgery between 1:00 to 2:30 hours.

Exclusion criteria:

1. Patient refusal

2. Patients with preexisting renal problems

3. Allergy to any of the study medications

4. Preoperative hypotension

5. Local infection at lumbar area

6. Pre-existing neurological disorders

7. Coagulation defects and patient on anticoagulants

Preoperative assessment:

- Routine clinical examination

- Biochemical investigations

- Electrocardiogram and chest x-ray were examined thoroughly for the conduct of anaesthesia.

Conduct of anaesthesia

Patients were allocated randomly into two equal groups (20 in each group). Group P (placebo) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2ml) plus 25 µg of fentanyl (0.5 ml) plus 0.9% NaCl solution (1 ml) . Total intrathecally injected volume is 3.5 ml.

Epidural infusion of 0.9% NaCl solution is given in first hour of surgery at the rate of 5 ml/hr.

Group M (Magnesium) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2 ml) plus 25 µg of fentanyl (0.5 ml) plus 50 mg of 5% magnesium sulphate (1 ml). Total intrathecally injected volume is 3.5 ml. Epidural infusion of 2 % magnesium sulphate is given at the rate of 100 mg/hr (5 ml/hr) during first hour of surgery.

5 % magnesium sulphate solution is prepared by mixing 1 ml of 50% magnesium sulphate with 9 ml of preservative free sterile water. 2% magnesium sulphate is prepared by mixing 1 ml of 50% magnesium sulphate with 24 ml of preservative free sterile water.

No premedication was given. On arrival in the operating room, baseline cardiorespiratory parameters viz., Heart Rate(HR), Systolic blood pressure(SBP), Diastolic blood pressure(DBP),Mean arterial pressure(MAP), Respiratory rate(RR) and Ramsay Sedation Score(RSS) were recorded.

A good intravenous access was established using 18G IV cannula. Preloading was done with crystalloids (10 ml/kg).

A standard anaesthetic technique was followed in all patients.

With the patient in sitting posture, after informing the procedure to the patient & under strict aseptic precautions, epidural space was identified at L2-L3 interspace using 16G Tuohy needle by loss of resistance technique. 18G epidural catheter was threaded in a cephalad direction & 3 cm catheter length was kept inside the epidural space. A test dose of 3 cc of 1.5 % lignocaine with adrenaline (5 µg/ml) was given. Spinal anaesthesia is performed at L3-L4 interspace. Epidural catheter was fixed and secured with tapes.The epidural catheter is then connected to infusion pump that is disconnected after first hour of surgery.

Patients with duration of surgery between 1-2:30 hours were only included in the study. Unanticipated prolonged duration of surgery were excluded from the study.

Time of incision is noted.

Intra-operatively the patient was monitored with ECG, BP and SpO2.

The following parameters were monitored every 10 mins:

1. Heart rate (HR)

2. Systolic blood pressure (SBP)

3. Diastolic blood pressure (DBP)

4. Mean arterial pressure (MAP)

5. Respiratory rate (RR)

6. Oxygen saturation (SpO_2)

Ramsay sedation scale (RSS) was also noted every 30 min during intraoperative period.

Urine output was monitored hourly.

All patients were given oxygen supplementation (4-5 L/min) through Hudson's face mask. No intravenous opioid analgesics were supplemented during the study. Intravenous fluid management was done based on mean arterial blood pressure and surgical blood loss.

RAMSAY SEDATION SCALE:

1. Patient is anxious and agitated or restless, or both

2. Patient is co-operative, oriented and tranquil

3. Patient responds to commands only

4. Patient exhibits brisk response to glabellar tap or loud auditory stimulus

5. Patient exhibits sluggish response to glabellar tap or loud auditory stimulus.

6. Patient exhibits no response

POST- OPERATIVE MONITORING :

- The epidural catheter was retained in position. Postoperatively the patient was transferred to the Post Anaesthetic Care Unit(PACU) where PR,SBP ,DBP, SPO2 & RR monitored continuously and recorded every hour.

- The intensity of pain was measured by using the verbal rating pain scale.

Pain Score (Verbal Rating Score):

Grade 0 - No complaint of pain

Grade 1 - Patient complaints of pain but tolerable (mild pain)

Grade 2 - Patient complaining of severe pain and demands relief (Moderate pain)

Grade 3 - Patient restless and screaming with pain(Severe pain)

When the patient complaints of pain , the pain intensity was assessed based on verbal rating scale & if pain score reaches 1, epidural top up of 6ml of 0.125% bupivacaine was given to the patient.

The time of first rescue analgesia(TFA) was calculated from the time of injection of study drug in the central neuraxial block to the time when the verbal rating pain score reached 1 in the postop period.

Number of epidural top-ups (6 ml of 0.125% bupivacaine) required by each patient for a period of 48 hours was noted in both the groups.

OBSERVATIONS

LIST OF ORTHOPAEDIC LOWER LIMB SURGERIES

S.NO	DIAGNOSIS AND SURGICAL PROCEDURES	NO. OF CASES	
		GROUP P	GROUP M
1.	Fracture shaft of femur- ORIF with interlocking nailing / plating	6	7
2.	Fracture both bones leg- ORIF with intramedullary nailing / plating	6	5
3.	Fracture neck of femur- Hemiarthroplasty	5	5
4.	Supracondylar fracture femur – ORIF with Dynamic Condylar Screw (DCS)	2	3
5.	Fracture Patella- ORIF with Tension Band Wiring	1	-
	TOTAL CASES	20	20

STATISTICS AND ANALYSIS

40 Patients were allocated randomly into two equal groups (20 in each group). Group P (placebo) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2 ml) plus 25 µg of fentanyl (0.5 ml) plus 0.9% NaCl solution (1 ml) . Total intrathecally injected volume is 3.5 ml. Epidural infusion of 0.9% NaCl solution is given in first hour of surgery at the rate of 5 ml/hr.

Group M (Magnesium) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2 ml) plus 25 µg of fentanyl (0.5 ml) plus 50 mg of 5% magnesium sulphate (1 ml). Total intrathecally injected volume is 3.5 ml. Epidural infusion of 2 % magnesium sulphate is given at the rate of 100 mg/hr (5 ml/hr) during first hour of surgery.

A standard anaesthetic technique was followed in all patients. The patient were assessed by the same observer in the postoperative period.

All the data were expressed as mean ± standard deviation (SD). Qualitative variables were compared with `Chi-square test' and quantitative variables were compared with 'the student 't' test'. The level of statistical significance was set at $P < 0.05$.

DEMOGRAPHIC PROFILE

TABLE- 1
COMPARISON OF AGE DISTRIBUTION

S.NO	PARAMETERS	GROUP		P VALUE
		GROUP P	GROUP M	
		MEAN ± SD	MEAN ± SD	
1.	Age (yrs)	40.60 ± 7.40	36.85 ± 9.59	P-0.183(NOT SIGNIFICANT)

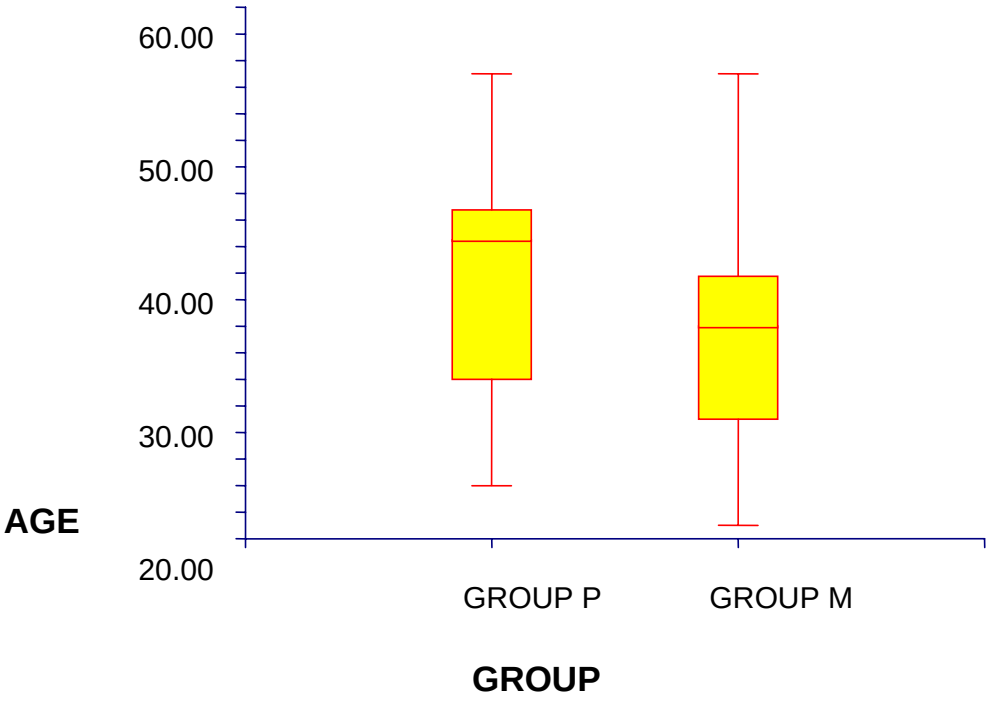


Figure 1: BOX- PLOT compares the age distribution of GROUP P and GROUP M

TABLE – 2

SEX DISTRIBUTION

	GROUP P	**GROUP M**	**TOTAL**
MALE	15 (75%)	17 (85%)	32 (80%)
FEMALE	5 (25%)	3 (15%)	8 (20%)
TOTAL	20	20	40

TABLE – 3

COMPARISON OF HEIGHT AND WEIGHT

S.NO	**PARAMETERS**	**GROUP**		**P value**
		GROUP P	**GROUP M**	
		MEAN±SD	**MEAN±SD**	
1.	HEIGHT	164.00±5.73	166.65±6.01	P-0.152(Not Significant)
2.	WEIGHT	59.60±5.16	59.50±6.10	P-0.956(Not Significant)

FIGURE – 2

SEX DISTRIBUTION

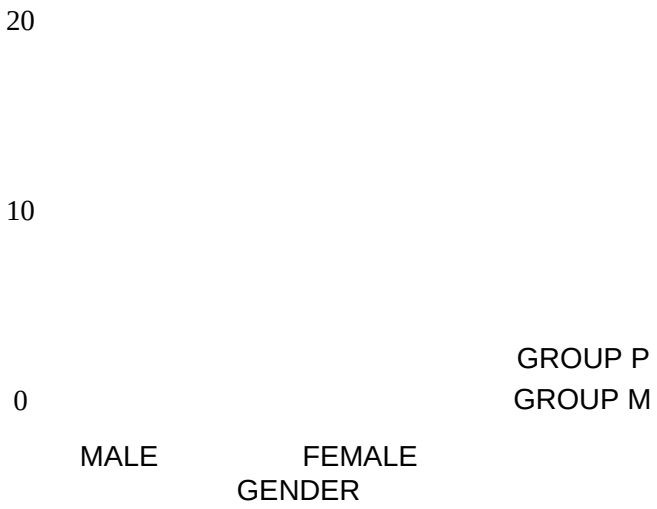


FIGURE – 3

HEIGHT AND WEIGHT

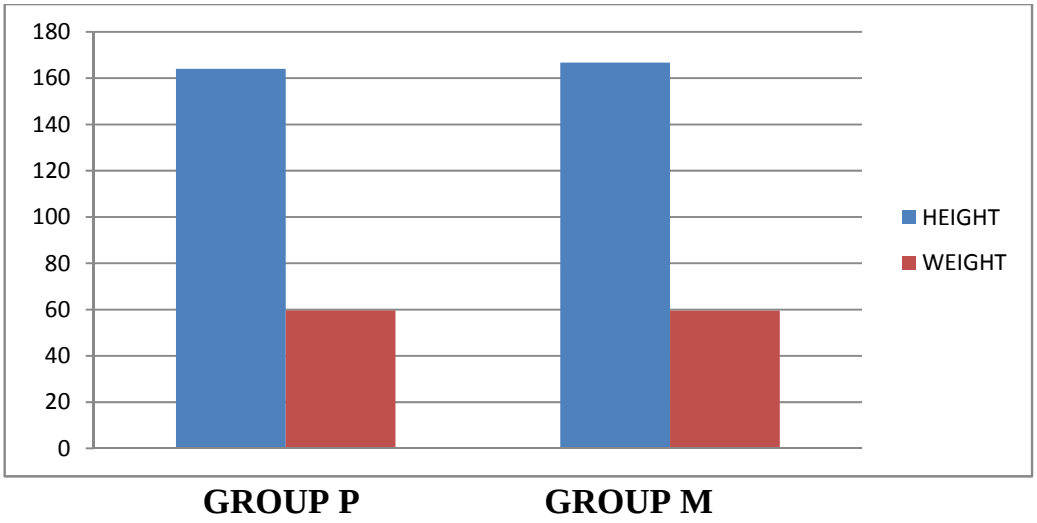


TABLE – 4

DURATION OF SURGERY

	GROUP P	GROUP M	P VALUE
DURATION OF SURGERY	2.14 ± 0.07	2.12 ± 0.07	P – 0.359 NOT SIGNIFICANT

FIGURE - 4

DURATION OF SURGERY

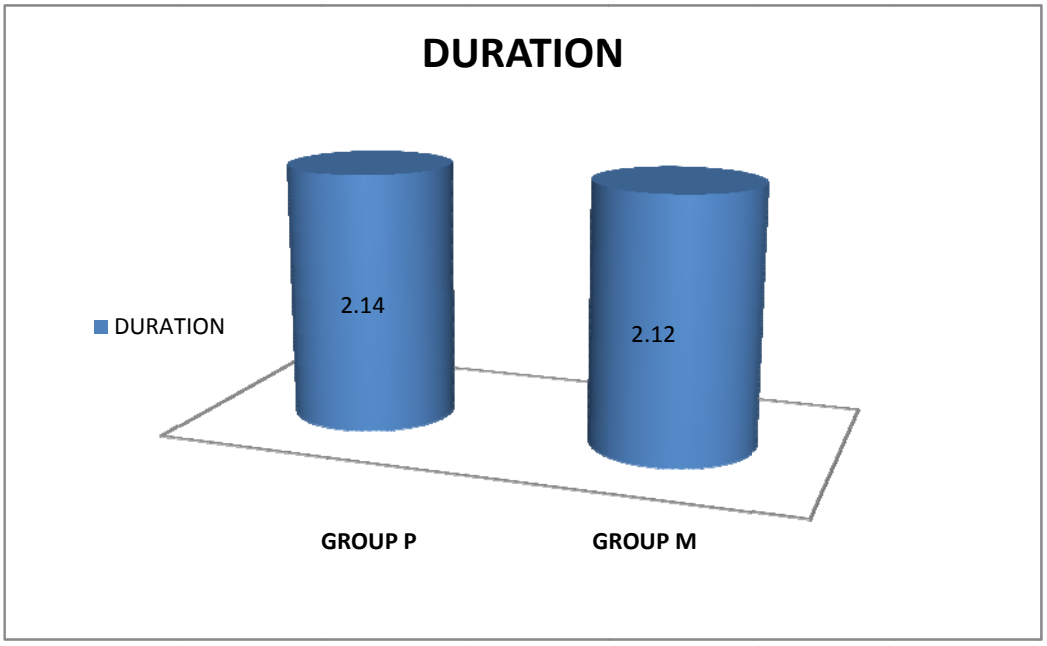


TABLE - 5

HEART RATE

S NO.	PARAMETERS (MINUTES)	GROUP		P VALUE P<0.05-SIG
		GROUP P	GROUP M	
		MEAN ± SD	MEAN ± SD	
1.	HR PRE-OP	94.10 ± 11.81	97.05 ± 12.81	.441(NOT SIG)
2.	HR10	92.20 ± 8.16	94.70 ± 11.69	.438(NOT SIG)
3.	HR20	88.90 ± 8.70	90.40 ± 12.12	.656(NOT SIG)
4.	HR30	85.95 ± 7.52	87.30 ± 11.77	.668(NOT SIG)
5.	HR40	84.80 ± 8.29	87.10 ± 12.81	.504(NOT SIG)
6.	HR50	83.85 ± 8.34	85.45 ± 13.03	.646(NOT SIG)
7.	HR60	82.75 ± 8.66	84.90 ± 11.79	.515(NOT SIG)
8.	HR70	81.95 ± 9.24	82.55 ± 10.73	.851(NOT SIG)
9.	HR80	82.35 ± 8.96	81.65 ± 9.9.52	.812(NOT SIG)
10.	HR90	83.00 ± 9.59	82.00 ± 11.94	.908(NOT SIG)
11.	HR100	84.55 ± 9.02	83.6 ± 10.51	.761(NOT SIG)
12.	HR110	86.30 ± 7.55	85.7 ± 10.26	.834(NOT SIG)
13.	HR120	84.15 ± 10.00	86.85 ± 10.21	.594(NOT SIG)
14.	HR130	87.30 ± 8.41	86.20 ± 10.28	.713(NOT SIG)
15.	HR140	87.00 ± 8.60	88.65 ± 11.08	.602(NOT SIG)
16.	HR150	90.70 ± 8.98	90.70 ± 10.53	1.00(NOT SIG)

TABLE - 6

SYSTOLIC BLOOD PRESSURE

S NO.	PARAMETERS (MINUTES)	GROUP		P VALUE P<0.05- SIG
		GROUP P	GROUP M	
		MEAN ± SD	MEAN ± SD	
1.	SBP PRE-OP	128.80 ± 6.68	130.20 ± 6.47	0.505(NOT SIG)
2.	SBP 10	120.20 ± 11.70	118.65 ± 5.85	0.600(NOT SIG)
3.	SBP 20	110.05 ± 11.64	107.40 ± 10.88	0.462(NOT SIG)
4.	SBP 30	113.85 ± 13.51	112.70 ± 6.85	0.736(NOT SIG)
5.	SBP 40	114.90 ± 9.29	108.30 ± 22.37	0.231(NOT SIG)
6.	SBP 50	116.00 ± 8.57	111.05 ± 7.16	0.055(NOT SIG)
7.	SBP 60	115.70 ± 9.81	110.25 ± 5.98	0.041(SIG)
8.	SBP 70	116.00 ± 7.38	108.70 ± 8.97	0.008(SIG)
9.	SBP 80	114.80 ± 7.96	112.95 ± 7.51	0.454(NOT SIG)
10.	SBP 90	114.50 ± 7.04	111.80 ± 8.47	0.280(NOT SIG)
11.	SBP 100	113.65 ± 8.56	110.35 ± 7.88	0.212(NOT SIG)
12.	SBP 110	118.35 ± 5.38	112.45 ± 7.30	0.006(SIG)
13.	SBP 120	120.35 ± 5.33	113.75 ± 8.90	0.007(SIG)
14.	SBP 130	117.55 ± 5.05	113.00 ± 8.37	0.044(SIG)
15.	SBP 140	118.70 ± 6.34	114.80 ± 7.46	0.083(NOT SIG)
16.	SBP 150	124.10 ± 3.74	120.00 ± 8.03	0.045(SIG)

FIGURE – 5

HEART RATE

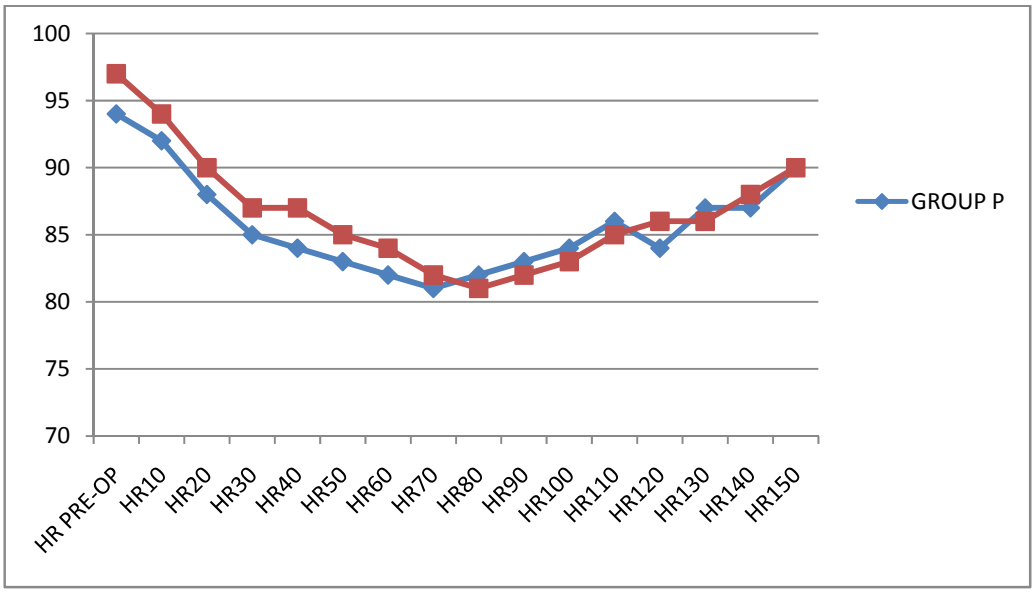


FIGURE – 6

SYSTOLIC BLOOD PRESSURE

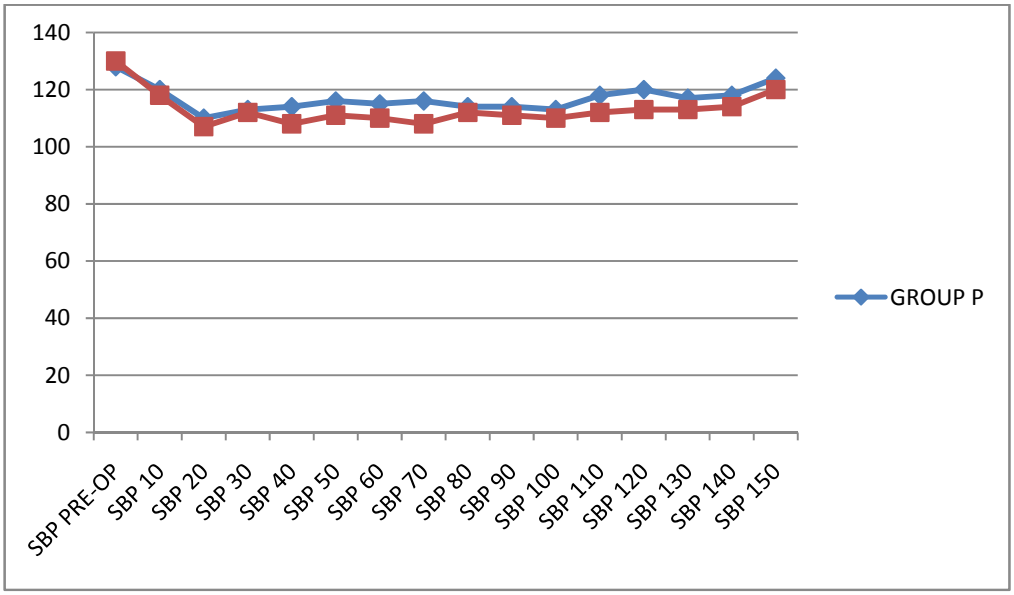


TABLE – 7

DIASTOLIC BLOOD PRESSURE

S NO.	PARAMETERS (MINUTES)	GROUP		P VALUE P<0.05- SIG
		GROUP P	GROUP M	
		MEAN ± SD	MEAN ± SD	
1.	DBP PRE OP	82.40 ± 3.01	81.85 ± 4.93	0.673(NOT SIG)
2.	DBP 10	75.20 ± 8.70	74.00± 6.02	0.615(NOT SIG)
3.	DBP 20	68.15± 10.38	65.50 ± 10.18	0.420(NOT SIG)
4.	DBP 30	69.40 ± 9.63	69.15 ± 6.36	0.923(NOT SIG)
5.	DBP 40	71.60 ± 7.80	67.65 ± 15.14	0.306(NOT SIG)
6.	DBP 50	72.20 ± 8.35	68.70 ± 4.47	0.107(NOT SIG)
7.	DBP 60	73.20 ± 7.88	67.85 ± 3.74	0.009(SIG)
8.	DBP 70	72.55 ± 7.75	66.95 ± 5.60	0.013(SIG)
9.	DBP 80	71.75 ± 6.48	70.70± 4.95	0.568(NOT SIG)
10	DBP 90	72.65 ± 6.55	69.45 ± 4.87	0.088(NOT SIG)
11.	DBP 100	72.50 ± 7.49	69.85 ± 5.54	0.211(NOT SIG)
12.	DBP 110	74.30 ± 5.10	70.45 ± 4.42	0.015(SIG)
13.	DBP 120	75.35 ± 6.67	71.85 ± 5.61	0.080(NOT SIG)
14.	DBP 130	73.30 ± 5.19	70.95 ± 5.07	0.156(NOT SIG)
15.	DBP 140	74.90 ± 6.20	71.65 ± 4.33	0.062(NOT SIG)
16.	DBP 150	79.15 ± 3.04	78.10 ± 4.61	0.401(NOT SIG)

TABLE – 8

MEAN ARTERIAL PRESSURE

S NO.	PARAMETERS (MINUTES)	GROUP		P VALUE P<0.05- SIG
		GROUP P	GROUP M	
		MEAN ± SD	MEAN ± SD	
1.	MAP PRE OP	97.85 ± 3.51	97.90 ± 4.74	0.970(NOT SIG)
2.	MAP 10	90.40 ± 9.34	88.80 ± 5.61	0.516(NOT SIG)
3.	MAP 20	81.85 ± 10.05	78.85 ± 10.35	0.359(NOT SIG)
4.	MAP 30	83.85 ± 9.94	83.80 ± 5.52	0.984(NOT SIG)
5.	MAP 40	86.20 ± 8.15	84.65 ± 4.58	0.463(NOT SIG)
6.	MAP 50	86.70 ± 8.15	83.00 ± 4.66	0.086(NOT SIG)
7.	MAP 60	88.25 ± 8.97	82.05 ± 4.31	0.008(SIG)
8.	MAP 70	86.90 ± 7.38	80.85 ± 6.44	0.009(SIG)
9.	MAP 80	86.00 ± 6.58	84.70 ± 5.55	0.504(NOT SIG)
10.	MAP 90	86.40 ± 6.32	83.45± 5.77	0.132(NOT SIG)
11.	MAP 100	85.85 ± 7.76	83.65± 5.31	0.302(NOT SIG)
12.	MAP 110	89.35 ± 5.30	84.60 ± 5.04	0.006(SIG)
13.	MAP 120	89.80 ± 6.13	85.85 ± 6.22	0.050(NOT SIG)
14.	MAP 130	88.25 ± 4.35	85.05 ± 5.79	0.055(NOT SIG)
15.	MAP 140	88.90 ± 6.07	86.20 ± 4.80	0.127(NOT SIG)
16.	MAP 150	94.00 ± 2.95	91.75 ± 5.15	0.098(NOT SIG)

FIGURE – 7

DIASTOLIC BLOOD PRESSURE

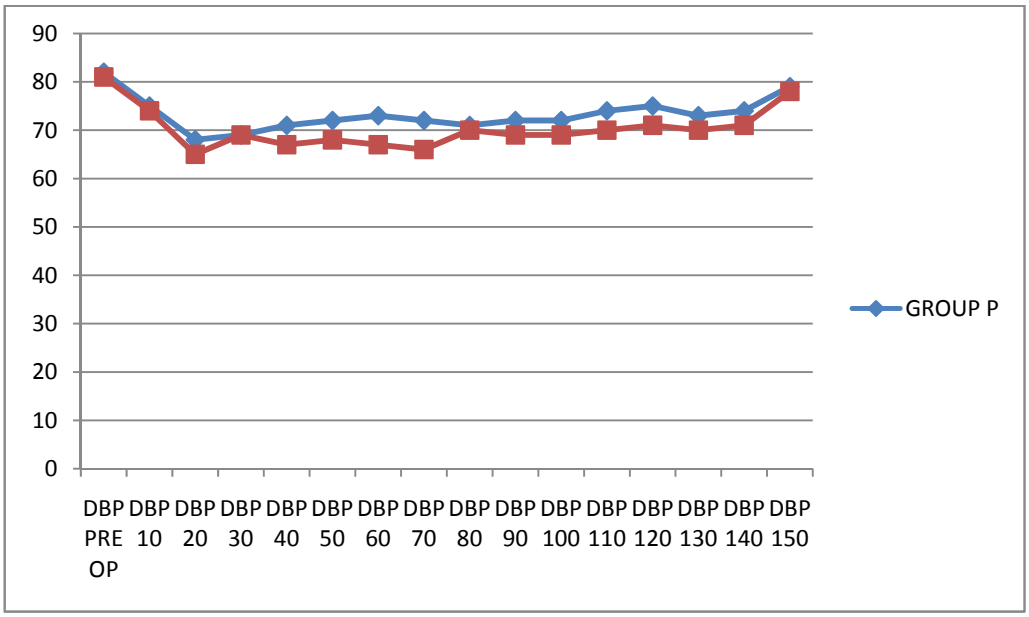


FIGURE – 8

MEAN ARTERIAL PRESSURE

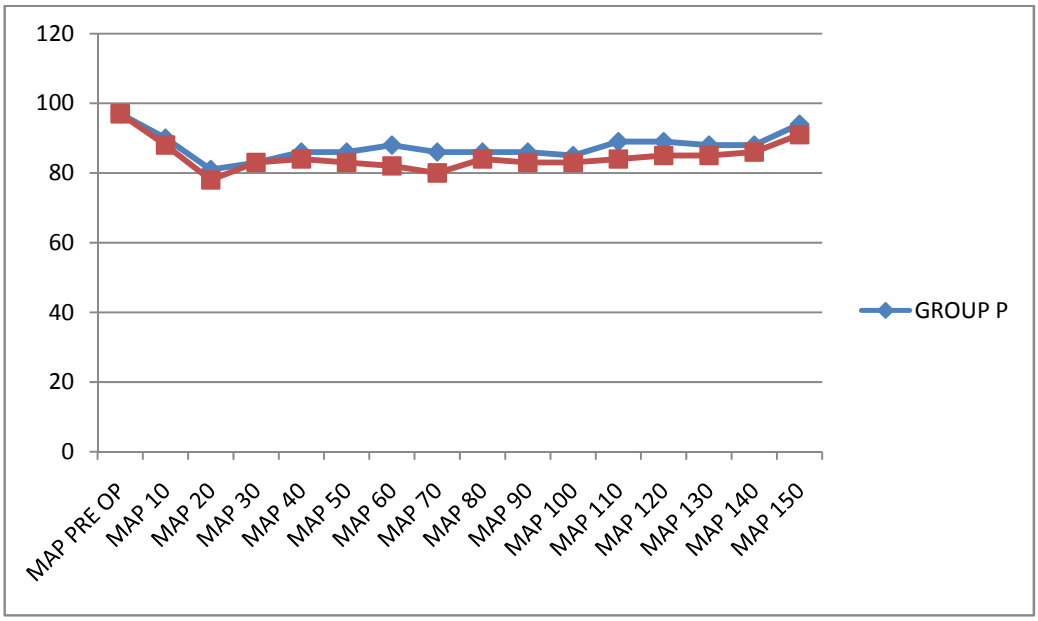


TABLE – 9

RESPIRATORY RATE

S NO.	PARAMETERS (MINUTES)	GROUP		P VALUE P<0.05- SIG
		GROUP P	GROUP M	
		MEAN ± SD	MEAN ± SD	
1.	RR PRE OP	15.80 ± 1.58	19.75 ± 1.56	0.268(NOT SIG)
2.	RR 10	14.45 ± 1.47	15.20 ± 1.28	0.093(NOT SIG)
3.	RR 20	14.65 ± 1.87	15.10 ± 1.41	0.396(NOT SIG)
4.	RR 30	14.40 ± 2.37	14.55 ± 1.76	0.822(NOT SIG)
5.	RR 40	14.10 ± 2.04	14.30 ± 1.45	0.724(NOT SIG)
6.	RR 50	14.25 ± 1.58	14.30 ± 1.49	0.919(NOT SIG)
7.	RR 60	14.45 ± 2.01	14.45±1.27	1.000(NOT SIG)
8.	RR 70	14.55 ± 2.44	14.65 ± 1.27	0.872(NOT SIG)
9.	RR 80	14.70 ± 2.12	14.85 ± 1.35	0.792(NOT SIG)
10	RR 90	14.50 ± 1.76	14.35 ± 1.56	0.777(NOT SIG)
11.	RR 100	14.60 ± 1.50	14.35 ± 1.35	0.583(NOT SIG)
12.	RR 110	14.80 ± 1.73	14.40 ± 1.53	0.445(NOT SIG)
13.	RR 120	14.75 ± 2.07	14.80 ± 1.05	0.923(NOT SIG)
14.	RR 130	15.50 ± 2.91	15.00 ± 1.17	0.480(NOT SIG)
15.	RR 140	14.95± 1.47	14.90 ± 0.97	0.899(NOT SIG)
16.	RR 150	15.00 ± 1.45	15.05 ± 0.99	0.900(NOT SIG)

TABLE – 10

RAMSAY SEDATION SCALE

RSS			GROUP P	GROUP M	TOTAL
30	1	COUNT	20	12	32
		%WITH IN GROUP	100%	60%	80%
	2	COUNT	0	8	8
		%WITH IN GROUP	0%	40%	20%
60	1	COUNT	20	0	20
		%WITH IN GROUP	100%	0%	50%
	2	COUNT	0	20	20
		%WITH IN GROUP	0%	100%	50%
90	1	COUNT	20	6	26
		%WITH IN GROUP	100%	30%	65%
	2	COUNT	0	14	14
		%WITH IN GROUP	0%	70%	35%
120	1	COUNT	20	19	39
		%WITH IN GROUP	100%	95%	97.5%
	2	COUNT	0	1	1
		%WITH IN GROUP	0%	5%	2.5
150	1	COUNT	20	20	40
		%WITH IN GROUP	100%	100%	100%

According to Chi- square test, RSS was significant at 30 min (P-0.003), 60 min (P<0.001) and 90 min (P<0.001). RSS was not significant at 120 min and 150 min respectively.

FIGURE – 9

RESPIRATORY RATE

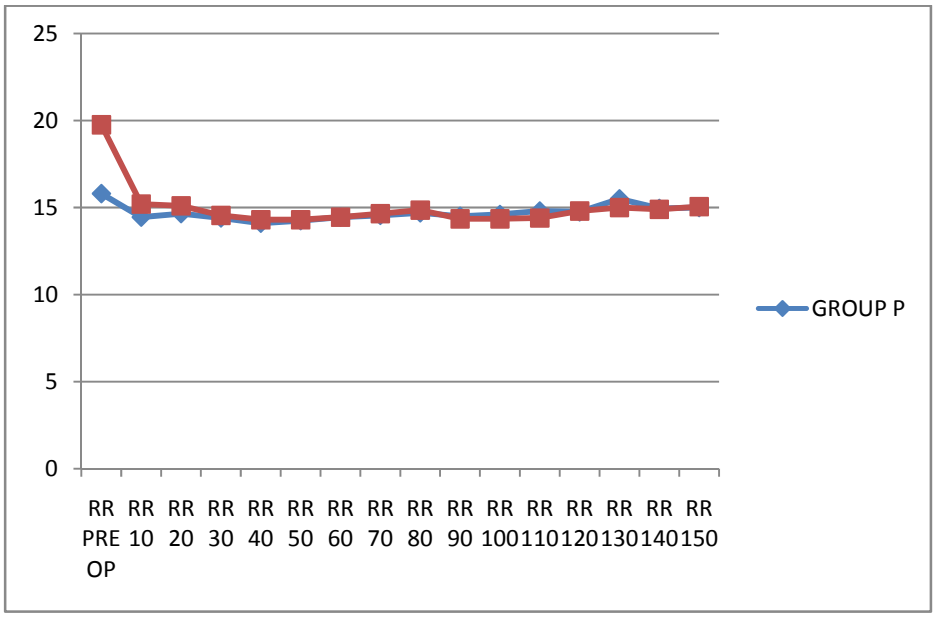


FIGURE – 10

RAMSAY SEDATION SCALE

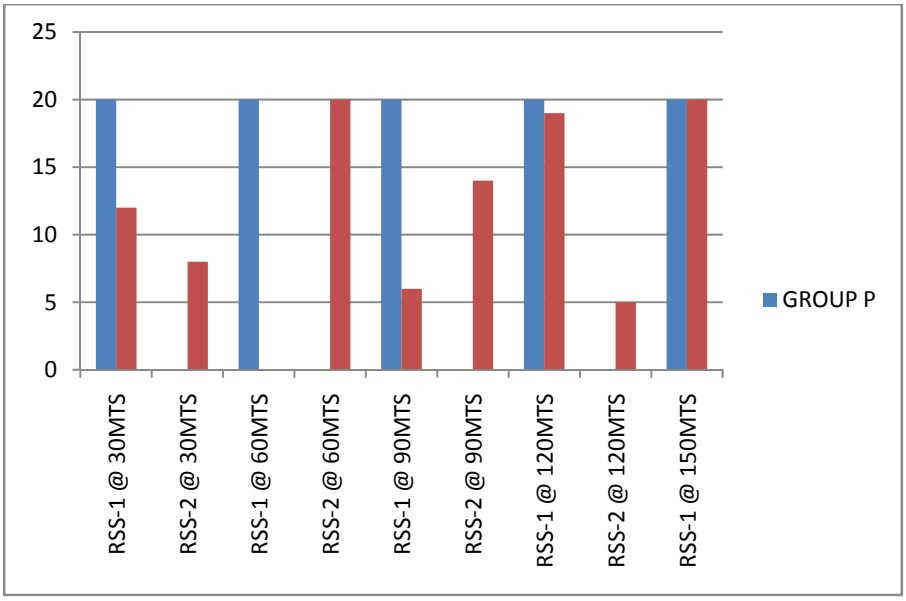


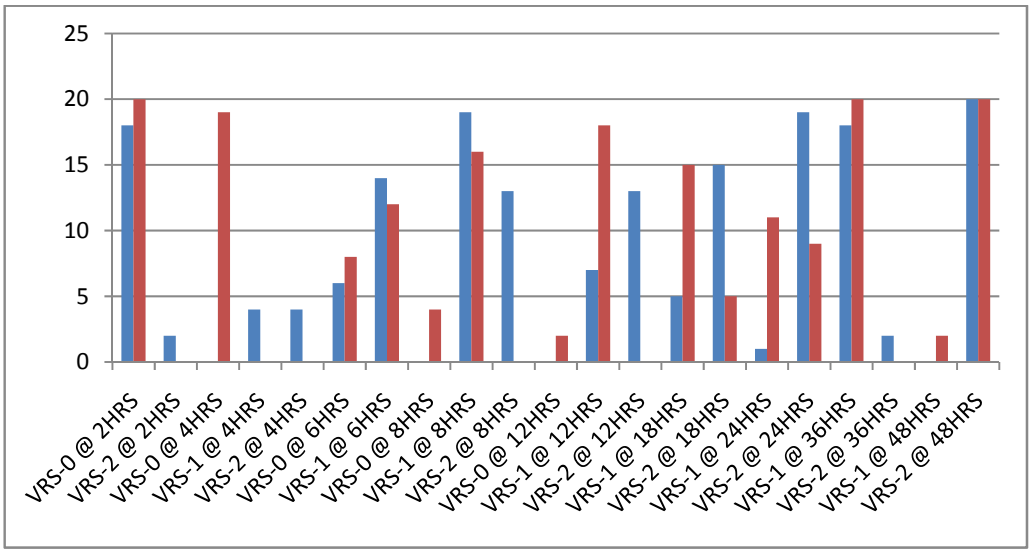
TABLE – 11

VERBAL RATING SCALE

TIME IN HOURS	VERBAL RATING SCALE		GROUP P	GROUP M	TOTAL	CHI-SQUARE TEST
2	0	COUNT	18	20	38	P-0.487
		%WITH IN GROUP	90%	100%	95%	NOT SIG
	2	COUNT	2	0	2	
		%WITH IN GROUP	10%	0%	5%	
4	0	COUNT	0	19	19	P<0.001
		%WITH IN GROUP	0%	95%	47.5%	SIG
	1	COUNT	16	1	17	
		%WITH IN GROUP	80%	5%	42%	
	2	COUNT	4	0	4	
		%WITH IN GROUP	20%	0%	10%	
6	0	COUNT	6	8	14	P-0.741
		%WITH IN GROUP	30%	40%	35%	NOT SIG
	1	COUNT	14	12	26	
		%WITH IN GROUP	70%	60%	65%	
8	0	COUNT	0	4	4	P-0.072
		%WITH IN GROUP	0%	20%	10%	NOT SIG
	1	COUNT	19	16	35	
		%WITH IN GROUP	95%	80%	87.5%	
	2	COUNT	1	0	1	
		%WITH IN GROUP	5%	0%	2.5%	
12	0	COUNT	0	2	2	P<0.001
		%WITH IN GROUP	0%	10%	5%	SIG
	1	COUNT	7	18	25	
		%WITH IN GROUP	35%	90%	62.5%	
	2	COUNT	13	0	13	
		%WITH IN GROUP	65%	0%	32.5%	
18	1	COUNT	5	15	20	P-0.004
		%WITH IN GROUP	25%	75%	50%	SIG
	2	COUNT	15	5	20	
		%WITH IN GROUP	75%	25%	50%	
24	1	COUNT	1	11	12	P-0.001
		%WITH IN GROUP	5%	55%	30%	SIG
	2	COUNT	19	9	28	
		%WITH IN GROUP	95%	45%	70%	
36	1	COUNT	18	20	38	P-0.487
		%WITH IN GROUP	90%	100%	95%	NOT SIG
	2	COUNT	2	0	2	
		%WITH IN GROUP	10%	0%	5%	
48	0	COUNT	0	2	2	P-0.487
		%WITH IN GROUP	0%	10%	5%	NOT SIG
	1	COUNT	20	18	38	
		%WITH IN GROUP	100%	90%	95%	

FIGURE - 11

VERBAL RATING SCALE



GROUP P

GROUP M

TABLE – 12

TIME OF FIRST RESCUE ANALGESIA

	GROUP		**P VALUE**
	GROUP P	**GROUP M**	
	MEAN ± SD	**MEAN ± SD**	
Time of first rescue analgesia(hrs)	3.27 ±0.53	6.05 ± 0.65	0.001 SIGNIFICANT

FIGURE – 12

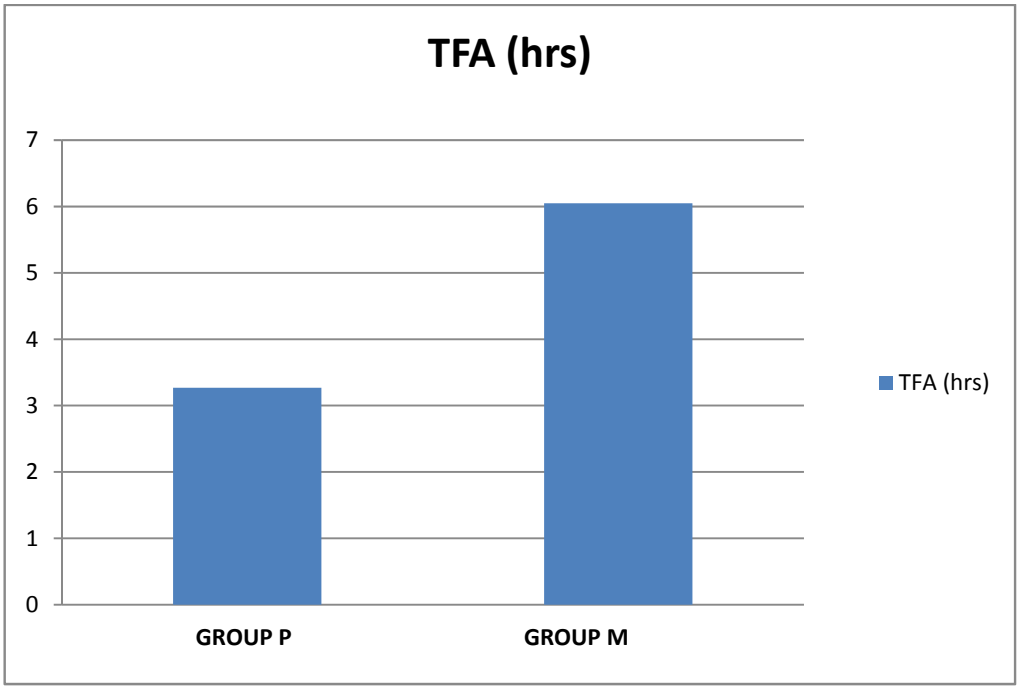


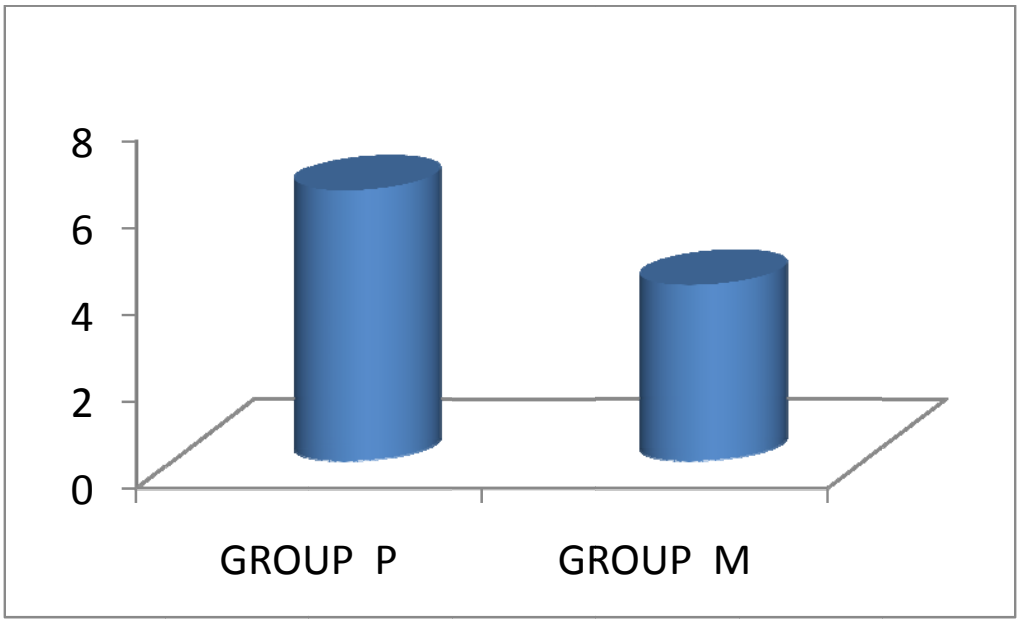
TABLE – 13

NO.OF POST OPERATIVE EPIDURAL TOP-UPS

GROUPS	NO. OF EPIDURAL TOP UPS				AVERAGE NO. OF EPIDURAL TOP UP
	4	5	6	7	
GROUP P	-	-	15	5	6.25
GROUP M	19	1	-	-	4.05

FIGURE – 13

NO.OF POST OPERATIVE EPIDURAL TOP-UPS



DISCUSSION

Our knowledge of acute pain mechanisms has advanced sufficiently over the past decade so that rational rather than empirically derived therapy can be used by aiming specifically at interrupting the mechanisms responsible for the generation of clinical pain. Breakthrough pain after surgical procedures is now beginning to be recognized as constituting suboptimal management. This is an active research area. A number of clinical trials have been conducted to prove the efficacy of anti- nociceptive effect of magnesium using different techniques and different types of drugs with conflicting results. The use of epidural techniques also offer the advantage of effective prolonged postoperative analgesia as compared to nerve blocks and local infiltrations.

Noxious stimulation leads to the release of neurotransmitters which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors. So NMDA receptor antagonists may play a role in the prevention and treatment of post injury pain. Magnesium blocks calcium influx and non-competitively antagonizes NMDA receptor channels[25]. Non competitive NMDA receptor antagonists can have an effect on pain when used alone, but it has also been shown that they can reveal the analgesic properties of opioids[2, 25] .

The safety of intrathecal and epidural magnesium administration has been evaluated in animal and human studies that concluded that magnesium has a good safety profile with no serious side effects[26, 27] . Since the amount of magnesium used in this is study is only 150 mg (50 mg intrathecally and 100 mg through epidural infusion), serum magnesium levels was not monitored during the study. In this study we found that magnesium administered intrathecally and epidurally reduced the amount of analgesic that patients required postoperatively suggesting that magnesium may enhance the analgesic effect of bupivacaine and fentanyl.

In this randomized control study, we have evaluated the analgesic efficacy of bupivacaine with fentanyl and magnesium mixture given through spinal route and epidural magnesium in patient undergoing elective orthopaedic lower limb surgeries.

The level of sedation intraoperatively was monitored using Ramsay Sedation Scale. The patients in group M were well sedated and comfortable than in group P.

Pain intensity was assessed using the verbal rating scale (VRS) post-operatively. Significant lower VRS scores after 2,4,6,8,12,18,24,26,48 hours has in group M demonstrated the clinical

advantage of administering mixture of bupivacaine, fentanyl and magnesium through spinal route for effective postoperative analgesia.

Duration of analgesia was significantly more in group M patients receiving bupivacaine, fentanyl and magnesium mixture (6.05±0.64 hrs) as compared to group P (3.26±0.53 hrs). The demand for supplementary epidural top-ups over 48 hours postoperatively was significantly low in group M than group P.

Hala El-Kerdawy et al[22] in 2008 conducted a similar study but they had a little different results. Duration of spinal anaesthesia was prolonged in magnesium group (182.8±19.1 mins) when compared to placebo group (164.4±16.9 mins). In our study the duration of spinal anaesthesia in magnesium group is 363±38 mins when compared to placebo group(195±32 mins). The difference in the results may be explained by the fact that El-Kerdawy et al performed spinal at L3-L4 interspace or L4-L5 interspace whereas we did it in L2-L3 space and L3-L4 interspace. Total intrathecally injected volume of drug is also different. They used 3 ml whereas in our study it is 3.5 ml.

Time for first rescue analgesia is also different in both studies. In our study, time for first rescue analgesia (TFA) in magnesium group is 363±38 mins. But in my parent study, time for first rescue analgesia (TFA) in magnesium group is 79 mins. This gross difference can be

explained by difference in the definition of TFA in both studies. El-Kerdawy et al defined time for first rescue analgesia as the time from the completion of surgery till the time of first use of rescue medication by PCEA. Since each surgery may have different durations, in our study, we defined time for first rescue analgesia as the time from the injection of the study drug in spinal anaesthesia to the time when verbal rating pain score reaches 1 in the postoperative period.

Two patients of placebo group (10% of group P) and two patients of magnesium group (10% of group M) had episodes of hypotension with a MAP< 70 mm Hg during intraoperative period who were managed with a single dose of ephedrine 6 mg iv and crystalloids , and this may be as a result of epidural bupivacaine as such.

Postoperatively none of the patients had episode of hypotension. No incidence of any bradycardia was noted in both the group during intraoperative and postoperative period.

The significant decrease in postoperative analgesic use obtained in this study is comparable with other studies[5, 19, 20] that proved that intrathecal and epidural magnesium prolongs opioid analgesia and reduce postoperative analgesic requirements.

This finding is different from some studies[16, 18] which suggests that magnesium is not effective in anaesthesia. Their finding can be explained by the different route of magnesium administration (intravenous) they used,which may lead us to the fact that the true site of action of magnesium is spinal cord NMDA receptors[17].

SUMMARY

This randomized control study was designed to assess the effectiveness of using intrathecal and epidural magnesium (Mg) in reducing intra and post operative analgesic requirements and to compare the quality of analgesia of intrathecal bupivacaine-fentanyl-magnesium mixture with intrathecal bupivacaine-fentanyl mixture.

Forty ASA I & II patients undergoing elective orthopaedic lower limb surgical procedure under epidural anaesthesia were randomly allocated into one of the two groups.. Group P (placebo) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2 ml) plus 25 µg of fentanyl (0.5 ml) plus 0.9% NaCl solution (1 ml) . Total intrathecally injected volume is 3.5 ml. Epidural infusion of 0.9% NaCl solution is given in first hour of surgery at the rate of 5 ml/hr.

Group M (Magnesium) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2 ml) plus 25 µg of fentanyl (0.5 ml) plus 50 mg of 5% magnesium sulphate (1 ml). Total intrathecally injected volume is 3.5 ml. Epidural infusion of 2 % magnesium sulphate is given at the rate of 100 mg/hr (5 ml/hr) during first hour of surgery.

Pain in the post-operative period was assessed using a verbal rating scale (VRS). Time of first rescue analgesic(TFA) and the supplementary analgesic doses required for 24 hours were noted for the two groups. Pain score were significantly less in Group M at 2,4,6,8,12,24,48 hours ($P < 0.05$) than in group P. Overall pain score over 48 hours period also revealed better pain relief in group M ($P<0.05$) as compared to Group P.

Time of first rescue analgesic (TFA) in group M was significantly prolonged compared with group P. The postoperative analgesic consumption was also significantly less in group M than in group P. The incidence of hypotension did not differ significantly between the two groups & there was no bradycardia in both the groups.

So this study demonstrates that addition of magnesium to bupivacaine-fentanyl mixture definitely improves the quality of analgesia by reducing the overall pain score, prolonging the duration of the time of first rescue analgesia and causing reduction of total analgesic consumption in the postoperative period without any hemodynamic instability.

CONCLUSION

1. Single dose administration of intrathecal and epidural magnesium to intrathecal bupivacaine-fentanyl mixture provides effective postoperative analgesia in patients undergoing elective orthopaedic lower limb surgeries, without any hemodynamic instability.

2. Epidural magnesium significantly reduces the postoperative analgesic requirements.