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EFFECT OF CLONIDINE AND MAGNESIUM SULFATE USED AS ADJUVANT TO EPIDURAL BUPIVACAINE FOR LOWER LIMB ORTHOPAEDIC SURGERY

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Abstract

Aim: Aim of our study was to evaluate the onset, extent and duration of sensory and motor block and side effects of clonidine or magnesium sulfate when used as an adjuvant to bupivacaine in epidural anaesthesia in lower limb orthopaedic surgery.

Methods:This prospective randomized double blind study was conducted on 60 patients of American society of anaesthesiologists status I and II, posted for lower limb orthopaedic surgery. All patients were randomly allocated into two groups of 30 each; group BC was bupivacaine - clonidine group and group BM was bupivacaine – magnesium sulfate group. Group BC patients received 16 ml of 0.5% bupivacaine and clonidine 2mcg/kg. Group BM patients received 16 ml of 0.5% bupivacaine and magnesium sulfate (50 mg). The onset, extent, duration of sensory and motor blocks, and side effects were recorded.

Results: Magnesium sulfate had earlier onset of sensory and motor block but duration of analgesia was more in clonidine group. Sedation scores were statistically significant with clonidine group in comparison to magnesium sulfate group.

Conclusion: Magnesium sulfate is a better alternative to clonidine as an adjuvant to ropivacaine in epidural anaesthesia in orthopaedic lower limb surgeries for rapid onset of action but clonidine provided prolonged duration of action.

Keywords- Clonidine**,** Magnesium sulfate , Bupivacaine, Orthopaedic**.**epidural

Introduction

.Epidural anaesthesia is a safe and popular technique for surgical anaesthesia as well as for post operative analgesia.[1] It has been shown to blunt the stress response to surgery, decrease intraoperative blood loss, reduce the incidence of postoperative thromboembolic events and decrease morbidity and mortality in high risk surgical patients.[2] It can be used to extend analgesia into postoperative period providing better analgesia than can be achieved with various adjuvants like opioids and other drugs.[3]Clonidine has been used as an adjuvant in regional anaesthesia in various settings.[3] It is an alpha-2 adrenergic agonist that produces analgesia via a non-opioid mechanism. It is also helpful in sparing local anaesthetic doses, which consequently reduces the incidence of side effects associated with larger doses of these anaesthetics.[4] The combination of epidural clonidine with bupivacaine for analgesia has

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been extensively studied and it has been shown to improve analgesia.After sodium, potassium and calcium, magnesium is the most abundant cation in our body. It has antinociceptive effects in animal and human models of pain.[5,6]Noxious stimulus produces an influx of calcium ion through both voltage sensitive calcium channels that facilitates presynaptic release of neurotransmitters and post synaptic N-methyl D-aspartate calcium channels which triggers the sequence of events leading to cellular hyper excitability.[7] Studies in animal models of persistent pain in which central sensitization is present support this theory.[8,9]Magnesium is a relatively harmless molecule, non expensive may provide perioperative analgesia on the biological basis for its potential antinociceptive effect.[10,11,12] These effects are primarily based on physiological calcium antagonism, that is voltage-dependent regulation of calcium influx into the cell, and noncompetitive antagonism of N-methylD-aspartate(NMDA)receptors.[13,14]As, there is no ideal adjuvant drug available for perioperative epidural analgesia, the present study was conducted to compare epidural plain bupivacaine with clonidine and plain bupivacaine with magnesium sulphate in patients undergoing elective lower limb surgery in respect of Onset and duration of sensory analgesia and anaethesia ,Onset and duration of motor block.Hemodynamic parameters and incidence of side effects.

Methods

After getting approval of the Institutional Ethical Committee randomized double blind prospective study was done in 60 patients posted for elective lower limb surgery. This study was conducted in a tertiary care hospital in Odisha.Patients included in the study were of ASA grade I and II,Age from 20 to 60 years,of Either Sex ,Weight 40-70kg. Local infection in the lumbar region, Known hypersensitivity to amide local anaesthetic,Bleeding diathesis,Spinal deformity and chronic pain syndromes were excluded from this study.And Known neurological, cardiac, renal, metabolic and psychological disorder.Randomisation was done by a computer derived random number sequence.Patients were visited on the preoperative day for pre-anaesthetic checkup. Detailed history of present illness, any relevant past history of disease was recorded. Clinical examination of respiratory system, cardiovascular system and central nervous system were done. Vertebral spine was also examined. Laboratory investigations were noted. The patients were explained in detail about the procedure of lumbar epidural block. All their queries and doubts were answered to get their confidence and support.Patients were kept fasting overnight after a light meal.All patients received Tab Alprazolam 0.25 mg orally night before surgery. All patients had an intravenous line with 18G cannula before arriving in the operation theater. After arrival of patients in the operation theater a base line pulse rate, blood pressure, ECG, respiratory rate, SpO_2 were noted. All patients were preloaded with 15ml-20ml/kg of Ringer's Lactate solution over 15-20 minutes before administering epidural block.The drugs were prepared by an anaesthesiologist who was not involved in the study .The patients were kept in sitting position. For epidural anaesthesia 18G Tuohy needle was used. Epidural space(L_{2-3},L_{2-4}) was identified by loss of resistance to air technique. After negative aspiration test for blood and CSF, a test dose was administered with 3 ml of inj. Lignocaine hydrochloride 2% with adrenaline(1:200000). After ensuring proper epidural placement of the needle tip, the study drug was slowly injected in small increments with repeated aspiration test as per protocol. After placement of study drug, epidural catheter was introduced. Monitoring of vital signs

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was continued throughout the procedure. The patients were made supine. No other analgesic was given to the patients intraoperatively. Group BC (n=30) patients with - received total volume of 16ml (15ml of plain 0.5% bupivacaine + clonidine 2mcg/kg made up to 1ml by adding normal saline . On the other hand, Group BM (n=30) -received a total volume of 16ml (15 ml of 0.5% bupivacaine + magnesium sulphate 1ml containing 50 mg). The patients were administered O_2, 3 L/min through face mask. Onset of Sensory Block was assessed by pin prick method at every minutes interval. Time duration was assessed from local anaesthetic solution injection to epidural space to start of loss of pain sensation to pin prick .Duration of Sensory Block: Assessed every 15 minutes postoperatively by pin prick method[15]. Time duration was assessed from onset of sensory block to regression of dermatome of two segments.Onset of Motor Block was Assessed by modified Bromage scale[16] as follows: 0 - no paralysis,1-inability to raise extended leg.2-inability to flex knee,3-Inability to flex ankle joint.Duration of Analgesia : Assessed every 15 minutes postoperatively by 10 cm Visual Analogue Scale (VAS)17. 0 - no pain,10 - worst possible pain.[17]Time duration (minute) was assessed from onset of sensory block to first request for rescue analgesic or VAS score 5 or more.[18]Rescue analgesic injection Tramadol 2mg/kg was given intravenously.Haemodynamic parameters like Heart rate, Systolic BP, Diastolic BP, Respiratory rate were noted at 0, 15, 30, 60, 75, 90, 120, and at 240 mins from administration of epidural anaesthesia. Side effects like nausea, vomiting, hypotension,sedation, shivering, headache, etc were noted.Sedation was assessed on 4 point sedation scale.0-awake and alert,1-mildly sedated,2-moderately sedated,3-deeply sedated.[19]Sample size calculation was done by taking duration of analgesia as primary outcome variable of interest. It was estimated that n = 26 (recruitment target achieved - n = 30 in each group) will be required per group to detect 60 minutes difference in this parameter with 80% power and 5% probability of Type I error. This calculation assumed a standard deviation of 75 minutes in duration of analgesia. For statistical analysis, raw data entered into a MS Excel spread sheet and analyzed by SPSS 21 (statistical software version 21). Unpaired student's t– test was used to compare normally distributed numerical variables. All analysis were two-tailed and p value <0.05 was taken to be statistically significant.

Results:

There was no statistical difference regarding age, sex, weight, height and duration of surgery.

Table 1: Epidural block characteristics

Block characteristics	GROUP BC (mean±SD)	GROUP BM (mean±SD)	P Value
Onset time of sensory block at T 10 (mins)	6.15±2.84	4.54±2.51	0.04
Time to max sensory block (mins)	13.74±3.96	10.34±3.75	0.02
Time for complete motor block (mins)	17.14±5.34	13.36±6.81	0.03
Total ephedrine requirement (mg)	6.35±2.1	5.55±1.8	0.13

Time to achieve T10 block was less in BM group than BC group which was statistically significant.

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Table 2: Epidural block characteristics

Parameters	GROUP BC (mean±SD)	GROUP BM (mean±SD)	P Value
Mean time to two segment regression (mins)	140.45±9.76	150.64±10.15	0.003
Mean time to sensory regression at S 1(mins)	300.18±34.65	350.54±35.84	0.007
Mean time to regression to bromage 1(mins)	260.22±28.26	290.52±25.44	0.008
Time to first rescue top up (mins)	325.18±24.81	360.66±25.8	0.001

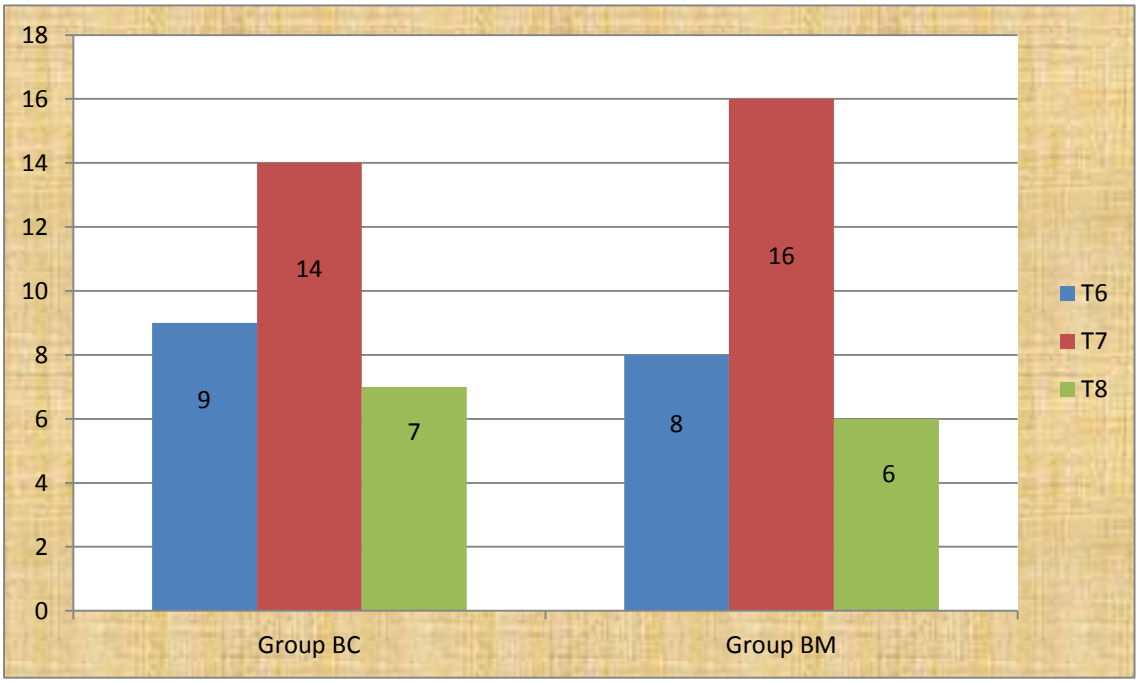

Fig 1: Distribution of block height between study groups

The bar diagram (Fig 1) showing distribution of block height between the groups and it showed no significant differences between the groups.

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Fig:2 Comparison of mean heart rate variability between study groups

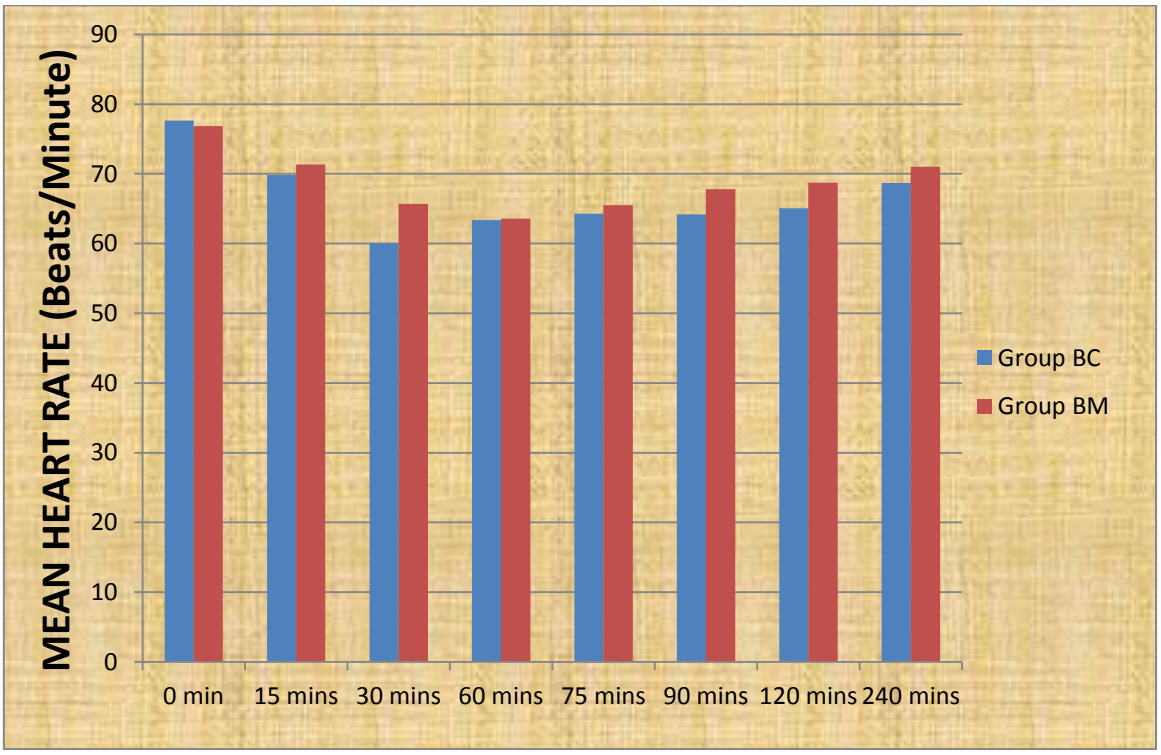
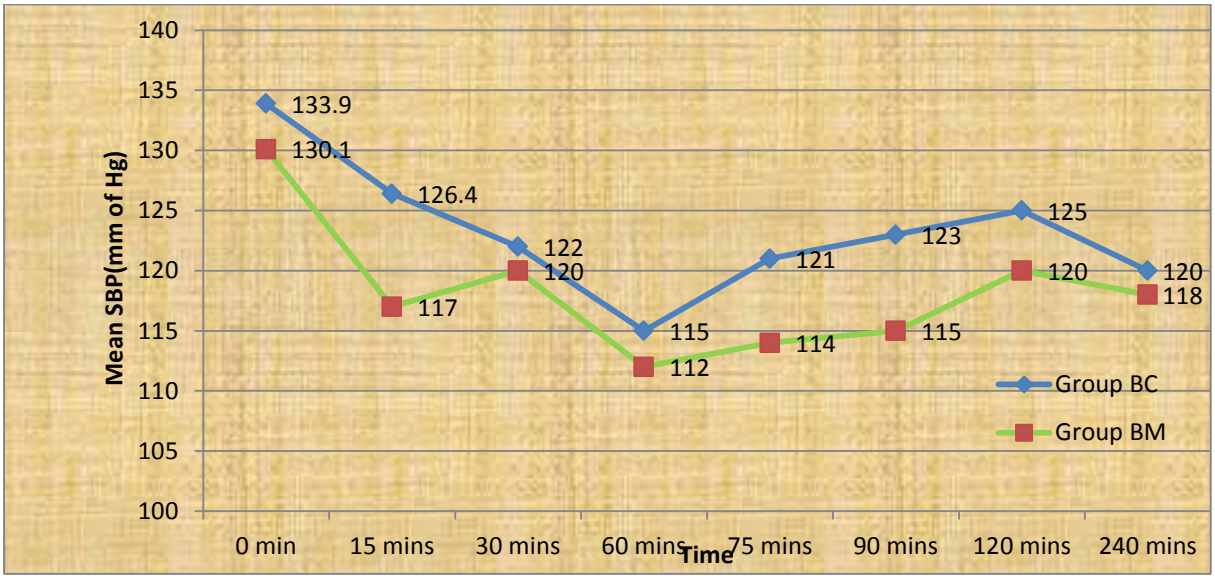


Fig: 3 Comparison of mean systolic blood pressure (SBP) variability between study group.



There was no significant deference for hemodynamic parameters between the groups (Fig 2 & 3)

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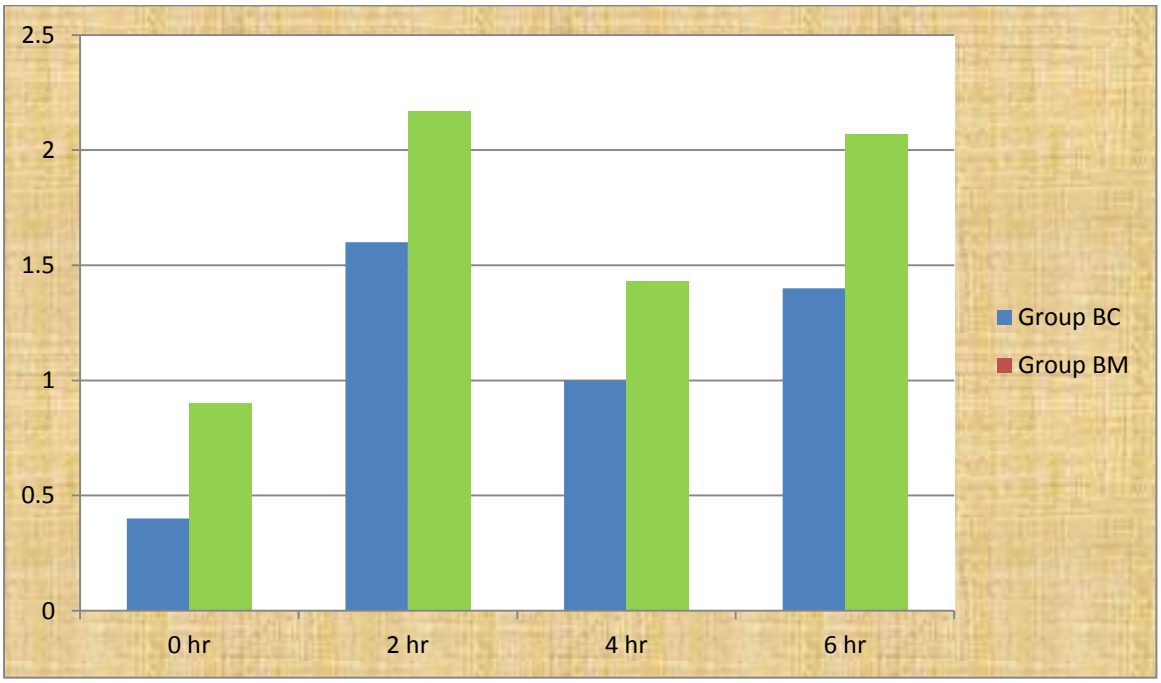
Fig 4: Comparison of VAS score between two groups(postoperatively)



Comparison of VAS score had shown between two groups at 0 hr, 2 hr, 4 hr, 6 hr in post operative period (Fig 4). The VAS was less in 0, 4 and 6 hr in Group BC.Sedation was significantly high in BC group.There was no significant difference in incidence of other side effects between study groups .

Discussion

. The reasonably extensive clinical experience with clonidine reflects the broader experience with alpha2 -adrenergic agonists in regional anesthesia and is consistent with our knowledge of the pharmacology of these agents from the laboratory. Epidural clonidine appears to offer unique advantages over existing agents. Clonidine also produces side effects, primarily hypotension, bradycardia, and sedation.[20]Till now very few studied magnesium as an adjuvant. Mechanism of intrathecal $MgSO_4$ is postulated to be supraspinal. However KO et al with 50mg/kg IV failed to demonstrate an increase in the CSF $MgSO_4$ level. Also they did not find any significant increase in the post-operative analgesia.[21] A. Bilir et al showed that Epidural magnesium reduces postoperative analgesic requirement.[22]Again the primary mechanism of action of $MgSO_4$ being antagonism of NMDA receptors, it can be postulated that quicker onset and relatively prolonged analgesia of $MgSO_4$ with bupivacaine may be due to their direct effects on the nerve roots in the epidural space alone.Ghatak et al showed that addition of magnesium sulphate, a competitive NMDA receptor antagonist as adjuvant to epidural bupivacaine reduces the time of onset of anaesthesia in comparison to clonidine.Both clonidine and magnesium groups were similar in respect to haemodynamic parameters.[23]Their findings were similar to ours.Eisenach et al showed in their study that Clonidine prolongs and intensifies epidural anesthetics without increasing hypotension during surgical epidural anesthesia. In his study clonidine has produced haemodynamic stability which was similar to our study.[24] Riham et al in 2013 showed epidural single dose magnesium sulphate when added to bupivacaine and fentanyl in labor resulted in significantly faster onset and longer duration of action of epidural analgesia compared to bupivacaine and fentanyl only.[25] It was observed in another study that addition of 50mg of

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$MgSO_4$ to 0.5% bupivacaine administered epidurally reduces the onset of sensory block compared to epidural 0.5% bupivacaine with clonidine which was statistically significant.[26] There were no significant change in blood pressure, pulse rate and respiratory rate in both groups. There was no significant increase in side effects except sedation. The onset of motor block was comparable in the two groups. Duration of sensory and motor block was also comparable in the both groups.Duration of analgesia is significantly high in BC group.VAS score is less in BC group.Vital parameters were well maintained during intraoperatively and postoperative period. No significant difference in vital parameters was seen in the two groups.Sedation was found more in BC group in comparison to BM group which was statistically significant.Few other minor side effects like nausea, vomiting, and shivering were found in both study groups but they were statistically not significant.

Conclusion- Epidural magnesium sulfate with bupivacaine produces rapid onset of surgical anaesthesia without any side-effects, but addition of clonidine to epidural bupivacaine produces prolonged duration of anaethesia with negligible side effects.

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