Original Research Article

"Comparative analysis of Magnesium Sulphate Versus Clonidine as an Adjuvant to Epidural Bupivacaine 0.5% in Lower Abdominal and Lower Limb Surgeries"

Ramesh Kumar[1], Jogendra Singh Rajpurohit[2], Pradeep Kumar Saini[3], Fateh Singh Bhati[4]

[1]Department of Anaesthesiology & Intensive Care, Dr. S.N.M.C, Jodhpur, Rajasthan, India
[2]Department of Anaesthesiology & Intensive Care, Dr. S.N.M.C, Jodhpur, Rajasthan, India
[3]Department of Anaesthesiology & Intensive Care, Dr. S.N.M.C, Jodhpur, Rajasthan, India
[4]Department of Anaesthesiology & Intensive Care, Dr. S.N.M.C, Jodhpur, Rajasthan, India

Received: 21-12-2020 / Revised: 30-01-2021 / Accepted: 20-02-2021

Abstract

Introduction: A prospective, randomized, controlled clinical trial was carried out to evaluate the effects ofMagnesium sulphate as an adjuvant to epidural bupivacaine and compared with clonidine along with epidural bupivacaine.**Aims and Objective:** Main objective to evaluate the efficacy of epidural magnesium sulphate& clonidineused as an adjuvant to bupivacaine.**Material and method:** After approval from institutional ethical committee 60 patients undergoing lowerabdominal &lower limb surgeries selected and divided in 2 groups Clonidine group and Magnesium group and different parameters observed.**Observation:** Co-administration of inj. Magnesium sulphate 50 mg. or Clonidine 3µg/kg (150µg maximum) to epidural bupivacaine produced predictable rapid onset of surgical anaesthesia without significant side effects. Addition of clonidine to epidural bupivacaine produced prolonged duration of analgesia with mild sedation compared to magnesium sulphate.**Conclusion:** From the study it is suggested that magnesium sulphate can be a useful alternative as anadjuvant to epidural bupivacaine without any side effects.

Keywords: Magnesium sulphate, clonidine, epidural bupivacaine

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue harm or described in terms of such damage (International Association for Study of Pain). Pain is usually protective and warns of tissue damage prompting treatment. Post-operative pain management can thus improve functionality and reduce the in-hospital stay and also improve the quality of life[1]. Because proactive treatment of acute postoperative pain is considered to be so beneficial, "The Joint Commission on Accreditation of Healthcare Organizations" has recognized that "pain is the fifth vital sign". The aim of good pain management is to reduce it to a comfortable or tolerable level, not necessarily to eliminate it completely. A multi-model approach to pain management combining regional anaesthesia, centrally acting analgesics like paracetamol, peripheral nonsteroidal anti-inflammatory drugs and opioids leads to improved pain relief, better patient outcomes, improved efficacy and reduced side effects, including the long-term benefit of reduced risk of developing chronic pain[1-3].Neuraxial block for lower abdominal and lower limb surgeries are becoming popular as it has many advantages over general anaesthesia. Once administered, it provides an unvarying dense analgesia unlike general anaesthesia (GA), where both the sedation anaesthesia. Once administered, it provides an unvarying dense analgesia unlike general anaesthesia (GA), where both the sedation and the analgesia are dynamic, keep varying and require constant Manipulations[3].Various opioids have been used along with bupivacaine to prolong its effect, to improve the quality of analgesia and minimize the requirement of postoperative analgesics.Clonidine which is one of the adjuvant added to bupivacaine is a centrally acting partial alpha 2 adrenergic agonist that inhibits voltage gated Na+ channels and suppresses the generation of action potentials in dorsal horn cells causing analgesia. Also it decreases activity of second-order neurons and reduces the input from peripheral nociceptive A delta and C fibers. Magnesium is a relatively harmless molecule and not expensive which may provide perioperative analgesia on the biological basis for its potential anti-nociceptive effect.Magnesium ions and NMDA receptors are involved in the modulation of pain as NMDA receptor signalling is important in determining the duration of acute pain. The mechanism of action is the competition between calcium and magnesium in the stimulus-secretion coupling processes in transmitter release, mainly inhibiting pre-synpatic release of acetylcholine at neuromuscular junction.

**Correspondence*
Dr. Fateh Singh Bhati
Department of Anaesthesiology&Intensive Care, Dr. S.N.M.C, Jodhpur,Rajasthan, India.
E-Mail: drraazramesh@gmail.com

Materials And Methods

Following ethical committee approval, a double-blind randomized controlled clinical study was conducted on 60 adult patients admitted for lower abdominal and lower limb procedures under epidural block.

Inclusion Criteria

1. American Society of Anaesthesiologists (ASA) I and II patients
2. Age group of 25-70 years
3. Patient with written valid consent
4. Weight between 45 and 95 kgs,
5. Height between 145 and 170 cms

Exclusion Criteria

1. Patient's refusal
2. Contra indications to the epidural block like

a) Patients with coagulation disorders
b) Patients with pre-existing neurological disease

c) Patients with anatomical abnormalities of spine
d) Infection at the local site
e) Patients with known allergy to local anesthetics
3. Patients with obesity, diabetes, received corticosteroids or immunosuppressive drugs in last 6 months
4. Contraindication to corticosteroids
5. Patients having compromised renal pulmonary and cardiac status
6. Patients on medications like hypnotics, narcotic analgesics or sedatives
7. Patients having known allergy to anesthetic agents used in study
8. Presence of hypotension or any vascular disease
9. History of any seizure disorders
10. Patients with anticipated difficult intubation
11. Patients with ASA grade 3, 4 and 5

Patients were randomly allocated into two groups. Each group consists of 30 patients. They received either of drug solution as below .

1. Group BM:Patients will receive epidural 0.5% bupivacaine 19ml and inj magnesium sulphate (preservative free) 50mg ,1ml (total 20 ml)
2. Group BC:Patients will receive epidural 0.5% bupivicaine 19ml and inj clonidine 3mcg/kg dissolved in NS up to 1ml(maximum 150 mcg) ,total 20 ml.

Preanesthetic evaluation was done to all patients under inclusion criteria. All relevant investigations were done and patient was kept 6 hours fasting overnight. Tablet Alprazolam 0.25 mg and tablet Pantoprazole 40 mg were advised at bedtime on night before surgery. On the day of surgery, in the recovery room, an intravenous line with 18-gauge (G) cannula was secured. Each patient was given injection Ondansetron 0.1 mg/kg on day of surgery. After receiving the patient in the operating room, all routine monitoring namely, non-invasive blood pressure (NIBP), peripheral oxygen saturation by pulse oximetry (SpO2), and electrocardiogram (ECG) were started. Baseline values of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO2) were recorded. The patient was placed in sitting position. Under all aseptic precautions, after painting the area and draping the back, skin overlying L2-L3 or L3-L4 inter-vertebral space was infiltrated with 2% Lignocaine. Epidural block is given using 18 G Tuohy needle. A 20G epidural catheter was advanced for 3 to 5 cm into the epidural space & secured. Correct placement of epidural catheter was verified with test dose of 2% lidocaine with adrenaline (1:200,000) 3 ml. Drug was injected slowly after negative aspiration of cerebrospinal fluid and blood. Injection Midazolam 0.5 mg intravenously(i.v), was given to the patient to allay the anxiety and apprehension. Motor block was assessed by modified bromagescale.Visual analogue scale (VAS) 100 point was used to assess post operative analgesia. Sedation was assessed by Ramsay sedation scale. Mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), oxygen saturation (SpO2) and respiratory rate (RR) measured and recorded before and after epidural drug injection, every 5 min till 30 min and thereafter every 15 min till the end of surgery and then 2 hourly postoperatively for next 24hr. The operation was started on achieving adequate sensory block at T_8 dermatome.Duration of effective analgesia [i.e., time of onset of sensory block to the first request of analgesia] was calculated from Visual analogue scale (VAS) score. VAS was measured every ½ hour, till 3 hour, then every 1hour, till 6hour followed by every 2 hour, till next 24 hour postoperatively either by an observing nurse in the recovery room or the trained ward nurse. During the observation, whenever VAS score was ≥ 4 or the patient was request pain medication, rescue analgesia provided with 10ml bupivacaine (0.20%) via epidural catheter. Duration of analgesia was defined as time interval between activation of epidural block and time to first epidural analgesic requirement. Total dose of rescue analgesic consumed during 24hr postoperative period also be recorded. The time at which patient demanded first dose of rescue analgesia was the primary end point of this study because at this time the effect of epidural block had weaned off. Hypotension was categorized as fall in SBP to less than 90 mmHg or decrease in MAP of more than 20% from the baseline. Bradycardia was when a decrease in heart rate greater than 20% from the baseline present. Respiratory depression defined as SpO2 < 90% on room air. Other side-effects like pruritus, nausea, vomiting, sedation also recorded. Hypotension was treated with intravenous crystalloid/colloid and bolus dose of intravenous Mephentermine 6 mg was given. Bradycardia episodes were treated with injection Atropine 0.6 mg as bolus dose. Nausea and vomiting was treated with injection Ondansetron 4 mg intravenously and pruritus with anti-histaminics.[4-7].

Statistical Methods

The sample size of 30 per group was determined by power analysis; due to the preliminary study results of decrease in onset of time measurements, when delta was assumed to be 3.10 and SD as 4.45, with 80% power and $\alpha = 0.05$, the sample size (n) was calculated to be minimum 30 for each group.All statistical analyses were performed by using SPSS 22.0 software package (SPSS Inc., Chicago, IL, USA). *T* test for independent samples was used to compare two groups for data with normal distribution and Mann---Whitney *U* test was used for comparing data with non-normal distribution. Yates continuity correction test *(Chi square test) ,Fisher's exact test and Fisher---Freeman---Halton test were used for comparison of qualitative data.

Results

There was nil statistical difference pertaining to age, sex, weight and height. The BM group achieved the T_{10} block faster than the BC group which was statistically significant. Maximum height of sensory block and complete motor block was achieved earlier with statistical significant difference by group BM compared to group BC.

Table 1: Demographic Data

Parameter	Group BC	Group BM	P Value
Age	39.13±13.15	42.46±10.76	P=0.287
Weight	57.46±3.97	58.56±5.23	P=0.361
Height	158.53±3.68	158.63±4.27	0.923

Table 2:Inter-group comparison of motor block, sensory block and analgesia in the two study groups

Parameter	Group BC	Group BM	P Value
Onset of sensory block	9.03±1.32	7.70±0.95	<0.0001
Onset of motor block	19.13±4.39	13.43±1.35	<0.0001
Two segment sensory regression	142.66±4.49	134.0±5.63	< 0.0001
Sensory regression to S1	368.33±31.19	313.76±25.00	<0.0001
Motor regression to bromage 1	331.33±43.10	261.26±17.88	< 0.0001
Total Duration of analgesia	414.33±44.69	339.60±22.58	0.164

Time needed for first dose of rescue top up was more in Group BC, which was statistically significant. Likewise the group BC had more ,mean time for two segment regression, sensory regression to S1, motor regression to bromage score 1 when compared to group BM and all were statistically significant.

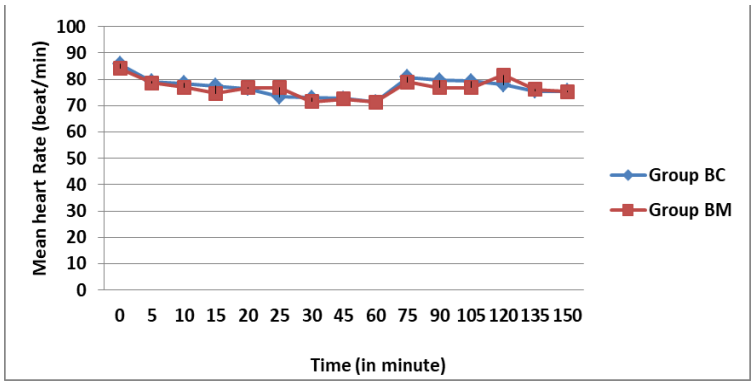

Fig 1:Mean heart rate in both groups

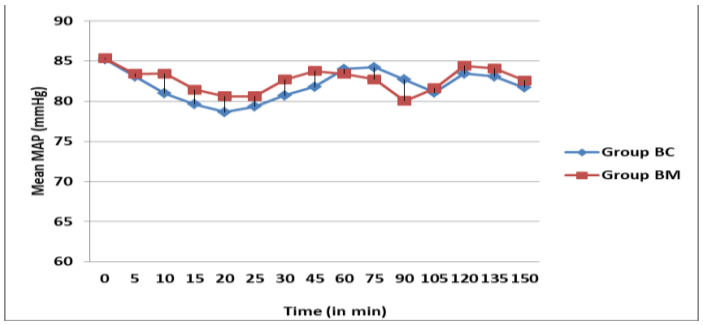

Fig 2:Mean arterial pressure in both groups

No significant changes in the hemodynamic parameters were noticed between the groups

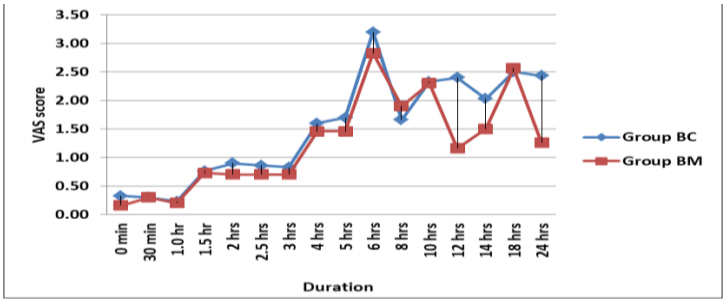

Fig 3:Postoperative visual analog score in both groups

Comparison of VAS score had shown between two groups at 0 hr, 2 hr, 4 hr, 6 hr during the post operative period in the above figure. Group BC had low VAS at 0, 4th&6th hours

Table 3: Adverse effects

Types	Group BC (n=30)	Group BM (n=30)	P value
Hypotension	02(6.67%)	00	0.491
Bradycardia	00	01(3.33%)	0.313
Nausea	03(10%)	04(13.33%)	0.687
Others (shivering)	02(6.67%)	04(13.33%)	0.667

Discussion

In past times many drugs have been used as an adjuvant with local anesthetics. The vast clinical experience with clonidine shows the wider experience with alpha2 –adrenergic agonists in regional anaesthesia. Epidural clonidine seems to offer unique advantages over the prevailing adjuvants. Clonidine also gives rise to side effects like hypotension, bradycardia, and sedation. By far very few studied magnesium sulfate as an adjunct to local anaesthetics in epidural anaesthesia. Mechanism of intrathecal $MgSO_4$ is postulated to be supraspinal. However Ko et al concluded that $MgSO_4$ 50mg/kg IV

failed to demonstrate an increase in the CSF $MgSO_4$ level.Also there is no increase in the post operative analgesic action .Bilir et al found that epidural magnesium sulfate reduces postoperative analgesic requirement. Again the foremost mechanism of action of MgSO4 being antagonism of NMDA receptors, it can be postulated to have faster onset of action and relatively prolonged analgesic effect with bupivacaine could 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 decreases the time of initiation of anaesthesia in compared to clonidine. Clonidine and magnesium groups were identical in respect to hemodynamic parameters.Their findings were similar to ours. Eisenach et al showed in his study that Clonidine prolongs and deepens epidural anaesthesia without causing extreme hypotension during epidural anaesthesia. In his study clonidine has caused hemodynamic stability similar to that of our study. Riham et al showed that epidural single dose magnesium sulphate with bupivacaine in labour analgesia resulted in tremendous faster onset and longer duration of action of epidural analgesia when compared to bupivacaine with fentanyl combination. It was observed in the current study that adding 50mg of MgSO4 to 0.5% bupivacaine given epiduraly decreases the onset of sensory block and onset of motor block when compared to epidural given with 0.5% bupivacaine added to clonidine, which was statistically significant. There were no significant change in blood pressure, pulse rate and respiratory rate in both groups. There was no noticeable increase in side effects except sedation. The BC group had a longer duration of analgesia and lower VAS score. Vital parameters were maintained well intraoperatively and postoperatively with almost nil difference in vital parameters between the two groups. Sedation was found more in BC group in comparison to BM group, which was of statistic significance. Minor side effects like nausea, vomiting, and shivering which were of no significance was seen in both study groups[8-11].

Conclusion

Co-administration of epidural magnesium sulfate 50 mg with bupivacaine produces predictable rapid onset of surgical anaesthesia without any side-effects but addition of clonidine 3µg/kg (150µg maximum) to epidural bupivacaine produces prolonged duration of anaethesia with negligible side effects except sedation. From the study it is suggested that magnesium sulphate can be a useful alternative to clonidine as an adjuvant to epidural bupivacaine without any side effects in lower abdominal and lower limb surgery.

Conflict of Interest: Nil
Source of support:Nil

References

1. Farquhar, Smith WP. Anatomy, physiology and pharmacology of pain. Anaesthesia& Intensive Care Medicine. 2008; 9:3-7.
2. Forster JG, Rosenberg PH. Clinically useful adjuvants in regional anaesthesia. CurrOpinAnaesthesiol. 2003; 16:477-86.
3. Greenberg CP.Practical,cost-effective regional anesthesia for ambulatory surgery. J Clin.Anesth.1995; 7:614-21.
4. Corning JL. Spinal anaesthesia and local medication of the cord. NY Med J. 1885; 42:483-5.
5. Zarr GD, Werling LL, Brown SR, Cox BM.Opioid ligand binding sites in the spinal cord of the guinea-pig. Neuropharmacology. 1986; 25:47–80.
6. Yoon JY, Jee YS, Hong JY. A Comparison of analgesic effects and side effects of intrathecal morphine, nalbuphine and morphine-nalbuphine mixture for pain relief during a caesarean section. Korean J Anaesthesiol. 2002; 42:627-33.
7. Culebras X, Gaggero G, Zatloukal J, Kern C,Marti RA. Advantages of intrathecal nalbuphine,compared with intrathecal morphine, after cesarean delivery An evaluation of postoperative analgesia and adverse effects. AnesthAnalg. 2000; 91:601-5.
8. Tiwari AK, Tomar GS, Agrawal J.Intrathecal Bupivacaine in Comparison With a Combination of Nalbuphine and Bupivacaine for Subarachnoid Block:A Randomized Prospe-ctive Double-Blind Clinical Study. Am J Ther. 2013; 20: 592-5.
9. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N. Intrathecal nalbuphine as an adjuvant to subarachnoid block: What is the most effective dose?Anesth Essays Res. 2011; 5: 171-5.
10. Mostafa MG, Mostafa MF, Farrag WSH. Which has greater effect, intrathecal nalbuphine or intrathecal tramadol. J Am Sci. 2011; 7:480-4.
11. Romagnoli A, Keats AS.Ceiling effect for respiratory depression by nalbuphine.ClinPharmacolTher. 1980; 27:478-85.