

ORIGINAL ARTICLE

COMPARISON OF EFFECTS OF MAGNESIUM SULPHATE V/S CLONIDINE AS AN ADJUVANT TO EPIDURAL BUPIVACAINE IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES

Bhumika A Munshi¹, Ankit Munshi²

Author's Affiliations: ¹Tutor, Dept. of Anesthesia, SMIMER, ²Consultant, Surat, Gujarat

Correspondence: Dr Bhumika Munshi Email: munshibhumi@yahoo.com

ABSTRACT

Introduction: A prospective, randomized, controlled clinical trial was carried out to evaluate the effects of Magnesium 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 & clonidine used as an adjuvant to bupivacaine.

Material and method: After approval from institutional ethical committee 90 patients undergoing lower abdominal & lower limb surgeries selected and divided in 3 groups Control group, magnesium group and clonidine 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 an adjuvant to epidural bupivacaine without any side effects.

Keywords: Magnesium sulphate, clonidine, epidural bupivacaine

INTRODUCTION

Epidural anaesthesia is a safe, well practiced, inexpensive neuraxial block technique with the advantage of providing surgical anaesthesia and postoperative pain control. Bupivacaine is a commonly used local anaesthetic agent for epidural anaesthesia. In many studies various drugs like opioids, ketamine, midazolam, clonidine or neostigmine were added to bupivacaine to prolong its action without any adverse effects. Clonidine is a centrally acting partial α_2 adrenergic agonist which 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 attenuates the input from peripheral nociceptive A δ and C fibers.¹ NMDA antagonists have been shown to be useful in the reduction of acute postoperative pain, analgesic consumption or both.¹ Magnesium ions and NMDA receptors are involved in the modulation of pain as NMDA receptor signalling is important in determin-

ing the duration of acute pain. The mechanism of action at synapses is related to competition between calcium and magnesium in the stimulus-secretion coupling processes in transmitter release, mainly inhibiting presynaptic release of acetylcholine at neuromuscular junction.¹ A prospective, randomized, controlled clinical trial was carried out to evaluate the effects of Magnesium sulphate as an adjuvant to epidural bupivacaine and compared with clonidine along with epidural bupivacaine.

Aims and Objective: We carried out the study to evaluate the efficacy of epidural magnesium sulphate & clonidine used as an adjuvant to bupivacaine and to compare the onset, duration of sensory and motor blockade as well as quality of anaesthesia in both the groups further to compare the hemodynamic status of patients perioperatively in both the groups. Also to compare the duration of postoperative analgesia in both groups and to observe the side effects of magnesium sulphate and clonidine.

METHODOLOGY

After approval from institutional ethical committee 90 patients undergoing lower abdominal & lower limb surgeries aged 20 to 60 years of either sex belonging to ASA I & II were selected for this study. Patients were divided into three different groups. (Each group 30 patients).

Thorough preanaesthetic evaluation was carried out on the previous day of surgery & patients were explained regarding the procedure. Informed consent was taken. We excluded patients with H/O peripheral neuropathy, coagulopathy, spinal deformity, local infection, hypersensitivity to study drugs, patients with renal & cardiac disease, taking antihypertensive medications, history of analgesic use, chronic pain syndrome were excluded from the study.

Preloading was done with I/V infusion of inj. Ringer lactate 20ml/kg. Inj. Glycopyrrolate 0.004mg/kg was given intramuscularly as premedication 1/2 hour before surgery. All patients received lumbar epidural block with 18 G Tuohy needle.

The epidural space was identified at L2-L3 or L3-L4 level, in sitting position, using loss of resistance technique under strict aseptic and antiseptic precaution. 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.

The patients were randomly divided into 3 groups of 30 patients each according to the epidural medication received:

Group A (n =30) (Control group): Inj 0.5% Bupivacaine (19ml) +Inj.0.9% Normal Saline (1ml)

Group B (n =30)(Magnesium group): Inj 0.5% Bupivacaine (19ml) +Inj. Magnesium sulphate (preservative free) 50mg (1ml)

Group C (n= 30) (Clonidine group): Inj. 0.5% Bupivacaine (19ml) + 3µg/kg Clonidine (1ml) (150µg maximum) Volume of epidural injection was kept 20ml in all three groups. Sensory Block was assessed by pinprick method. Motor block was assessed by modified Bromage scale.

Visual analogue scale (VAS) 100 point was used to assess post operative analgesia.

Sedation was assessed by four point sedation scale.

Intra operatively, heart rate, blood pressure and SpO₂ were recorded at every 5 minutes for half an hour then every 15 minutes for 2 hours then half hourly till end of the surgery. Postoperatively heart rate, blood pressure SpO₂ were recorded every hourly up to 6 hrs and 4 hourly up to 24 hours.

The following parameters were observed:

- Time to achieve T6 sensory block.
- Time from epidural medication to two segment regression.
- Time for requirement of 1st rescue analgesic dose. Postoperatively, When VAS \geq 40, epidural tramadol 50mg was given as a rescue analgesic.
- Duration of analgesia-Time to achieve T6 sensory block to time for requirement of 1st analgesic dose.
- Requirement of total rescue analgesics within 24 hours was calculated.
- Sideeffects like hypotension / bradycardia / respiratory depression / sedation / shivering / nausea / vomiting were noted perioperatively.

RESULTS

In our study, time of onset and establishment of epidural block was least in bupivacaine with magnesium group (13.7 \pm 1.7minutes) compared to clonidine group and control group & comparatively less in clonidine group(15 \pm 0.6minutes) than control group (20.3 \pm 1.52minutes). The difference between the groups was statistically highly significant. (p<0.001).

Time from epidural medication to two segment regression(142 \pm 13min in Group A, 145 \pm 14.9min in Group B and 151 \pm .0.6min in Group C) were not statistically significant(p>0.05).

No difference in quality of sensory and motor block noted among the groups.

Table 1: Showing time effects of T6 block in Magnesium sulphate and clonidine groups in different study.

Different study	Magnesium adjuvant group	Clonidine adjuvant group
Tanmoy Ghatak et al (2010)	11.8mins	16.93mins
Noha Sayed Hussien (2011)	10.80mins	13.63mins
Our study	13.7mins	15.2mins

Heart rate, systolic blood pressure, diastolic blood pressure and oxygen saturation remained comparatively stable in group A and group B.

After 30 minutes of epidural injection, fall in heart rate and blood pressure were observed in group C, but no medication was required.

Thus, the difference in pulse rate and blood pressure were significant in Group C compared to Group A and Group B. (P<0.001)

When VAS was ≥ 40 , rescue analgesic was supplemented with inj. Tramadol 50mg epidurally. Variation in VAS score were observed throughout the study period. Statistically significant differences were seen after 90 minutes among three groups. In clonidine group, VAS score remained significantly low (351 ± 32 minutes) up to 6 hour and up to 5 hour (310 ± 37.6 minutes) in magnesium group but group A patients require 1st rescue analgesic dose at 3 hour (179 ± 14 minutes). The difference was statistically highly significant. ($p < 0.001$)

Time for first rescue analgesic was maximum (351 ± 32 minutes) in group C, than (310 ± 37.6 minutes) in group B and while it was minimum (179 ± 14 minutes) in group A. The difference was statistically highly significant. ($p < 0.001$)

Thus, requirement of first rescue analgesic was early in group A compared to group B and C.

Duration of analgesia was maximum in group C 336 ± 31.4 minutes and minimum in group A 158.7 ± 12.48 , whereas it was 296.3 ± 35.9 minutes in group B. The difference was statistically significant. ($p < 0.001$)

Analgesia lasted longer in group C compared to other groups.

Table 2: Showing different side effects of different group

Side effects	Clonidine group	Magnesium group
Sedation	Present	Absent
Shivering	Present	Absent
Heart rate	Reduced	No Change
Blood pressure	Reduced	No Change
Pain	Less compared to magnesium group	More as compared to Clonidine

None of the patients in any group had significant hypotension (i.e. $< 30\%$ of preinduction value) and bradycardia (heart rate < 60 /min).

Total 5 patients (16.7%) in group C had sedation (score 1) at different time interval from 25 to 120 min of epidural injection ($p < 0.05$). patients were closely observed in recovery room.

Shivering experienced in three patients (10%) in control group and five patients (16.7%) in clonidine group where as no patients in magnesium group suffered from shivering, difference among groups were statistically significant. ($p < 0.05$).

DISCUSSION

Tanmoy Ghatak et al (2010) observed that time to achieve T6 block was least in epidural magnesium adjuvant group (11.8 ± 3.21 mins) and highest (18.73 ± 2.79 mins) in control group, where it was 16.93 ± 3.43 mins in clonidine group.² In our study, we also found that addition of magnesium as an adjuvant to epidural bupivacaine had early onset (13.7 ± 0.6 minutes) and establishment of epidural block up to T6 level compared to clonidine (15.2 ± 0.6 mins) and control group (20.3 ± 1.52). They found that addition of clonidine prolongs anaesthesia duration (180.33 ± 29.97 mins). Similarly in our study, duration of analgesia was longer in clonidine group (~ 5-6 hours) than magnesium group (~ 4-5 hours) and control group (~ 3 hours). They had not found significant arterial blood pressure differences in all three groups. The findings were similar with our study. They found sedation in seven patients of clonidine group. Shivering was experienced in seven patients in clonidine group and four patients in magnesium group perioperatively. We also observed sedation in five patients of clonidine group. Incidence of shivering was high in clonidine group (16.7%) compared to control group (10%). Noha Sayed Hussien (2011) observed that time to reach T6 sensory level was 17.71 ± 2.66 mins in control group, 10.80 ± 3.24 mins in magnesium group and 13.63 ± 3.72 mins in clonidine group.³ Similarly in our study shorter onset of duration was found in magnesium group. They observed that time to first postoperative rescue analgesic was longest in clonidine group (162.22 ± 26.92 mins). The results were comparable with our study. They found that patients in clonidine group had decreased in both mean arterial blood pressures and heart rates compared to patients in other two groups. The results were comparable with our study. They observed sedation in clonidine group (6 patients) shivering was present more in clonidine group (8 patients) compared to control group (5 patients) and patients in magnesium group remained hemodynamically stable throughout surgery. Similarly in our study, we observed sedation and shivering in clonidine group and patients in magnesium group remained hemodynamically stable without any side effects.

S.Farouk et al (2008) observed that analgesic consumption in pre-magnesium group was significantly less (78.5ml) than other two groups and dose consumed in post-magnesium group was significantly smaller (91.2ml) than control group (104.6ml).⁴ There were no cases of postoperative hemodynamic or respiratory instability in their study. Similarly in our study, epidural magnesium had effective postoperative analgesia (~ 4-5hour) with good hemodynamic stability.

De Kock et al (1996) observed that after operation epidural clonidine infusion provided complete analgesia lasting 30 ± 21 min in group 1 compared with 251 ± 237 min in group 2 or 369 ± 256 min in group 3.⁵ They concluded that larger doses of epidural clonidine used in the study provide substantial intra and postoperative analgesia without any side effects. In our study, we used single dose of epidural clonidine $3\mu\text{g}/\text{kg}$ had provided longer duration of analgesia (336 ± 31.4 minutes).

Yaun-Shiou Huang et al (2007) observed that clonidine groups experienced less postoperative pain.⁶ The cumulative volume of analgesic solution consumed were C0, 71.8 ± 19.5 ml; C1, 49.6 ± 12.3 ml; C2, 48.1 ± 9.3 ml; C4, 39.4 ± 9 ml. Group C4 used a significantly lower volume of analgesic solution & experienced less intense pain with longer lasting sensory and motor blockade. We used epidural clonidine in dose of $3\mu\text{g}/\text{kg}$ & observed longer duration of analgesia in clonidine group as compared to other group. (~ 5 -6 hour). **Andrew d. Farmery et al** observed that morphine consumption was significantly lower in clonidine group.⁷ The mean consumption at 36 hr was 35mg in clonidine group, compared with 61mg in control group. Similarly in our study, patients who received epidural clonidine required lesser rescue analgesic doses up to 24hour postoperatively. (2.3 ± 0.5)

They also observed lower pain scores in clonidine group as compared to other group. The findings were similar with our study. They observed reduction in heart rate (11-17% patients) and blood pressure in (8-12% patients) in clonidine group but not in other group. Similarly in our study we observed fall in blood pressure and heart rate in clonidine group patients only but no medication required.

CONCLUSION

Co-administration of inj. Magnesium sulphate 50 mg. or Clonidine $3\mu\text{g}/\text{kg}$ ($150\mu\text{g}$ 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. From the study it is suggested that magnesium sulphate can be a useful alternative as an adjuvant to epidural bupivacaine without any side effects.

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