

# Single bolus dose of epidural magnesium prolongs the duration of analgesia in cardiac patients undergoing vascular surgeries

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## ABSTRACT

**Background and Aims:** Magnesium, a physiological antagonist of calcium and N-methyl-d-aspartate, has a role in the prevention of pain in patients undergoing surgery for peripheral vascular diseases with cardiac comorbidities such as ischaemic heart disease and coronary artery disease. The objective of our study was assessment of effects of epidural magnesium in cardiac patients undergoing vascular surgery. **Methods:** Sixty patients of either sex American Society of Anesthesiologists physical status III undergoing surgeries for peripheral vascular diseases were enrolled. The control group had 30 patients who received levobupivacaine 0.25% 10 ml with fentanyl 50 µg while 30 patients in study group received levobupivacaine 0.25% 10 ml with fentanyl 50 µg and magnesium 100 mg. The primary outcome was duration of analgesia. Sedation score, pain assessment using visual analogue scale (VAS), systolic blood pressure (SBP) and diastolic blood pressure (DBP), heart rate (HR), respiratory rate (RR) and fentanyl consumption were also recorded. Statistical analyses were performed using Minitab 15 statistical software. **Results:** Both groups were similar demographically and with respect to baseline HR, SBP, DBP and RR. In the study group, compared to the control group, duration of analgesia was  $4.17 \pm 1.07$  h versus  $1.55 \pm 0.47$  h ( $P < 0.01$ ), sedation score were better ( $P = 0.003$ ) and the VAS scores was lower ( $P < 0.01$ ). **Conclusion:** Epidural magnesium, added to levobupivacaine and fentanyl as a single bolus dose effectively prolongs the duration of analgesia in high-risk cardiac patients undergoing peripheral vascular surgery.

**Key words:** Epidural anaesthesia, magnesium sulphate, N-methyl-d-aspartate receptor, post-operative pain, rescue analgesia

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## INTRODUCTION

Patients with peripheral vascular diseases have associated cardiac, renal, cerebrovascular, and respiratory co-morbidities.<sup>[1]</sup> Regional anaesthesia in these patients has the advantage of reducing respiratory morbidity and postoperative cognitive dysfunction (POCD) while providing good quality post-operative pain relief.<sup>[1]</sup> Effective post-operative analgesia blunts autonomic, somatic and endocrine responses leading to better outcome in cardiac patients.<sup>[2]</sup> The biological basis for the antinociceptive effect of magnesium is the physiological calcium channel and N-methyl-d-aspartate [NMDA] antagonism.<sup>[2,3]</sup> The antiarrhythmic properties make parenteral magnesium efficacious in atrial

and ventricular arrhythmias. It may also have anticoagulant properties, a feature which is receiving greater attention in recent times.<sup>[4]</sup> Magnesium is a predictable and safe adjunct to epidural anaesthesia.<sup>[5]</sup> Hence, it can be useful in patients undergoing surgery for peripheral vascular diseases having cardiac co-morbidities such as coronary artery disease, left

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ventricular dysfunction and ischaemic heart disease in whom robust postoperative analgesia is beneficial. Therefore we designed this study to assess the effects of addition of single bolus dose of magnesium to local anaesthetic and opioid for epidural anaesthesia with respect to improvement in the duration and the quality of analgesia.

## METHODS

After obtaining ethical committee approval and written informed consent, sixty patients of either sex with the age of 40–65 years and American Society of Anesthesiologists physical status III undergoing surgery for peripheral vascular diseases posted for femoral popliteal bypass, with an expected duration of 2 hours, were enrolled in the study. Exclusion criteria were patients with renal dysfunction, hepatic impairment, spine deformity, neuropathy, coagulopathy and those with severe cardiac comorbidities such as triple vessel coronary artery disease or left main coronary artery disease.

Patients were familiarised with the visual analogue pain scale (visual analogue scale [VAS]: 0 - no pain and 100 - worst pain). All patients were premedicated with tablet lorazepam 1–2 mg. The cardiac drugs such as statins, beta-blockers and calcium channel blockers were continued perioperatively. Antiplatelet drugs were stopped 7 days prior while angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers were discontinued 24 hours before the procedure.

On arrival in the operating room, intravenous (IV) access was established with an 18-gauge IV cannula. Monitoring was done by electrocardiogram, pulse oximeter and invasive arterial blood pressure by radial artery cannulation done before epidural catheter placement. Under all aseptic precautions, epidural anaesthesia was administered in the sitting position. Epidural catheter was threaded after locating the epidural space with loss of resistance technique at L3–L4 or L2–L3 intervertebral space with 18-Gauge Tuohy needle and kept 5 cms inside the epidural space. Test dose of 3 ml of 1.5% lignocaine with 1:200,000 adrenaline was given.

Randomization of patients was based on a computer generated code prepared at remote site and sealed in opaque sequentially numbered envelopes. Patients were then allocated as control group having thirty patients who received levobupivacaine 0.25%

10 ml with fentanyl 50 µg and thirty patients in study group who received levobupivacaine 0.25% 10 ml with fentanyl 50 µg and magnesium sulphate 100 mg (0.2ml). The study drug was prepared by another anaesthesiologist unaware of the study. The anaesthesiologist doing the study, the surgeon and the staff were blinded to the drug used.

Sensory block was evaluated by loss to pinprick with a short beveled needle and checked at T10 level. Any pain on pinprick was considered as ineffective sensory block. Intraoperatively sensory block was checked every 20 minutes. The motor block was checked by modified Bromage scale as: 0 – No motor block; 1 – Inability to raise extended leg; able to move knees and feet; 2 – Inability to raise extended leg or move knee but able to move feet; 3 – Complete motor block of limb.<sup>[6]</sup>

Patients were given Injmidazolam 1 mg IV. Hypotension was defined as systolic blood pressure (SBP) <80 mmHg or >30% decrease from baseline which was treated with injection phenylephrine 20–40 µg IV and 50–100 ml bolus of normal saline. Tachycardia was considered significant at heart rate (HR) >120 bpm and bradycardia <50 bpm. Failed epidural was considered when analgesia to pinprick upto T10 level did not occur within 30 minutes. Additional drug administration was not planned owing to the high risk patients in our study groups. If the sensory block did not reach T10 level, the plan was to withdraw the patient from further efficacy of epidural assessment and administer general anaesthesia with endotracheal intubation.

Sedation was assessed on a 5-point sedation score as 1: awake and alert, 2: easily arousable to verbal command, 3: aroused by gentle shaking, 4: aroused by vigorous shaking and 5: unarousable.<sup>[5]</sup>

SBP, HR, RR, onset of sensory block, total intraoperative fentanyl consumption, pain assessment by VAS, analgesia duration, sedation score were recorded postoperatively every hourly up to 10 hours.

Adverse effects such as sedation, respiratory depression, nausea and vomiting, shivering and prolonged motor block were watched closely in the postoperative period.

In the postoperative period patients with VAS <40 were considered to have adequate pain relief. After

the epidural analgesia of the single bolus dose wore off, supplementary IV tramadol 1 mg/kg was given as rescue analgesic whenever patient had VAS >40 and patient's first analgesic requirement was recorded. The duration of post-operative analgesia was defined as time from administration of epidural drug administration to time to first analgesic requirement.

Post-operative monitoring consisted of pulse rate, electrocardiogram, invasive blood pressure monitoring, pulse oximetry, VAS, modified Bromage scale and any complications such as excessive sedation, pruritus, shivering, post-operative nausea and vomiting, urinary retention and respiratory depression (RR <10 breaths per minute or SpO<sub>2</sub> <95% on room air).

All the patients were also observed for any neurologic complications like POCD until 24 h after surgery. Post-operative monitoring was recorded at 30 min interval for 6 h and 1 hourly thereafter for 12 h. Pruritus was assessed and graded as 1: no pruritus, 2: pruritus without scratching, treatment not requirement, 3: pruritus with scratching, 4: severe pruritus and scratching, treatment required and 5: intractable pruritus and scratching.<sup>[6]</sup>

Patients were shifted to ward after fulfilling all the discharge criteria which were completely resolved motor block, stable haemodynamics, satisfactory pain relief, absence of nausea vomiting, drowsiness and respiratory depression.

The sample size estimation was done before the study using duration of analgesia as the primary outcome. Increase by more than one hour in the duration of analgesia in the study group was an important goal. A sample size of 27 subjects in each group was required with the power of 80% for detecting the difference in duration of analgesia at a level of alpha = 0.05. Statistical analyses were performed using the Minitab 15 statistical software (Minitab Inc.) and graphical presentations using MS-Excel. Data were expressed as mean ± standard deviation. Unpaired Student's *t*-tests were used to compare between two groups. *P* < 0.05 was considered statistically significant.

## RESULTS

Sixty patients posted for femoral popliteal bypass surgery were divided into thirty each in study and control group. These patients had single coronary artery disease, mild to moderate left ventricular

dysfunction and ischaemic heart disease along with the peripheral vascular disease. The study group showed increased duration of analgesia 4.17 ± 1.07 h versus 1.55 ± 0.47 h (*P* = <0.01) [Table 1], improved sedation score (*P* = 0.003) [Table 1] and importantly reduced VAS score (*P* = <0.01) [Graph 1]. The total fentanyl consumption was 76.66 µg in study group and 92.5 µg in control group (*P* = 0.002) [Table 1]. The onset of analgesia in study group was 10.13 ± 2.41 min and in control group was 10.53 ± 2.38 min (*P* = 0.522) [Graph 2]. Side effect such as shivering was noticed in four patients in control group and none in the study group. Prolongation of motor blockade did not occur in any patient. Also there was no failed epidural in any group. Nausea, vomiting, pruritus, bradycardia and severe hypotension did not occur in any patient postoperatively [Graph 3-5].

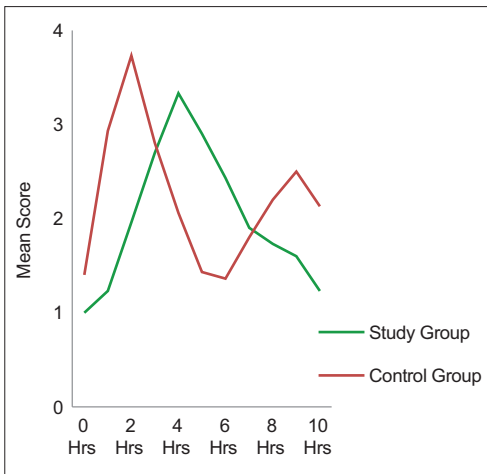
## DISCUSSION

The results of this study show that a single bolus of epidural magnesium 100 mg as an adjuvant to epidural levobupivacaine with fentanyl 1 µg/kg results in prolonged duration of analgesia as compared to levobupivacaine and fentanyl alone in high risk patients.

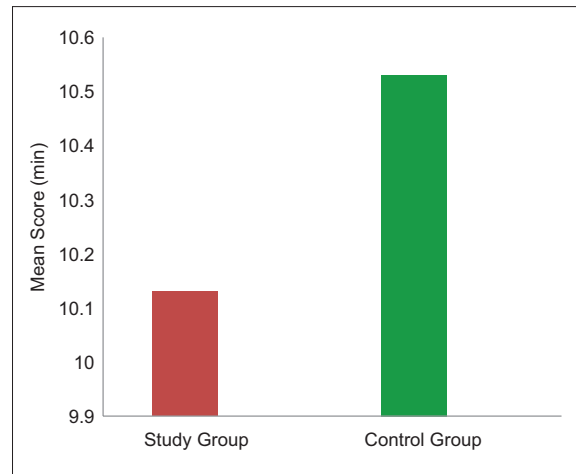
Magnesium blocks calcium influx and non-competitively antagonises NMDA receptor channels. Non-competitive NMDA receptor antagonists have an effect on pain, and they also accentuate the analgesic properties of opioids.<sup>[1]</sup> Administered intravenously, intrathecally or epidurally, the true site of action of magnesium is probably at the spinal cord NMDA receptors.<sup>[7]</sup> The duration and intensity of post-operative analgesia depends on the degree of inhibition of NMDA receptor signal transmission.<sup>[7]</sup> Co-administration of epidural magnesium for post-operative patient-controlled epidural analgesia reduced fentanyl consumption without any side effects.<sup>[2]</sup> Administration of epidural magnesium perioperatively was associated with less analgesic requirement in the post-operative period.<sup>[7]</sup> Bilir *et al.* also reported reduction in post-operative fentanyl consumption without any side effects.

Table 1: Characteristics of epidural anaesthesia

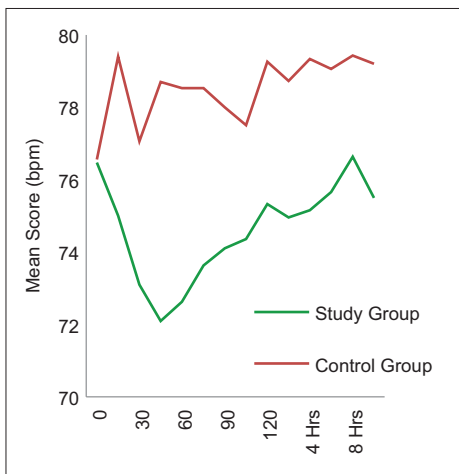
Parameter	Mean±SD		<i>P</i>
	Study group	Control group	
Analgesia duration (h)	4.17±1.07	1.55±0.471	<0.01
Sedation score (h)	1.20±0.40	1.56±0.50	0.003
Intraoperative Fentanyl consumption (µg)	76.66±9.12	92.50±24.69	0.002



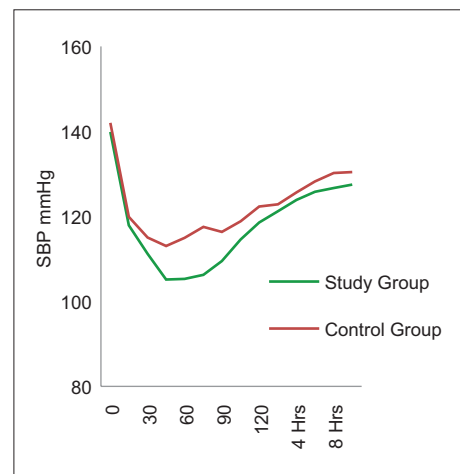
Graph 1: Postoperative VAS – Comparison between two groups



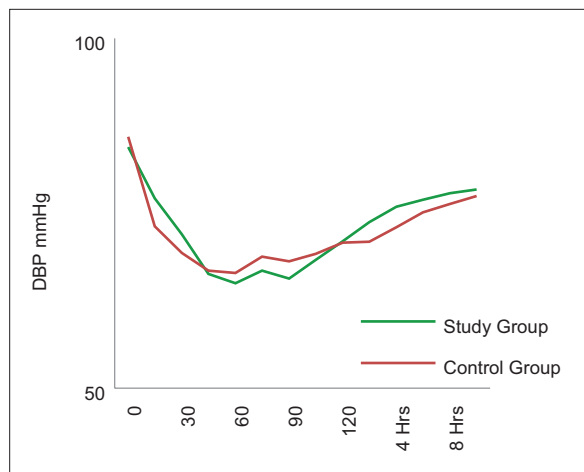
Graph 2: Comparison of onset of analgesia



Graph 3: Comparison of heart rate



Graph 4: Comparison of systolic blood pressure



Graph 5: Comparison of diastolic blood pressure

Hasanein *et al.* concluded that magnesium sulphate in addition to bupivacaine and fentanyl for labour analgesia led to early onset, longer duration of action and reduced breakthrough pain.<sup>[8]</sup>

Furthermore, the neurological outcome after inadvertent administration of large doses of epidural magnesium has been studied and no neurologic deficit has been reported.<sup>[2]</sup>

As fentanyl consumption was less, sedation score was less. Kandil *et al.* mentioned the total amount of fentanyl infusion over 24 h postoperatively is reduced in magnesium group and rescue analgesia is also reduced.<sup>[9]</sup> Co-administration of magnesium with epidural bupivacaine and morphine as a single shot dose decreases intraoperative and post-operative narcotic consumption.<sup>[10]</sup>

Intrathecal magnesium potentiates opioid spinal analgesia while parenteral magnesium reduces intraoperative and postoperative opioid requirement.<sup>[6]</sup> IV magnesium also prolongs opioid-induced analgesia while minimising nausea, pruritus and somnolence.<sup>[11]</sup> And, epidural magnesium has shown to lower the

cumulative dose of local anaesthetic ropivacaine.<sup>[12]</sup> Apart from this, epidural magnesium had no effect on the incidence of chronic post-operative pain after video-assisted thoracic surgery.<sup>[13]</sup>

The limitation of our study was serum magnesium levels were not checked in our study. The drawback of using magnesium in patients undergoing general anaesthesia is increased serum concentration of magnesium *per se* may produce profound paralysis of skeletal muscles. However, in the presence of normal renal function, elimination of magnesium is rapid. Furthermore magnesium may interact with calcium ions at vascular membranes and decrease peripheral vascular resistance.<sup>[14]</sup>

## CONCLUSION

Epidural magnesium as a single bolus dose prolongs the duration of analgesia effectively without any side effects and proves efficacious in high-risk cardiac patients undergoing non-cardiac surgery.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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