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EVALUATION OF SINGLE EPIDURAL BOLUS DOSE OF MAGNESIUM SULPHATE AS AN ADJUVANT TO FENTANYL FOR POSTOPERATIVE ANALGESIA IN ORTHOPAEDIC HIP SURGERIES

M. Santhisree¹, P. Krishnaprasad², B. Sowbhagyalakshmi³, S. Narasimha Rao Babji⁴

HOW TO CITE THIS ARTICLE:

M. Santhisree, P. Krishnaprasad, B. Sowbhagyalakshmi, S. Narasimha Rao Babji. "Evaluation of Single Epidural Bolus Dose of Magnesium Sulphate as an Adjuvant to Fentanyl for Postoperative Analgesia in Orthopaedic Hip Surgeries". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 27, July 07; Page: 7581-7587, DOI: 10.14260/jemds/2014/2940

ABSTRACT: BACKGROUND AND OBJECTIVES: Magnesium has been used as an adjuvant by various routes, including intravenous, intrathecal and epidural in different dosage regimens. This is a prospective, randomized, controlled study designed to assess the efficacy of single bolus administration of Magnesium epidurally as an adjuvant to epidural fentanyl for postoperative analgesia in patients undergoing orthopedic hip surgeries under combined spinal epidural anesthesia. **MATERIALS and METHODS:** 50 Patients of ASA grade I and II aged 35 to 50 years of either gender undergoing orthopedic hip surgeries enrolled in study received combined spinal epidural anesthesia with 3 ml of 0.5% hyperbaric bupivacaine intrathecally. After surgery patients were randomized into Group F (epidural fentanyl 50µg in 10ml saline) and Group FM (epidural magnesium 75 mg along with fentanyl 50µg in 10 ml saline). Rescue analgesic is provided by intravenous tramadol if VAS score >4. Patient's first analgesic requirement time and duration of analgesia were recorded. **RESULT:** The duration of analgesia was significantly longer for Group FM compared to Group F. The frequency of rescue analgesics required in 24 hr postoperative period in Group FM was significantly less than that in Group F. **CONCLUSION:** The administration of magnesium as an adjuvant to epidural fentanyl for postoperative analgesia results in significantly lower VAS with prolonged duration of analgesia as compared to epidural fentanyl alone.

KEYWORDS: Epidural, magnesium, N-methyl-d-aspartate receptor, post-operative pain, rescue analgesia.

INTRODUCTION: Postoperative epidural analgesia after combined spinal epidural anesthesia is one of the accepted techniques of postoperative pain relief.⁽¹⁾ The CSE technique is used routinely for major orthopedic surgeries and in obstetrics.⁽²⁾ The role of epidural anesthesia and analgesia in reducing the incidence and severity of perioperative physiologic derangements, in addition to relieving pain has been reported in several studies.⁽³⁻⁶⁾

Various adjuvants in addition to opioids have been used epidurally to prolong analgesia and reduce the incidence of adverse events observed when opioids are used alone.⁽⁷⁾ Because of its greater lipophilic nature, fentanyl offers some advantages for epidural analgesia. The rapidity of analgesic effects of epidural fentanyl administration and relatively short duration of action makes it the drug of choice for postoperative acute pain.⁽⁸⁾

Magnesium, the non-competitive NMDA antagonist, administered intrathecally or epidurally, is proved to prolong the duration of spinal opioid analgesia.⁽⁹⁾ Co-administration of epidural magnesium for postoperative epidural analgesia has provided a pronounced reduction in patient controlled epidural fentanyl consumption without any side-effects.⁽¹⁰⁾

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N-methyl-d-aspartate (NMDA) receptors present in the dorsal horn of spinal cord have a role in the modulation of central sensitization of noxious stimulus.⁽¹¹⁾ Calcium channel blockers and NMDA receptor antagonists have shown to be beneficial in preventing initiation of pain. Magnesium, a divalent cation through non-competitive mechanism blocks the NMDA receptor in a voltage – dependant manner and results in natural calcium antagonism.⁽¹²⁾

Magnesium possessing anti-nociceptive action has been used as an adjuvant by various routes, including intravenous, intrathecal and epidural in different dosage regimens.^(13,14) On the basis of these evidences, a study was undertaken to compare the effects of epidural fentanyl and fentanyl plus magnesium on duration of analgesia, hemodynamic stability and side effects in patients undergoing orthopedic hip surgeries.

AIMS AND OBJECTIVES: Aim of our study is to evaluate the analgesic efficacy of single bolus dose of magnesium sulphate as an adjuvant to epidural fentanyl for postoperative analgesia.

MATERIALS and METHODS: The present study was a Prospective, randomized double blind comparative study conducted during 2013 June to 2014 March. After obtaining institutional Ethics committee approval, written and informed consent, 50 patients of ASA grade I and II aged 35-50 years of either gender, undergoing orthopedic hip surgeries were enrolled for the study. Thorough pre-anesthetic evaluation and investigations were carried out to find out any associated systemic illness.

Exclusion Criteria: Patients for whom central neuraxial block was contraindicated and those with history of reaction to study drugs, on analgesic therapy and calcium channel blockers, major hepatic, renal or cardiovascular dysfunction were excluded from the study.

Patients were briefed before operation on visual analogue pain scale (vas 0: no pain, 10: Worst pain ever). They were advised overnight fasting and pre-medicated with 0.5mg oral alprazolam at night. On arrival at the operating room, electro cardiogram, non- invasive blood pressure and pulse oximeter monitoring were started. Baseline pulse rate, blood pressure (systolic, diastolic and mean), and oxygen saturation were noted. An intravenous access was established and all the patients were preloaded with lactated Ringer's solution (10ml/kg body weight).

Under all aseptic precautions, patient received CSE anesthesia. The epidural space was identified at L3-L4 or L4-L5 space using a loss of resistance technique. Dural puncture was performed by a needle-through-needle technique with a whitacre 26G needle and 3ml of 0.5% hyperbaric bupivacaine was injected into intrathecal space. Epidural catheter was threaded 4cms in addition to the distance of epidural space and fixed with adhesive plaster on patients back. Sensory block was assessed bilaterally by using pinprick method with short beveled needle. Motor block was evaluated using modified Bromage scale (Table I).

An epidural test dose of 45 mg lignocaine and 1:200000 adrenaline in a volume of 3ml was administered. During the course of operation, epidural bupivacaine 0.5% was given, if required to achieve a block above T8 level. When surgery was complete patients were randomized by computer generated random number assignment into 2 groups of 25 each. After surgery patients were shifted to post anesthesia care unit and Group F (n=25) Patients received epidural fentanyl 50µg in 10ml

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normal saline. Group FM (n-25) Received epidural magnesium 75mg along with fentanyl 50µg diluted in isotonic saline to a total of 10ml.

The drug was prepared by an independent investigator who was not involved in the perioperative management of the patient. Fentanyl was prepared from an ampoule containing 50µg/ml, whereas magnesium dose was prepared from an ampoule containing 50% magnesium (500 mg / ml) which was diluted to 5% in 10ml normal saline and 1.5ml was administered.

Patients were monitored 24 hrs postoperatively for vitals, VAS score for pain and any other side effects such as excessive sedation, pruritis, postoperative nausea vomiting (PONV), urinary retention and respiratory depression. Sedation was assessed on a 4 point scale (Table II).

All the patients were observed for any neurological complications until 24 hrs after surgery. Postoperative monitoring was recorded at 5 minutes intervals for 30 minutes, hourly for the first 6hrs, and 2nd hourly for 12 hrs period and then 24 hrs. If the patients need analgesia, rescue analgesic (intravenous tramadol 50 mg) is given.

Statistical Analysis: The data was compiled and analyzed statistically by using the students't test and a 'p' value of <0.05 was considered as significant and p <0.001 was considered as highly significant. All the scores in our study were analyzed by using the students 't' test and standard error of difference between the two means and chi-square test. Statistical analysis was done by using Graphpad software.

RESULTS: The groups were comparable with respect to age, gender, ASA status (Table III), (Bar diagram I). The duration of surgery was comparable in both the groups (159±22.5 min in Group F vs 163±20.6 min in Group FM (p=0.473).

The sensory and motor block level were comparable prior to administration of epidural drugs in the 2 groups (p=0.7 and 0.52 respectively).

The duration of analgesia after the epidural drug administration was significantly longer for Group FM 340±28.8 minutes, compared with Group F (164±17.1min (p=0.001) (Table IV) (Bar diagram II).

The frequency of rescue analgesic (intravenous tramadol 50mg) required in 24hrs postoperative period in Group FM (2.3±0.5) was significantly less than in Group F (4.3±0.5) (p=0.001) (Tab V). Postoperative pulse rate, systolic, diastolic and mean blood pressure were comparable in both groups and statistically insignificant. (p>0.05).

There was no incidence of hypotension or bradycardia in either of the group postoperatively. There was no incidence of respiratory depression in either of the groups. No patients experienced excessive sedation (median sedation score 0 in both the groups), PONV or pruritis. Two patients each in both the group had urinary retention (p=1).

DISCUSSION: The results of present study show that a single bolus dose of epidural magnesium (75mg) as an adjuvant to epidural fentanyl (50µg) results in prolonged duration of analgesia as compared with epidural fentanyl (50µg) alone. Also VAS was lower in the study group as compared with control group. Concomitant administration of magnesium also reduces the requirements of rescue analgesic with no increased incidence of side effects.

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Noxious stimulation leads to the release of neurotransmitters, which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors. NMDA receptor signaling may be important in determining the duration of acute pain.⁽¹⁵⁾ Therefore NMDA receptor antagonists play a role in the prevention and treatment of post-injury pain. Magnesium blocks calcium influx and non-competitively antagonizes NMDA receptor channels. Magnesium can have an effect on pain when used alone, but it has also been shown that it potentiates the analgesic properties of opioids.⁽¹⁶⁾

In this way the co-administration of magnesium with fentanyl prolongs fentanyl analgesia. In our study 75 mg dose of epidural magnesium in Group FM resulted in lower VAS scores at 2, 3 and 4 hrs postoperatively and our observation coincided with study of Biliar et al.⁽¹⁰⁾ The frequency of rescue analgesia requirement was lower in Group FM in 24 hr study period and our observation coincided with study of Arcioni et al.⁽¹⁷⁾ who studied the effect of combined intrathecal and epidural infusion of magnesium sulphate supplementation.

They concluded that supplementation of spinal anesthesia with combined intrathecal and epidural magnesium significantly reduces patient's postoperative analgesic requirements. The concern of neuromuscular blockade after epidural magnesium administration is emphasized in literature but no impact was noted on motor function in our study when magnesium was administered epidurally (as suggested by modified Bromage score).⁽¹⁸⁾

Also neurologic outcome after inadvertent administration of larger doses of intrathecal and epidural magnesium has been studied and no neurologic deficit has been reported.^(19,20) There were no increased incidence of side effects in magnesium group, although 2 patients in both the groups complained of urinary retention which might have resulted from epidural administration of fentanyl.⁽²¹⁾ Thus in present clinical study epidurally administered magnesium is shown to prolong the duration of fentanyl analgesia without significant side effects.

CONCLUSION: We conclude that the administration of epidural magnesium (75 mg) as an adjuvant to epidural fentanyl (50µg) for postoperative analgesia resulted in prolonged duration of analgesia when compared with epidural fentanyl (50µg) alone. Concomitant administration of magnesium also reduces the requirement for rescue analgesic with no increased incidence of side effects.

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0	No motor block
1	Inability to raise extended legs
2	Inability to flex knees
3	Inability to flex ankle joints

Table I: Showing Modified Bromage Scale

0	Awake and alert
1	Mildly sedated, easily awakened.
2	Moderately sedated, awakened by shaking.
3	Deeply sedated, difficult to be awakened by physical stimulation.

Table II: Showing Sedation – 4 point scale

Variable	Group F (n=25)	Group FM (n=25)
Age in years	39.92 ± 4.23	40.6 ± 4.46
M/F	18/7	18/7
ASA I/II	15/10	16/9

Table III: Showing age and gender distribution

Variable	Group F	Group FM	p Value
Duration of Analgesia (mint)	164±17.1	340 ± 28.8	0.001

Table IV: Showing comparison of duration of analgesia

Time	Group F	Group FM	p value
30 min	0±0	0±0	1
1h	1.4±0.6	1.3±0.7	0.411
2h	2.6±0.1	1.8±0.5	0.001
3h	6.2 ± 1.2	2.3 ± 0.6	0.001
4h	4.1 ± 0.9	2.7 ± 0.5	0.001
5h	2.9 ± 0.1	3.9±1.1	0.02
6h	2.5±0.9	6.2 ±1.4	0.001
8h	2.2 ± 0.7	3.1 ±0.9	0.001
10h	1.9 ± 0.7	2.5 ±0.6	0.001
12h	1.8 ± 0.7	2.2 ± 0.4	0.004
24h	1±0.6	1±0.6	1

Table V: Showing VAS scoring

Bar Dia I: Showing age distribution in the two groups

Bar Dia II: Showing comparison of duration of analgesia

AUTHORS:

1. M. Santhisree
2. P. Krishnaprasad
3. B. Sowbhagyalakshmi
4. S. Narasimha Rao Babji

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesiology, Rangaraya Medical College, Kakinada.
2. Associate Professor, Department of Anaesthesiology, Rangaraya Medical College, Kakinada.
3. Professor and HOD, Department of Anaesthesiology, Rangaraya Medical College, Kakinada.

4. Assistant Professor, Department of Biochemistry, Rangaraya Medical College, Kakinada.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. M. Santhisree,
13-2-2, Saikrishna Towers,
4th Floor, D1, Opposite NGO Home,
Latchiraju Street, Kakinada-533001,
East Godavari District, Andhra Pradesh.
Email: santhisreemulam@gmail.com

Date of Submission: 30/06/2014.
Date of Peer Review: 01/07/2014.
Date of Acceptance: 04/07/2014.
Date of Publishing: 07/07/2014.