Evaluation Of Intravenous Magnesium Sulphate For Postoperative Analgesia In Upper Limb Orthopaedic Surgery Under General Anaesthesia: A Comparative Study

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Citation

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Abstract

Background- This randomised, placebo-controlled, double-blind study designed to assess the efficacy of intravenous magnesium sulphate to reduce postoperative pain in upper limb orthopaedic surgery (duration of surgery≤120minutes) under general anaesthesia using thiopentone, fentanyl, vecuronium,N_2O/O_2 and isoflurane.Method- After obtaining written informed consent from 100 ASA I-II patients, they were divided randomly into two groups of 50 each. Group M received magnesium sulphate 30 mg/kg as a bolus before induction and 10 mg/kg/hour by infusion. Group S patients received same volume of normal saline. All the vital parameters were recorded at the time of start of administering drugs and at 10 minutes interval till the end of study. All patients received injection meperidine 0.5-1mg/kg intramuscular (IM) and diclofenac 75 mg IM as soon as they complained of pain or when the visual analogue scale (VAS) became >3cm. Pain by using VAS, during first hour and 3, 6, 12, 18 and 24 hours after surgery was noted. The timing and dosage of rescue analgesic during first 24hrs after operation was noted.Result- Pain in the postoperative period was significantly lower in group M compared to in group S during first hour and 3,6,12 and 18 hrs postoperatively. Patients in group M were more sedated as compared to group S [sedation score 1.32 vs. 1.88 (p=0.000)]. Rescue analgesia requirement postoperatively was significantly lower in patients of group M than group S.Conclusion- Intravenous Magnesium sulphate decreases postoperative pain and cumulative analgesic requirement without any clinically significant adverse reaction.

INTRODUCTION

Acute pain management came into force as a speciality in 1988 in Seattle where Brain Ready published his concept of acute pain services.[1] It is well documented that pain inadequately relieved is deleterious and can lead to a number of complications in the postoperative period, therefore the pain of surgery must be relieved totally. One intravenous adjuvant medication that has shown potential in pre-emptive analgesia is magnesium sulphate.

Magnesium acts as antagonist at the N-methyl-D-aspartate (NMDA) glutamate receptor in central nervous system.[2] The suggested mechanisms underlying antinociceptive effects of magnesium include the inhibition of Calcium influx (Calcium channel blockers augment morphine induced analgesia and decrease total opioid consumption), antagonism of NMDA receptors and the prevention of enhanced ligand induced NMDA signalling in a state of hypomagnesemia.[3,4] In addition, Magnesium seems to prevent central sensitization after peripheral tissue injury or inflammation because of inhibition of dorsal horn NMDA receptors.[5,6]

Recently the importance of magnesium in anaesthetic practice has been highlighted [7] and since there is no convincing evidence to support analgesic efficacy of magnesium sulphate, therefore it was planned to study the role of magnesium sulphate for postoperative analgesia.

MATERIAL AND METHOD

After hospital ethics committee approval and written informed consent from each patient, a total of 100 patients (18-50yrs) of either sex belonging to ASA physical status I or II, were allocated randomly to two groups. Group M (Magnesium sulphate group) and Group S (Normal saline group).The study was conducted in the Guru Gobind Singh Medical College and Hospital, Faridkot between August 2008 and July 2009. Patients with impaired hepatic and/or

renal function, hypertension, diabetes, neurological disorders, varying degree of heart blocks, history of allergy to anaesthetics or study drug, pregnant women, myopathy, endocrine disorder and patients treated with calcium channel blockers or magnesium were not included in the study.

The study was designed in a randomised, prospective, double blind, placebo-controlled manner. Patients who were included in the study were counselled and explained about visual analogue scale (VAS) for pain.

All patients were examined a day before surgery and were keep fasting for 6hrs before surgery. On arrived to the operation theatre ,monitors were attached and base line vital parameters like heart rate, mean arterial blood pressure (MAP), arterial oxygen saturation(SPO_2),end tidal CO_2 ($EtCO_2$), respiratory rate and ECG were recorded. Standard protocol was followed for all patients throughout surgery. After intravenous line establishment, each patient received injection Glycopyrrolate 0.2mg and injection Ondensetron 4mg intravenously as a premedication. For group M patients, 8ml distilled water was added to 12ml Magnesium sulphate (6000mg) in a 20ml syringe (1ml=300mg) and same volume of normal saline was used for group S patients. The solution were prepared by an anaesthesiologist, who was totally unaware of nature of the study .Patients received 0.1ml/kg of one of these above said solution as a bolus over a period of 15 minutes before induction. Same solution was administered at a rate of 0.03ml/kg /hr as continuous intravenous infusion throughout the surgical procedure.

After preoxygenation for 3mts, patients received Fentanyl (2µg/kg) and they were induced by injection Thiopentone (6mg/kg) and oral endotracheal intubation was facilitated by muscle relaxant Vecuronium bromide (0.1mg/kg). Anaesthesia was maintained with Isoflurane and nitrous oxide in oxygen (FiO_2=0.4). Muscle relaxation was achieved by intermittent bolus dose of Vecuronium. The patients were mechanically ventilated to keep $EtCO_2$ between 35 and 40 mm Hg and normothermia was maintained in operation theatre. Heart rate, MAP, SPO_2 and $EtCO_2$ were recorded throughout procedure at an interval of 10 minutes. During intraoperative period any episode of hypotension and/or bradycardia or any adverse events were noted. At the end of surgical procedure, all the infusions were stopped and residual neuromuscular block was reversed by using Neostigmine (0.05mg/kg) and Glycopyrrolate (0.02mg/kg).

Pain intensity was assessed using a 10cm VAS. Zero denoting no pain and 10 denoting intolerable pain. VAS was evaluated at 1,3,6,12,18 and 24hrs after surgery. Rescue analgesia was provided at VAS >3 in the form of Diclofenac sodium 75mg IM and Meperidine 0.5-1mg/kg IM. Postoperatively, HR, MeanBP, RR, SPO_2 were recorded at 0min., 30min.,1 st ,2 nd, 3 rd, 6 th, 12 th and 24 th hour. The total dose of postoperative analgesics was also recorded. The sedation score was monitored by using a four point rating scale (1- Patient fully awake, 2- Patient somnolent but respond to verbal command, 3- Patient somnolent but respond to tactile stimulation, 4- Patient asleep but respond to pain). During first 4 hrs the patients were kept in recovery room and after that they were sent to ward and analgesic was given on demand.

The data was compiled and represented as mean ± standard deviation (SD). Results were analyzed by Student's't' test for parametric data and Mann-Whitney U test for non parametric data. Differences among the group means were compared using analysis of variance or paired t-test. A 'p' value of <0.05 was considered significant and >0.05 was considered insignificant.

OBSERVATIONS

Both the groups were comparable with respect to age, sex, body weight and the duration of surgery (P>0.05) [Table-1]. Pain reported by the group M was significantly less at 1 st, 3 rd, 6 th, 12 th and 18 th hours after the operation in comparison with group S (P=<0.05). At the 24 th hours post operation, there was no significant difference between the two groups (P>0.05) [Table-2]. Intraoperative and postoperative haemodynamic parameters were very much comparable between the two groups (P>0.05) [Table 3 &Table 4]. Mean sedation score was found to be higher in group M patients then group S patients (P<0.05) [Table-5]. The cumulative requirement in 24hrs of both Meperidine and Diclofenac was statistically significantly less for group M vs. group S (P=<0.05) [Figure-1, ranging from 64+_42.36mg in group M vs 104+_45mg in group S for Meperidine and from 72+_35.82mg to 100+_50.03mg in group M & group S respectively for Diclofenac]. In group M, less patients required a single dose of Meperidine, during the first 24hrs postoperatively, where as in group S, more patients required 2 or more than 2 doses of Meperidine. Similarly, fewer patients required only one dose of Diclofenac sodium during first 24 hrs postoperatively in group M and in control group S more patients required a second dose of Diclofenac sodium to alleviate postoperative pain. No incidence of

bradycardia, hypotension, hypoxia or hypoventilation was recorded during intra as well as postoperative period.

Figure 5

Table 5-Postoperative Sedation score

Variable	Group M (n=50)	Group S (n=5)
Age (years)	35.26 ± 2.12	35.18 ± 2.23
Sex (Male/Female)	27/23	26/24
Weight (kg)	49.50 ± 4.33	51.04 ± 5.17
Duration of surgery(Minutes)	114 ± 10.20	120.74 ± 12.36

Figure 2

Table 2- Assessment of pain in post operative period. Visual analogue scale (1-10)

	Group M(Mean±SD)	Group S(Mean±SD)	P Value
1st	2.84±3.07	5.01±2.78	0.000
3rd	1.94±2.66	3.70±2.53	0.001
6th	2.14±2.69	5.21±3.17	0.000
12th	3.18±3.11	5.61±3.11	0.000
18th	3.68±3.43	6.11±3.40	0.01
24th	6.12±3.35	6.72±3.14	0.358

Figure 3

Table 3- Intraoperative Haemodynamic Monitoring

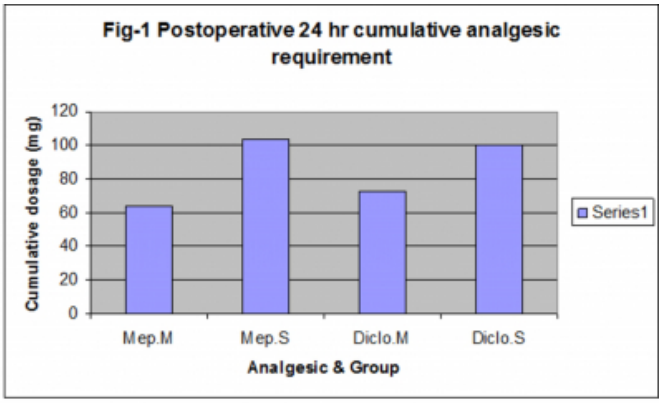
Time mins	HR		Mean BP (mm Hg)		SPO_2 (%)		RR		$EtCO_2$ (mm Hg)	
	Group M	GroupS	GroupM	GroupS	GroupM	GroupS	Group M	GroupS	Group M	GroupS
0	76±3.8	80±4.1	118±3.4	116±4.3	99.9±0.5	99.6±0.5	14±1.5	18±1.5	36±4	36±5
10	78±4.2	80±5.7	118±8.1	115±7.2	99±1.0	99±1.0	14±2.0	16±1.8	36±5	35±4
20	82±6.7	84±7.8	116±7.3	112±6.7	99.6±1.0	99.5±0.6	17±2.2	16±0.9	34±6	33±4
30	83±6.4	82±6.6	116±7.0	112±5.5	98.9±0.55	99.3±0.7	16±1.2	18±1.6	32±4	30±6
60	78±5.7	78±4.8	110±4.9	108±6.8	99.7±0.3	99.3±0.6	18±1.1	17±2.1	35±5	31±5
90	72±7.5	78±5.5	115±5.6	105±7.4	99±0.2	99.8±0.5	18±2.2	17±1.7	33±6	31±6
120	72±4.9	77±5.2	115±5.3	110±4.7	99.9±0.2	99±0.5	17±1.3	14±1.8	33±4	30±6

Figure 4

Table 4- Postoperative haemodynamic parameters

Groups	Mean BP	RR	SPO_2	HR
Group M	110±5.0	16±1.3	99.8±0.5	80±5.1
Group S	105±6.9	17.4±1.4	98.6±0.4	82±4.2
P value	0.94	0.54	0.82	0.68

Figure 6



Mep- Meperidine
Diclo.- Diclofenac
M- Magnesium Sulphate group
S- Normal Saline group

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DISCUSSION

The present study shows that infusion of magnesium sulphate started before induction of anaesthesia and continues throughout procedure, is associated with less postoperative pain and analgesic consumption in patients undergoing upper limb orthopedic surgery. Magnesium sulphate was administered in dosage of 30mg/kg as a bolus followed by 10mg/kg/hr infusion intra-operatively. The dose selected, significantly reduces postoperative pain without episode of severe hypotension and bradycardia. This finding is supported by a study of Ozcan, Tugrul & other[8]. They used same dose of magnesium sulphate as in present study for patients undergoing thoracotomy. However they used magnesium sulphate infusion for 48 hrs postoperatively. A study conducted by Telci & Esen[9] also used similar dose of magnesium sulphate as ours. Elsharnouby and Elsharnouby[10] used magnesium sulphate 40mg/kg over a period of 15 minutes before induction &15mg/kg/hour by continuous infusion intraoperatively. They noticed more episodes of severe hypotension, so in our study we reduced the dose of magnesium sulphate and there was no episode of severe hypotension and bradycardia.

The analgesic effect of magnesium sulphate has shown conflicting results. A study done by Tramer and others[11] observed that IV magnesium sulphate had no analgesic efficacy and no reduction in postoperative analgesic requirements, but they used only diclofenac suppository preoperatively and local nerve block at the end of hernia repair surgery resulting in consistently decreased pain scores. But in our study administration of intraoperative

fentanyl resulted in superior pain relief. This observation is similar to the observations made by Kiran et al[12]. Mentes O and others, Ferasatkish R and others[13,14] also observed the efficacy of magnesium sulphate in reducing postoperative pain following laproscopic cholecystectomy and coronary bypass grafting respectively.

It has been demonstrated in previous studies that after radical retropubic prostatectomy, administration of magnesium sulphate, concomitant with Ropivacaine for postoperative analgesia by infiltration method, leads to significant reduction in Tramadol requirement[15]. A study done by Unlugene H & others[16] also shown that supplementation of spinal anaesthesia with combined intrathecal and epidural Magnesium sulphate significantly reduces patients postoperative analgesic requirements in patients undergoing major abdominal surgery.

Similarly in our study the cumulative requirement of both Meperidine and Diclofenac, in 24hrs was significantly lesser in group M as compared to group S, thus shows a significant beneficial effect of magnesium sulphate. Our results were similar to study done by Bilir A & others[17] and Ray et al[18].

There are number of limitations in our study for example magnesium sulphate potentiates the effect of neuromuscular blocking agents[19]. In our study we did not monitor neuromuscular block. The duration of neuromuscular blockade of Vecuronium were similar because no clinical prolongation of block was observed in our study. Second limitation was that we did not measure serum magnesium concentration because facilities for measurement are not available at our institute.

Magnesium sulphate may induce hypotension by vasodilatation, sympathetic blockade and inhibition of catecholamine release. But we did not observe any hypotensive episode in our study, significant hypotension has been reported by some authors[10] . None of our patients had significant bradycardia.

In our study patients of group M were more sedated in comparison to control group. This effect may be due to central nervous system depression by magnesium sulphate. This result was similar to study done by Kiran et al[12]. Many studies evaluating the effect of magnesium sulphate in postoperative analgesia have not measured the postoperative sedation scores.

To conclude, administration of magnesium sulphate 30mg/kg before induction as bolus & then 10mg/kg/hr by infusion intraoperatively significantly reduces postoperative pain in patients undergoing upper limb orthopedic surgery without any significant increase in adverse effects.

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