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Original Research Article

Impact of $MgSO_4$ Infusion on Elective Neurosurgery Propofol Dosage Reduction

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Abstract:

The potential benefits of using magnesium sulphate as an adjunct to propofol-fentanyl anaesthesia were explored due to propofol's inability to enhance neuromuscular block and the requirement for early postoperative analgesia with fentanyl. This study examines the impact of mgs04 infusion on the necessary propofol dose during elective neurosurgery procedures conducted under propofol infusion anaesthesia. The study was conducted in a hospital in Varanasi, India. Following approval from the Institutional Ethical Committee, patients were required to provide written informed consent prior to their inclusion in the study. The age range of patients in both groups is 20-60 years. The mean age in group T ($MgSO_4$ group) is 41 years with a standard deviation of 12.21 years, while in group C (saline group) it is 37 years with a standard deviation of 10.08 years. In summary, the use of magnesium during surgery has beneficial effects such as anaesthesia, pain relief, and muscle relaxation. This results in a decreased need for anaesthesia drugs during total intravenous anaesthesia.

Introduction

Neuroanaesthesiology today is a fast-growing specialty. The anaesthetic techniques and agents that are used in modern day anaesthesia strongly influence the end result of any neurosurgical procedure. In order to preserve the neuronal function and metabolism and to achieve stable perioperative vitals there is always a constant search of newer and better anaesthetic agents. Preservation of neuronal function by avoiding complications such as hypoxia, hypercarbia and cardiovascular instability has always been priority in neuroanaesthesia [1, 2, 3]. The patients presenting with raised intracranial pressure are at increased risk of developing cerebral ischemia, if the anaesthetic agent causes significant alteration in cerebral haemodynamics. Apart from preserving the neuronal function, the chosen anaesthetic agent should also minimally interfere with cerebral autoregulation and carbon dioxide (CO_2) reactivity [4, 5].

Propofol is the most commonly used induction agent in present day anaesthesia and is fast gaining popularity in neurosurgical anaesthesia due to its favorable effect in neurophysiology. Propofol causes a dose dependent decrease in intracranial pressure, while maintaining cerebral perfusion at modest doses [6, 7, 8]. The other features of propofol for which it is preferred in neurosurgical anaesthesia are reduction in cerebral metabolic rate (CMR) with unaltered glucose and lactate metabolism, undisturbed cerebral reactivity to carbon dioxide and autoregulation during continuous infusion and cerebral protective effects by attenuating changes in ATP, sodium and potassium concentrations after cerebral injury and also by its antioxidant property [9].

Magnesium (Mg) is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist with anti-nociceptive effects. Parenteral magnesium sulphate ($MgSO_4$) has been used for many years as an antiarrhythmic agent and for prophylaxis against seizures in pre-eclampsia. Recently, the importance of magnesium in anaesthetic practice has been highlighted [10]. Noxious stimulation leads to the release of glutamate and aspartate neurotransmitters, which bind to various subclasses of excitatory amino acid receptors, including the N-methyl D-aspartate (NMDA) receptor. Activation of NMDA receptors leads to calcium and sodium influx into the cell, with an efflux of potassium and initiation of central sensitization and windup. Magnesium blocks NMDA channels in a voltage-dependent way, and its addition produces a reduction of NMDA-induced currents [11, 12]. Anaesthetic effect of magnesium is believed to be due to magnesium and calcium ions competition in pre-synaptic calcium channels [13]. The effects of magnesium on the neuromuscular junction can be explained by a reduced release of acetylcholine at the motor nerve terminal, diminished depolarizing action of acetylcholine, and depressed excitability of the muscle fiber membrane, with the first effect being the most important [14].

Magnesium sulphate has been previously investigated as a possible adjuvant for intraoperative and postoperative analgesia. Although magnesium has been used successfully to potentiate opioid analgesia and in treating neuropathic pain in experimental studies [15, 16] clinical trials investigating the analgesic efficacy of magnesium have shown conflicting results [17, 18]. This study aims to evaluate the effect of $MgSO_4$ infusion in reducing intraoperative dose requirement of propofol during elective neurosurgery procedures performed under propofol infusion anaesthesia.

Materials and Methods

The study was conducted in S. S. Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, INDIA. After the approval by the Institutional Ethical Committee, written informed consent was obtained from all the patients before being included in the study. Sixty adult male and female patients of ASA physical status 1 & 2 with average weight and height, aged between 20-60 years and posted for elective neurosurgery were included in the study. The patients were randomly allocated in to two groups by computerized draw of lots namely:

- Group T: The TEST GROUP in which patients received $MgSO_4$ with other anaesthetic medication.
- Group C: It's the CONTROL GROUP in which patients will receive isotonic saline with other anaesthetic medication.

Inclusion criteria

Sixty ASA I–II patients with average weight and height aged between 20 and 60yr of both sex undergoing elective neuro-surgery.

Exclusion criteria

Following categories of patients were excluded from the study-

- Patients with Allergy to magnesium sulphate or any other study drug.
- Patients with Glasgow coma scale score <14/15.
- Patients with any other neurological disorder other than the concerned surgical illness.
- Patients with any Renal, hepatic, or cardiovascular dysfunction.
- Patients with Atrioventricular conductance disturbance.
- Patients with systemic disorders like Hypertension, Diabetes mellitus, respiratory disease.
- Patients with history of Alcohol or Opioid or Analgesic drug abuse.
- Patients receiving chronic treatment with calcium channel blockers or magnesium.
- Patients taking treatment of Anti Tubercular drugs.

Statistical Analysis:

Statistical analysis was done with windows SPSS software version 12.0. The mean and standard deviation of the parameters studied during observation were calculated for two groups and compared using unpaired" t" test. The critical value of "P" indicating the probability of significance difference was taken as < 0.05 for comparison. To test the degree of linear relationship between two variables Kari-Pearson co-efficient of co-relation (r) was determined.

Results

Age distribution

Age of the patients in both the group is between 20-60 yr. Mean age in mgso4 group (group T) is 41yr with SD 12.21yr while that in saline group (group C) is 37 yr with SD 10.08yr. By applying independent sample" t"- test, the P-value was found to be 0.175 which was statistically insignificant and hence both the groups were comparable.

Table 1: comparison of age between group T and group C

AGE		t-value	p-value	Result
Group T Mean±SD	**Group C Mean±SD**			
41.00±12.214	37.03±10.081	1.372	0.175	NS

Sex distribution

Out of 30 patients in group T, 20 were male and 10 were female while in group C, 18 were male and 12 were female. Sex of participants in both groups are comparable and statistically non-significant (p value >0.05).

Table 2: Comparison of sex between group T and group C

SEX	Group T	Group C
	No. (%)	**No.(%)**
Male	20 (66.7)	18 (60.0)
Female	10 (33.3)	12 (40.0)
Total	**30 (100)**	**30 (100)**

Weight of patients

Mean wt of the patients in group T was 55kg with SD 12.21kg while that in group C was 54.33kg with SD 8.31 kg. After applying independent sample "t" test, the P-value was fond to be 0.747 which was statistically insignificant and hence both the groups were comparable.

Table 3: Comparison of weight of patients in group t and group c

WEIGHT			
Group T Mean±SD	**Group C Mean±SD**	**t-value**	**p-value**
55.03±8.483	54.33±8.310	0.323	0.748

Table 4 below shows comparison of average propofol dose requirement in both groups during induction (dose per kg body wt) and maintenance (dose per kg body wt per min of anaesthesia). It was observed that the required mean propofol dose for induction after receiving mgso4 loading dose in group T was lower than group C(not receiving mgso4), but it was statistically not much significant ($p>0.05$).

But required mean propofol dose during maintenance in group T patients (who received fixed dose continuous mgso4 infusion) is significantly lower than group C ($p<0.05$). There for it is also observed that mean total required propofol dose during surgery in group T (0.1192±.02574 mg/kg/min) is much lower than patients in group C (0.1640 ± .01948) and it was statistically very much significant ($p<0.05$).

Table 4: Comparison of total propofol dose requirement during surgery in both groups

	Group T (Mean±SD)	Group C (Mean±SD)	t-value	p-value
Induction propofol dose (mg/kg)	1.5005±.25527	1.5336±.24220	.515	0.608
Maintenance Propofol dose (mg/kg/min)	0.1063±.02087	0.1529±.01545	-9.826	<0.001
Total Propofol dose (mg/kg/min)	0.1192±.02574	0.1640±.01948	-7.590	<0.001

Discussion

Propofol is an excellent agent for neurosurgical procedures due to its favorable effects on neurophysiology. Propofol causes reduction in cerebral metabolic rate (CMR) and intra cranial pressure (ICP) with unaltered lactate and glucose metabolism [19]. Cerebral auto-regulation in response to change in systemic blood pressure and reactivity of cerebral blood flow to changes in $PaCO_2$ are not affected by propofol. In addition, propofol exerts cerebral protective effect by attenuating changes in ATP, sodium and potassium concentrations after cerebral injury and also by its antioxidant property [20].

This study shows that when used with propofol infusion anaesthesia, magnesium sulphate produced similar intraoperative conditions and haemodynamic parameters during the surgery as control. Although it is known that magnesium might induce hypotension directly by vasodilation and decreasing systemic vascular resistance, as well as indirectly by sympathetic blockade and inhibition of catecholamine release. However in our study we did not find any episodes of hypotension or bradycardia that warrant the use of vasopressor or atropine. This is in contrary to some of the studies where episodes of hypotension and bradycardia were observed [20]. This might be due to the preloading that we have done in our patients with 500 ml of Normal saline solution. The heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and the mean arterial pressure (MAP) were on the lower side in magnesium group but were statistically insignificant. In a study Choi et al [13] has maintained the base line values of hemodynamic parameter by changing the propofol infusion rate when the MAP and HR changed and he concluded that the $MgSO_4$ group required less propofol infusion than the other group. These results are also in accordance with the result of Telci et al [21] who adjusted the dose of the remifentanyl and propofol according to the hemodynamic changes. In another study, Tramer et al [9] observed that a bolus of 4gm $MgSO_4$ resulted in rapid but transient decrease in MAP in hypertensive patients but no significant change in normotensive patients. We also observed there was more stable haemodynamics during laryngoscopy and tracheal intubation (LTI) in magnesium group. However the changes in DBP, MAP, and HR were not significant.

We studied the possible effect of magnesium sulphate in reducing the anaesthetic requirements of propofol infusion during general anaesthesia with 50% oxygen-air mixture, vecuronium and fentanyl. More importantly we used Bispectral index (BIS); which is an objective, quantifiable measure of 'depth of anaesthesia' and to maintain the similar anaesthetic depth by propofol we required to keep the BIS between 40 to 60 and ideally towards 50 in both the groups. The BIS value derived from electroencephalogram data has been used as statistical predictor of the level of hypnosis and has been proposed as a tool to reduce the risk of intraoperative awareness. We have chosen BIS monitoring as a measure of an appropriate level of hypnosis in our study, because previous studies have clearly demonstrated a reduction in the incidence of intraoperative awareness using BIS monitoring. In most studies the researchers have reported a nearly 80% reduction in the intraoperative awareness by maintaining a BIS score of 40-60 [19, 20]. Holzer and associates [22], maintained a BIS score of 40-50 and used phenylephrine and glycopyrrolate to treat intraoperative hypotension and bradycardia respectively in their study.

It has been shown that when $MgSO_4$ is co-administered with propofol, it potentiates the anaesthetic effect and NMDA antagonism of propofol. Another mechanism could involve the reduction of catecholamine release through reduced sympathetic outflow and decrease the stress response to surgery which lead to reduced propofol requirement for maintaining anaesthetic depth. This means magnesium act as a part of balanced general anaesthesia with propofol [23]. These result are in accordance with the result of Telci et al [21] who had shown that co-administration of $MgSO_4$ lead to reduction of anaesthetic drug requirement of propofol, remifentanyl and mivacurium during total intravenous anaesthesia (TIVA).

Adequate bolus and infusion doses of MgSO4 are important for effective analgesia intraoperatively and postoperatively. In a comparison of the effects of three different dose regimens of Mg on postoperative morphine consumption [24], a single bolus injection at 40 mg/kg was found to reduce postoperative morphine consumption, and when this was followed by a maintenance infusion of 10 mg/kg/h, the effect was enhanced. Moreover, increasing the maintenance infusion to 20 mg/kg/h provided no additional advantage and induced unwarranted haemodynamic effects. Pre- and intraoperative administration of $MgSO_4$ (50 mg/kg bolus and maintenance 15 mg/kg/hr) in gynaecology patients receiving total intravenous anaesthesia reduced rocuronium requirement and improved the quality of analgesia without any significant side-effects [12]. Accordingly, in the present study, we administered a 50 mg/kg bolus and a maintenance dose of 8 mg/kg/hr.

Limitation of this study

Firstly, we did not measure the preoperative serum magnesium level of our subjects and did not assess the correlations between the magnesium level versus total anaesthetic requirement intraoperatively. Secondly, we used only one regimen for magnesium infusion, while clinical studies showed that magnesium causes a dose dependent CNS depressant and negative ionotropic effect which could be the main reason for decreased anaesthetic requirement in our study. Thirdly, we also did not measure postoperative serum magnesium level in any patient, but we did not find any postoperative symptom related to magnesium toxicity like respiratory depression, decreased urine output or sluggish reflexes in any of patient receiving $MgSO_4$ infusion. Lastly, we did not evaluate the cost effectivity of $MgSO_4$ propofol combination compared to other anaesthetic medication. Schulz et al166 showed that 21-35% reduction in cost with magnesium in a 2hr anaesthesia.

Conclusion

In conclusion, magnesium has anaesthetic, analgesic and muscle relaxant properties and its intraoperative use leads to a significant reduction in the doses of anaesthetic drugs required during total intravenous anaesthesia. Although a number of studies suggest a clinically relevant effect of magnesium, its actual efficacy as an adjuvant to analgesics and anaesthetics to induce and maintain general anaesthesia remains unclear and requires evaluation in larger and randomized clinical trials. The high therapeutic index and cost-effectiveness of magnesium still makes it a potent adjuvant drug for maintaining anaesthesia and with its appropriate use it can improve surgical outcome and patient's satisfaction.

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