Effect of single-dose magnesium sulfate on total postoperative analgesic requirement in patients receiving balanced general anesthesia- A prospective, randomized, placebo controlled study

Vinod Kumar Verma[1], Arvind Kumar[2,*], Chandrakant Prasad[3], Mumtaz Hussain[4]

[1]Professor, [2]Associate Professor, [3]Junior Resident, [4]Associate Professor, Dept. of Anaesthesiology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

***Corresponding Author: Arvind Kumar**
Email: arvind007kumar@yahoo.com

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Abstract

Aim: The aim of this study was to see the effect Single-Dose Magnesium Sulfate on total Postoperative analgesic requirement in patients receiving balanced general anesthesia.

Materials and Methods: 100 ASA status I & II patients of age >20 years & < 60 years posted for elective abdominal surgeries under general anaesthesia were randomly allocated into two groups. Group M (n=50) - patients were given magnesium sulphate 50 mg/kg in 100 ml NS infused over 10 minutes just prior to induction of balanced general anaesthesia & Group P (n=50) – patients were given 100 ml NS infused over 10 minutes as placebo just prior to induction. Balanced general anaesthesia was given as per preset protocol and intraoperative vitals were recorded at regular intervals. In PACU after complete recovery from anaesthesia NRS score was noted. Tramadol was given when NRS > 4. Total tramadol consumtion over 24 hours after surgery was calculated for each group.

Results: In group P post-operativly NRS score was significantly higher in at 6, 12, 18 and 24 hours. Consumption of tramadol was significantly more in group P.

Conclusion: Ten minutes before induction of balanced general anaesthesia 50 Mg/Kg magnesium sulphate mixed in 100 ml of normal saline given to alley post-operative pain and significantly reduces post-operative analgesic consumption after open abdominal surgeries.

Keywords: Magnesium sulfate, Post-operative analgesia, Placebo, Balanced general anesthesia.

Introduction

Postoperative peace and comfort depends upon postsurgical pain. There are intense inflammatory response associated with abdominal surgery resulting in moderate to severe postoperative pain perception.[1–3]

The major goal in postoperative pain management is to provide good analgesia using minimal drugs especially narcotics to reduce side effects. Earlier mobilization, shortened hospital staying, reduced hospital costs, and increased patient satisfaction depends upon good post-operative pain relief.[4,5]

Narcotics are the most common analgesics which are used after the surgeries but there is continuous search for replaceable methods with fewer side effects and cost.[6,7]

Before any painful stimulus, Preemptive analgesia is a better choice to decrease the physiological effects of nociceptive stimulation. Preemptive analgesia is an anti-nociceptive measures for prevention of altered central processing of afferent input from injuries. Magnesium sulphate is one of the agents that can be used as premptive analgesic agents. Magnesium sulphate is also used as an anticonvulsant or antiarrhythmic agent. The analgesic effects of magnesium sulphate may be due to interference with calcium channels and N-methyl-D-aspartate (NMDA) receptor, but exact mechanism of action is not yet clear. It seem that altering nociceptive central sensitization are responsible for analgesic action of N-methyl-D-aspartate (NMDA) receptor. Reduction of catecholamine release and thus decreasing peripheral nociception or the stress response to the surgery may be the another mechanism of analgesic action.[6,13-15] This study was done to find out the total post-operative analgesic requirement in patients undergoing balanced general anaesthesia after pretreatment with single dose magnesium sulphate.

Materials and Methods

This study was conducted at Indira Gandhi Institute of Medical Sciences, Patna, and Bihar, India after taking approval from the Institutional ethics Committee and getting it registered with clinical trial registry of India viz. registration number CTRI/2017/10/010088. The duration of study was 6 months and was done from October 2017 to April 2018 to. This is a prospective randomized double blind placebo controlled clinical study. From every patient written informed consent was taken. 100 ASA status I & II patients of age >20 years & < 60 years posted for elective abdominal surgeries under general anesthesia, who were willing to give written consent were taken in this study. Patients with co-morbidities such as cardiac, renal, respiratory, and hepatic or any other systemic illness, having allergy to $MgSO_4$ & patients with extreme of ages were excluded from the study. They were assigned according to a computer-generated table of random numbers into two different groups of fifty each. Group M patients were given magnesium sulphate 50 mg/kg IV in 100 ml NS prior to induction. Group P patients were given 100 ml NS as placebo prior to induction.

Pre-anaesthetic checkup were done for all patients. Patients were shifted to the operation theatre, non-invasive blood pressure monitor, pulse oximeter and ECG leads were connected to all patients and baseline values were recorded. After securing 18G IV canula, Group M patients were given magnesium sulphate 50 mg/kg in 100 ml NS infused over 10 minutes just prior to induction of balanced general anaesthesia. Group P patients were given 100 ml NS infused over 10 minutes as placebo just prior to induction. General anaesthesia was induced with fentanyl 2 µg/kg and propofol 2 mg/kg. Intubation was facilitataed with vecuronium 0.1 mg/kg. Maintenance of anaesthesia was done with O_2, N_2O, isoflurane and vecuronium top-up as per requirement. Paracetamol 15 mg/kg was given to every patient intraoperatively as a part of multimodal analgesia. At the end of surgery neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrolate 0.01 mg/kg. HR, MAP and SPO_2 were monitored every 5 minutes intra operatively and every 15 minutes post operatively in PACU and any significant variation (>20%) were taken care of with documentation. Symptoms of hypermagnesemia was monitored intra and post operatively. In PACU after complete recovery from anaesthesia, NRS (Numeric Rating Scale) with 10 cm length (starting from 0, no pain, to 10, worst pain score was recorded at emergence of anesthesia and at 6, 12, 18 and 24 h. When NRS > 4 IV tramadol 1mg/kg was given. After surgery the dosage of post operative analgesia was recorded at 0, 6, 12, 18 and 24hours in both groups. Total tramadol consumption over 24 hours after surgery was calculated for each group.

Blinding: Two Anaesthesiologists were involved in each case enrolled in this study. One Anaesthesiologist was engaged in giving drug to the patients and to allot a random number to the patient in that study. Second Anaesthesiologist was blinded to the study drug being given and was recording all the data for that case.

Statistical Analysis

Data were entered into Microsoft Excel spread sheet. Sample size was calculated using lambda- Willis formula based on data of previous studies. With power of study 80% and alpha error 5%, the sample size came to 46 for each group. Considering drop outs, 50 patients were recruited in each group. SPSS for Windows 21 (SPSS, Chicago, IL, USA) was used for statistical analysis. Unpaired t test was used to analysis for continuous variables and Chi-Square Test and Fisher Exact Test was used to analysis categorical variables. Statistical significance was taken as $P < 0.05$.

Results

The demographic profile of both the groups were comparable as shown in Table 1. Intra-operative vitals (HR, MAP & SpO_2) were comparable and almost stable in both the groups except for usual variations. Post-operatively NRS score was significantly higher in Group P at 6, 12, 18 and 24 hours Table 2). In group P total post-operative tramadol consumption was significantly higher (Table 3).

Table 1: Demographic profile of both the groups

Variable	Group M	Group P	P-value	Remarks
Age (yrs)	44.2 ± 5.3	47.1 ± 3.1	0.325	Non-significant
Weight (kgs)	58.49 ± 3.35	54.35 ±3.61	0.655	Non-significant
Height (cms)	165.21 ± 8.35	163.35 ±5.61	0.421	Non-significant
Sex ratio (M:F)	34:16	38:12	0.432	Non-significant
Duration of surgery (mins)	98.55 ± 8.82	94.27 ± 10.84	0.524	Non-significant

Table 2: Post-operative NRS score in both the groups

Duration	Group M	Group P	P-value	Remarks
At emergence	2.94 ± 0.3	3.43 ± 0.7	0.125	Non-significant
6 hours	3.49 ± 0.35	6.35 ±0.61	0.001	significant
12 hours	3.91 ± 0.85	7.35 ±0.61	0.001	significant
18 hours	4.11 ± 0.56	7.41 ± 0.55	0.001	significant
24 hours	4.55 ± 0.82	6.27 ± 0.74	0.001	significant

Table 3: Total post-operative tramadol consumption in both the groups

	Group M	Group P	p-value	Remarks
Total post-operative tramadol consumption(mgs)	112.94± 12.3	232.23± 21.3	<0.001	Highly significant

Discussion

Here in our study we found that 10 minutes before the induction of balanced general anesthesia pre-treatment with 50mg/kg magnesium sulphate in 100mL of normal saline significantly reduces post-operative tramadol consumption after open abdominal surgeries. Post –operative NRS was significantly lower at 6, 12, and 18 and 24 hours in patients who were given magnesium sulfate pre-operatively.

Adverse effects of opioids such as respiratory depression, nausea, vomiting or hypotension make this category of drugs undesirable analgesic after surgery. So using magnesium sulfate pre-treatment before induction can

be a useful technique to reduce total post-operative opioid consumption and hence can minimize their adverse effects.

Magnesium has many established roles in anesthesiology viz as an anticonvulsant or antiarrhythmic agent. Before any painful stimulus, Preemptive analgesia is a better choice to decrease the physiological effects of nociceptive stimulation. Preemptive analgesia is an anti nociceptive measures for prevention of altered central processing of afferent input from injuries. Magnesium sulphate is one of the agents that can be used as premptive analgesic agents. Magnesium sulphate is also used as an anticonvulsant or antiarrhythmic agent. The analgesic effects of magnesium sulphate may be due to interference with calcium channels and N-methyl-D-aspartate (NMDA) receptor, but exact mechanism of action is not yet clear. It seem that altering nociceptive central sensitization are responsible for analgesic action of N-methyl-D-aspartate (NMDA) receptor. Reduction of catecholamine release and thus decreasing peripheral nociception or the stress response to the surgery may be the another mechanism of analgesic action.[6,13-15]

There are so many studies showing the conflicting results of clinical efficacy of magnesium sulfate on postoperative pain relief.

Ryu and colleagues (2008) assessed the effect of Mg sulfate on intraoperative anesthetic requirement and postoperative analgesia in gynecologic patients in TIVA and concluded that IV Mg sulfate improves the quality of postoperative analgesia during TIVA.[8]

Lysakowski and colleagues in 2007 didn't find convincing evidence that perioperative Mg has favorable effects on postoperative pain intensity and analgesic requirement.[9]

Mavrommati and colleagues (2004) concluded that infusion of low dose Mg sulfate in hernioplasty is an effective adjuvant for perioperative analgesic management.[16]

Kiran and colleagues (2011) evaluated the efficacy of single-low-dose of IV Mg sulfate for prevention of postoperative pain after inguinal surgery and concluded it could decrease post operative pain and equivalent of rescue analgesia.[17]

Wilder-Smith and colleagues (1997) studied perioperative infusion of magnesium levulinate in patients undergoing elective TAH and concluded that preoperative magnesium infusion does not improve postoperative analgesia. A small study group size and inadequate dose of magnesium might have been possible causes of this finding.[18]

Taheri et al (2015) found Single dose of magnesium sulfate during balanced general anesthesia could be considered as effective and safe method to reduce postoperative pain and opioid consumption in hysterectomy patients.[19]

Agrawal et al (2015) evaluated the effect of magnesium sulphate on post operative analgesia in patients undergoing lower segment caesarean section and found that I.V. magnesium sulphate administration during spinal anaesthesia improves postoperative analgesia without any notable complications.[20]

We did not notice any feature of magnesium toxicity (loss of patellar reflexes, decreased urine output, respiratory depression) in any patients. So we can say that toxic level of magnesium doesn't reach with the dose used in the study. But this statement would have been more authentic if we were co-relating the findings with serial serum magnesium level which can be taken as the limitation of this study.

Conclusion

We concluded that pre-treatment with magnesium sulfate (50mg/kg in 100mL of normal saline solution) 10 minutes before the induction of balanced general anesthesia alleviates post-operative pain and significantly reduces post-operative analgesic consumption after open abdominal surgeries.

Conflict of Interest: None.

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