Original Article

Indian Journal of Anesthesia and Analgesia
2017, 4 (4, Part-II), 1115-1120
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4417.32

Effect of Preemptive Intravenous Magnesium Sulphate on Post Operative Analgesia for Surgeries Done under General Anaesthesia: A Prospective Randomised Study

Santpur Unmesh S.[1], Santpur Madhavi U.[2], Karri Laxmi Priyanka[3]

[1]Associate Professor, Department of Obstetrics and Gynaescology [2]Associate Professor, Department of Anaesthesia, Maharishi Markendeshwar Institute of Medical Sciences and Research, Mullana, Ambala, Haryana 133207, India. [3]Assistant Professor, Department of Anaesthesia, Kamineni Institute of Medical Sciences, Narketpally, Telangana 508254, India.

Abstract

Context: Effective postoperative analgesia is always a challenge. Drug therapies in vogue have their own merits and demerits. Thus a concept of preemptive analgesia has evolved. *Aims:* The present study was aimed to evaluate the efficacy of preemptive intravenous magnesium sulphate on post operative analgesia for surgeries done under general anaesthesia. *Settings and Design:* A prospective randomized double blind study. *Methods and Material:* Sixty patients of ASA grade I or II between 20 to 50 years age, of either gender were divided into two groups of 30 each. Group I received 40 mg/kg of intravenous infusion of magnesium sulphate preoperatively and 10 mg/kg/hr intraoperatively and Group II received same volume of normal saline preoperatively and intraoperatively. *Statistical analysis used:* Observations were analysed using'students unpaired t-test'. *Results*: The pain score, sedation score at recovery and number of rescue analgesics required in 24 hours was observed. The decrease in pain scores and the higher level of sedation in group I was statistically significant ($p<0.05$). *Conclusions:* Preemptive magnesium sulphate significantly reduces postoperative pain, provides sedation and reduces analgesic requirement .

Keywords: Preemptive; Intravenous Magnesium Sulphate; Postoperative Analgesia; Sedation.

Introduction

Postoperative pain relief is an essential component of care of all surgical patients. Effective postoperative analgesia may facilitate recovery and reduce morbidity in surgical patients by blunting autonomic, somatic and endocrine reflexes [1]. Drug therapies used for postoperative analgesia include parenteral and oral non steroidal anti inflammatory drugs (NSAID), opioids, GABA analogues, parenteral NMDA receptor antagonists [2]. One of the intravenous adjuvant that has shown potential in preemptive analgesia is magnesium sulphate [3] ($MgSO_4$). Magnesium (Mg) is a non-competitive NMDA receptor antagonist with antinociceptive effects [4]. The present study was designed to evaluate the efficacy of preemptive intravenous $MgSO_4$ on post operative analgesia for surgeries done under general anaesthesia (GA).

Materials and Methods

After obtaining an approval of Institutional Ethical Committee, the present study was conducted at Kamineni Institute of Medical Sciences, Narketpally, Telangana , over a period of one year from November 2012 to December 2013. All the patients were randomly allocated into two groups of 30 each using computer generated random numbers.

An informed, written consent was obtained. The patient and the anesthesiologist were blinded to the allocation to the groups.

Corresponding Author: Santpur Madhavi Unmesh, Associate Professor, Department of Anaesthesia, Maharishi Markendeshwar Institute of Medical Sciences and Research, Mullana, Ambala, Haryana 133207 India.
E-mail: madhavisantpur90@gmail.com

Received on 15.07.2017, **Accepted on** 14.08.2017

Inclusion Criteria

- ASA grade I and II patients.
- Age between 20 – 50 years
- Elective surgeries under general anaesthesia.

Exclusion Criteria

- Patients with cardiovascular disorders like heart blocks, hypertension etc. hepatic, renal diseases, diabetes mellitus, asthma, chronic obstructive pulmonary disease, hematological disorders and neurological and patients receiving treatment with calcium channel blockers
- Patients with any known allergy to $MgSO_4$ or other drugs.
- Surgeries extending beyond two hours of duration.

After a thorough clinical examination and relevant laboratory investigations of all patients an informed, valid written consent was obtained for the administration of GA. Patients were explained preoperatively about visual analogue scale (VAS). All patients were kept nil by mouth for eight hours before surgery and tablet alprazolam (0.01mg/kg body weight) was administered per orally at bed time the day before surgery. Intravenous access was established with an 18G intravenous cannula and hemodynamic parameters i.e. HR, SBP, DBP, MAP and electrocardiogram were monitored. Neuro-muscular monitoring was also done.

All patients were allocated into one of the two groups of 30 each. In Group I, MgSO4 infusion was administered at the rate of 40mg/kg in 100 ml NS intravenous (IV) over 15 mins and same volume of normal saline was administered in group II in the preoperative period inside the theatre. IV glycopyrrolate 0.1 mg, IV fentanyl (1 µg/kg body weight) and IV midazolam (0.02mg/kg body weight) were given as pre-medication. In group I, IV infusion of MgSO4 was administered at the rate of 10mg/kg/hr till the end of surgery, whereas in group II, IV infusion of same volume of NS was given.

GA was induced with IV propofol (2mg/kg body weight), intubated with appropriate sized portex cuffed endotracheal tube after administration of IV atracurium (0.5mg/kg body weight). Balanced anaesthesia was maintained with O_2:N_2O in the ratio of 40:60, isoflorane and incremental doses of IV atracurium. At the end of surgery, neuromuscular blockade was reversed with IV neostigmine (0.05mg/kg body weight) and IV glycopyrrolate 0.1 mg.

After recovery from anaesthesia, sedation level was assessed using four point rating scale as shown in Table 1. In the recovery room patient was kept for four hrs for assessment of analgesia using VAS score and measurement of hemodynamic parameters every hour.

Level of pain at 0,1,2,3,4,8,16 and 24 hours postoperatively was assessed by using VAS scoring as shown in Figure 1. When VAS ≥ 3, rescue analgesia was provided in the form of IV tramadol (2mg/kg body weight) .

All the data was collected, tabulated and analysed statistically. p value of <0.05 was considered as statistically significant.

Statistical analysis was done using student's unpaired t-test for statistical analysis.... with thehelp of statistical software SPSS version 16) for analysis.

Table 1: Sedation score (four point rating scale)

Points	Parameter
1	Patient fully awake
2	Patient somnolent but responds to verbal commands
3	Patient somnolent but responds to tactile stimulation
4	Patient asleep but responds to pain

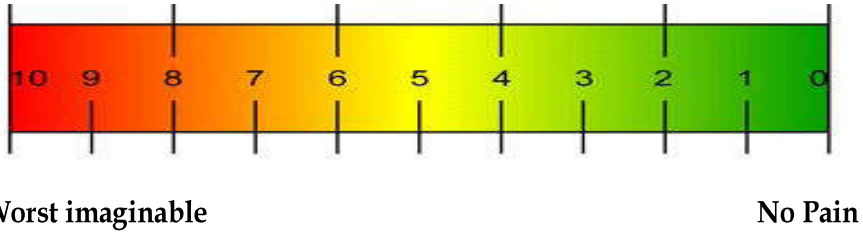

Fig. 1: Visual analogue scale

Results

Mean sedation score at recovery was significantly higher in group I

VAS scores at different intervals were significantly lower in group I ($p<0.05$) except at emergence from anaesthesia ($p>0.05$).

Mean number of rescue analgesics required post operatively was lesser in group I compared to group II.

Table 2: Comparision of sedation score (mean±sd) at recovery in both the groups (n = 60)

Mean sedation score	Group 1(n=30)	Group II (n=30)	p value
At recovery	1.93±0.63	1.56±0.56	0.0194

p value < 0.05 was taken as significant.

Table 3: Comparision of pain score (mean±sd) vas at different intervals in both the groups (n = 60)

Time at hours	Group I	Group II	p value
0 Hr	2.10±0.66	2.34±0.56	0.13
1 Hr	1.46±0.50	1.96±0.41	0.0001
2 Hr	1.20±0.48	1.76±0.56	0.0001
3 Hr	1.33±0.47	1.96±0.41	0.0001
4 Hr	1.43±0.62	2.30±0.53	0.0001
8 Hr	3.00±0.45	4.16±0.69	0.0001
16 Hr	1.70±0.53	2.36±0.61	0.0001
24 Hr	0.86±0.34	2.00±0.26	0.0001

Table 4: Comparision of mean number of rescue analgesics required in both the groups (n = 60)

Mean number of rescue analgesics required	Group 1(n=30)	Group II (n=30)
	1.23	2.43

Discussion

The International Association for the study of pain had described pain as unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage [5]. Modern day anaesthesia is not just concerned with relieving pain during surgeries but also during post operative period. Ineffective postoperative pain management may lead to deep vein thrombosis, pulmonary embolism, coronary stress, atelectasis, pneumonia, poor wound healing, insomnia and demoralization. The idea of pain prevention was first introduced into clinical practice by Crile in 1913 and further developed by Wall and Woolf who suggested that "simple changes in the timing of treatment can have profound effects on postoperative pain [6,7,8]."

In the present study, pain management was started prior to initiation of pain on the basis of preemptive analgesia..The aim of preemptive analgesia, which has been investigated in recent years, is to provide analgesia prior to a painful stimulus to prevent central sensitization caused by the painful stimulus such as tissue injury during surgery [2], in an attempt to obtain better pain relief compared with when the same analgesic intervention is used after the painful stimulus is given. Most commonly used intravenous agents as preemptive analgesics are NSAIDs, opioids and NMDA receptor antagonists. Recently the importance of Mg in anaesthetic practice has been highlighted [9]. Magnesium has the potential to treat and prevent pain by acting as an antagonist of NMDA receptors [10,11]. No adverse effects of $MgSO_4$ are seen in the study dosage as the drug is considered to be safe [12].

The Demographic Profile of the Patients in two Groups was Statistically Insignificant

In the present study, mean sedation score at recovery in group I and II was 1.93±0.63 and 1.56±0.56 respectively (Table 5). Thus, mean sedation score at recovery was higher in group I as compared to group II. ($p <0.05$) This was in accordance with the study of Kiran S et al [3] (2011) having scores (1.86±0.64 and 1.40±0.49) respectively.

Table 5: Comparision of sedation score (at recovery in present study with other study

Mean sedation score	(Kiran S et al[3](2011) N = 100		Present study (N=60)	
	study	Control	study	Control
At recovery	1.86±0.64	1.40±0.49	1.93±0.63	1.56±0.56

Table 6: Comparision of mean pain scores (mean±sd) at different intervals in present study with other studies

VAS Score	Kiran S et al[3] (N = 100)		*Mohammed Shawagfeh* [13] *(N = 200)*		*S Kaur et al*[14] *(N = 100)*		*Present study (N=60)*	
	Study	Control	Study	Control	Study	Control	Study	Control
0 Hr	1.86±0.70	1.96±0.53	1.48±0.60	1.58±0.40	--	--	2.10±0.66	2.34±0.56
1 Hr	--	--	--	--	2.84±3.07	5.01±2.78	1.46±0.50	1.96±0.41
2 Hr	1.22±0.76	1.82±0.96	1.21±0.73	1.77±0.33	--	--	1.20±0.48	1.76±0.56
3 Hr	--	--	--	--	1.94±2.66	3.70±2.53	1.33±0.47	1.96±0.41
4 Hr	1.32±0.84	1.88±0.44	--	--	--	--	1.43±0.62	2.30±0.53
8 Hr	2.74±1.43	3.84±1.46	--	--	--	--	3.00±0.45	4.16±0.69
16 Hr	1.36±0.69	2.00±0.76	--	--	--	--	1.70±0.53	2.36±0.61
24 Hr	0.78±0.68	1.30±0.46	0.56±0.64	1.10±0.24	6.12±3.35	6.72±3.14	0.86±0.34	2.00±0.26

Table 7: Comparison of heart rate (mean±sd) of present study with other Studies Heart Rate in Beats/Minute

Time	S.Kaur et al[14] (N=100)		Present study (N=60)	
	Study	Control	Study	Control
Base line	76.0±3.8	80±4.1	77.4±4.42	78.0±4.44
Before induction	--	--	80.0±4.47	81.0±4.35
Before intubation	--	--	74.6±3.24	75.2±3.81
After intubation	-	--	82.0±4.62	83.0±3.35
15	--	--	75.4±12.01	76.7±3.04
60	78±5.7	78±4.8	77.7±5.34	79.0±5.40
120	72±4.9	77±5.2	71.2±3.3	73.0±3.96

Table 8: Comparison of mean arterial pressure (mean±sd) of present study with other studies mean arterial pressure

Time	S.Kaur et al[14] (N=100)		Present study (N=60)	
	Study	Control	Study	Control
Base line	118 ±3.4	116 ±4.3	101.49±4.63	101.62±2.08
Pre- induction	--	--	99.00±3.37	99.78±3.03
Pre- intubation	--	--	96.47±3.56	94.46±6.63
After intubation	--	--	107.44±3.55	106.80±2.56
15 minutes	--	--	99.71.±2.91	98.16±2.56
30 minutes	116±7.0	112±5.5	99.62 ±2.34	100.56±2.24
60 minutes	110±4.9	108±6.8	102.20±3.11	102.67±3.23
120 minutes	115±5.3	110±4.7	99.20 ±3.11	99.13±3.29

In the present study, mean VAS scores at different intervals in group I were lesser than in the group II which was statistically significant ($p < 0.05$) but at emergence from anaesthesia, mean VAS score was statistically insignificant (Table 6).

The mean VAS score in the present study was in accordance with the VAS scores in Kiran S et al [3] (2011), Mohammed Shawagfeh et al [13] (2012) and S Kaur et al [14] (2012) at different intervals post-operatively. Shariat Moharari R et al [15] (2014) stated that postoperative pain was significantly lower dur-ing the first 24 hours in study group. Manna EM et al [16] (2012) reported that postoperative pain assessments by VAS showed significantly lower pain scores in study group compared to control group. Koinig et al [17] (1998) stated that the mean intraoperative and postoperative fentanyl consumption in the control group was significantly higher than that in the study group, thus concluding that preoperative administration of magnesium reduces not only postoperative but also intraoperative, analgesic requirements and thus magnesium can be be an adjuvant to perioperative analgesic management.

The number of mean rescue analgesics required postoperatively was lesser in group I (1.23) compared to that in group II (2.43). Kiran S et al [3] (2007) have stated that rescue analgesic requirement

of patients in study group was lesser than that in the control group. Ryu JH et al [12] (2008) and Kaur S et al [14] (2012) also have observed that cumulative postoperative analgesic consumption was significantly lesser in study group compared to that in control group.

In the present study, the changes in mean values of HR in both the groups were not statistically significant. The findings of present study were in accordance to the study conducted by S. Kaur et al [14] which stated that intraoperative and postoperative haemodynamic parameters were very much comparable between the two groups (P>0.05). Kiran S et al [3] and Mohammed Shawagfeh [13] and Koinig et al [17] stated that comparison of haemodynamic paremeters during study medication and intraoperative period between the two group at different time intervals was statistically insignificant. No adverse effects like bradycardia, hypotension, post operative nausea vomitting, dysrthymias etc were observed during the study.

Conclusion

From the present study it was concluded that preemptive administration of intravenous $MgSO_4$ in the dosage of 40mg/kg preoperatively and 10mg/kg/hr intraoperatively for surgeries done under GA had distinct advantages. Magnesium is an adjuvant preemptive analgesic, significantly reducing postoperative pain and analgesic requirement. It produces sedation in which patients are easily arousable. It is haemodynamically stable and not associated with any adverse effects and hence can be a good alternative for other analgesics like opioids, NSAIDs etc. However, study with larger samples are required to confirm the above findings.

Acknowledgement

This study was conducted at Kamineni Institute of Medical Sciences, Narketpally, Telangana.

Conflict of Interest

Nil

Key Messages

Effective preemptive analgesia with intravenous magnesium sulphate in surgeries under general anaesthesia

References

1. Kehlet H. Surgical stress: the role of pain and analgesia. Br J Anaesth1989;63:189–195.
2. Kissin I. Preemptive analgesia. Anesthesiology 2000;93:1138-1143.
3. Kiran S, Gupta R, Verma D. Evaluation of a single-dose of intravenous magnesium sulphate for prevention of postoperative pain after inguinal surgery. Indian J Anaesth 2011;55(1):31-35.
4. McCarthy RJ, Kroin JS, Tuman KJ, Penn RD, Ivankovich AD. Antinociceptive potentiation and attenuation of tolerance by intrathecal co-infusion of magnesium sulfate and morphine in rats. Anesth Analg 1998;86:830–836.
5. Arthur CG, John EH. Somatic sensations:pain, headache and thermal sensations. In: (editors) Textbook of Medical Physiology. 11thedn. Philadelphia:Elsevier; 2006.p.598-605.
6. Crile GW. The kinetic theory of shock and its prevention through anoci-association. Lancet 1913;185:7-16.
7. Wall PD. The prevention of postoperative pain. Pain 1988;33:289-290.
8. Woolf CJ. Central mechanisms of acute pain. In: Bond MR, Charlton JE, Woolf CJ. Proc. 6th World Congress on Pain. Amsterdam:Elsevier; 1991.p.25-34.
9. James MFM. Clinical use of magnesium infusions in anesthesia. Anesth Analg 1992;74:129-136.
10. Feria M, Abad F, Sanchez A, Abreu P. Magnesium sulphate injected subcutaneously suppresses autonomy in peripherally deafferented rats. Pain 1993; 53:287-293.
11. Woolf CJ, Thompson SWN. The induction and maintenance of central sensitization is dependent on N-methyl-D-aspartic acid receptor activation: implications for the treatment of post injury pain and hypersensitivity states. Pain 1991;44:293-299.
12. Ryu JH, Kang MH, Park KS, Do SH. Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. Br J Anaesth 2008;100:397–403.
13. Mohammed Shawagfeh. Efficacy of intravenous magnesium sulphate on postoperative pain. Middle east journal of internal medicine July 2012;5(4):24-26.
14. Kaur S, Baghla N. Evaluation Of Intravenous Magnesium Sulphate For Postoperative Analgesia In Upper Limb Orthopaedic Surgery Under General Anaesthesia: A Comparative Study. The Internet Journal of Anesthesiology 2012;30(2):1-6.
15. Shariat Moharari R, Motalebi M, Najafi A, Mohammed Zamani M, Imani F, Etezadi F, et al. Magnesium Can Decrease Postoperative Physiological Ileus and Postoperative Pain in Major non Laparoscopic Gastrointestinal Surgeries:A

Randomized Controlled Trial. Anesth Pain Med 2013;4(1):e12750.

16. Manaa EM, Alhabib AF. Effect of Magnesium Sulfate on the Total Anesthetic and Analgesic Requirements in Neurosurgery. J Neurol Neurophysiol 2012;11:1-5.
17. Koinig H, Thomas W, Peter M, Harald A, Klaus H, Nikolaus M. Magnesium Sulfate Reduces Intra- and Postoperative Analgesic Requirements. Anesth Analg 1998;87:206-210.