



Mediscope



The Journal of GMC

**ORIGINAL ARTICLE**DOI: <https://doi.org/10.3329/mediscope.v6i2.43156>**Pretreatment with Magnesium Sulfate to Alleviate Pain on Propofol Injection: A Prospective Randomized Double Blind Study****MS Hossain<sup>1</sup>, MM Rashid<sup>2</sup>, MM Rashid<sup>3</sup>, MAR Babu<sup>4</sup>, A Sultana<sup>5</sup>, D Saha<sup>6</sup>, MI Hasan<sup>7</sup>****Abstract**

**Background and aim of study:** Propofol is one of the most frequently used medications for inducing and maintaining anesthesia. However, propofol injection causes pain and discomfort in more than 70% of patients. This study was performed to determine the effect of magnesium sulfate on reducing pain at the onset of anesthesia induced by propofol injection. **Materials and methods:** A total of 80 healthy adult patients were selected in this study with either sex, scheduled for routine elective surgical procedure under general anesthesia. The patients enrolled were divided randomly into two groups of 40 patients each. Group I received 30 mg/kg of intravenous magnesium sulfate in 5 ml. Group II (placebo group) received 5ml of 0.9% intravenous normal saline 1 minute before propofol injection. The patients were asked to report their pain during injection of propofol. For all statistical tests,  $p < 0.05$  was taken to indicate a significant difference. **Results:** The incidence of pain experienced in magnesium sulfate group was 30% patients and in saline group was 60% patients, which is statistically significant  $p < 0.05$ . The severity of POPI was also lower in magnesium sulfate group than the saline group ( $p < 0.05$ ). The incidence of mild and moderate pain in groups I versus group II was 22.5% versus 37.5% and 7.5% versus 22.5% respectively  $p < 0.05$ . There was no severe pain recorded in any groups. **Conclusion:** Magnesium sulfate can be used before induction of anesthesia to reduce pain on propofol injection.

**Key words:** Magnesium sulfate, general anesthesia, pain on propofol injection (POPI).

**Introduction:**

Propofol is one of the most popular intravenous anesthetic drugs. It has been used widely because of its numerous advantages including rapid induction and recovery and

reducing postoperative nausea and vomiting. However, the incidence of pain following propofol injection is seen in almost 70% of patients, in the absence of other pretreatments.<sup>1-3</sup> The mechanism by which

1. Dr. Muhammad Sazzad Hossain MBBS PhD FCPS (anes) Associate Professor and Head Department of Anesthesiology National Institute of ENT. Tejgaon, Dhaka. E mail: sazzadicu786@yahoo.com
2. Dr. Md. Mamunur Rashid DA Associate Professor (cc) Department of anesthesiology Gazi Medical College. Khulna.
3. Dr. Mohammad Mamunur Rashid DA Junior Consultant, Department of anesthesiology. NIENT.
4. Dr. Md. Anisur Rahman Babu DA Medical officer, Department of anesthesiology. NIENT.
5. Dr. Afsana Sultana DA Medical officer, Department of anesthesiology. NIENT.
6. Dr. Devashis Saha MBBS Research officer, Department of anesthesiology. NIENT.
7. Dr. Mohammad IftaKhairul Hasan. MBBS. Medical officer. Anesthesiology Department of anesthesia, analgesia, palliative and Intensive care medicine Dhaka Medical College Hospital.

propofol causes pain on injection is not fully understood. However, the activation of pain mediators, such as the kinin cascade system, has been suggested as a possible cause.<sup>3</sup> A number of different interventions have been used to alleviate pain incidence and intensity during propofol injection, including administering lignocaine, heating or cooling, diluting propofol, injecting it into a large vein, and using ondansetron, metoclopramide, clonidine, ketamine, narcotics, thiopentone and magnesium sulfate. It is not clear, which is the most effective.<sup>4-8</sup>

Magnesium sulfate is used to reduce propofol-induced pain.<sup>9</sup> It is a natural calcium antagonist, which can be used as an adjuvant agent to reduce postoperative pain.<sup>10-12</sup> Various studies have shown that magnesium sulfate can reduce the need for opiates, such as propofol, remifentanyl, and vecuronium.<sup>13,14</sup>

This study was undertaken to evaluate the efficacy of 30 mg/kg of intravenous magnesium sulfate in comparison with placebo (normal saline) on incidence and severity of pain on propofol injection (POPI).

### Materials and methods

This randomized double blinded controlled trial was performed in National Institute of ENT Dhaka, during July to September of 2018. Eighty patients with ASA class (American Society of Anesthesiologists) I-II aged 20-50 years, who were scheduled for elective ENT surgery under general anesthesia, were included and written informed consent was obtained separately before surgery. Patients with history of allergy to magnesium sulfate, neurological disorders, use of analgesic or sedative drugs in the 24 hours prior to surgery were excluded. All routine investigations were done for GA fitness.

The patients enrolled were divided randomly into two groups of 40 patients each. Group I was allocated to receive 30 mg/kg of intravenous magnesium sulfate. Group II (placebo group) was allocated to receive 5ml of 0.9%

intravenous normal saline. Study drugs were prepared in the same shape of 5ml syringe, by an anesthesiologist who was not involved in the study.

On arrival to the operation room, standard monitoring was applied to all patients including pulse oximeter, electrocardiogram and noninvasive arterial blood pressure. A 20-gauge intravenous cannula was placed on the dorsum of non-dominant hand of the patient and Ringer's solution was started. Patients received no premedication. While the venous drainage was occluded by placing an air-filled tourniquet (pressure inflated to 70 mm Hg) on the upper arm by an assistant; a blinded anesthesiologist injected prepared study drug or saline according to the allocation. The occlusion was released after one minute. First one-fourth of induction dose (2 mg/kg) of propofol was injected slowly over 10 seconds. The pain intensity was measured based on McCririck and Hunter scale.<sup>15</sup> After the assessment of pain, induction of anesthesia was completed with the remaining dose of propofol then tracheal intubation was facilitated with the injection of succinylcholine. Anesthesia was maintained with injection of fentanyl, vecuronium, oxygen, nitrous oxide (66%) and halothane. When surgery was completed general anesthesia was reversed as usual.

Grading of pain: As per McCririck and Hunter scale<sup>15</sup>

0= No pain

1=Mild pain (pain reported only in response to questioning without any behavioral signs)

2= Moderate pain (pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning).

3= Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears).

Statistical analysis: For comparison of quantitative variables between the two groups, the unpaired t-test and for qualitative variables

the Chi-squared test was used. The statistically significant level was  $P < 0.05$ .

### Results

There was no significant demographic difference between the groups (Table 1).

Basal MAP and HR were comparable in both groups. There was no significant difference of MAP and HR between magnesium sulfate and saline groups during pre-intubation or three minutes post-intubation period ( $p > 0.05$ ) (Table II).

The incidence of pain experienced in magnesium sulfate group (group I) was 30% patients and in group II (saline group) was 60% patients, which is statistically significant  $p < 0.05$  (Table III). The severity of POPI was also lower in magnesium sulfate group than the saline group ( $p < 0.05$ ) (Table III). The incidence of mild and moderate pain in groups I versus group II was 22.5% versus 37.5% and 7.5% versus 22.5% respectively  $p < 0.05$ . There was no severe pain recorded in any groups.

### Discussion

Propofol, an excellent IV anesthetic agent belonging to the phenol group, can irritate the skin, the mucous membrane and the venous intima. The mechanism of pain is attributed to the activation of the kinin-kallikrein system that releases bradykinin, causing vasodilatation and hyper-permeability, thereby increasing contact between the aqueous phase propofol and the free nerve endings. Several authors have studied the mechanisms and methods of reducing propofol injection pain.

The results obtained from the present study showed, the overall incidence and severity of pain were significantly less in magnesium group compared to placebo group. The incidence of pain experienced in magnesium sulfate groups 30% patients and insaline group is in 60% patients. The severity of POPI is also lower in magnesium sulfate group than the saline group.

Khoshferrat et al.<sup>16</sup> had a study on prevention of propofol injection induced pain using

**Table 1: Comparison of demographic data between the two groups**

Parameters	Group I (Magnesium sulfate group) n=40.	Group II (Saline group) n=40.	p value
Age in years (mean±SD)	36.23±8.34	38.12±9.54	$p > 0.05$
Weight in kg (mean±SD)	65.28±8.47	64.54±8.62	$p > 0.05$
Sex (male/female)	27/13	28/12	$p > 0.05$
ASA Physical status I/II	37/3	36/4	$p > 0.05$

**Table 2: Changes of mean arterial pressure and heart rate between two groups**

Hemodynamic parameter	Basal Group I / Group II	Pre intubation Group I / Group II	Post intubation Group I / Group II
Mean arterial pressure (MAP) mm Hg	94/98	91/93	102/105
Heart rate per minute	81/84	73/76	92/90

**Table 3: Incidence and severity of pain following propofol injection between two groups**

Characteristics of pain	Group I (Magnesium Sulfate group) n=40. Number and %	Group II (Saline group) n=40. Number and %	p value
No pain	28 (70%)	16 (40%)	$p < 0.05$
Pain	12 (30%)	24 (60%)	$p < 0.05$
Mild pain	9 (22.5%)	15 (37.5%)	$p < 0.05$
Moderate pain	3 (7.5%)	9 (22.5%)	$p < 0.05$
Severe pain	0	0	-

magnesium, ketamine and lignocaine. They observed 20% patients experienced pain during propofol injection in magnesium pretreatment group.

A study done by Safavi et al.17 on attenuation of pain induced by injection of propofol by pretreatment of magnesium and found 34% patients experienced pain during propofol injection.

The study on prevention of pain on propofol injection using magnesium sulfate by Akbari et al.8 observed 36% patients experienced pain during injection of propofol.

Another study done by Memis et al.9 in their report showed that magnesium sulfate can reduce the pain due to propofol injection. In their study, the patients were divided into normal saline and magnesium groups and their observation showed, also 36% of patients reported pain in the magnesium group.

In another study, titled "Paracetamol, Ondansetron, Granisetron, Magnesium Sulfate and Lidocaine and Reduced Propofol injection pain" by Alipour et al.18 showed pain observed with Paracetamol in 72% patients, Ondansetron 61%, granisetron 30% Magnesium 48% and Lidocaine 30% patients.

Galgon et al.19 showed in his study, on prevention of Propofol injection pain using magnesium sulfate and Lidocaine and they found, 57% patients complained pain in magnesium sulfate group and 29% patients complained pain in lidocaine group.

Li M et al. 20 has a Study titled "Effects and safety of Magnesium sulfate on Propofol-induced injection pain, a meta-analysis of randomized controlled trials". They also concluded that pretreatment with Magnesium sulfate intravenously before injecting Propofol significantly reduced Propofol injection induced pain.

Present study shows, complains of pain in 30% patients in magnesium group which is lower than those studies by Alipour et al.18

and Galgon et al.19 but nearly similar to those studies of Safavi et al.17, Akbari et al.8 and Memis et al.9

### Conclusion

Pretreatment with a dose of 30 mg/kg magnesium sulfate intravenously administered one minute before propofol injection can reduce the incidence and severity of pain on propofol injection without significant adverse effects.

### References

1. Zahedi, H, Maleki, A. Ondansetron Pretreatment Reduces Pain on Injection of Propofol. *ActaMedicalIranica*. 2012; 50(4):239-43.
2. Tan CH, Onsiung MK. Pain on injection of propofol. *Anaesthesia* 1988; 53:468-76.
3. Cheong MA, Kim KS, Choi WJ. Ephedrine reduces the pain from propofol injection. *AnesthAnalg*. 2002; 95(5):1293-96.
4. Macario A, Weinger M, Truong P, Lee M. Which clinical anesthesia outcomes are both common and important to avoid? The perspective of a panel of expert anesthesiologists. *AnesthAnalg* 1999; 88(5):1085-91.
5. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: a randomized, controlled, double-blinded study. *Anesth Analg*.1999; 89(1):197-9.
6. Ishiyama T, Kashimoto S, Oguchi T, Furuya A, Fukushima H, Kumazawa T. Clonidine-ephedrine combination reduces pain on injection of propofol and blunts hemodynamic stress responses during the induction sequence. *J Clin-Anesth*. 2006; 18(3):211-5.
7. Saadawy I, Ertok E, Boker A. Painless injection of propofol: pretreatment with ketamine vs thiopental, meperidine, and lidocaine. *Middle East J Anesthesiol*. 2007; 19(3):631-44.
8. Akbari H, Nasiri E, Nikkhah A, Ardehali

- SH. Analgesic Effects of Ketamine, Magnesium Sulfate, and Sodium-Thiopental on Propofol Injection Pain: A Single-Blind Randomized Clinical Trial. *Tanaffos* 2018; 17(1): 22-8.
9. Memi D, Turan A, Karamanlioğlu B, Süt N, Pamukçu Z. The use of magnesium sulfate to prevent pain on injection of propofol. *AnesthAnalg* 2002;95(3):606-8,
10. LevauxCh, Bonhomme V, Dewandre PY, Brichant JF, Hans P. Effect of intraoperative magnesium sulphate on pain relief and patient comfort after major lumbar orthopaedic surgery. *Anaesthesia* 2003;58(2):131-5.
11. Bhatia A, Kashyap L, Pawar DK, Trikha A. Effect of intraoperative magnesium infusion on perioperative analgesia in open cholecystectomy. *J ClinAnesth* 2004;16(4):262-5.
12. Seyhan TO, Tugrul M, Sungur MO, Kayaçan S, Telci L, Pembeci K, Akpir K. Effects of three different dose regimens of magnesium on propofol requirements, haemodynamic variables and postoperative pain relief in gynaecological surgery. *Br J Anaesth* 2006;96(2):247-52.
13. Choi JC, Yoon KB, Um DJ, Kim C, Kim JS, Lee SG. Intravenous magnesium sulfate administration reduces propofolinfusion-requirements during maintenance of propofol-N<sub>2</sub>O anesthesia: part I: comparing propofol requirements according to hemodynamic responses: part II: comparing bispectral index in control and magnesium groups. *Anesthesiology* 2002; 97(5):1137-41.
14. Telci L, Esen F, Akcora D, Erden T, Canbolat AT, Akpir K. Evaluation of effects of magnesium sulphate in reducing intraoperative anaesthetic requirements. *Br J Anaesth* 2002;89(4):594-8.
15. McCrerrick A, Hunter S. Pain on injection of propofol: the effect of injected temperature. *Anaesthesia* 1990; 45: 443-4.
16. Khoshferrat M, Beirami F, Panah FS, Keykha A. A comparison of premedication injections of magnesium sulfate, ketamine and lidocaine on severity of pain induced by intravenous injection of propofol. *Archives of Anesthesiology and Critical Care* 2017; 3(4): 382-84.
17. Safavi M, Honarmand A. Magnesium sulfate pretreatment to alleviate pain on propofol injection: a comparison with ketamine or lidocaine. *Journal of Mazandaran University of Medical Sciences*. 2007; 17(60):30-8.
18. Alipour M, Tabari M and Alipour M. Paracetamol, Ondansetron, Granisetron, Magnesium Sulfate and Lidocaine and Reduced Propofol Injection Pain. *Iran Red Crescent J* 2014;16:e16086.
19. GalgonRE, Strube P, HeierJ Groth J, Wang S and Schroeder KM. Magnesium Sulfate with Lidocaine for preventing Propofol injection pain: a randomized, double-blind, placebo controlled trial. *J Anesth* 2014;206-11.
20. Li M, Zhao X, Zhang L, Niu X, GuoT, Yang B Liu Z. *Int J ClinExp Med* 2015;8(5):6813-6821.