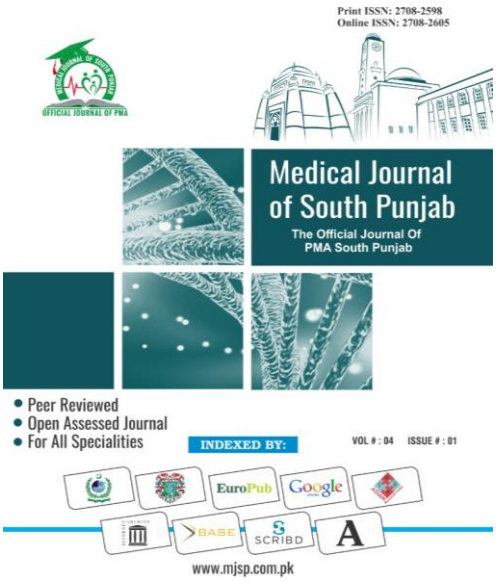
ISSN (E): 2708-2601
ISSN (P): 2708-2598

Medical Journal of South Punjab
Article DOI:10.61581/MJSP.VOL05/01/19
Volume 5, Issue 1, 2024



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Publication History

Received: Feb, 12 2024 Revised: Feb 16, 2024
Accepted: Mar 20, 2024 Published: Mar 30, 2024

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Conflict of Interest:

Author(s) declared no conflict of interest.

Acknowledgment:

No Funding received.

Citation: Farooq FM, Shuja ZS, Hameed J , Nadeem A, Alam A , Raza A. Efficacy of different techniques in attenuation of the pain caused by intravenous propofol injection. Medical Journal of South Punjab. 2024 March 30; 5(1):119-124

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An official publication of
Medteach Private Limited, Multan, Pakistan.
Email: farman@mjsp.com.pk, Website: https://mjsp.com.pk/index.php/mjsp

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Volume 5, Issue 1, 2024; pp: 119-124
Original Article

Efficacy of different techniques in attenuation of the pain caused by intravenous propofol injection

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ABSTRACT

Objective: *to compare the effectiveness of various drugs in attenuation of intravenous propofol injection pain.*

Methods: *Study was conducted at the department of anesthesia Lady Reading Hospital Peshawar, Pakistan from March 2023 to February 2024. Patients were assigned randomly to one of three groups using sealed envelopes. Each group consisted of 25 individuals. Drug solutions were prepared by a co-supervisor and dispensed in 5 ml doses by an observer. Group A received intravenous magnesium sulfate, Group B received intravenous granisetron, Group C received intravenous nitroglycerine.*

Results: *Pain score 0 grade at 5 seconds in Group A, B and C was 36.0%, 40.0% and 44.0%, respectively. [χ^2=1.71, p=0.789]. Pain score 0 at 10 seconds in Group A, B and C was 32.0%, 76.0% and 32.0%, respectively. [χ^2=12.64, p=0.002]. Pain score 0 at 15 second in Group A, B and C was 40.0%, 60.0% and 36.0%, respectively. [χ^2=3.34, p=0.198]. Whereas, pain score 0 at 20 second in Group A, B and C was 4 (16.0%), 44.0% and 24.0%, respectively. [χ^2=5.16, p=0.076].*

Conclusion: *The present study suggests that pain experienced during intravenous injection of propofol can be reduced by using various medications. Among these medications, most effective drug was granisetron, followed by nitroglycerin and magnesium sulfate, with no significant complications in postoperative time.*

Keywords: *Propofol injection, Pain, Granisetron, Magnesium sulfate, Nitroglycerine*

1. INTRODUCTION

Propofol, widely favored for intravenous induction and various surgical procedures since its clinical debut in 1977, is renowned for its efficacy; however, its frequent drawback of causing injection-site pain, particularly in small veins on the hand dorsum, poses significant discomfort to patients, potentially diminishing the agent's overall acceptability despite its manifold benefits in ambulatory surgeries, day care, short-duration, as well as sedation.

The incidence of pain associated with intravenous administration of propofol ranges widely, in adults from 28% to 90% and in children 28% to 85%, with younger children experiencing higher rates and intensity. Various factors including injection site, vein size, injection speed, blood buffering, propofol temperature, and concurrent medication use such as local anesthetics and opiates contribute to this variability.

Various pharmacological interventions such as pre-treatment with nitroglycerine, ketamine, nafamostat, ketorolac, ondesteron, lignocaine with propofol, or diluting propofol with 10% intralipid or 5% dextrose, have been explored to mitigate pain upon propofol injection, yet their efficacy varies. Additionally, non-pharmacological methods have been investigated, but the search for the ideal agent to alleviate pain associated with propofol injection remains ongoing.

In subanesthetic doses, ketamine which is NMDA receptors antagonist, alleviates propofol injection pain due to its properties of local anesthesia, while magnesium, another NMDA antagonist, demonstrates antinociceptive effects in humans by regulating calcium ion influx into cells, which serves analgesic because of natural physiological properties, prompting studies on magnesium sulfate to potentially attenuate pain associated with propofol injection.

2. METHODOLOGY

After receiving approval from the hospital ethics committee and obtaining informed consent from the patients, a study was conducted on 100 patients within the ASA status I and II, spanning both sexes and age limit 21-50 years, who were planned for surgery under general anesthesia. Exclusion criteria comprised patients those falling under ASA grades III and IV, individuals with a history of systemic illness, allergy to study drugs, as well as those currently taking analgesics prior to surgery, obese patients, and surgery performed on emergency basis.

Patients were randomly assigned to one of three groups using sealed envelopes. Each group consisted of 25 individuals. Drug solutions were prepared by a co-supervisor and dispensed in 5 ml doses by an observer. Group A received intravenous magnesium sulfate, Group B received intravenous granisetron, Group C received intravenous nitroglycerine. Pre-surgery, all patients underwent standard investigations; only those with normal results were included. Patients fasted for 8 hours, premeditated with 10mg diazepam the night before and 5mg 2 hours before surgery.

Intravenous access was established on dorsal side of hand using an 18-G intravenous line, with saline infusion at 100 ml per hour. ECG and vital signs monitoring was done, and the procedure was explained to the patient. No analgesic was administered before propofol injection. Venous occlusion was applied with a tourniquet to enhance drug concentration locally. Propofol was injected over 10 seconds following occlusion removal, with an initial 25% of the calculated dose administered over 20 seconds. Pain intensity was assessed using a verbal rating scale at specified intervals.

The observer was unaware of the administered drug. Induction of anesthesia proceeded with propofol. Fentanyl (2 µg/kg) was administered for analgesia. Endotracheal intubation was performed using vecuronium. Maintenance anesthesia was given with combination of Nitrous oxide and Oxygen 66-33% and isoflurane. The collected data underwent standard statistical analysis, employing descriptive statistics including range, mean, and SD to summarize the baseline clinical and demographic data. Chi-square (χ^2) test was applied on categorical data.

3. RESULTS

All the three groups were not statistically significant with respect to age, sex and ASA grades, (p>0.050). Most of the patients in all three groups were males and had ASA grade I. (Table. I).

Pain score 0 grade at 5 seconds in Group A, B and C was 9 (36.0%), 10 (40.0%) and 11 (44.0%), respectively. [χ^2=1.71, p=0.789]. Pain score 0 at 10 seconds in Group A, B and C was 8 (32.0%), 19 (76.0%) and 8 (32.0%), respectively. [χ^2=12.64, p=0.002]. Pain score 0 at 15 second in Group A, B and C was 10 (40.0%), 15 (60.0%) and 9 (36.0%), respectively. [χ^2=3.34, p=0.198]. Whereas, pain score 0 at 20 second in Group A, B and C was 4 (16.0%), 11 (44.0%) and 6 (24.0%), respectively. [χ^2=5.16, p=0.076]. (Table. II).

Table. I

Demographic parameters

	Group A n=25	Group B n=25	Group C n=25	Test of sig.
Age (years)	36.41±8.41	37.24±7.21	38.36±7.29	F=0.412 p=0.664
Sex				
Male	18 (72.0)	18 (72.0)	17 (68.0)	χ^2=0.129 p=0.938
Female	7 (28.0)	7 (28.0)	8 (32.0)	
ASA grades				
I	20 (80.0)	21 (84.0)	22 (88.0)	χ^2=0.595 p=0.743
II	5 (20.0)	4 (16.0)	3 (12.0)	
Mean±S.D, N (%)				

Table. II: Pain scores at 5, 10, 15 and 20 seconds

Pain score	Group A n=25	Group B n=25	Group C n=25	Test of sig.
Pain score at 5 second				
Grade 0	9 (36.0)	10 (40.0)	11 (44.0)	χ^2=1.71 p=0.789
Grade 1	12 (48.0)	10 (40.0)	12 (48.0)	
Grade 2	4 (16.0)	5 (20.0)	2 (8.0)	
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	
Pain score at 10 second				
Grade 0	8 (32.0)	19 (76.0)	8 (32.0)	χ^2=12.64 p=0.002
Grade 1	17 (68.0)	6 (24.0)	17 (68.0)	
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	
Pain score at 15 second				
Grade 0	10 (40.0)	15 (60.0)	9 (36.0)	χ^2=3.34 p=0.198
Grade 1	15 (60.0)	10 (40.0)	16 (64.0)	
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	
Pain score at 20 second				
Grade 0	4 (16.0)	11 (44.0)	6 (24.0)	χ^2=5.16 p=0.076
Grade 1	21 (84.0)	14 (56.0)	19 (76.0)	
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	
Mean±S.D, N (%)				

4. DICSCUSSION

The reported incidence of pain caused by propofol injection in adults varies widely, ranging from 28 to 90%, attributed to its classification within the phenol group known for irritating skin, mucous membranes, and venous intima, potentially due to factors such as endothelial irritation, differences in activation of pain mediators, osmolality, and unphysiological pH [11].

In this study, a verbal categorical scoring system was selected over a visual analogue score (VAS) due to its simplicity, making it easier for patients to use. Similar scoring system was used by Sing et al[12]. Ohnhaus et al[13] also used same scoring system and provide logic behind this that

decision was particularly relevant given that not all patients may have appropriate hand-eye coordination, especially at the time of induction and rapid changing conscious level.

In this study male patient ration was much higher in all groups and patients were having young age group. Sing et al[12] conducted a study where they found no significant difference in the demographic data of the patients across all groups, as indicated in Table 1. The majority of patients in each group were males, accounting for 59% of the total.

Scott et al[14] suggested that injection pain may be triggered by the activation of the Kallikrein-Kinin system, potentially by propofol or its lipid solvent, leading to the generation of kinins, particularly bradykinin, while Coderre et al[15] similarly proposed that bradykinin could induce local vasodilation and hyperpermeability, potentially increasing the interaction between free nerve ending and propofol's aqueous phase, causing pain upon injection with a delayed onset of 10-20 seconds.

In the study, the pain score was 0 at 10 seconds in the magnesium sulphate group, while in the granisetron and nitroglycerine groups, the pain scores were 32.0% and 76.0%, respectively. Ambesh et al[16] found 25% reduction in pain when using ondansetron group drugs 55% in saline group at the time comparison. Ye et al[17] suggested that this reduction in pain with ondansetron could be attributed to its dual mechanism of action as a 5HT3 receptor antagonist and sodium-channel blocker, where peripheral 5HT3 receptors are involved in nociceptive pathways. However, the exact mechanism responsible for the alleviation of pain caused by propofol injection.

Dilek et al[18] conducted a study where they found that pre-treatment with magnesium sulfate significantly reduced the incidence of pain upon propofol intravenous injection, with only 36% of patients experiencing pain compared to 86% in the control group receiving saline. On the other hand, Wilkinson et al[19] reported that in their study involving 60 patients, 67% of those pre-treated with nitroglycerine did not experience pain upon injection, whereas only 33% of patients in the placebo group had a similar outcome. These findings suggest that both magnesium sulfate and nitroglycerine can effectively reduce pain associated with propofol injection, highlighting their potential as pre-treatment options in clinical practice.

In their study, Lohmann and colleagues[20] provided evidence of significant venous dilation, with an increase of more than 50% observed in the diameter of the vein, in over half of the subjects who were treated with nitroglycerin within a timeframe of 15 minutes following application.

5. CONCLUSION

The present study suggests that pain experienced during intravenous injection of propofol can be reduced by using various medications. Among these medications, most effective drug was granisetron, followed by nitroglycerin and magnesium sulfate, with no significant complications in postoperative time.

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