

Original Article



Management of Pain During Propofol Injection Using Intravenous Nitroglycerine

Muhammad Sazzad Hossain¹, Mohammad Mamunur Rashid², Md. Anisur Rahman Babu³, Afsana Sultana⁴, Md. Sirajul Islam Mahfuz⁵, Abdur Rahman⁶, Muhammad Alamgir Mandal⁷.

Abstract

Background: Propofol is an intravenous (IV) anesthetic agent, can irritate the skin, mucous membrane and venous intima. The main drawback is the pain at injection site following its intravenous injection. **Objectives:** This study was performed to evaluate the effect of intravenous nitroglycerine on pain in patients following propofol injection. **Materials and Methods:** Eighty adult patients of both sexes, aged 20-50 years, according to American Society of Anesthesiologists (ASA) physical status were divided into two equal groups (n=40) to receive 200 mcg intravenous nitroglycerine diluted in 10 ml saline (group A) and 10 ml normal saline as placebo (group B) at an ambient operating room temperature in a randomized and double blinded fashion to compare the pain-relieving effects of the drugs during propofol injection before the patients lost consciousness. The pain on propofol injection was assessed according to the Mc Crirrick and Hunter scale. **Results:** The overall incidence and severity of pain were significantly less in Groups A (nitroglycerine group) than group B (placebo group) ($p < 0.05$). The incidence of mild and moderate pain in Group A versus group B was 25% vs 45% and 15% vs 30% respectively ($p < 0.05$). The incidence of score '0' (no pain) was higher in Group A (60%) than Group B (25%) ($p < 0.05$). **Conclusion:** Pretreatment with 200 mcg nitroglycerine with venous occlusion for one minute is effective pretreatment in alleviating propofol injection pain when compared to placebo.

Keywords: Nitroglycerine, Propofol, General anesthesia, Pain on propofol injection.

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Introduction

Propofol, a widely used induction agent in general anesthesia, has the main drawback of pain on injection that ranged 24-90%;^{1,2} this ranks seventh in order of frequency and clinical importance.³ Several interventions have been advocated to alleviate the pain associated with propofol injection, which include addition of lignocaine, ketamine,⁴ acetaminophen,⁵ tramadol,⁶ different doses of lidocaine,⁷ and different concentrations of propofol⁸ and topical nitroglycerin.⁹ Other studies have suggested other methods for controlling pain, including the injection of low doses of narcotics such as

sufentanil and butorphanol^{10,11} injection in large vessels and lignocaine injection together with tourniquet closure,¹² cold or warm propofol,¹³ metoclopramide injection as a premedication,¹⁴ magnesium,¹⁵ beta blocker,¹⁶ midazolam,¹⁷ 5-HT₃ receptor antagonists,¹⁸ or Alpha-2 agonists like dexmedetomidine.¹⁹

A few studies have been conducted to evaluate the use of nitroglycerine for pain reduction in the patients undergoing propofol injection.²⁰⁻²³ This effect might be due to the pain modulating and anti-inflammatory characteristics of Nitric Oxide (NO), which is a metabolite of nitroglycerine in smooth

1. Associate Professor and Head, Department of Anesthesiology National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
2. Junior Consultant, Department of Anesthesiology National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
3. Medical officer, Department of Anesthesiology. National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
4. Medical officer, Department of Anesthesiology. National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
5. Professor of ENT (Unit-3), National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
6. Associate Professor, Department of Anesthesiology, National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
7. Associate Professor & Head, Department of Physical Medicine & Rehabilitation. TMSS Medical College & Hospital, Bogura, Bangladesh.

Correspondent: Dr. Muhammad Sazzad Hossain, Associate Professor and Head, Department of Anesthesiology, National Institute of ENT, Tejgaon, Dhaka, Bangladesh. Mobile: +8801779849059, E mail: sazzadicu786@yahoo.com

muscle cells of vessels.²⁴⁻²⁷ Considering the contradictory results obtained in previous studies and the necessity of using propofol as an induction agent for general anesthesia, it was decided to conduct the current study aiming to compare premedication injections of nitroglycerine and placebo in reducing the pain induced by intravenous injection of propofol.

Material and Methods

This prospective, randomized, double-blind study included 80 patients according to ASA physical status I to II patients aged between 20 and 50 years for whom elective ENT surgery was planned with general anesthesia. The study was conducted at National Institute of ENT Dhaka, during October 2018 to January 2019 after obtaining written informed consent from the patients. Patients with a history of drug abuse, psychiatric disease, seizures, uncontrolled hypertension, renal or hepatic impairment, allergy to the study drugs, pregnant females and those who received any kind of analgesic or sedative in the 24-hrs prior to surgery were excluded from the study. Patients were randomly divided into two groups. The study drug was administered by an anesthesiologist who was blinded to the constituents of the drug. Group A (nitroglycerine group) received 200 mcg nitroglycerine diluted in 10 ml normal saline and Group B (placebo group) received 10 ml normal saline. Electrocardiogram, noninvasive arterial blood pressure and peripheral oxygen saturation (SpO2) measurements along with standard monitoring techniques were used in the operating room. Patients did not receive preoperative medication. A 20-gauge intravenous cannula was placed on the dorsum of the non-dominant hand. It was explained to the patients prior to anesthetic induction that they might feel some pain in their arms due to the application of the intravenous anesthetic. The anesthesiologist who administered the study drug was unaware of the identity of the solution that was being administered to each patient. To provide standardized venous occlusion, an automated blood pressure cuff was placed on the ipsilateral upper arm and pressure was maintained 50 mm Hg to guarantee venous occlusion. The study drug was administered over 20 second after venous occlusion. The tourniquet was opened after one minute, and then propofol was used at 2.5 mg/kg for anesthetic induction. Patients received 25% of the calculated dose of propofol over five seconds. Another anesthesiologist who did not know which study drug had been administered, graded the pain using the four point verbal rating scale published by McCrirrick and Hunter.²⁸

The pain responses were evaluated as

- 0 = no pain;
- 1 = mild pain (pain reported in response to questioning only, no behavioral signs);
- 2 = moderate pain (pain reported in response to questioning and accompanied by behavioral signs);
- 3 = severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears).

After pain assessment the remaining propofol was injected. After induction, patients were intubated using succinylcholine

and anesthesia was maintained with nitrous oxide, oxygen, fentanyl, halothane and vecuronium. At the end of surgery, residual neuromuscular blockade was antagonized with 0.05 mg/kg of neostigmine and 0.02 mg/kg of atropine. Extubation was done when the patients were fully awake and obeying commands. 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 I). Basal mean arterial pressure and heart rate were comparable in both groups. There were no significant differences of mean arterial pressure and heart rate between nitroglycerine and placebo groups during pre-intubation or three minutes post-intubation period (Table II). The incidence of pain experienced in nitroglycerine group (group A) was 40% patients and in group B (placebo group) was 75% patients, which was statistically significant p<0.05 (Table III). The severity of POPI was also lower in nitroglycerine group than the control group (p<0.05) (Table III). The incidence of mild and moderate pain in Groups A versus group B was 25% vs 45% and 15% vs 30% respectively p<0.05.

Table I: Comparison of demographic data between the two groups

Parameters	Group A (n=40)	Group A (n=40)
Age in years (mean±SD)	38.16±7.27	39.78±8.1 6
Weight in kg (mean±SD)	68.12±5.34	66.25±7.72
Sex (male/female)	25/15	26/14
ASA Physical status I/II	38/2	37/3

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

Hemodynamic parameter	Basal Group A/ Group B	Pre intubation Group A / Group B	Post intubation Group A / Group B
Mean arterial pressure (MAP) mm Hg	96/93	84/86	102/104
Heart rate per minute	78/76	65/67	92/90

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

Characteristics of pain	Group A (n=40) Number and %	Group B (n=40) Number and %	p value
No Pain	24 (60%)	10 (25%)	p <0.05
Pain	16 (40%)	30 (75%)	p <0.05
Mild Pain	10 (25%)	18 (45%)	p <0.05
Moderate Pain	6 (15%)	12 (30%)	p <0.05
Severe Pain	-	-	-

Discussion

Propofol is one of the most widely used drugs for induction of general anesthesia, whose common application is due to high clearance and fast awakening of patient. Propofol-induced anesthesia is associated with adverse complications, including pain on injection, myoclonus, apnea, reduced blood pressure and rarely thrombophlebitis. The pain is one of the common side effects of propofol injection. A number of drugs were tried to attenuate the pain caused by propofol injection. A number of drugs were tried to attenuate the pain on propofol injection.

The present study compared the efficacy of nitroglycerine to placebo as pretreatment agent in decreasing the incidence and severity of pain on propofol injection (POPI) in patients undergoing elective surgery under general anesthesia. This study result shows the incidence of pain experienced in nitroglycerine group (Group A) was 40% patients and in placebo group (Group B) is 75% patients ($p < 0.05$). The severity of POPI is also lower in nitroglycerine group than the control group ($p < 0.05$). The incidence of mild and moderate pain in Group A versus group B was 25% vs 45% and 15% vs 30% respectively ($p < 0.05$).

Derakhshan et al.²⁹ had a comparative randomized, double blind placebo controlled study between nitroglycerine and placebo on prevention of pain on propofol injection. Their result showed, pain experienced on propofol injection in nitroglycerine group was 36% patients and in placebo group 82% patients.

Goktug et al.³⁰ conducted a study titled Lidocaine alleviates propofol related pain much better than metoprolol and nitroglycerine and reported POPI was experienced in 31% patients in nitroglycerine group.

Another study done by Jeon Y³¹ on propofol injection induced pain with pretreatment by lignocaine and combination of lignocaine and nitroglycerine and showed 43% patients experienced pain in contrast to 7% patients complained pain in combination group.

The study done by Sing et al.³² on attenuation of pain caused by propofol injection by nitroglycerine, granisetron and magnesium sulfate and showed 36% patients experienced pain in nitroglycerine group.

The result of present study is nearly similar to those of studies done by Derakhshan et al.,²⁹ Goktug et al.³⁰ and Sing et al.³²

Conclusion

It can be concluded that, venous priming with a dose of 200 mcg nitroglycerine administered with mid-arm tourniquet applied for one minute before propofol administration can significantly reduce the incidence and severity of pain on propofol injection without any adverse effect.

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