Original Article

Efficacy of Intravenous Paracetamol Pretreatment for Prevention of Pain on Propofol Injection: A Randomized Placebo-Controlled Study

Muhammad Sazzad Hossain[1], Md. Shahidul Islam[2], Mohammad Mamunur Rashid[3], Md. Anisur Rahman Babu[4], Devashis Saha[5]

[1]Associate Professor and HOD, Department of Anesthesiology, National Institute of ENT. Tejgaon, Dhaka, [2]Professor of Pediatric Anesthesiology, Dhaka Shishu Hospital, [3]Junior Consultant, department of anesthesiology. NIENT, [4]Medical officer, department of anesthesiology. NIENT, [5]Research officer, department of anesthesiology. NIENT

Corresponding Author: E mail: sazzadicu786@yahoo.com

Abstract

Background and aim of study: *Propofol, most frequently used intravenous anesthetic, is used for induction of routine elective surgical procedure. Pain on propofol injection (POPI) still remains a considerable concern for the anesthesiologist. A number of techniques has been tried to minimize propofol-induced pain with variable results. Aim of this prospective randomized study is to observe the efficacy of intravenous paracetamol injection as pretreatment for the prevention of pain caused by the propofol injection.*

Materials and Methods: *A total of 80 patients were selected in this study with the age group of 20 to 50 years of either sex, ASA grade I and II, scheduled for routine elective surgical procedure under general anesthesia with endotracheal intubation. The patients enrolled were divided randomly into two groups of 40 patients each. Group I received 50 mg of intravenous paracetamol in 10 ml. Group II (placebo group) received 10 ml of 0.9% intravenous normal saline. The patients were asked to report their pain during injection of propofol according to the McCririck and Hunter S scale.*

For all statistical tests, $p<0.05$ was taken to indicate a significant difference.

Results: *The incidence of pain experienced in paracetamol group is 25% patients and in saline group is 70% patients, which is statistically significant $p<0.05$. The severity of POPI is also lower in paracetamol group than the saline group ($p<0.05$). The incidence of mild and moderate pain in paracetamol groups versus saline group was 17.5% versus 45% and 7.5% versus 25% respectively $p<0.05$. There was no severe pain recorded in any groups.*

Conclusion: *Pretreatment of intravenous paracetamol is effectively reduces pain on propofol injection.*

Keywords: *Paracetamol, propofol, pain on propofol injection (POPI).*

(JBSA 2019; 32(1): 24-27)

Introduction

Patient satisfaction with perioperative care is assuming more importance in the recent years. Propofol is an intravenous (IV) sedative and hypnotic agent commonly used for induction of general anesthesia. Its rapidity and reliability in causing loss of consciousness and quick smooth recovery are favorable features. However pain on injection when given intravenously is a common problem with propofol, the incidence of which is between 40-86%.[1] The mechanisms of pain on propofol injection are not known completely but a number of factors may be responsible for the pain. Several strategies to attenuate this pain include the use of antecubital vein,[1] with venous occlusion,[1] lignocaine,[1,2] cooling[3] or warming[4] of the drug, diluting propofol solution,[5] pretreatment with antiemetics,[6,7] metoclopramide,[8] opioids,[8] ketamine,[1,9] flurbiprofen[10]and paracetamol.[11] Other alternative strategies include various formulations of propofol emulsions such as nano emulsions.[12]

It has been shown that paracetamol selectively suppresses peripheral PGE_2 and increases COX 2 gene expression in a clinical mode of acute inflammation.[13] Propofol characteristically causes vascular pain that occurs in response to prostanoids, particularly PGE_2, which is selectively suppressed by paracetamol.[14] This study was undertaken to evaluate the efficacy of intravenous paracetamol 50mg in comparison with placebo (normal saline) on incidence and severity of pain on propofol injection (POPI).

Materials and methods

The present prospective, randomized study was conducted in National Institute of ENT Dhaka, during the period of August to October 2017. After obtaining written informed consent, a total of 80 patients, ASA grade I and II were taken up in the study with the age group of 20 to 50 years of either sex scheduled for routine elective surgical procedure under general anesthesia with endotracheal intubation. Patients excluded were those who had history of adverse effects to propofol, study drugs, presence of hepatic or renal dysfunction, patients with seizure disorder, history of drug abuse and uncontrolled hypertension. Pre-anesthetic check-up was done a day before surgery including a detailed history, a thorough physical and systemic examination. Routine investigations included CBC, routine urine test, electro-cardiogram, serum urea, serum creatinine, blood sugar and chest radiograph. The patients were fasted for 8 hours preoperatively.

In the operating room, monitors including non-invasive arterial pressure, electrocardiography and pulse oximetry were applied. The patients enrolled were divided randomly into two groups of 40 patients each. Group I was selected for pretreatment with 50 mg of intravenous paracetamol in 10 ml volume and group II was selected for pretreatment with 10 ml of intravenous normal saline. A 20 G intravenous cannula was placed in a vein on the dorsum of the no-dominant hand and Ringer's Lactate solution was started 100 ml/ hour. The mid arm of the side on which cannula was placed on the dorsum of hand was occluded by a BP cuff. The study drug was then injected and maintained in the vein for 1 minute. After 1 minute, the occlusion was released and one fourth of total calculated dose of propofol was injected over 5 seconds. Then the patients were asked by a blinded investigator to any sensation of pain during injection of propofol as per the McCririck and Hunte S scale.[15]

After the assessment of pain, induction of anesthesia was completed with the remaining dose of propofol, and 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 usal.

Grading of pain: As per McCririck and Hunter S scale[15]

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 is no significant demographic difference between the groups (Table I).

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

The incidence of pain experienced in paracetamol group (group I) is 25% patients and in group II (saline group) is 70% patients, which is statistically significant $p<0.05$ (Table III). The severity of POPI is also lower in paracetamol group than the saline group ($p<0.05$) (Table III). The incidence of mild and moderate pain in groups I versus group II was 17.5% versus 45% and 7.5% versus 25% respectively $p<0.05$. There was no severe pain recorded in any groups.

Table I *Comparison of demographic data between the two groups*

Parameters	Group I (Parecetamol group) n=40	Group II (Saline group) n=40	p value
Age in years (mean±SD)	38.53±8.42	37.53±9.67	p>0.05
Weight in kg (mean±SD)	63.68±8.42	64.72±9.16	p>0.05
Sex (male/female)	25/15	24/16	p>0.05
ASA Physical status I/II	37/3	36/4	p>0.05

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

Hemodynamic parameter	BasalGroup I / Group II	Pre intubation Group I / Group II	Post intubation Group I / Group II
Mean arterial pressure (MAP) mm Hg	94/97	90/92	105/108
Heart rate per minute	78/81	73/77	91/93

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

Characteristics of pain	Group I (Parecetamol group) n=40. Number and %	Group II (Saline group) n=40. Number and %	p value
No pain	30 (75%)	12 (30%)	p <0.05
Pain	10 (25%)	28 (70%)	p <0.05
Mild pain	7 (17.5%)	18 (45%)	p <0.05
Moderate pain	3 (7.5%)	10 (25%)	p <0.05
Severe pain	0	0	-

Discussion

Pain on propofol injection is a common problem, can be immediate or delayed. The immediate pain could be the result of a direct irritant effect, but the kinin cascade is probably the cause of delayed pain. The lipid solvent for propofol activates the plasma kallikrein–kinin system which results in bradykinin production that increases local vein permeability and dilation. The aqueous-phase propofol diffuses into more free nerve endings outside the endothelial layer of the vessel which is more permeable and dilated because of bradykinin effect, thereby intensifying pain on injection.

In present study, the overall incidence of pain on propofol injection experienced in paracetamol group is 25% patients and in saline group is 70% patients, which is statistically significant p<0.05. The severity of POPI is also lower in paracetamol group than the saline group (p<0.05). The incidence of mild and moderate pain in paracetamol groups versus normal group was 17.5% versus 45% and 7.5% versus 25% respectively p<0.05. There was no severe pain recorded in any groups.The study done by Canbay et al.[16] on efficacy of intravenous acetaminophen (paracetamol) and lidocaine on propofol injection pain and recorded the overall incidence of pain during IV injection of propofol in the control (saline) group was 64% compared with 22% in IV paracetamol and with 8% in lidocaine group, suggesting that IV acetaminophen injection is effective in reducing propofol injection pain compared with control. The results of present study correlated with the results of the study by Canbay O et al on prevention of POPI by paracetamol.

In the study conducted by Biswal S et al.[11] the overall incidence of POPI during IV administration of paracetamol is 56.7% compared to 26.7% with IV lignocaine group. In contrast to present study, the incidence of POPI is higher in the study

conducted by Biswal S et al. (25% versus 56.7%). Further study with large number of patients may be required for prevention of propofol injection pain by pretreatment with intravenous paracetamol.

A study done by Borazan et al, [17] they concluded pretreatments 1 min before propofol, paracetamol 1 mg/ kg and lidocaine 0.5 mg/ kg were equally effective in attenuating pain during intravenous injection of propofol whereas pretreatment with paracetamol 2 mg/ kg was shown to be the most effective treatment.

Conclusion

Pretreatment with a dose of 50 mg paracetamol intravenously administered with mid-arm occlusion applied for one minute before propofol administration can effectively reduce the incidence and severity of pain on propofol injection.

References

1. Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, et al. Prevention of pain on injection of propofol: Systematic review and meta analysis. BMJ 2011;342:1110.
2. Picard P, Tramèr MR. Prevention of pain on injection with propofol: A quantitative systematic review. Anesth Analg 2000;90:963 9.
3. Barker P, Langton JA, Murphy P, Rowbotham DJ. Effect of prior administration of cold saline on pain during propofol injection. A comparison with cold propofol and propofol with lignocaine. Anaesthesia 1991;46:1069 70.
4. Fletcher GC, Gillespie JA, Davidson JA. The effect of temperature upon pain during injection of propofol. Anaesthesia 1996;51:498 9.
5. Klement W, Arndt JO. Pain on injection of propofol: Effects of concentration and diluent. Br J Anaesth 1991;67:281 4.
6. Draškoviæ B, Kne•eviæ S, Radovanoviæ D, Rakiæ G. Ondansetron, alfentanil and nitrous oxide in the prevention of pain on injection of propofol. Srp Arh Celok Lek 2013;141:61 5.
7. Ahmed A, Sengupta S, Das T, Rudra A, Iqbal A. Pre treatment with intravenous granisetron to alleviate pain on propofol injection: A double blind, randomized, controlled trial. Indian J Anaesth 2012;56: 135 8.
8. Rasmussen KG, Ritter MJ. Anesthetic induced pain on injection in electroconvulsive therapy: Review of the literature and suggestions for prevention. J ECT 2014; 30:203 9.
9. Wang M, Wang Q, Yu YY, Wang WS. An effective dose of ketamine for eliminating pain during injection of propofol: A dose response study. Ann Fr Anesth Reanim 2013;32: e103 6.
10. Zhang L, Zhu J, Xu L, Zhang X, Wang H, Luo Z, et al. Efficacy and safety of flurbiprofen axetil in the prevention of pain on propofol injection: A systematic review and meta analysis. Med Sci Monit 2014;20:995 1002.
11. Biswal S, Moningi S, Ramachandran G. Effect of intravenous tramadol, acetaminophen in attenuating pain on propofol injection: Comparison with lignocaine: A randomized, Double-blind, controlled study. Karnataka Anaesth J 2015;1:118-22.
12. Rodrigues TA, Alexandrino RA, Kanczuk ME, Gozzani JL, Mathias LA. A comparative study of non lipid nanoemulsion of propofol with solutol and propofol emulsion with lecithin. Rev Bras Anestesiol 2012;62:325 34.
13. Lee YS, Kim H, Brahim JS, Rowan J, Lee G, Dionne RA. Acetaminophen selectively suppresses peripheral prostaglandin E2 release and increases COX 2 gene expression in a clinical model of acute inflammation. Pain 2007;129:279 86.
14. Ando R, Watanabe C. Characteristics of propofol evoked vascular pain in anaesthetized rats. Br J Anaesth 2005;95:384 92.
15. Mc Crirrick A, Hunter S. Pain on injection of propofol: the effect of injectate temperature. Anaesthesia 1990; 45: 443–4.
16. Canbay O, Celebi N, Arun O, Karagoz AH, F. Sarýcaoglu F,Ozgen S. Efficacy of intravenous acetaminophen and lidocaine on propofol injection pain. BJA 2008;100(1:)95-8.
17. Borazan H, Erdem TB, Kececioglu M, Otelcioglu S. Prevention of pain on injection of propofol: a comparison of lidocaine with different doses of paracetamol. Eur J Anaesthesiol. 2010 Mar;27(3):253-7.