Original Article

Prevention of Propofol Injection-Induced Pain, Using Lignocaine in large Volume: A Prospective Randomized Double-Blind Study

Muhammad Sazzad Hossain[1], Md. Afzalur Rahman[2], Md. Mahiuddin Alamgir[3], Md. Waliullah[4], Muhammad Alamgir Mandal[5],

Abstract

Background: *Propofol is a common intravenous (IV) anesthetic drug, used for induction of general anesthesia. Pain during bolus injection is a major drawback of propofol. Different methods of propofol formulations and drugs have been used to decrease pain on propofol injection (POPI), but still it remains an unresolved problem. It is assumed that IV administration of diluted lignocaine in a large volume before propofol injection could be more effective in prevention of both immediate and delayed types of pain associated with propofol injection than the most commonly used method of mixing lignocaine with propofol (20 mg lignocaine added to the 20 ml propofol).* ***Objectives:*** *The aim of this study was to compare the effect of lignocaine used in a large volume for prevention of propofol injection pain.* ***Materials and methods:*** *Eighty adult patients undergoing general anesthesia for elective ENT surgery were included in this study. Patients were classified into two groups, Group A (study group), in which 20 mg lignocaine diluted into a total volume of 20 ml using normal saline was given IV after venous occlusion for with BP cuff followed by propofol injection. In group B (control group), 20 mg lignocaine was mixed with propofol and given to the patient as commonly used.* ***Results:*** *This study showed statistically significant reduction in pain on propofol injection (POPI) in the study group compared to control group.* ***Conclusion:*** *Lignocaine when used diluted with normal saline in large volume after venous occlusion has significantly reduced propofo linjection pain in adults.*

Keywords: *Propofol, lignocaine, Pain on propofol injection (POPI)*

Date of received: *05.09.2017*

Date of acceptance: *07.08.2018*

KYAMC Journal.2018;9(3): 125-128 .

DOI: http://dx.doi.org/10.3329/kyamcj.v9i3.38784

Introduction

Propofol is the most widely used intravenous (IV) anesthetic agent for induction and maintenance of anesthesia as well as for sedation inside and outside of operation theatre. It is almost an ideal IV anesthetic agent, but pain on its injection still remains problem. The pain may not be a serious complication, but most patients remember it as one of the unpleasant encounters with anesthesiologists. Pain on propofol injection (POPI) is a common problem in adults, which varies between 30 and 90%.[1] Several strategies have been suggested to prevent or reduce pain at the site of propofol administration. Most previous and recent work in this area has been performed on the adjuvant use of hypnotic, analgesic, anti-inflammatory or local anesthetic drugs, which include adding lignocaine to propofol, cooling or warming propofol, diluting the propofol solution, injection of propofol into a large vein[2-4] and pretreatment with intravenous injection of lignocaine, ondansetron, opioids,[5-7] granisetron,[8,9] thiopentone,[10] metoclopramide,[11] ketorolac,[12] dexamethasone[13] and magnesium,[14] with or without tourniquet. All these drugs have been tried with variable and sometimes conflicting results.

Propofol belongs to a group of phenol that can irritate the skin, mucous membrane and venous intima. The pathophysiology of this pain is attributed till this moment to one and a combination of more than one of the three proposed mechanisms. The first mechanism relates to the pain to the triggering of the local kallikrein-kinin cascade,[15] which explains the decrease in the incidence and severity of non-immediate (delayed) pain resulting from propofol administration when the drug is premixed with lignocaine[16] or a non-steroidal anti-inflammatory agents, which inhibit the

1. Associate Professor and HOD, Department of Anesthesiology, National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
2. Junior consultant, Department of Anesthesiology, National Institute of ENT, Tejgaon, Dhaka, Bangladesh.
3. Research 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. Assistant Professor and Head, Department of Physical Medicine and Rehabilitation, Khwaja Yunus Ali Medical College and Hospital, Enayetpur, Sirajgonj, Bangladesh.

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

prostaglandins synthesis.[17] Another suggested mechanism was the stimulation of the nociceptive receptors at the free nerve endings located between the intima and media layers of venous wall, in which a direct and immediate response is transmitted through the A-delta fibers; drugs like lignocaine,[18] fentanyl, morphine[19] and procaine are effective when administered few seconds before propofol injection. The third proposed mechanism relates the pain to the pH and concentration of propofol; which when lowered by premixing it with lignocaine or 10% intralipids[20] causes less pain.

In this study, it is assumed that IV administration of diluted lignocaine in large volume (20 mg lignocaine diluted in 20 ml of normal saline) before propofol injection could be more effective in prevention of both immediate and delayed types of pain associated with propofol injection than the most commonly used method of mixing lignocaine with propofol (20 mg lignocaine added to 20 ml propofol). Lignocaine diluted in such volume and injected during venous occlusion may give a chance for larger volume of drug to spread over larger surface area to block more pain producing nerve endings, not only within the veins but also by passing to block perivascular nerve endings, which could prevent both immediate and delayed types of pain caused by propofol.

Material and Methods

This prospective randomized double-blind study was conducted on 80 patients of American Society of Anesthesiologists (ASA) physical status I and II, aged 20-55 years of both sexes, at National Institute of ENT, Dhaka from February to April 2018. Written informed consent was obtained from all patients. Patients with known history of allergy to either propofol or lignocaine were excluded. Eligible patients were randomly divided into two groups: Group A (study group) and Group B (control group). All patients were cannulated with a 20 gauge intravenous cannula on the distal part of the forearm. On arrival to the operation room, all patients were monitored with electrocardiogram, pulse oximetry, non-invasive arterial blood pressure, and capnography. Mean arterial blood pressure and heart rate were recorded for statistical comparison between the two groups at baseline, just before intubation, and 1 min after intubation.

In Group A (study group), 20 mg lignocaine diluted with sterile saline into a total volume of 20 ml was injected intravenously after venous occlusion using blood pressure cuff around middle of the arm limiting inflation pressure to just above 50 mmHg and locked in order to be sure that venous outflow was completely restricted, which was maintained 90 s after lignocaine injection, and then after release cuff pressure, propofol in a dose of 2 mg/kg was injected slowly over 30 seconds. In Group B (control group), BP cuff was applied similarly as the study group and a total volume of 20 mL of sterile normal saline without any drug was injected as a placebo, so the anesthesia providers administering the propofol would still remain blinded to the mixed or unmixed propofol. After release of cuff pressure, propofol mixed with 20 mg lignocaine (total volume 20 ml) was injected in a dose of 2 mg/kg over 30 seconds. Each dose was prepared by an anesthesiologist in the operating room immediately prior to induction but was given by another anesthesiologist, who was blinded to the content of each syringe. Assessment of pain was recorded during and within 1 min after propofol injection (Table I). After propofol injection, and pain assessment, fentanyl 1 mcg/kg and vecuronium 0.1 mg/kg were given. Intubation was done 3 min after vecuronium administration; anesthesia was maintained by a mixture of nitrous oxide and oxygen supplemented with halothane. At the end of the operation, muscle relaxant was reversed by neostigmine and atropine as usual.

Table I: Grading of pain

Number	Description of
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)

The chi-squire test was used to compare pain on propofol injection (POPI) between two groups. Comparison of age and weight between the two groups was obtained by unpaired t-test. The results were expressed as number or mean ±SD. p value <0.05 was considered to be statistically significant.

Results

There is no significant demographic difference between the groups (Table II). In both groups MAP and HR decreases during pre-intubation and post intubation from basal reading. There is some difference of MAP and HR between the two groups but is not significant (Table III). The incidence of pain in group A (study group) is 5% patients and in group B (control group) is 20% patients, which is statistically significant p<0.05. In both groups we found only mild pain, no moderate or severe pain was recorded (Table IV).

Table II: Comparison of demographic data between the two groups

Parameters	Group A (n=40)	Group B (n=40)
Age inyears (mean±SD)	37.73±7.12	38.53±8.42
Weight in kg (mean±SD)	65.52±8.64	6612±6.89
Sex (male/female)	21/19	20/20

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

Hemodynamic parameter	Basal Group A/ Group B	Pre intubation Group A/ Group B
Mean arterial pressure (MAP) mm Hg	102/104	87/89
Heartr ate per minute	94/96	84/86

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

Characteristics of pain	Group A (n=40)%	G roup B (n=40)%	p value
No pain	38(95%)	32(80%)	p<0.05
Pain	2(5%)	8(20%)	p<0.05
Mild Pain	2(5%)	8(20%)	p<0.05
Moderatpain	0	0	
Severe pain	0	0	

Discussion

In this study it is found that, the incidence and severity of propofol injection induced pain were significantly less in pre treatment lignocaine diluted in large volume with normal saline using tourniquet, than the premixed lignocaine with propofol. It has been suggested that lignocaine is not effective in reducing the pain of propofol injection except when a tourniquet is use.[21] The mechanism of action is possibly the blockade of the nerve fibers responsible for pain transmission resulting from direct irritation of the inner walls of blood vessels by propofol; this direct anesthetic effect of lignocaine is achieved when sufficient time is allowed for the drug to work.[22] However, the results of studies related to the amount of time lignocaine remains in blood vessels when a tourniquet is used are controversial.[23] Local anesthetic activity of lignocaine may be high due to long duration, but in the study of Ewart and Whitwam,[23] lignocaine was most effective at reducing pain when administered immediately before applying propofol. Liaw et al [24] found that IV lignocaine was retained in the veins for 1 minute, and injecting propofol after releasing the rubber tourniquet was found to be effective in reducing pain when compared with the saline group. In a study Picard and Tramer [2] compared three different methods of using lignocaine in prevention of propofol injection pain. The first was lignocaine bolus injection before propofol injection. Second was mixing lignocaine with propofol, and the third by giving lignocaine after venous occlusion with tourniquet. They reported that using the tourniquet was the most effective method. We studied lignocaine pretreatment because propofol pain may hinder smooth induction of anesthesia which is associated with patient agitation and enhancement of the stress response, so pretreatment for prevention of this pain become the standard technique in anesthesia practice. Overbaugh et al[25] concluded that lignocaine more effectively reduces pain on injection of propofol when it is administered as a mixture thanwhen given as a pretreatment before the propofol injection. Our technique is different because of using markedly diluted lignocaine under tourniquet which may explain the different results between our study and Overbaugh et al.[25] The present study was both cost and time effective as it can be used during the period of pre-oxygenation. In this study, the reduction of the pre-intubation and post-intubation measurements of mean arterial blood pressure and heart rate in the study group compared to the control one could be explained by attenuation of the stress response as a result of reduction of the propofol injection pain in thestudy group.

Conclusion

Lignocaine pre treatment decreases pain on propofol injection (POPI)using in large volume under venous occlusion significantly than premixed lignocaine with propofol injection in adult patients. This method has no wastage of time, without adding cost and also easy to apply. This method causes reduced pain on propofol injection so it is associated with smooth induction of general anesthesia and attenuation of stress response.

Acknowledgement

We are extremely grateful to Prof. Dr. Mahmudul hassan, Professor of Department of ENT, Director, National Institute of ENT, Dhaka. It is our great pleasure to express our regards to all the staffs of Department of Anesthesiology of National Institute of ENT, Dhaka for their endless support during the study period.

References

1. Pang WW, Mok MS, Huang S, Hwang MH. The analgesic effect of fentanyl, morphine, meperidine and lignocaine in the peripheral veins: A comparative study. Anesth Analg. 1998;86:382-386.

2. Picard P, Tramer MR. Prevention of pain on injection with propofol: A quantitative systemic review. Anesth Analg. 2000;90:963-969.

3. Fields HL, Emson PC, Leigh BK, Gilbert RF, Iversen LL. Multiple opiate receptor sites on primary afferen tfibres Nature. 1980;284:351-353

4. Zhou L, Zhang Q, stein C, Schafer M. Contribution of opioid receptors on primary afferent versus sympathetic neurons to peripheral opioid analgesia. J Pharmacol ExpTher. 1998;286:1000-1006.

5. Wong WH, Cheong KF. Role of tramadol in reducing pain on propofol injection. Singapore Med J. 2001;42:193-195.

6. Aouad MT, Siddik-Sayyid SM, Ai-Amin AA, Baraka AS. Pretreatment with remifentanil and lidocaine versus remifentanil or lidocaine alone. Anesth Analg. 2007;104:1540-1544.

7. Agarwal A, Reza M, Dhiraaj S, Pandey R, gupta D, Pandey CK, Pain during injection of propofol:The effect of prior administration of butrophenol. Anesth Analg. 2004; 99:117-119.

8. Asik I, Yorukoglu D, Gulay I. Tulunay M. Pain on injection of propofol: Comparison of metoprolol with lidocaine. Eur J Anesthesiol. 2003;20:487-289.

9. Dubey PK. Prasad SS. Pain on injection of propofol: The effect of granisetron pretreatment. Clin J Pain. 2003;9:121-124.

10. Agarwal A, Ansary MF, Gupta D, Pandey R, Reza M, Sing PK. Pretreatment with thiopental for prevention of pain associated with propofol injection. Anesth Analg. 2004;98: 683-686.

11. Scott RP, Saunders DA, Norman J. Propofol: Clinical. 1988;43:492-494.

12. Huang YW, Buerkle H, Lee TH, Lu CY, Lin CR, et al. Effect of pretreatment with ketorolac on propofol injection pain. Acta Anesthesiol Scand. 2002;46:1021-1024.

13. Sing M, Mahota M, Sethi AK, Tyagi A. Efficacy of dexamethasone pretreatment for alleviation of propofol injection pain. Eur J Anesthesiol. 2005;22:888-890.

14. Memiu D, Turan A, Karamanlioglu B, Sut N, Pamukcu Z. The use of magnesium sulphate to prevent pain on injection of propofol. Anesth Analg. 2002;95:606-608.

15. Srbel PS, Lowon JP. Propofol a new intravenous anesthetic. Anesthesiol. 1989;71:260-277.

16. Scott RPF, Saunders DA, Norman J. Propodfol: Clinical strategies for preventing pain on injection. Anesthesia. 1988;43:492-494

17. Fuji Y, Shiga Y. Flurbiprofen Axetil preceded by venous occlusion in the prevention of pain on propofol injection in the hand: a prospective, randomized, double blinded, vehicle-controlled, dose finding study in Japanese adult surgical patients. Clin Ther. 2005;27:588-593.

18. Arndt Jo, Klement W. Pain evoked by polymodal stimulation on the hand veins in human. J Physiology. 1991;440:467-468.

19. Pang WW, Mok MS, Huang S, Hwang MH. The analgesic effect of fentanyl, morphine, meperidine and lidocaine in the perepheral veins: a comparative study. Anesth Analg. 1998; 86:382-386

20. Klement W, Arndt JO. Pain on injection of propofol: effect of concentration and diluents. Br J Anesth. 1991;67:281-284

21. Sasaki T, Okamura S, Kisara A, Effect oflidocaine on pain caused by injection of propofol: Comparison of three methods at two injection rates. J Anesth. 1999;13:1416.

22. Massad IM, Abu-Ali HM, Abu-Halaweh SA, Badran IZ. Venous occlusion with lidocaine for preventing propofol induced pain. A prospective double-blind randomized study. Saudi Med J. 2006; 27:997-1000.

23. Ewart MC, Whitwam JG. Prevention of pain during injection of propofol. Lancet. 1990;335:798-799.

24. Liaw WJ, Pang WW, Chang DP, Hwang MH. Pain on injection of propofol: The mitigating influence of metoclopramide using different techniques. Acta Anaesthesiol/Scand. 1999;43:24-25.

25. Overbaugh R, Jones P, Nguyen A. Effect of mixed versus unmixed lidocaine with propofol. I J Anesthesiol. 2003; (2) 212-214