A Comparative Study between Intravenous Tramadol Versus Lidocaine Pretreatment in Reducing Pain on Propofol Injection

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Abstract

Background: Propofol gains popularity due to its smooth induction and rapid recovery. But one of its side effects is pain during injection. So, the aim of this study was to compare the efficacy of tramadol and lidocaine pretreatment for alleviation of pain on propofol injection in our setting.

Materials and methods: 80 patients of either sex (ASA grade I and II, age 20-50 years) who underwent elective Surgery under general anaesthesia were randomized into two equal groups (n=40). Group L (Control group) received pretreatment injection 2% lidocaine 40mg (2ml) Group T received pretreatment injection tramadol 50 mg (2ml). After that, 1/4th of calculated induction dose of propofol (2mg/kg) was administered. The level of pain was evaluated by four point verbal response scale.

Results: The overall incidence of pain on propofol injection was lower in lidocaine (20%) than in tramadol group (22.5%). The incidence of score '0' (No pain) was higher in lidocaine (80%) than in tramadol group (77.5%) but it is not statistically significant (p >0.05).

Conclusion: pretreatment with 2% lignocaine and tramadol effectively reduced the incidence and severity of propofol injection pain.

Key words: Lidocaine; Pain; Propofol; Tramadol.

Introduction

Propofol is one of the most commonly used induction agents around the globe. This is due to its fast onset and short duration of action. The commercial preparation is 1% formulation in an oil and water emulsion having egg lecithin 1.2%, soybean oil 10% and glycerol 2.25%.[1] Propofol has many characteristics of an ideal intravenous anaesthetic agent, providing smooth induction and rapid recovery. But it causes pain when given intravenously and incidence can be very high, with a range of 28 to 90%.[1-3] The cause of pain upon intravenous injection of propofol remains a mystery.[4] Some patient recalls the induction of anaesthesia as the most painful part of the perioperative period.[5] As a result the pain associated with injection of propofol remains a challenge and several interventions have been investigated to alleviate the pain associated with propofol injection.

Various methods have been used to decrease this discomfort, including cooling, diluting, adding lidocaine, applying nitroglycerine ointment to the venepuncture site and injecting cold saline prior to the injection of propofol.[6] A Quantitative Systematic Review reported IV lidocaine should be given with a rubber tourniquet on the forearm, 30 to 120 seconds before the injection of propofol, lidocaine will prevent pain in approximately 60% of the patients treated in this manner.[7] Venous flow inhibition of the upper extremities using a tourniquet can be effectively used as a model for studying peripheral reactions to drugs without whole-body effects.[8] Previous study have shown that, Lidocaine pretreatment reduces the incidence of pain.[9,10] As lidocaine has both a local anesthetic effect and a kinin cascade-stabilizing effect, it can be used for injection pain prevention.[11]

Tramadol is one of the widely used analgesic agents. Tramadol is a centrally acting analgesic. It has two different mechanisms of action. One is that, it acts as weak opioid agonist and another is that, it inhibits reuptake of monoamine neurotransmitter. Its role in perioperative pain management is established.Recently, a $5HT_3$

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Submitted on : 15.11.2021
Accepted on : 26.12.2021

antagonist, ondansetron also used as pretreatment has been shown to reduce propofol induced pain.[3,12]

In addition, pretreatment with tramadol have a peripheral site of action was as effective as lignocaine in reducing pain on propofol injection.[13]

Therefore the aim of this study is to evaluate the comparative efficacy of Tramadol and lidocaine pretreatment to relief pain during injection of propofol.

Materials and methods

The randomized, controlled study was conducted in the department of Anaesthesiology in Chittagong Medical College Hospital after ethical committee approval. Study duration was six months, from 6th June 2018 to 28thDecember 2018. Total 80 patients of aged between 20-50 years either of sex underwent surgical procedures under general anaesthesia were randomly allocated into two equal groups of 40 patients each. Patients excluded were who had history of allergy and known hypersensitivity to propofol or lignocaine or tramadol, history of taking analgesics or sedative or anti anxiety or pain modifying drugs, history of convulsion and head injury, pregnant patient, infection on the dorsum of their non dominant hand. Informed written consent was taken from each patient fulfilling inclusive criteria. Group L (Control group) was given pretreatment with injection 2% lidocaine 40mg (2ml) and Group T was given pretreatment injection tramadol 50 mg (2ml). Prior to the procedure, purpose of the study were explained to the patients and informed written consent was obtained and a careful general examination, systemic examination, airway examination were done in preoperative room.

Patients were assigned by block randomization (10 cards in each block, 5 cards were marked as T and 5 cards were marked as L) into two groups by a supervisor. On arrival of the operation theatre, an 18G cannula was inserted into a vein on the dorsum of the patient's non-dominant hand and Hartmann solution was infused. Heart rate, SPO_2 and mean blood pressure were measured as baseline value.

The volume of each pretreatment drug was 2 ml. Patients and the principal investigator was blinded about the constituents of the drugs. The selected patients were asked to take any one of the cards from the box. Then the name of the patient, cards name (Either T or L) and serial number were enrolled in a note book. The drug solutions were prepared by the co-worker who enrolled the patients and card name. We used venous occlusion by sphygmomanometer cuff because they used a tourniquet to give a "Bier's block like effect" for lidocaine.[14, 15] Following the venous occlusion at mid-arm by inflation of sphygmomanometer cuff to 70 mmHg, the pretreatment drugs were given by the principal investigator at the rate of 0.5ml/seconds. One minute later, the occlusion of venous drainage was released. After that one-fourth of the calculated dose (2 mg/kg) of propofol 1% was injected over 5 seconds because speed of propofol injection directly correlates with pain on injection.[15] The patient then asked about any sensation of pain within 15 seconds after injection of propofol. The intensity of Pain was assessed using four point verbal response scales and it was assessed by the principal investigator. The adverse effects, if any, also noted and managed accordingly during this period. Later, Induction of anesthesia was achieved with injection propofol and the study was completed at this point. The anaesthestic procedure was continued according to the standard protocol. Every patient was monitored for any allergic reaction at the injection site and nausea, vomiting, headache for 24 hour from the pretreatment. If any adverse reaction occurs, it was noted in data collection sheet and managed accordingly.

Results

Table I Age and Sex distribution of the patients (n=80)

Age (Years)	Number of patients		Total (%)
	Group L (n = 40) No. (%)	Group T (n = 40) No. (%)	
<30	7(17.5%)	6(15.0%)	13(16.2%)
31-40	14(35.0%)	16(40.0%)	30(37.5%)
41-50	19(47.5%)	18(45.0%)	37(46.2%)
Mean ± S.D.	41.4±9.7	42.1±8.5	
Sex(Male/Female)	21/19	22/18	

Table I showed age distribution of patients. This study was conducted on patients with age ranging from 20 to 50 years. It was observed that majority, e.g. 37(46.2%) patients belonged to age 41-50 years, followed by 30(37.5%) of patients belonged to age 31-40 years. The mean age was found 41.4±9.7 years in Group-L and 42.1±8.5 years in Group-T.

Table II American Society of Anesthesiologist (ASA) physical status distribution of the patients (n=80)

ASA Status	Number of Patient	
	Group L (n = 40) No. (%)	Group T (n = 40) No. (%)
ASA I	27(67.5%)	22(55.0%)
ASA II	13(32.5%)	18(45.0%)

Table II shows patient distribution according to ASA physical status. ASA I was higher in group L than group T and ASA II was higher in group T than group L.

Table III Degree of pain sensation using four point verbal response scale prior and after administration of propofol (n = 80)

Four point Verbal response scale	Number of patients		p value
	Group L (n = 40) No. (%)	Group T (n = 40) No. (%)	
Degree of pain just after (Within 15 seconds) giving inj. propofol			
0	32(80%)	31 (77.5%)	
1	8(20%)	8 (20%)	0.602
2	0	1(2.5%)	(ns)
3	0	0	

The incidence and severity of pain during propofol injection is shown in Table III. The overall incidence of pain on propofol injection was lower in group L (20%) than in group T (22.5%). The incidence of score '0' (No pain) was higher in group L (80%) than in group T (77.5%) but it is not statistically significant (p >0.05).

Table IV Trends of Heart Rate (HR) in the studied group (n=80)

	Heart rate		p value
	Group L (n = 40) Mean ± S.D.	Group T (n = 40) Mean ± S.D.	
Before giving inj. propofol	102.2 ± 6.3	105.5 ± 7.2	0.182(ns)
1 min. after inj. propofol	117.5 ± 9.1	122.4 ± 9.1	0.206(ns)
3 min. after inj. propofol	97.4± 8.1	84.3 ± 8.9	0.001(s)

Before giving inj. propofol, mean heart rate was 102.2 ±6.3 beat/min and 105.5±7.2 beat/min in group L and group T respectively. After 1minute of inj. propofol, mean heart rate was found 117.5±9.1 beat/min in group L and 122.4±9.1 beat/min in group T. Then 3 minutes later of inj. Propofol, it was found that in group-L mean heart rate detected 97.4±8.1 beat/min and in group T mean heart rate detected 84.3±8.9 beat/min. The difference was statistically significant ($p<0.05$) between two groups (Tab le IV).

Table V Trends of Mean blood pressure among studied group (n=80)

	Mean blood pressure		p value
	Group L (n = 40) Mean ± S.D.	Group T (n = 40) Mean ± S.D.	
Before giving inj. propofol	93.025 ± 0.338	92.925 ± 0.360	
1 min. after inj. propofol	93.025 ± 0.338	92.925 ± 0.360	0.8(ns)
3 min. after inj. propofol	93.025 ± 0.338	92.925 ± 0.360	

No gross variation was observed in the mean blood pressure at different time in the studied groups (Table V).

Table VI Trends of SPO_2 among studied group (n=80)

	SPO_2		p value
	Group L (n = 40) Mean ± S.D.	Group T (n = 40) Mean ± S.D.	
Before giving inj propofol	96.5 ± 0.506	96.8 ± 0.51	
1 min. after inj. propofol	96.5 ± 0.506	96.8 ± 0.408	0.8(ns)
3 min. after inj. propofol	96.5 ± 0.506	96.8 ± 0.408	

No gross variation was observed in the SPO_2 at different time in the studied groups (Table VI).

Discussion

Considering the extensive use of propofol in clinical practice, the high incidence of pain (28-90%) on induction of anaesthesia cannot be neglected.[1-3] In our study, we observed and compared the effect of pretreatment with lidocaine and tramadol for reducing pain associated with propofol injection.

In our study, the mean age was found 41.4±9.7 years in Group lidocaine and 42.1±8.5 years in Group tramadol. Harprit et al done a prospective,

randomized, double blinded study in total 100 patients for 01 year.[4] They randomly divided into 4 groups of 25 patients each Group L (Lignocaine) Group T (Tramadol) Group K (ketorolac) and Group N (Normal saline) Mean age was 37.52 ± 9.68 and 38.40 ± 7.94 in group-lidocaine and tramadol respectively which was closer to our study age group.[4,13,3]

We have done a randomized, double blinded study where 67.5% patient in lidocaine group was ASA I and 32.5% patient was ASA II. In tramadol group 55% patient was ASA I and 45% patient was ASA II. The unequal distribution of ASA physical status between two groups was due to randomization process.[16,17]

The overall incidence of pain on propofol injection in our study was lower in group L (20%) than in group T (22.5%) in our study. The incidence of score '0' (No pain) was higher in group L (80%) than in group T (77.5%) but it is not statistically significant ($p > 0.05$).[18,19]

Shah et al performed a randomized clinical trial in 100 patients, Group A received 50 mg intravenous tramadol, whereas Group B received 2 ml of 2 % lidocaine. Pain was present in 7 patients (14%) in group A as compared to 11 patients in group B (22%) [p value=0.298]. This showed that there was no significant statistical difference between pretreatment with Tramadol and Lignocaine.[1] Similar results were observed in our study, pain was present in 8 patients (20%) in lidocaine group as compared with 9 patients (22.5%) in tramadol group ($p > 0.05$).[17,20,21]

Another prospective, randomized, double blinded, single centre study was done where 100 adult patients (ASA grade I and grade II) scheduled for elective surgery under general anaesthesia.[22,23] Patients were randomly divided into 4 groups of 25 patients each Group L (Lignocaine) Group T (Tramadol) Group K (Ketorolac) and Group N (Normal saline). There was no statistically significant difference among group L (24%), T (28%) and K (28%) for pain on injection but statistically significant difference of all 3 groups was found when compared with group N.[4] In our study we had no placebo (normal saline) group but beside that our observations were similar to this study regarding propofol injection pain. [24,25]

According to our study, we observed the mean SPO_2 value in lidocaine group was 96.5 ± 0.506% before giving inj. Propofol and 96.5± 0.506% after 3 minutes of giving inj. Propofol, mean SPO_2 value in tramadol group was 96.8 ± 0.51% before giving inj. Propofol and 96.8± 0.408% after 3 minutes of giving inj. Propofol. The change of SPO_2 was not statistically significant ($p > 0.05$).[18,19]

Thus, we can conclude that both lidocaine and tramadol pretreatment is equally effective in order to decrease the pain caused by propofol injection in addition with stable haemodynamics.

Limitations

- Our study had few limitations. The duration of study was short and sample size was small.
- It was a single centre study. Only patients admitted in Chittagong Medical College Hospital, Chittagong were taken for the study. So this will not reflect the overall picture of the country. A large scale study needs to be conducted to reach to a definitive conclusion
- Sample were taken by purposive method in which question of personal biasness might arise.
- Pain is a subjective perception. We didn't perform any psychological evaluation of patient that interfere pain assessment during the study.

Conclusions

The findings of our study suggest that pretreatment with either 2% of 2ml lignocaine or Tramadol 50mg was equally effective in reduction of propofol injection pain.

Recommendation

We can recommend that, Tramadol can be used as an alternative pretreatment drug for reducing propofol injection pain where lidocaine is contraindicated. In addition, tramadol is a widely available drug now a day and can be used as a cost effective pretreatment technique at the time of propofol induction.

Acknowledgement

All the authors confer their gratefulness to all the staffs of Department of Anesthesiology, Chittagong Medical College for their continuous support and co-operation without this, the study would not have been possible.

Contribution of authors

MHOR-Conception, acquisition of data, drafting & final approval.

MSI-Acquisitation of data, data analysis, drafting & final approval.

RKN-Interpretation of data, critical revision & final approval.
PKD-Data analysis, critical revision & final approval.
SAB-Interpretation of data, drafting & final approval.
GAC-Design, critical revision & final approval.

Disclosure

All the authors declared no competing interests.

References

1. Shah SARA, Bukhari RH, Naqvi SSN. Efficacy of intravenous tramadol in reduction of propofol induced pain. Anaesth Pain & Intensive Care. 2016; 20(2):150-153.

2. Prashant J, Pachore, Sonal A, Chaudhar, Abhimanyu S, Tarkase, Ganesh K, Nikam. Comparative Study of Ondansetron with Lignocaine to Alleviate Pain during Injection of Propofol. Journal of Evolution of Medical and Dental Sciences. 2014; 3(44): 10828-10835.

3. Ansari. M Umar, Garg. Gangashankar, Lodha L.R, Qureshi. S. U, Porwal. S. Pre- treatment with intravenous ondansetron to alleviate pain on propofol injection: A randomized, controlled & double-blind study. J Pharm Biomed Sci. 2013; 32(32): 1274-1278.

4. Madan H, Singh R, Sodhi G. Comparsion of Intravenous Lignocaine, Tramadol and Keterolac for Attenuation of Propofol Injection Pain. J Clin Diagn Res .2016; 10(7):5-8.

5. Jalota L, Kalira V, George E, Shi Y, Hornuss C, Radke O, Pace NL, Apfel CC. Prevention of pain on injection of propofol: systematic review and meta-analysis. BMJ. 2011; 342:1-18.

6. Shaban E. Comparative study between Lignocaine, pethidine, Dexamethasone, Ephedrine and placebo for prevention of pain on propofol injection. AAMJ. 2006; 4:1.

7. Picard P, Tramer M. Prevention of Pain on Injection with Propofol: A Quantitative Systematic Review. Anesth Analg. 2000; 90:963–969.

8. 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; 27: 253-257.

9. Patilbuwa PV, Yarramalle SP. A randomized comparative study of metoclopramide, ketamine and lignocaine given intravenously to attenuate pain due to propofol. International Journal of Contemporary Medical Research. 2016; 3(9):2746-2749.

10. Sai V, Kamath S. Does Granisetron Pretreatment Relieve Pain Due to Propofol Injection? American Journal of Advanced Drug Delivery. AJADD. 2015; 3(1):104-109.

11. Scott RP, Saunders DA, Norman J. Propofol: clinical strategies for preventing the pain of injection. Anaesthesia. 1988; 43: 492-494.

12. Zahedi H, Maleki A , Rostami G. Ondansetron Pretreatment Reduces Pain on Injection of Propofol. Acta Medica Iranica. 2012; 50(4): 239-243.

13. W H Wong, K F Cheong. Role of Tramadol in Reducing Pain on Propofol Injection. Singapore Med J. 2001; 42(5):193-195.

14. Johnson RA, Harper NJN, Chadwick S, Vohra A. Pain on injection of propofol: methods of alleviation. Anaesthesia. 1990;45: 439–442.

15. Hiller A, Saarnivaara L. Injection pain, cardiovascular changes and recovery following induction of anaesthesia with Propofol in combination with alfentanil or lidocaine in children; Acta Anaesthesia Scandinavia. 1992; 36(6): 564-568.

16. Sennur U, Burcu A, Banu A. Effects of different propofol injection speeds on blood pressure, dose, and time of induction. Turk J Med Sci. 2011; 41 (3): 397-401.

17. Mattila MA, Koski EMZ. Venous sequelae after intravenous propofol:a comparison with methohexitone in short anaesthesia. Postgrad med J. 1985; 61 (3):162-164.

18. Singh D, Jagannath S, Priye S, Kadli C and Reddy D. Prevention of propofol injection pain: Comparison between lidocaine and ramosetron. Journal of Anaesthesiology Clinical Pharmacology 2014 April-June; 30(2):213-216.

19. Briggs LP, Clarke RS, Dundee JW, Moore J, Bahar M, Wright PJ. Use of di-isopropyl phenol as main agent for short procedures. Br J Anaesth. 1981; 53(11):1197-1202.

20. Yull DN, Barkshire KF, Dexter T. Pretreatment with ketorolac and venous occlusion to reduce pain on injection of propofol. Anaesthesia. 2000;55(3):284-287.

21. Kay B, Rolly G. a new intravenous induction agent. Acta Anaesthesiol Belg. 1977;28(4):303-316.

22. 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;1:118-122.

23. Yadav M, Durga P, Gopinath R. Role of Steroids in Prevention of Pain on Propofol Injection. J Anesthe Clinic Res. 2011; 2:132.

24. Khouadja H, Arnous H, Tarmiz K, Beletaifa D, Brahim A, Brahem W, Sakhri J, Jazia KB. Pain on Injection of Propofol: Efficacy of Paracetamol and Lidocaine. Open Journal of Anesthesiology. 2014; 4: 81-87.

25. Nadkarni M, Mahajan J. Comparison of Pre-Treatment with Ondansetron Versus Tramadol For Reduction of Pain on Injection of Propofol- A Prospective, Randomized Study. Journal of Dental and Medical Sciences. 2016;15(9): 82-84.