Original Article

Efficacy of Propofol Mixed With Lidocaine Versus Lidocaine Followed By Propofol To Reduce Injection Pain Due To Propofol In Patients Undergoing General Anaesthesia

Muhammad Adnan Akram, Syed Musharraf Imam, Shahid Maqsood

ABSTRACT

Introduction: Propofol is widely used for induction and maintenance of anaesthesia and possesses many characteristics of an ideal anaesthetic. A disadvantage of propofol is pain on injection, which is sometimes very distressing to patients. Many different methods have been proposed to reduce the incidence and severity of this adverse effect of propofol. **Objective:** To determine the efficacy of premixed inj lidocaine and propofol versus separately giving them, for reducing propofol injection pain. **Study Design:** Randomized clinical trial. **Place and duration of study:** Study was conducted in main operation theatre Combined Military Hospital Peshawar over a period of six months from 1st July 2010 to 31st Dec 2010. **Methodology:** One hundred and twenty patients in ASA I & II were enrolled by non probability consecutive sampling, who were scheduled for different elective surgical procedures under general anaesthesia. The patients were randomized into two groups (A and B). Patients of Group A received pretreatment with lidocaine 2% (0.5 mg/kg body weight) followed by inj propofol 1% (2mg/kg body weight).Group B received premixed inj propofol with lidocaine on similar weight base doses. **Results**: In group-A pain was reported by 19 patients (30.9%) and in group B pain developed in 6 patients (9.7%) (P=0.003). **Conclusion** Premixed Propofol and lidocaine was more effective in reducing propofol induced pain incidence on injection than giving these two injections separately.

Key Words Pain, propofol injection, lidocaine, anaesthesia

INTRODUCTION

Propofol is widely used for induction and maintenance of anaesthesia and possesses many characteristics of an ideal anaesthetic. It is known to cause severe, sharp, itching or burning pain on injection that can be distressing to the patient. This pain is considered to be clinically unacceptable as it can cause agitation and hinder the smooth induction of anesthesia [1]. During induction of anaesthesia, the incidence of injection pain has been shown to vary between 28% and 90% in adults [2]. Different methods and formulations has been tried to reduce pain on injection with propofol [3] including mixing lidocaine with propofol in the same syringe, pretreatment with lidocaine or procaine, cooling or warming or diluting the propofol solution, injection of propofol into a large vein [4], prior injection of ondansetron, ketamine, opioids, magnesium sulfate, ketorolac or tramadol. In previous studies, metoclopramide pre-treatment and propofol premixed with lidocaine were introduced as two effective and safe methods [5]. Two of the most commonly accepted techniques are the administration of lidocaine immediately before propofol or mixing lidocaine with propofol itself [6, 7]. There is a significant statistical data showing incidence of pain is 8% with mixed lidocaine

Corresponding Author
Dr. Muhammad Adnan Akram
Graded Anaesthesiologist
Combined Military Hospital Peshawar
E-mail: dr_adnanakram@yahoo.com

and propofol as compared to 28% pain with separate administration of these drugs [6].

The rationale of the study is to decrease pain on injection with propofol, which is most commonly used for induction of anaesthesia having number of advantages over other anaesthetic drugs with respect to cost effectiveness and other anaesthetic qualities. It will benefit patients in terms of smooth induction and good anaesthetic experience

METHODOLOGY

Study was conducted in main operation theatre Combined Military Hospital Peshawar. It was randomized clinical trial and was carried out over a period of six months from 01-07-2010 to 31-12-2010. A total of 120 patients divided into two groups (group A and group B) were included in the study. Sample size was calculated by using WHO sample size calculator taking level of significant 5%, power of test 90% population. All ASA I and II booked patients with good IQ in both genders between the ages 20 to 50 years undergoing elective surgical procedures were included in the study. Patients with low IQ, having history of allergy to lidocaine and propofol, disoriented patients, were excluded from the study.

The study was conducted after approval of the Hospital ethical committee and all the data was recorded on the pre designed proforma bearing the informed consent and explaining the risk and benefits to the patients.

An 18G intravenous cannula was inserted in dorsal vein of hand of each patient before start of surgery. Randomization was done by computer generated table of random numbers.

In the operating room non-invasive blood pressure monitoring and pulse oximetry was applied to each patient. Group A received pretreatment with 2% lidocaine intravenously on body weight basis just after the venous occlusion by tourniquet followed by injection propofol intravenously in calculated dose over a period of 5 seconds. Group B received intravenous injection of premixed calculated doses of propofol and lidocaine. Patients were explained about Numerical pain scale ranging from 0 to 10. They were taught to describe their pain perception by numbering from 0 to 10. Pain was assessed as per patient response by the anesthetist and was recorded. Those patients who were unable to speak their pain score before becoming unconscious were excluded from the study. The level of unconsciousness was established by drop of a pencil held by the patient with his thumb and index finger.

All the data collected was entered into the statistical package for social sciences (SPSS) version 10 and analyzed through the statistical package. Mean and standard deviation was used for demographic data while frequency and percentages were calculated for assessment of pain. Pain intensity was assessed using Numerical Pain Scale. Chi Square was used to compare pain response between the two groups. P value of less than 0.05 was taken as significant.

RESULTS

The demographic data of the patients are given in Table 1. No statistical difference was found between two groups regarding mean age, body weight and heights. Baseline hemodynamics is shown in Table 2 showing no demonstrable differences. Pain of mild intensity was taken as numerical scale 1-3, and moderate pain was nominated by verbal scale from 4-7 and severe pain was labeled for numbers 8 and above.

Table-1
Comparison of demographic data of patients in two groups

Parameters	Group A n=60	Group B n=60
Age (yrs.) Mean ± SD	55 ± 5	53 ± 7
Body Wt. (kg) Mean ± SD	64 ± 4	65 ± 3
Height (cm) Mean ± SD	166±2	164±2

Table-2
Comparison of baseline hemodynamics in two groups (Mean ± SD)

Parameters	Group A n=60	Group B n=60
SystolicBlood Pressure	118±7	117±9
Diastlic Blood Pressure	68± 12	66±10
Mean Blood Pressure	82±12	86± 11
Base line Heart Rate(b/min)	98±12	102±14
Base line Respiratory Rate	20±4	19±6
SaO2(%)	98±2	97±3

Table-3
Pain response

Pain on injection	Group-A (n=60)		Group-B (n=60)	
	Number of patient	%	Number of patient	%
Yes	19	30.6	06	09.7
No	43	69.4	56	90.3
Total	**62**	**100.0**	**62**	**100.0**

Chi Square = 8.47
df = 1
P value = 0.003

Pain of mild intensity was neglected for making the study simple. Only the moderate to severe pain was considered for the study. In group-A, moderate to severe pain was reported by 19 patients (30.9%) and in group-B, moderate to severe pain was noted in 6 patients (9.7%). There was a statistically significant difference between two groups with p value 0.003 (Table 3).

DISCUSSION

Propofol is frequently used intravenous aesthetic induction agent, especially for brief cases, day care surgery or when a laryngeal mask airway is to be used. Pain on injection with propofol is a common problem and can be very distressing to the patient. Incidence of pain varies between 28% and 90% [8] in adults and 28%-85% in children [9,10].

The younger the child, the higher is the incidence and severity of propofol injection pain. This could be due to small veins in hand. Many factors appear to affect the incidence of pain, which includes site of injection, size of vein, speed of injection, buffering effect of blood, temperature of propofol and concomitant use of drugs such as local anesthetics and opiates [11].

Pain on injection of propofol can be immediate or delayed. Immediate pain probably results from a direct irritant effect whereas delayed pain probably results from an indirect effect via the kinin cascade. Delayed pain has latency of between 10 and 20s [12].

Administration of lidocaine - either before or pre-mixed with propofol is the most widely used method. Lidocaine is more effective when it is added to the propofol and not injected before it [6]. So the admixture of the lidocaine-propofol used in our study is the best form thus studied to effectively control such pain. The addition of lidocaine may lead to destabilization of the propofol solution. When applying the emulsion in a 9:1 mixture of propofol lidocaine within a short time frame (< 30min), this effect is negligible. Lidocaine in propofol reduced the pain on injection [13]. Our study has also showed similar results. The analgesic effect of lidocaine may occur because of a local anesthetic effect.

Lilley et al. [14] showed that adding lidocaine to propofol emulsion increased the lipid droplet size and caused an oil droplet to form in a time- and dose dependent manner [14]. The propofol / lidocaine ratios used in the study ranged from 200:10 to 200:50 mg, similar to ratios used in clinical practice to reduce the pain of propofol injection [15].

The addition of 10 mg of lidocaine to 90 mg of propofol also caused a time-dependent reduction of propofol concentration in the emulsion as propofol separated out to form an oily layer [16]. Despite these changes, Lilley et al [14]. suggested that the changes in droplet size with freshly prepared mixtures using up to 20 mg of lidocaine to 200 mg of propofol were unlikely to have clinically significant effects. This is supported by the results of our study.

In contrast to our findings, two other studies suggested a decrease in anesthetic potency of propofol when administered as a propofol / lidocaine mixture.

Eriksson et al. [17] found that mixing 20 mg of lidocaine with 200 mg of propofol increased the dose of propofol required to induce hypnosis in rats by 64%–68% [17].

Another study, looking at pain reduction with the addition of lidocaine and/or prilocaine to propofol in women undergoing dilation and curettage, showed a 34% increase in the total amount of propofol required to induce and maintain anesthesia in those who received a propofol / lidocaine mixture compared with those who received a propofol/saline mixture [18]. The study compared the total doses of propofol, not induction doses or doses per kilogram of body weight. Although the mean duration of surgery and body weight was similar between the two groups, the actual figures were not stated.

CONCLUSION

It is concluded in current study, after comparing the two methods, that propofol mixed with lidocaine during injection of propofol is more effective in reducing propofol induced pain on injection than pretreatment with 2% lidocaine.

Further studies are required to uncover the underlying mechanism of action of the premixing the two drugs that is lidocaine and propofol.

REFERENCES

1. So SY, Kim YH, Ko YK, Park SI, Pak HJ, Jung WS. Effect of lidocaine (40 mg) mixed to prevent injection pain of propofol on the intubating conditions and onset time of rocuronium**.** Korean J Anesthesiol. 2013; 64: 29-33.
2. Jeon Y. Reduction. of pain on injection of propofol: combination of nitroglycerin and lidocaine. J Anesth. 2012; 26: 728-31.
3. Canbay O, Celebi N, Arun O, Karagöz AH, Saricaoğlu F, Ozgen S. Efficacy of intravenous acetaminophen and lidocaine on propofol injection pain. Anaesth 2008;100:95-8.
4. Tariq M A, Kamran M. Incidence of pain on Propofol injection and efficacy of addition of Lignocaine or selecting big vein or both combined in reducing it. J Postgrad Med Inst 2006; 20: 8-11.
5. Fujii Y, Nakayama M. A lidocaine/metoclopramide combination decreases pain on injection of propofol. Can J Anaesth. 2005; 52: 474-7.
6. Depue K, Christopher NC, Raed M, Forbes ML, Besunder J, Reed MD. Efficacy of intravenous lidocaine to reduce pain and distress associated with propofol infusion in pediatric patients during procedural sedation. Pediatr Emerg Care. 2013; 29: 13-6.
7. LeeHY, KimSH, SoKY. Prevention of microemulsion propofol injection pain: a comparison of a combination of lidocaine and ramosetron with lidocaine or ramosetron alone. Korean J Anesthesiol 2011; 61: 30-4.
8. Canbay O, Celebi N, Arun O, Karagöz AH, Saricaoğlu F, Ozgen S. Efficacy of intravenous acetaminophen and lidocaine on propofol injection pain. Anaesth 2008; 100: 95-8.
9. Mannarino R, Luna SP, Monteiro ER, Beier SL, Castro VB. Minimum infusion rate and hemodynamic effects of propofol, propofol-lidocaine andpropofol-lidocaine-ketamine in dogs. Vet Anaesth Analg. 2012; 39: 160-73.
10. Basaranoglu G, Erden V, Delatioglu H, Saitoglu L. Reduction of pain on injection of propofol using meperidine and remifentanil. Eur J Anaesthesiol 2005; 22:890-2.
11. Polat R, Aktay M, Ozlü O. The effects of remifentanil, lidocaine, metoclopramide, or ketamine pretreatment on propofolinjection pain. Middle East J Anesthesiol. 2012; 21: 673-7.
12. Mahmood I, Yasmine M. Prevention of pain on propofol injection: a comparative, randomized, double blind study between lignocaine, ketamine, dexamethasone and placebo. Professional Med J 2010; 17: 405-10.
13. Chaudhary K, Gupta P, Gogia AR. A prospective, randomized, double-blind study to compare the efficacy of lidocaine + metoclopramide and lidocaine + ketamine combinations in preventing pain on propofol injection. J Anesth. 2012 Dec 12
14. Choi YJ, Park HS, Lee H, Yoon SZ. Single pretreatment of remifentanil may reduce pain after propofol androcuronium injection i n rapid sequence induction. Korean J Anesthesiol. 2012; 63: 413-8.
15. Sethi N, Jayaraman L, Sethi M, Sharma S, Sood J. Prevention of propofol pain: a comparative study. Middle East J Anesthesiol. 2009; 20: 71-4.
16. Aldrete JA, Otero P, Alcover J, Parietti A, Johnson SC, Montpetit FH, Torrieri A, Quiroga D. Pain on injection from propofol may be avoided by changing its formulation. Acta Anaesthesiol Scand. 2010; 54: 442-6.
17. Brock MF, Grace BE, Morley B, Hillegass G, Houle TT, Groban L. Does lidocaine more effectively prevent pain upon induction with propofol or etomidate when given preemptively than when mixed with the drug?. J Clin Anesth. 2010; 22: 505-9.
18. Koo SW, Cho SJ, Kim YK, Ham KD, Hwang JH. Small-Dose Ketamine Reduces the Pain of Propofol Injection. Anesth Analg 2006; 103: 1444-7.

AUTHORS

- **Dr. Muhammad Adnan Akram**
  Anaesthesiologist
  Combined Military Hospital Peshawar
  Email address: dr_adnanakram@yahoo.com
- **Dr. Syed Musharraf Imam**
  Classified Anaesthesiologist
  Combined Military Hospital Peshawar
- **Dr. Shahid Maqsood**
  Anaesthesiologist
  Combined Military Hospital Peshawar

Submitted for Publication: 04-04-2013

Accepted for Publication: 04-05-2013
After minor revisions