ORIGINAL ARTICLE

A single-centre randomized-controlled trial to study effect of dilution on propofol-induced injection pain at injection site

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ABSTRACT

Background: Propofol is a commonly used short-acting intravenous anaesthetic agent. A major disadvantage of propofol is pain at injection site with high incidence up to 90%. Various modalities have been tried to obtund propofol-induced pain; however, search for an ideal agent continues. We assessed the effect of double and triple dilution of 1% propofol emulsion with normal saline on pain at injection site. **Methods:** This randomized, double-blinded study was done on 60 adult patients of both sexes, belonging to ASA grade I and II scheduled for elective surgery under general anesthesia, divided into three groups named I, II, III of 20 patients each. The patients of group I, II, and III received 1% propofol 2 ml, 0.5% propofol 4 ml, and 0.33% propofol 6 ml, respectively, over a period of 4 s and pain felt was assessed. **Results:** There was no statistically significant difference in the pain score in group II as compared to patients in group I. However, there was a statistically significant decrease in the pain score in group III as compared to patients in group I (*P* value 0.02) and group II (*P* value 0.03). **Conclusions:** We found a significant decrease in both incidence and severity of pain during injection with a 0.33% propofol solution without significant adverse hemodynamic effects. The small size of data was a limitation in our study and a large-scale study will be needed to prove its therapeutic beneficence.

Key words: *Dilution, injection, pain, propofol*

INTRODUCTION

Propofol is one of the most commonly short-acting intravenous anesthetic used and has a rapid onset of action. It is available as milky white isotonic emulsion containing propofol, soyabean oil, and egg lecithin. It produces smooth induction and rapid recovery of general anesthesia–the feature that makes the agent suitable for day care anesthesia. It is frequently used for sedation, induction, and maintenance of anesthesia. A major disadvantage of propofol is pain at site of injection with a high incidence up to 90%.[1] It is distressing and uncomfortable for the patient and should be controlled or prevented to make the induction of anesthesia pleasant. It is hypothesized that the concentration of free propofol in the aqueous phase of emulsion is responsible for the pain. Various modalities have been tried to obtund propofol-induced pain. These include drugs like Lignocaine, Ondansetron, Fentanyl, Metoclopramide, Ketamine, Ephedrine, etc.[2-6] These drugs have been administered in various ways and doses. Other physical methods like microfiltration, double line intravenous set, warming the propofol to 37°C, cooling of propofol to 4°C, and reducing the pH of propofol injectate have also been tried.[7-11] However, some investigators have shown that the addition of lidocaine to propofol resulted in a coalescence of oil droplets , and it is thought that the concentration of free propofol in the aqueous phase can be changed.[12] However, search for an ideal technique for relief of propofol-induced pain on injection still continues. In the present study, we assessed the effect of double and triple dilution of 1% propofol emulsion with normal saline on pain at injection site.

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METHODS

The present randomized, double-blind study was

conducted in the Department of Anesthesiology and Critical Care at a tertiary care teaching hospital. Ethical approval was obtained from Institution Ethical Committee and informed consent was obtained from each patient to participate in study.

Sixty adult patients of both sexes belonging to ASA grades I and II scheduled for elective surgery under general anesthesia were randomly selected for the study. All patients were pre-medicated orally with tablet Diazepam 10 mg 2 hr prior to surgery. The patients having cardiovascular, respiratory, renal, or hepatic diseases were excluded from the study. Monitoring for continuous ECG, heart rate, NIBP (systolic, diastolic and mean BP), and SPO_2 was started and intravenous line of 18-G cannula was established in all patients over dorsum of either hand or forearm. All patients were divided by an anesthesiologist by draw of lots into three groups named I, II, III of 20 patients each.

The patients of group I received 1% propofol 2 ml. Patients of group II were given 0.5% propofol 4 ml and patients of group III were given 0.33 % propofol 6 ml over a period of 4 s in each case. The available 1% solution of propofol was diluted with normal saline to make it 0.5% or 0.33% solution (double or triple dilution). During injection the pain felt by patient was assessed by the second anesthesiologist (who was unaware of the group assignments) and graded by the patient on 4-point scale as, 0-no pain, 1-mild pain, 2-moderate pain, and 3-severe pain. Any involuntary movement of the limb due to injection pain was recorded. Data were analyzed by using appropriate statistical analysis. Rest of the inducing dose of propofol was injected after assessing pain to continue anesthesia.

The study protocol is depicted in Figure 1.

RESULTS

The study was done on 60 persons. Out of them 35 (58.33%) were males and 25 (41.67%) were females. All the three groups were comparable with respect to demographic variables (age, body weight, and sex ratio) as shown in Table 1. At pre-injection time (base line value) heart rates recorded were 90.70 ± 21.65, 82.70 ± 11.69, and 83.70 ± 16.01 beats per min which were changed to 93.90 ± 17.45, 78.05 ± 11.01, and 83.20 ± 16.56 beats per min at the end of study period in groups I, II, and III, respectively. On comparison, no statistical significant difference was found between the groups and also within the group at any point of time during the study period. There was also no statistical significant difference between the groups and also within the group at any point of time during study period in systolic BP. At pre-injection time it was 127.95 ± 15.23, 126.50 ± 09.23, and 129.95 ± 12.80 mmHg and at the end of study period (5 min) its values were 116.85 ± 23.23, 118.35 ± 11.41, and 119.15 ± 12.04 mmHg in groups I, II, and III, respectively. At pre-injection time, the diastolic BP was 78.60 ± 13.49, 80.10 ± 10.40, and 84.00 ± 8.66 mmHg and at the end of study period (5 min) its values were 74.85 ± 16.43, 76.70 ± 10.10, and 75.65 ± 10.32 mmHg in groups I, II, and III, respectively. There was no statistical significant difference between the groups and also within the group at any point of time during the study period. At pre-injection time (base line value) the mean BP values recorded were 97.90 ± 11.83, 97.15 ± 7.21, and 99.35 ± 8.94 which were changed to 89.35 ± 17.23, 91.30 ± 9.12, and 91.75 ± 10.54 mmHg at the end of study period in groups I, II, and III, respectively. On comparison, no statistical significant difference was found between the groups and also within the group at any point of time during the study period.

No pain was observed in four patients (20%) in group III as compared to 0 patients in groups I and II. Severe pain was observed in five patients in group I (25%) as compared to three patients (15%) and 0 patient in groups II and III,

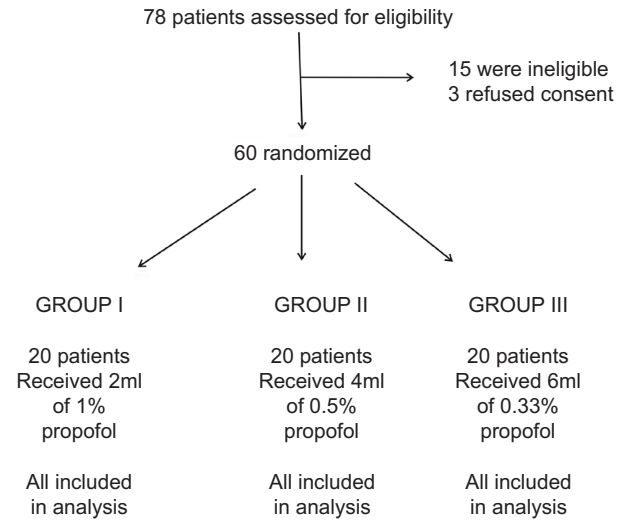

Figure 1: Study design

Table 1: Showing demographic data (mean ± SD) with sex ratio of all three groups ($P < 0.05$ significant)

	Demographic data			
	Group I ($n = 20$)	Group II ($n = 20$)	Group III ($n = 20$)	*P* value
Age (years)	35.55 ± 11.10	36.70 ± 16.25	38.40 ± 10.88	0.12
Body weight (kg)	56.00 ± 8.67	61.05 ± 7.66	60.00 ± 9.50	0.15
Male: Female	11:9	13:7	11:9	

Table 2: Pain score in three groups

Pain score	Pain severity		
	Group I (*n* = 20)	Group II (*n* = 20)	Group III (*n* = 20)
0 – No pain (%)	0 (0)	0 (0)	4 (20)
1 – Mild pain (%)	9 (45)	9 (45)	12 (60)
2 – Moderate pain (%)	6 (30)	8 (40)	4 (20)
3 – Severe pain (%)	5 (25)	3 (15)	0 (0)
Total patients	20	20	20

respectively. The pain score of patients in three groups is shown in Table 2. The reduction in pain was statistically significant in group III (*P* value < 0.05). There was no statistically significant difference in the pain score in patients in group II as compared to patients in group I (*P* value > 0.05). However, there was statistically significant difference in the pain score in group III as compared to patients in group I (*P* value 0.02) and patients in group II (*P* value 0.03)

DISCUSSION

We found a significant decrease in both incidence and severity of pain during injection of propofol with 0.33% propofol without significant adverse hemodynamic effects during induction.

Pain at the site of injection of propofol is well documented in the literature with the incidence up to 90%.[1] Its severity ranges from mild to severe and sometimes associated with limb retraction. The pain by propofol has an onset latency of between 10 and 20 s and is probably an indirect effect mediated via the kinin cascade.[13] Propofol belongs to the group of phenols that irritate the skin, mucous membranes, and venous intima. Propofol, by its indirect action on the endothelium, activates the kallikrein-kinin system and releases bradykinin, thus producing venous dilation and hyperpermeability.[14] It increases the contact between the aqueous phase of propofol and the free nerve endings, thus producing the sensation of pain. Propofol, when drawn up in a disposable syringe, may lead to formation of irritants and may result in producing pain sensation.[15] It has been confirmed that propofol strips the silicone lubricant from the inside barrel of plastic syringes. Pain on injection is obviously not important enough to negate its pharmacokinetic and pharmacodynamic advantages over other drugs that have led to this popularity. It is, however, troublesome and unpleasant, particularly during sedation. Various modalities have been tried to reduce the incidence and severity of propofol induced pain by using lignocaine, ondansetron, metoclopramide, ketamine, ephedrine, microbiological filter cooling the solution of propofol, etc.[2-7,9] But none of them was found to be ideal to reduce the propofol-induced pain. Lignocaine is widely used to control propofol-induced pain at the injection site, but unfortunately it has a failure rate of about 28-47%.[16] As the failure rate has been reported by various workers with the use of a single remedy, Kobayashi *et al.* used a combination of remedies to get 100% success.[17] In their study injection fentanyl was followed by injection of cold propofol premixed with lidocaine in a forearm vein without carrier IV fluid in the study group. In the control group, 90% patients experienced injection pain, whereas no patients complained of pain or discomfort in the study group. Thus, pain-free propofol injection was made possible by prior administration of fentanyl premixing of lidocaine, and rapid injection of cold propofol at 4°C via a forearm vein. In our study, no pain was experienced by 20% of patients receiving triple diluted (0.33%) propofol and severity of pain was significantly reduced in others as compared to 1% and 0.5% propofol. The small size of data was a limitation in our study and a large-scale study comparing the results with the lignocaine mixture will throw more light on therapeutic beneficence of triple dilution of propofol on pain during injection.

REFERENCES

1. Tan CH, Onsiong MK. Pain on injection of propofol. Anaesthesia 1998;53:468-76.
2. King SY, Davis FM, Wells JE, Murchison DJ, Pryor PJ. Lidocaine for the prevention of pain due to injection of propofol. Anesth Analg 1992;74:246-9.
3. Reddy MS, Chen FG, Ng HP. Effect of ondansetron pre-treatment on pain after rocuronium and propofol injection: A randomized,double blinbd controlled comparison with lidocaine. Anaesthesia 2001;56:902-5.
4. 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;43:24-7.
5. 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.
6. Cheong MA, Kim KS, Choi WJ. Ephedrine reduces the pain from propofol injection. Anesth Analg 2002;95:1293-6.
7. Davies AF, Vadodaria B, Hopwood B, Dexter T, Conn D. Efficacy of microfiltration in decreasing propofol induced pain. Anaesthesia 2002;57:557-61.
8. Angst MS, Mackey SC, Zupfer GH, Tataru CD, Brock-Utne JG. Reduction of propofol injection pain with a double lumen intravenous set. J Clin Anesth1997;9:462-6.
9. Fletcher GC, Gillespie JA, Davidson JA. The effect of temperature upon pain during injection of propofol. Anaesthesia 1996;51:498-9.
10. McCrirrick A, Hunter S. Pain on injection of propofol: The effect of injectate temperature. Anaesthesia 1990;45:443-4.
11. Eriksson M, Englesson S, Niklasson F, Hartvig P. Effect of lignocaine and pH on propofol-induced pain. Br J Anaesth 1997;78:502-6.
12. Park JW, Park ES, Chi SC, Kil HY, Lee KH. The effect of lidocaine on the globule size distribution of propofol emulsions. Anesth Analg 2003;97:769-71.
13. Briggs LP, Clarke RS, Dundee JW, Moore J, Bahar M, Wright PJ. Use of diisopropyl phenol as main agent for short procedures. Br J Anaesth 1981;53:1197-202.
14. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment

to alleviate pain on propofol injection: A randomized, controlled, double-blind study. Anesth Analg 1999;89:197-9.
15. Lomax D. Propofol injection pain. Anaesth Intensive Care 1994;22:500-1.
16. Minogue SC, Sun DA. Bacteriostatic saline containing benzyl alcohol decreases the pain associated with the injection of propofol. Anesth Analg 2005;100:683-6.
17. Kobayashi Y, Kamada Y, Kumagai A, Seki S, Ichimiya T, Tsuchida H, *et al*. Pain-free injection of propofol. Masui 1998;47:835-8.

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