Original Article

Efficacy of methylprednisolone and lignocaine on propofol injection pain: A randomised, double-blind, prospective study in adult cardiac surgical patients

Address for correspondence:
Dr. Sathyanarayan Jagannath, Department of Cardiac Anaesthesiology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India.
E-mail: sathyaforall2005@gmail.com

Shivaprakash Shivanna, Shio Priye, Dipali Singh, Sathyanarayan Jagannath, Syed Mudassar, Durga Prasad Reddy

Department of Cardiac Anaesthesiology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/0019-5049.193683

Quick response code

ABSTRACT

Background and Aims: Propofol (2, 6-di-isopropylphenol) used for the induction of anaesthesia often causes mild to severe pain or discomfort on injection. We designed this double-blind study to compare the efficacy of methylprednisolone and lignocaine in reducing the pain of propofol injection in patients scheduled for cardiac surgery. **Methods:** A total of 165 adult patients, scheduled for elective cardiac surgery, were divided into three groups: saline (group S, $n = 55$), lignocaine 20 mg (Group L, $n = 55$) and methylprednisolone 125 mg diluted into 2 ml of distilled water (Group MP, $n = 55$). Drugs were administered after tourniquet application and occlusion was released after 1 min and 1/4th of the total dose of propofol (2 mg/kg) was administered at the rate of 0.5 ml/s. Pain on propofol injection was evaluated by four-point verbal rating scale. Statistical methods used included Student's *t*-test and Chi-square test/Fisher's exact test. **Results:** The overall incidence of pain was 70.9% in the saline group, 30.9% in the lignocaine group and 36.4% in the methylprednisolone group. The intensity of pain was significantly less in patients receiving methylprednisolone and lignocaine than those receiving saline ($P < 0.012$). **Conclusion:** Pre-treatment with intravenous methylprednisolone was found to be as effective as lignocaine in reducing propofol injection-induced pain.

Key words: Lignocaine, methylprednisolone, pain, propofol

INTRODUCTION

Propofol is an intravenous (IV) anaesthetic drug used for induction and maintenance during anaesthesia. The incidence of pain with IV propofol varies between 28% and 90% in adults.[1] The quality of pain is described as extremely sharp, aching or burning. In addition, the hyperdynamic cardiovascular response to the pain can precipitate adverse events in high-risk patients with a history of coronary artery disease and/or abnormal heart rhythm. [2] Many factors appear to affect the incidence of pain, which include site of injection, size of vein, speed of injection, buffering effect of blood, temperature of propofol and concomitant use of drugs such as local anaesthetics and opiates. [3]

Corticosteroids are systemic anti-inflammatory agents, [4] systemic analgesics [5] and are known to block nociceptive C fibres when applied locally.[6] Dexamethasone has been shown to reduce propofol injection pain. [7] Methylprednisolone is commonly used during cardiopulmonary bypass to reduce inflammatory response at doses of 10–30 mg/kg body weight. Methylprednisolone sodium succinate for injection is available in 40 mg, 125 mg, 500 mg and 1000 mg strengths. We hypothesised that pre-treatment with methylprednisolone reduces pain of propofol injection.

How to cite this article: Shivanna S, Priye S, Singh D, Jagannath S, Mudassar S, Reddy DP. Efficacy of methylprednisolone and lignocaine on propofol injection pain: A randomised, double-blind, prospective study in adult cardiac surgical patients. Indian J Anaesth 2016;60:848-51.

METHODS

The study was approved by the hospital ethical committee and written informed consent was obtained from all the patients. In this study, 165 patients between 21 and 60 years irrespective of sex belonging to the American Society of Anesthesiologists (ASA) physical Status I and II undergoing elective cardiac surgery were included.

Patients with allergy to propofol, lignocaine, anticipated difficult venous access, patients with cardiac conduction defects, congenital heart disease, low ejection fraction, haemodynamically instability, diabetes mellitus, chronic pain syndromes, convulsions, head injury and systemic fungal infections were excluded from the study.

This was an interventional, randomised, prospective, double-blind, parallel group study. Five lead electrocardiogram and pulse oximeter were connected. A 20-gauge cannula was placed into the largest vein on the dorsum of the left hand. Right radial artery cannulation was performed after local skin infiltration with lignocaine. Patients were randomly assigned to three groups of 55 patients each according to a computer-generated random number sequence. Group S patients received 2 ml of normal saline as a placebo; Group L patients received pre-treatment with lignocaine (20 mg of 2% solution diluted to 2 ml with distilled water), and Group MP patients received pre-treatment with methylprednisolone sodium succinate (125 mg diluted into 2 ml of distilled water).

After limb elevation for 15 s, venous drainage was occluded by placing a tourniquet inflated to 40 mmHg. According to the experimental group, respective drug was injected, and the investigator was blinded to the content of the solution. Tourniquet was deflated after 1 min, and then 0.5 mg/kg of propofol (long chain triglycerides LCT) was administered at the rate of 0.5 ml/s. The drugs used in the study were stored at room temperature. The intensity of pain on injection of propofol was assessed by a second anaesthesiologist who was unaware of the group to which the patient had been allocated. Assessment included standard questions asked to the patients about the comfort of the injection, verbal response and behavioural signs (such as facial grimacing, arm withdrawal or tears from the eyes). Pain was graded using a four-point scale: 0 = no pain, 1 = mild pain (pain reported only in response to questioning without any behavioural signs), 2 = moderate pain (pain reported in response to questioning and accompanied by a behavioural sign or pain reported spontaneously without questioning) and 3 = severe pain (i.e. strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears).[8]

Anaesthesia induction was continued with fentanyl 3–5 μg/kg and midazolam 0.03 mg/kg intravenously. Tracheal intubation was facilitated with rocuronium, and anaesthesia was maintained with isoflurane. Haemodynamic parameters were monitored. In the post-operative period, the trachea was extubated and were assessed for pain, swelling or allergic reaction at the site of injection by a blinded anaesthesiologist.

Considering previous studies,[8] the incidence of propofol-induced pain was assumed as 80% and 50% reduction was considered significant. Based on the alpha value of 0.05 and a power value of 80%, our study required at least 41 patients per group. Assuming drop-outs, the sample size was increased to 55 per group. Continuous data are reported as mean ± standard deviation. Comparison of age, sex, weight and ASA between the three groups was obtained by Student's *t*-test. Categorical data are reported as numbers and percentages and are analysed using Chi-square test or Fisher's exact test as appropriate. $P < 0.05$ was considered statistically significant.

RESULTS

There were no significant differences in demographic characteristics between the three groups [Table 1]. No incidence of pain or discomfort was reported during the injection of pre-treatment solution in any group. The overall incidence of pain was 70.9% (64.2%–77.6%) in the saline group, 30.9% (21.2%–40.6%) in the lignocaine group, and 36.4% (31.5%–41.3%) in the methylprednisolone group [Table 2]. The incidence of pain was significantly less ($P < 0.012$) in patients receiving drugs for pre-treatment than those receiving saline. Moderate to severe pain was observed in

Table 1: Demographic data

Patients characteristics	Group S (*n*=55)	Group L (*n*=55)	Group MP (*n*=55)
Age (years)	42.84±9.62	43.56±10.00	43.49±9.33
Weight (kg)	61.42±9.43	61.64±9.23	61.56±9.33
Sex (male/female)	41/14	43/12	44/11
ASA (I/II)	17/38	16/39	14/41

Values are expressed as mean ± SD or number of patients. *n* – Number of patients; ASA – American Society of Anesthesiologists; SD – Standard deviation

Table 2: Incidence and severity of pain following propofol injection among groups

Groups	No pain (%)	Pain (%)	Mild pain (%)	Moderate pain (%)	Severe pain (%)
Group S	16 (29.1)	39 (70.9)	5 (9.1)	14 (25.5)	20 (36.4)
Group L	38 (69.1)*	17 (30.9)*	14 (25.5)	2 (3.6)*	1 (1.8)*
Group MP	35 (63.6)*	20 (36.4)*	16 (29.1)	3 (5.5)*	1 (1.8)*

χ^2=62.29, *P<0.012 compared with Group S respectively. Data are expressed as number of patients (%)

3 (5.4%) and 4 (7.3%) patients in Groups L and MP respectively as compared to 34 (62%) patients in S group. The difference in moderate to severe pain between the study Groups (L and MP) was not statistically significant.

DISCUSSION

In this study, the incidence of pain during the injection of propofol in the lignocaine group was 30.9%, whereas in the methyl prednisolone group, it was 36.4%. Moderate to severe pain was reported in 5.4% of the patients in the lignocaine group whereas 7.3% was reported in the methyl prednisolone group. There are very few studies on the use of pre-treatment with steroid-based drugs for the alleviation of pain on propofol injection.

The mechanism for propofol injection pain is unknown; however it could be due to irritation of the endothelium, osmolality differences, unphysiological pH and the activation of pain mediators.[9] The immediate vascular pain on propofol injection is attributed to direct irritation of the drug[10] by stimulating the venous nociceptive receptors or free nerve endings involving myelinated Aδ fibres.[11] The delayed pain of injection has a latency of 10–20 s mediated by activation of kallikrein–kinin system.[12]

There are many strategies to reduce the incidence of pain on injection which include the following: pre-treatment with IV lignocaine, adding lignocaine to propofol,[13] cooling or warming propofol,[14] injection of propofol into a large vein,[15] preadministration of 5-HT3 receptor antagonist,[16] dexamethasone,[17] hydrocortisone[18] with or without tourniquet.[19] Among these studies, the most commonly accepted technique is the administration of lignocaine just before the injection of propofol.[20]

Corticosteroids are used routinely in cardiac surgery to attenuate the release of pro-inflammatory cytokines. Dexamethasone in 2 ml of normal saline effectively reduces the pain on propofol injection.[17] Methylprednisolone is a commonly used steroid during cardiopulmonary bypass in our institute, so we choose methylprednisolone to test the efficacy in reducing pain on propofol injection.

A previous study found that 31% of patients felt pain ($P < 0.01$) after dexamethasone pre-treatment and moderate to severe pain was noticed in 17.14%.[21] Another study comparing lignocaine, pethidine and dexamethasone as pre-treatment found that 48% of the patients with dexamethasone pre-treatment had no pain.[17] The combination of lignocaine 20 mg and dexamethasone 6 mg with venous occlusion for 1 min was more effective than lignocaine 20 mg (34.3%) or dexamethasone 6 mg (37.1%) alone for pain control during propofol injection.[7] Dexamethasone given at higher analgesic doses reduces pain associated with the injection of propofol.[2] These results show an effective reduction in the incidence and severity of propofol injection pain after pre-treatment with dexamethasone.

Pre-treatment with either 10 mg or 25 mg of hydrocortisone was associated with no significant reduction of propofol injection pain (66.66% and 94.44% respectively) when compared to a placebo (94.44%). It was administered 30 s before the administration of propofol, which may be a short contact time. Hydrocortisone might not be effective on immediate pain.[18]

In this study, the incidence of pain was 70.9% in the Group S whereas in those pre-treated with lignocaine and methylprednisolone, it was 30.9% and 36.4%, respectively. These results show that there is a significant reduction in the propofol injection pain, and both lignocaine and methylprednisolone are equally effective. There is a significant decrease in moderate to severe pain (5.4% and 7.3% in each L and MP group) when compared with Group S (62%).

The outcome of this study may not be applicable in emergency induction. This technique is useful in elective surgery and adult participants who require methylprednisolone perioperatively. The use of methylprednisolone should be individualised with due consideration to the cost-effectiveness and benefit to the patient.

CONCLUSION

The analgesic efficacy of methylprednisolone given as pre-treatment with propofol is as effective as lignocaine in preventing propofol-induced pain. Therefore, it can be administered before propofol in patients who require methylprednisolone for other indications.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sim JY, Lee SH, Park DY, Jung JA, Ki KH, Lee DH, *et al.* Pain on injection with microemulsion propofol. Br J Clin Pharmacol 2009;67:316-25.
2. Ahmad S, De Oliveira GS Jr., Fitzgerald PC, McCarthy RJ. The effect of intravenous dexamethasone and lidocaine on propofol-induced vascular pain: A randomized double-blinded placebo-controlled trial. Pain Res Treat 2013;2013:734531.
3. 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:d1110.
4. Ali-Hassan-Sayegh S, Mirhosseini SJ, Haddad F, Karimi-Bondarabadi AA, Shahidzadeh A, Weymann A, *et al.* Protective effects of corticosteroids in coronary artery bypass graft surgery alone or combined with valvular surgery: An updated and comprehensive meta-analysis and systematic review. Interact Cardiovasc Thorac Surg 2015;20:825-36.
5. Tan PH, Liu K, Peng CH, Yang LC, Lin CR, Lu CY. The effect of dexamethasone on postoperative pain and emesis after intrathecal neostigmine. Anesth Analg 2001;92:228-32.
6. Johansson A, Hao J, Sjölund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. Acta Anaesthesiol Scand 1990;34:335-8.
7. Kwak KH, Ha J, Kim Y, Jeon Y. Efficacy of combination intravenous lidocaine and dexamethasone on propofol injection pain: A randomized, double-blind, prospective study in adult Korean surgical patients. Clin Ther 2008;30:1113-9.
8. Singh D, Jagannath S, Priye S, Shivaprakash, Kadli C, Reddy D. Prevention of propofol injection pain: Comparison between lidocaine and ramosetron. J Anaesthesiol Clin Pharmacol 2014;30:213-6.
9. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: A randomized, controlled, double-blinded study. Anesth Analg 1999;89:197-9.
10. Tan CH, Onsiong MK. Pain on injection of propofol. Anaesthesia 1998;53:468-76.
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. Nishiyama T. How to decrease pain at rapid injection of propofol: Effectiveness of flurbiprofen. J Anesth 2005;19:273-6.
13. Walker BJ, Neal JM, Mulroy MF, Humsi JA, Bittner RC, McDonald SB. Lidocaine pretreatment with tourniquet versus lidocaine-propofol admixture for attenuating propofol injection pain: A randomized controlled trial. Reg Anesth Pain Med 2011;36:41-5.
14. Ozturk E, Izdes S, Babacan A, Kaya K. Temperature of propofol does not reduce the incidence of injection pain. Anesthesiology 1998;89:1041.
15. Tariq MA, Kamran M. Incidence of pain on propofol injection and efficacy of addition of lignocaine or selecting big vein or both combined in reducing it: A randomized control trial. J Postgrad Med Inst 2006;20:8-11.
16. Sumalatha GB, Dodawad RR, Pandarpurkar S, Jajee PR. A comparative study of attenuation of propofol-induced pain by lignocaine, ondansetron, and ramosetron. Indian J Anaesth 2016;60:25-9.
17. Gupta M, Mishra S, Gupta D, Gujjar M, Bhatnagar S. Prevention of pain on propofol injection: A comparative, randomized, double blind study between lignocaine, pethidine, dexamethasone and placebo. Internet J Anesthesiol 2006;11:1-6.
18. Yadav M, Durga P, Gopinath R. Role of hydrocortisone in prevention of pain on propofol injection. J Anaesthesiol Clin Pharmacol 2011;27:470-4.
19. Kaya S, Turhanoglu S, Karaman H, Ozgün S, Basak N. Lidocaine for prevention of propofol injection-induced pain: A prospective, randomized, double-blind, controlled study of the effect of duration of venous occlusion with a tourniquet in adults. Curr Ther Res Clin Exp 2008;69:29-35.
20. Gharavi M, Sabzevari A, Ghorbanian E, Sajadi R, Akhondi M. Effect of lidocaine volume and concentration on preventing incidence and severity of propofol injection pain. Iran Red Crescent Med J 2014;16:e16099.
21. Singh M, Mohta M, Sethi AK, Tyagi A. Efficacy of dexamethasone pretreatment for alleviation of propofol injection pain. Eur J Anaesthesiol 2005;22:888-90.