A Comparative Study of 2 mg, 4 mg Intravenous Ondansetron and 2% Lignocaine Hydrochloride Pre-treatment to Alleviate Pain of Propofol Injection

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Abstract

Introduction: Propofol belongs to one of the commonly used intravenous (IV)-inducing anaesthetic agents. However, at least 70% of the patients experience pain on propofol injection. To reduce pain, various methods were tried. A randomised, double-blinded comparative study was done by us. Materials and Methods: A total of 180 patients belonging to American Society of Anesthesiologists Grade 1 and 2, who were for elective or emergency surgery, were randomly divided into three groups. All surgeries were under general anaesthesia. Group 1 was administered 2 ml of 2% IV lignocaine, Group 2 was administered IV ondansetron 2 mg and Group 3 was administered IV ondansetron 4 mg. One-fourth of the total dosage was injected over 5 s, and pain was assessed in the patients during injection of propofol by verbal rating scale. Results: The intensity and incidence of pain were comparatively less with lignocaine and ondansetron 4 mg overall. Even though there was better relief of pain with lignocaine, ondansetron 4 mg along with venous occlusion also reduced propofol injection pain. Conclusion: Ondansetron also can be used as an alternative in relief of pain on propofol injection just like lignocaine.

Keywords: Injection, ondansetron, lignocaine, propofol, pain, intravenous

Introduction

Propofol or di-isopropylphenol is one of the commonly used intravenous (IV)-inducing anaesthetic agents. It is used for daycare surgeries, for cases where laryngeal mask airway (LMA) is used and for maintenance of anaesthesia and sedation in the form of total IV anaesthesia. Other uses include its use for preventing vomiting,[1] intubating without using neuromuscular blocking drugs,[2] and treating pruritus[3] associated with liver disease.

Onset of action of propofol is rapid and it acts for a short duration. However, it was found that at least 70% of patients experience pain on injection when no other interventions or other forms of treatment[4-6] are used. Some recall propofol injection pain to be the most distressing during the perioperative period. American anaesthesiologists[7] have proposed it as the seventh most common problem encountered during the practice of anaesthesia.

Ondansetron, a commonly used antiemetic, has also been found to have a local anaesthetic effect.[9] Studies have demonstrated that ondansetron is a quite effective drug used for preventing and treating postoperative nausea and vomiting (PONV).[9-12]

In our study, we compared two different doses of IV ondansetron that is 2 and 4 mg and lignocaine hydrochloride in attenuation of pain due to propofol injection during induction of anaesthesia.

Materials and Methods

The institution’s ethical committee clearance was obtained. The study comprised 180 patients. Patients belonging to American Society of Anesthesiologists (ASA) Grade 1 and 2 were selected. They were for elective surgery or emergency surgery under general anaesthesia. A total of 180 patients were randomly divided into three groups. Group 1 was administered 2 ml of 2% IV lignocaine, Group 2 was administered IV ondansetron 2 mg and Group 3 was administered IV ondansetron 4 mg. One-fourth of the total dosage was injected over 5 s, and pain was assessed in the patients during injection of propofol by verbal rating scale.

Results: The intensity and incidence of pain were comparatively less with lignocaine and ondansetron 4 mg overall. Even though there was better relief of pain with lignocaine, ondansetron 4 mg along with venous occlusion also reduced propofol injection pain.

Conclusion: Ondansetron also can be used as an alternative in relief of pain on propofol injection just like lignocaine.

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2, of 15–65 years of age of either sex, posted for elective or emergency surgery under general anaesthesia were included in the study. Before surgery, informed consent was obtained and the procedure was explained to the patients.

Patients were randomly divided into one of the three groups (60 in each group) based on computer-generated random numbers. A blinded anaesthetist prepared the solutions at an operating room temperature range of 21°C–23°C.

The investigator was not aware of the contents of the solutions. The anaesthesiologist who was blinded about the constituents of the drug administered the drug solution.

Group 1 was administered 2 ml of 2% IV lignocaine, Group 2 was administered IV ondansetron 2 mg and Group 3 was administered IV ondansetron 4 mg. Ondansetron 2 mg was made to a volume of 2 ml by adding normal saline.

All the patients underwent thorough pre-anaesthetic check-up and the required investigations before the surgery.

All patients were kept fasting for 6 h for solids. In the operation theatre, IV cannula of 20-gauge was passed in a suitable vein on the dorsal aspect of non-dominant hand, and Ringer’s lactate solution was started.

The vital parameters monitored were a non-invasive blood pressure monitor, a lead II electrocardiogram, end-tidal carbon dioxide and pulse oximetry. Premedication was not administered. Above the cannula, a tourniquet was attached to the arm and inflated to 80 mmHg.

The patients were then given 2 ml of the pre-treatment drug IV, containing either (Group 1) 2 ml of 2% IV lignocaine (Loxicard 2%, Neon Laboratories Ltd, Mumbai, India), (Group 2) 2 mg of IV ondansetron or (Group 3) 4 mg of IV ondansetron (Gaptroin, GAPL). Following this, injection of 1% propofol was given which was drawn immediately before use at a dose of 2 mg/kg. Troypofol®, Troikaa Pharmaceuticals, Ahmedabad, Gujarat, India, diluted in Long chain triglyceride (LCT) was used.

One-fourth of the total dosage was injected over 5 s, and the pain was assessed in the patient during injection of propofol by verbal rating scale. The degree of pain was classified into none, mild, moderate and severe [Table 1]. Adverse effects if present were identified.

The remaining dose of propofol was used to complete induction of anaesthesia. The patients were either intubated or LMA was inserted depending on the case.

Intubated patients were maintained with vecuronium, nitrous oxide, and sevoflurane.

Neostigmine at a dose of 0.05 mg/kg and glycopyrrolate at a dose of 0.01 mg/kg were used to reverse residual neuromuscular blockade at the end of surgery. Once the patients were fully awake and obeying commands, extubation was done.

For comparison of quantitative variables among the three groups, the ANOVA test was used. Chi-square test or Fisher’s exact test was used to analyse qualitative variables. A $P < 0.05$ was considered statistically significant. For statistical analysis, SPSS software (IBM corporation) for Windows was used.

**Results**

A total of 180 patients with 60 patients in each group in our study group were included. There is significantly higher pain score in the ondansetron groups. The ondansetron 2 mg group has 45 people with score 1 and 7 people with score 2, which is significantly higher than both lignocaine and ondansetron 4 mg group [Figure 1].

The ondansetron 4 mg group is also less effective than the lignocaine group as it had 31% showing score 1 in comparison to only 10% in lignocaine group, $P < 0.001$ [Figure 1].

There was no statistical significance between age, sex, ASA grade, and weight between the study groups.

**Discussion**

Compared to the other IV anaesthetic drugs, propofol was found to have a higher association of pain on injection.

Although many factors have been proposed for the cause of pain on injection of propofol, the exact mechanism for pain has not been found out.

Different methods have been tried to solve this problem. They include use of drugs as well as other interventions. Among the various drugs tried are aspirin, Non steroid anti inflammatory drugs (NSAIDs), opioids, thiopentone sodium, use of premedication, glyceryl trinitrate, metoclopramide, ondansetron, ephedrine, nafamostat mesilate or ketamine.[3,13-22]

The other methods tried were speed of injection, injection site, rate of infusion of carrier IV fluid, local anaesthetics usage, different temperatures, dilution of propofol, different syringe material, the aspiration of blood and increasing the usage, different temperatures, dilution of propofol, different syringe material, the aspiration of blood and increasing the infusion rate.

Our study showed that 54 patients (90%) in lignocaine group had no pain. In contrast, 41 patients (68%) in ondansetron

**Table 1: Assessment of pain during injection of propofol**

| Pain score | Degree of pain | Response |
|------------|----------------|----------|
| 0          | None           | Negative response to questioning |
| 1          | Mild           | Pain reported in response to questioning only, without any behavioural signs |
| 2          | Moderate       | Pain reported in response to questioning and accompanied by behavioural sign or pain reported spontaneously without questioning |
| 3          | Severe         | Strong vocal response or response accompanied by facial griming, arm withdrawal or tears |

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4 mg group had no pain, whereas in ondansetron 2 mg group, only 8 patients (13%) had no pain.

In our study, there were only 31% patients in ondansetron 4 mg group with mild pain compared to 75% in ondansetron 2 mg group. Lignocaine group had only 10% of patients with mild pain. Moderate pain was shown by 11% of patients in ondansetron 2 mg group. Ondansetron 4 mg group did not show any patient with moderate pain. No patient complained of severe pain. This shows that lignocaine is better than ondansetron in reducing pain. This was statistically significant (P < 0.01).

However, this shows that ondansetron 4 mg is also effective in reducing pain due to propofol injection. Ondansetron 4 mg is more effective than ondansetron 2 mg.

Studies by Ye et al.[3] in rats showed that ondansetron, which is a specific 5-HT₁ receptor antagonist, blocks sodium channels in the neurons of brain. When ondansetron was injected under the skin, they found that it is 15 times more potent than lignocaine in causing numbness. Ondansetron also reduces pain[21] by binding to the opioid µ-receptors and hence shows agonist activity. The nociceptive pathways also involve 5-HT₁ receptors, and hence, ondansetron exhibits its analgesic effect through this mechanism. These properties of ondansetron have made it be an effective alternative to reduce pain.[15,24]

Ambesh et al.[13] in their study showed that although pre-treatment with ondansetron did not reduce the incidence of pain on propofol injection in all patients, it was helpful in reducing pain in around 50% of patients.

Likewise, studies were done by Ryu and Kim[16] with palonosetron on propofol-induced pain. It was noted that on pre-treatment by palonosetron (0.075 mg), 72.5% of patients felt a reduction in the incidence of propofol injection pain.

Studies done by Sunny et al.[25] showed comparable results. In their study, 40% of patients in ondansetron 4 mg group had mild pain whereas none in lignocaine group had any pain. They showed that although control of pain was better with lignocaine, ondansetron had no untoward side effects and can be used as an alternative to lignocaine in reducing pain on propofol injection.

Sumalatha et al.[26] showed that there was no significant difference between demographic and baseline characteristics in the study groups. They noted that pre-treatment with IV ramosetron and lignocaine significantly reduced the propofol-induced pain when compared to ondansetron 4 mg.

Piper et al.[27] did studies with dolasetron. They noted that the severity but not the incidence of pain on propofol injection was decreased significantly by 50% compared with placebo. There was no significant difference between the studies comparing dolasetron and lignocaine.

Lee et al.[28] did studies on ramosetron, a recently developed 5-HT₁ receptor antagonist, and noted that the incidence of pain in the groups pre-treated with 0.3 mg ramosetron or combination with ramosetron and 20 mg lignocaine was 60% and 38%, respectively.

These studies show that 5-HT₁ receptor antagonists are effective in reduction of pain on propofol injection. Similarly, in this study, pain was significantly reduced with lignocaine as well with ondansetron 4 mg.

The advantage with ondansetron is that it is used for the prevention of PONV[9-12] during induction of anaesthesia. It is given at a dose of 4 mg usually in adults.

**Conclusion**

Even though lignocaine was better for control of pain, ondansetron can also be used as an alternative to decrease propofol injection pain.

**Ethical statement**

The study was approved by the institutional Ethics Committee of Goa Medical College ethical committee. (Approval No: 25.9.2015).

**Declaration of patient consent**

All patients and participants have agreed to use their clinical information anonymously for the purpose of this study in a written consent as per the regulation of Goa Medical College ethical committee.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Weir PM, Munro HM, Reynolds PI, Lewis IH, Wilton NC. Propofol infusion and the incidence of emesis in pediatric outpatient strabismus surgery. Anesth Analg 1993;76:760-4.

2. Beck GN, Masterson GR, Richards J, Bunting P. Comparison of intubation following propofol and alfentanil with intubation following thiopentone and suxamethonium. Anaesthesia 1993;48:876-80.

3. Borget A, Wilder-Smith OH, Mentha G. Subhypnotic doses of propofol relieve pruritus associated with liver disease. Gastroenterology 1993;104:244-7.

4. Picard P, Tramèr MR. Prevention of pain on injection with propofol: A quantitative systematic review. Anesth Analg 2000;90:963-9.
5. Nathanson MH, Gajraj NM, Russell JA. Prevention of pain on injection of propofol: A comparison of lidocaine with alfentanil. Anesth Analg 1996;82:469-71.
6. Tan CH, Onsiong MK. Pain on injection of propofol. Anaesthesia 1998;53:468-76.
7. Macario A, Weinger M, Truong P, Lee M. Which clinical anesthesia outcomes are both common and important to avoid? The perspective of a panel of expert anesthesiologists. Anesth Analg 1999;88:1085-91.
8. Ye JH, Mui WC, Ren J, Hunt TE, Wu WH, Zbuzek VK. Ondansetron exhibits the properties of a local anesthetic. Anesth Analg 1997;85:1116-21.
9. El-Radaideh KM. Effect of pretreatment with lidocaine, intravenous paracetamol and lidocaine-fentanyl on propofol injection pain. Comparative study. Rev Bras Anestesiol 2007;57:32-8.
10. Peroutka SJ, Snyder SH. Antiemetics: Neurotransmitter receptor binding predicts therapeutic actions. Lancet 1982;1:658-9.
11. El-Radaideh KM. Effect of pretreatment with lidocaine, intravenous paracetamol and lidocaine-fentanyl on propofol injection pain. Comparative study. Rev Bras Anestesiol 2007;57:32-8.
12. Bhardwaj N, Bala I, Kaur C, Chari P. Comparison of ondansetron with ondansetron plus dexamethasone for antiemetic prophylaxis in children undergoing strabismus surgery. J Pediatr Ophthalmol Strabismus 2004;41:100-4.
13. 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.
14. Dubey PK, Prasad SS. Pain on injection of propofol: The effect of granisetron pretreatment. Clin J Pain 2003;19:121-4.
15. Singh D, Jagannath S, Priye S, Shivaprakash, Kadri C, Reddy D. Prevention of propofol injection pain: Comparison between lidocaine and ramosetron. J Anaesthesiol Clin Pharmacol 2014;30:213-6.
16. Ryu HB, Kim SJ. Analgesic effects of palonosetron in the intravenous propofol injection. Korean J Anesthesiol 2014;66:99-104.
17. Eriksson M, Englesson S, Niklasson F, Hartvig P. Effect of lignocaine and pH on propofol-induced pain. Br J Anaesth 1997;78:502-6.
18. Nishiyama T. How to decrease pain at rapid injection of propofol: Effectiveness of flurbiprofen. J Anesth 2005;19:273-6.
19. Sawa S, Pal A, Chatterjee S, Saha D, Dawar N. Ondansetron, ramosetron, or palonosetron: Which is a better choice of antiemetic to prevent postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy? Anesth Essays Res 2011;5:182-6.
20. Lee JW, Park HJ, Choi J, Park SJ, Kang H, Kim EG. Comparison of ramosetron’s and ondansetron’s preventive anti-emetic effects in highly susceptible patients undergoing abdominal hysterectomy. Korean J Anesthesiol 2011;61:488-92.
21. McCrirrick A, Hunter S. Pain on injection of propofol: The effect of injectate temperature. Anaesthesia 1990;45:443-4.
22. El-Radaideh KM. Effect of pretreatment with lidocaine, intravenous paracetamol and lidocaine-fentanyl on propofol injection pain. Comparative study. Rev Bras Anestesiol 2007;57:32-8.