*Original Research Article*

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# The Effect of Lignocaine versus Ramosetron on Attenuation of Propofol Induced Pain

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**Abstract**

*Background and Aims:* Propofol is widely used for induction of anaesthesia, although the pain during its injection remains a concern for all anaesthesiologists. A number of techniques have been adopted to minimise propofol induced pain. Various 5 hydroxytryptamine 3 antagonists have shown to reduce propofol induced pain. Hence, this placebo controlled study was conducted to compare the efficacy of ramosetron and lignocaine in terms of attenuation of propofol induced pain during induction of anaesthesia. *Methods:* Hundred adult patients, aged 18–60 years, posted for various elective surgical procedures under general anaesthesia were randomly assigned to two groups of 50 each. Group R received 0.3 mg of ramosetron, Group L received 0.5 mg/kg of 2% lignocaine. After intravenous (IV) pre treatment of study drug, manual occlusion of venous drainage was done at mid arm with the help of an assistant for 1 min. This was followed by administration of propofol LCT after release of venous occlusion. Pain was assessed with a four point scale. Unpaired Student's *t* test and Chi square test/ Fisher's exact test were used to analyse results. *Results:* In our study out of 50 patients of each study group, 54% in lignocaine group and 60% in ramosetron group did not have pain, 34% in lignocaine group and 24% in ramosetron group had mild pain, 10% in both groups had moderate pain, 2% in lignocaine group and 6% in ramosetron group had severe pain. *Conclusion:* Pre treatment with IV ramosetron 0.3 mg is equally effective as 0.5mg/kg of 2% lignocaine in preventing propofol induced pain.

**Keywords:** Lignocaine; Pain; Propofol; Ramosetron.

## Introduction

Propofol is a common intravenous (IV) anesthetic drug used for induction and maintenance during general anesthesia with rapid onset and short duration of action [1]. However, the incidence of pain following propofol injection varies between 28 and 90% in adults if a vein on dorsum of hand is used [2,3]. The quality of pain was described as extremely sharp, aching, or burning. It has been arranged as the seventh most important problem in current practice of clinical anesthesia by American anesthesiologists [4].

Strategies to reduce the incidence of pain on injection include adding lidocaine to propofol, cooling or warming propofol, diluting the propofol solution, injection of propofol into a large vein, and pretreatment with IV injection of lidocaine, ondansetron, metoclopramide, an opioid, magnesium, or thiopental with or without tourniquet; all have been tried with variable results [5,6,7]. It has been demonstrated that ondansetron, a specific 5-hydroxytryptamine ($5HT_3$) receptor antagonist, provided numbness when injected under the skin and is 15 times more potent than lidocaine. It has been further demonstrated that ondansetron successfully relieved pain following

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propofol injection without any adverse effects in a significant number of patients [8,9]. In our practice, ramosetron is routinely administered as premedication to prevent postoperative nausea and vomiting (PONV) in patients scheduled for general anesthesia.

Ramosetron is a serotonin $5HT_3$ receptor antagonist and demonstrates superior efficacy and longer duration to granisetron [10]. We used ramosetron pretreatment to determine its efficacy to decrease the pain of propofol injection as equivalent to lidocaine.

## Materials and Methods

Institutional ethical committee approval was obtained and informed written consent was taken from all patients. Hundred adult patients belonging to American Society of Anesthesiologists (ASA) I and II class, scheduled for elective surgery under general anesthesia were randomly allocated to either of the two groups using computer generated random numbers (50 in each group), for this prospectively randomized, placebo-controlled, single-blinded study. Patients having problems in communication and history of allergic response to either propofol or $5HT_3$ antagonists, pregnant ladies were excluded from this study.

All patients were kept fasting for 6 h for solid food. On arrival to the operation theatre, a 20 G cannula was inserted into a vein on the dorsum of the patient's non dominant hand and lactated Ringer's solution was infused. The pretreatment solutions consisted of 2 ml (0.5 mg/kg, Group L, $n$ = 50) of lidocaine (Loxicard 2%, Neon laboratories ltd, Mumbai, India), and 2 ml (0.3 mg, Group R, $n$ = 50) of ramosetron (Nozia, Cadila Healthcare Ltd, Goa, India).

Pretreatment drug was injected after venous drainage was occluded manually at the mid-forearm for 1 min. Patient's then received one-fourth of the total calculated dose of propofol-LCT (long chain triglycerides) over 5s and 15 s later the patient was assessed for pain during injection of propofol.

The level of pain was assessed by standard questions asked to the patients about the comfort of the injection, verbal response, and behavioral signs (such as facial grimacing, arm withdrawal, or tears). Pain was graded using a four-point scale:0 = no pain, 1= mild pain (pain reported only in response to questioning without any behavioral signs), 2 = moderate pain (pain reported in response to questioning and accompanied by a behavioral 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) [11].

Later anesthesia was induced with intravenous propofol-LCT 2 mg/kg. All study drugs were kept at room temperature and used within 30 min of preparation. Tracheal intubation was facilitated with muscle relaxants and anaesthesia was maintained with inhalational drugs and analgesics.

### *Statistical Analysis*

Based on the literature, the incidence of pain on injecting propofol is assumed as 80%, and 50% reduction in pain was considered clinically significant. Fifty patients were calculated as the minimum size for each group assuming a-value of 0.05 and a power value of 80%. All measured values are presented as mean±standard deviation and numbers (%). The results were analyzed statistically using unpaired Student's $t$-test and chi-square test/ Fisher's exact test. Results were considered statistically significant when $P$-value of <0.05 was obtained. Statistical Packages for the Social Sciences (SPSS; Windows ver. 15.0, SPSS Inc., Chicago, IL) was used for statistical analysis.

## Results

There was no significant difference in the demographic characteristics among the two groups [Table 1]. No patients in any group experienced pain and discomfort during the injection of pretreatment solution. The incidence and severity of pain during IV injection of propofol in various groups is shown in Table 2.

**Table 1:** Demographic data

| Patients characteristics | Group L (n =50) | Group R (n=50) | P value |
|---|---|---|---|
| Age | 31 ± 9.8 | 32.1 ± 10.1 | 0.581 |
| Sex (M/F) | 19/31 | 21/29 | 0.683 |
| Weight | 49.7 ± 4.78 | 48.68 ± 3.68 | 0.234 |
| ASA 1/2 | 29/21 | 31/19 | 0.683 |

L = patients who received lignocaine, R= patients who received ramosetron, ASA= American society of Anaesthesiologist, M= Male F= Female

**Table 2:** Comparison of pain score among the study groups

| Pain score | Comparison of Pain score among the study groups | | | | |
|---|---|---|---|---|---|
| | Lignocaine group | | Ramosetron group | | |
| | Frequency | Percentage | Frequency | Percentage | P value |
| No Pain (0) | 27 | 54 | 30 | 60 | 0.544 |
| Mild Pain (1) | 17 | 34 | 12 | 24 | 0.271 |
| Moderate Pain (2) | 5 | 10 | 5 | 10 | >0.99 |
| Severe Pain (3) | 1 | 2 | 3 | 6 | 0.617 |
| Mean ± SD | 0.6 ± 0.8 | | 0.62 ± 0.9 | | 0.906 |

Both ramosetron 0.3mg and lignocaine 0.5mg $kg^{-1}$ significantly reduced pain on propofol injection but there was no statistical significance between the two groups.

## Discussion

Considering the extensive use of propofol in clinical practice, the pain frequently reported on induction of anesthesia cannot be neglected. Although it is not a serious complication, efforts are assumed to reduce the severity of the pain or discomfort. Propofol belongs to the group of phenols that can irritate the skin, mucous membranes, and venous intima [9]. Injection pain associated with propofol characteristically occurs immediately or later after the drug injection with a delayed response of 10-20s [12]. The explanation for the pain includes endothelial irritation, osmolality differences, unphysiological pH, and the activation of pain mediators [13].

Many methods have been used to reduce the incidence of pain on propofol injection with variable results. Lignocaine added to or given before injection of propofol is widely employed [6]. Gajraj and Nathanson [11] studied the optimal dose of lidocaine for propofol pain and concluded that 30 mg lidocaine is the optimal dose for attenuation of propofol pain. Cooling the propofol to 4°C reduces its injection pain possibly by delaying the activation of enzyme cascade of pain mediators [14]. Injecting into a large forearm vein also reduces the pain, probably by reducing contact between drug and endothelium [6].

Metoclopramide shares the structural and physiochemical properties with lidocaine and is a weak local anesthetic. It has also shown to be as effective as lidocaine in reducing propofol injection pain [15]. Ye *et al.*, [8] found in rats, that ondansetron is approximately 15 times more potent local anesthetic as lidocaine and this property probably contributes to its antiemetic action. Ondansetron had been shown to relieve pain by its multifaceted actions as a Na channel blocker, a $5HT_3$ receptor antagonist, and mu opioid agonist [8,16]. Ondansetron pretreatment may be used to reduce the incidence of pain on injection of propofol with an added advantage of prevention of PONV [9,17].

In a study by Ahmed *et al.* [18] the incidence of propofol injection pain was reduced from 60 to 15% after granisetron pretreatment. Pretreatment with granisetron/lidocaine may be effective not only in attenuating pains during IV injection of propofol, but also in preventing postoperative nausea, vomiting, and shivering [19,20]. In a study by Piper *et al.* [21] severity but not the incidence of pain on injection was significantly reduced by dolasetron (50%) compared with placebo and there was no significant difference between dolasetron and lidocaine. Ramosetron is a recently developed $5HT_3$ receptor antagonist. Lee *et al* [22] reported the incidence of pain in the groups pretreated with ramosetron 0.3 mg or combination with ramosetron and lidocaine 20 mg were 60 and 38%, respectively. These results show effective reduction in propofol injection pain. Pretreatment with ramosetron alone or with combined pretreatment of ramosetron and lidocaine also prevented pain effectively for moderate to severe pain.

In our study out of 50 patients of each study group, 54% in lignocaine group and 60% in ramosetron group did not have pain, 34% in lignocaine group and 24% in ramosetron group had mild pain, 10% in both groups had moderate pain, 2% in lignocaine group and 6% in ramosetron group had severe pain. Thus both ramosetron 0.3mg and lignocaine 0.5mg $kg^{-1}$ significantly reduced pain on propofol injection but there was no statistical significance between the two groups.

Our study had few limitations. Occlusion at mid forearm was done manually, which will vary from person to person, this could have been overcome by using tourniquet with constant pressure. Also drug could have been injected using syringe pump instead of injecting manually.

## Conclusion

We concluded that IV ramosetron when given as pretreatment is as effective as lidocaine on propofol associated pain with an added advantage of preventing PONV.

*Source of Support*

Nil

*Conflict of Interest*

None declared.

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