# Comparison Of Pretreatment With Lignocaine And Ondansetron For Pain On Injection Of Propofol During Induction Of Anaesthesia

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**Citation**

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**Abstract**

Propofol causes pain on IV injection in 28%–90% of patients. A number of techniques have been tried to minimize propofol-induced pain. We compared the efficacy of pretreatment with Lignocaine 50 mg and Ondansetron 4mg after venous occlusion for prevention of propofol-induced pain. Sixty adult patients, ASA physical status I or II, undergoing elective surgery were randomly assigned into 3groups of 20 each. Group A received normal saline, group B received lignocaine 1% (50 mg), and group C received Ondansetron 4mg. All pretreatment drugs were made in 5 mL and were accompanied by manual venous occlusion for 1 minute. Propofol was administered after release of venous occlusion. Pain was assessed with a four-point scale: 0 = no pain, 1 = mild pain, 2 = moderate pain, and 3 = severe pain at the time of propofol injection. Eighteen patients (90%) complained of pain in the group pretreated with normal saline as compared with none in Lignocaine group and Eight (40%) in Ondansetron group.

## INTRODUCTION

Propofol for induction of anaesthesia causes pain or discomfort on injection in 28% - 90% of patients1. Among 33 clinical problems, Propofol- induced pain has been ranked seventh, when both clinical importance and frequency were considered2. The addition of Lidocaine to propofol reduces the incidence of pain on injection3,4. However, mixtures of propofol and lidocaine are not stable and must be used within 30 minutes of preparation. Ye et al5 demonstrated that Ondansetron, a specific 5-Hydroxy tryptamine antagonist is 15 times more potent than lidocaine in causing numbness when injected under the skin.

With this background we conducted a placebo controlled study to compare the efficacy of Ondansetron and Lignocaine in reduction of pain on propofol injection during induction of anaesthesia.

## MATERIALS AND METHODS

We included 60 adult patients, ASA (American Society of Anaesthesiolgist) physical status I and II, scheduled for various elective surgical procedures under general anesthesia. The institutional ethical committee approved the study, and written, informed consent was obtained from all patients. We used a randomized, placebo controlled, double-blinded method for evaluation. The age groups ranged from 18 to 80 years and body weight between 35 & 80kgs.
Following patients were excluded from the study:
1. Patients with disorders of lipid metabolism
2. Patients with past history of an adverse response with propofol or lignocaine.
3. Patients with history of chronic pain syndromes / analgesic drugs.
4. Patients with history of convulsions, head injury.
7. Patients with cardiac conduction defects or on anti-arrythmic drugs
8. Patients with difficult airway.
9. Pregnant and lactating mothers
All subjects received 5-10mg oral diazepam as premedication the night before and 2 hours before induction of anesthesia on the day of surgery with sips of water.
During induction of anesthesia, patients were monitored with Electro cardiogram, Pulse oximetry, and non-invasive blood pressure.
The patients were then allocated randomly to one of three groups.
Group A – 5ml of 0.9% sodium chloride
Group B- 50mg Lignocaine ( 5ml of 1% solution)
Group C-4mg Ondansetron (OND) (diluted to 5ml)

Each patient received 5 mL of pretreatment solution (0.9% saline or 1% Lignocaine or Ondansetron 4 mg) Intravenous, followed by anesthetic induction with propofol 2.5 mg/kg (Propofol preparation used for all the cases were the same). The solutions were prepared by an independent anesthesiologist, and the investigator did not know the contents of the solutions. The patients received 5 mL of the pretreatment solution over a period of 20s while the venous drainage was occluded manually at midarm by an assistant6. The occlusion was released after 1 minute, and one fourth of the total calculated dose of propofol was administered for a period of 5seconds. No analgesic drug was given before propofol. The level of pain was assessed by a second, independent anesthesiologist who was unaware of the group to which the patient had been allocated. The patients were asked a standard question about the comfort of the injection; the verbal response and behavioral signs, such as facial grimacing, arm withdrawal, or tears, were noted1. A score of 0–3, which corresponded to no pain or mild, moderate, and severe pain, was recorded (Table1).
Adverse effects, if any, were noted. Induction of anesthesia was continued with propofol. Tracheal intubation was facilitated with Pancuronium, and anesthesia was maintained with inhaled technique supplemented with fentanyl. Monitoring during anaesthesia was continued with Electrocardiogram, Pulse Oximetry and Non-invasive blood pressure measurement. After the completion of surgical procedure, residual neuromuscular blockade was antagonised with 0.05mg/kg of Neostigmine and 0.02mg/kg of Atropine. Extubation was done when the patients were fully awake and obeying commands. The data obtained were analyzed statistically using the chi-square test. A p value of <0.05 was accepted as statistically significant.

ResultsThe ratio of men to women was 1.2:1. Age ranged from 18 to 80 years and the body weight ranged from 35 to 80 kgs. There was no significant difference between the two groups with regard to sex, age or weight (p>0.05). When pain score was analysed it was found that only 10% of patients in saline group had no pain(score of 0), 20% had moderate pain(score 2) and 70% had severe pain(score 3). In Ondansetron group 60% had no pain (score 0) & 40% had mild pain (score 1); moderate (score 2) and severe pain(score 3) was not noticed in this group. All the patients in Lignocaine group had a score of 0 (no pain) (Table 2).
Severity of pain was much less with Ondansetron and Lignocaine group than saline group. Pain score of 3 & 4 (moderate pain & severe pain) was not noticed in Ondansetron and Lignocaine group. 40% of patients in Ondansetron group had mild pain whereas none in Lignocaine group had.
After Propofol, one patient in the saline group had myoclonic movements and 10% ( 2 patients) in Ondansetron group had skin rashes in the limb into which Propofol was injected which was self limiting (Table:3). Statistical analysis revealed it to be insignificant (p>0.05)

**Table 1**

Assessment of Pain during Injection of Propofol

**Table 2**

Pain after propofol

**Pain After Propofol**

| | | | Drug | | | |
|---|---|---|---|---|---|---|
| | | | Placebo | Ondansetron | Lignocaine | Total |
| painprof | - | Count | 2 | 12 | 20 | 34 |
| | | % | 10.0% | 60.0% | 100.0% | 56.7% |
| | + | Count | 0 | 8 | 0 | 8 |
| | | % | .0% | 40.0% | .0% | 13.3% |
| | ++ | Count | 4 | 0 | 0 | 4 |
| | | % | 20.0% | .0% | .0% | 6.7% |
| | +++ | Count | 14 | 0 | 0 | 14 |
| | | % | 70.0% | .0% | .0% | 23.3% |
| Total | | Count | 20 | 20 | 20 | 60 |
| | | % | 100.0% | 100.0% | 100.0% | 100.0% |

a. $\chi^2$=66.353 P<0.001 VHS

(VHS= very highly significant)

**Table 3**

Side effects

**SIDE EFFECTS**

| | | Drug | | | |
|---|---|---|---|---|---|
| | | Placebo | Ondansetron | Lignocaine | Total |
| NIL | Count | 19 | 18 | 20 | 57 |
| | % | 95.0% | 90.0% | 100.0% | 95.0% |
| Myoclonus | Count | 1 | 0 | 0 | 1 |
| | % | 5.0% | .0% | .0% | 1.7% |
| Rashes | Count | 0 | 2 | 0 | 2 |
| | % | .0% | 10.0% | .0% | 3.3% |
| Total | Count | 20 | 20 | 20 | 60 |
| | % | 100.0% | 100.0% | 100.0% | 100.0% |

a. X2=6.105 P=.191 NS

NS: not significant

## DISCUSSION

In our study, we observed that pretreatment with Lignocaine 50mg or Ondansetron 4mg attenuated pain associated with Propofol injection. However Lignocaine was found to be slightly better than Ondansetron in reducing pain.

Chemically, propofol belongs to the group of sterically hindered phenols. Hence, like the phenols, propofol irritates the skin, mucous membrane and venous intima. Propofol causes pain on injection in 45-75% of patients, particularly when it is administered through the small veins at the back of the hand7. Various ways of minimizing this pain have been proposed, including using larger veins8, priming with lidocaine, an opioid (e.g., fentanyl, alfentanil, or meperidine), or midazolam before the injection of propofol7,9 diluting propofol with 5% glucose or 10% intralipid, injecting cold saline with the propofol or discontinuing fluid during the injection10, or the use of 5-hydroxytryptamine3 antagonists11.

Bradykinin, by producing local venous vasodilation and hyperpermeability, may increase the contact between the aqueous phase propofol and free nerve endings resulting in pain on injection12.

McCulloch MJ, Lees NW et al13 showed that Lidocaine pretreatment reduces the incidence of pain to 17.5% and 19.5% respectively. ). Others have shown that freshly mixed propofol and 1% lidocaine reduces the incidence of pain on injection significantly. In our study, all the patients in Lignocaine group had a score of 0 (no pain).

Ye et al.5 found, in rats, that Ondansetron is approximately 15 times more potent as local anesthetic than lidocaine. The local anesthetics currently in use contain hydrophilic and hydrophobic structures, separated by an intermediate amide or ester linkage. The hydrophilic group can be a tertiary or secondary amine; the hydrophobic domain must always be an aromatic moiety. Although Ondansetron does not have this aromatic moiety, it has the ability to block sodium channels. Peripheral 5-Hydroxytryptamine3 receptors involve nociceptive pathways5. Recently, Ondansetron has demonstrated binding at the opioid mu(μ) receptors in humans and exhibits agonist activity14. As a result of its multifaceted actions as a sodium channel blocker, a 5-Hydroxytryptamine3 receptor antagonist, and mu(μ)-opioid agonist, Ondansetron may potentially be used to alleviate pain produced by a drug similar to propofol. The usual dose of Ondansetron in adults is 4 mg. Pretreatment with the usual dose of Ondansetron could alleviate the pain produced by propofol, and one minute was allowed for its action to begin. We chose a one-minute interval with the presumption that this period might be sufficient, as most patients feel numbness after the intradermal injection of a local anesthetic. In our study, 40% of patients in Ondansetron group had mild pain whereas none in Lignocaine group had any pain.

## CONCLUSION

Though 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.

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