*Original Research Article*

Indian Journal of Anesthesia and Analgesia
2019; 6(2) (Part - I): 433-437
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6219.10

# Comparative Evaluation of Ondansetron and Fentanyl for Alleviation of Pain Caused By Propofol Injection

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**Abstract**

*Aim:* Pain associated with Propofol injection is quite distressing. This study was aimed to compare the effectivness of ondensetron and fentanyl for alleviation of pain caused by propofol injection. *Setting and design:* Prospective comparative observational study. *Methods and Material:* A prospective observational study was conducted on 90 patients who were scheduled for the elective surgeries under general anaesthesia and received inj.propofol as an induction agent. Patients who received pretreatment with ondensetron (4 mg) before Propofol injection formed group O (n=30) while patients who received fentanyl (100 µg) as a pretreatment or nothing formed group F (n=30) and group P (n=30) respectively. The primary outcome recorded was the incidence of pain after propofol injection. We also assessed severity of pain and local reaction at the site of injection. *Statistical analysis used:* Purposive sampling method used for calculation of sample size. Data were analysed using SPSS softwere version 16.0. ANOVA test were used to compare quantitative data while chi-square test and fisher's exact test were used to compare qualitative data. p value <0.05 was considered as a significant. *Results:* The incidence of pain was significantly low in group O (13.3%) and group F (13.3%) compared to group P (100%). Among all the patients who had pain, patients of group O and group F experienced only mild pain while patients of group P experienced moderate to severe pain. None of the patient had inflammatory reaction at local site. *Conclusion:* Pretreatment with Ondensetron or Fentanyl is equally effective for alleviation of pain caused by Propofol injection.

**Keywords:** Propofol; Ondansetron; Fentanyl; Lignocaine.

**How to cite this article:**

Hetal Hathiwala, Harsha Patel. Comparative Evaluation of Ondansetron and Fentanyl for Alleviation of Pain Caused By Propofol Injection. Indian J Anesth Analg. 2019;6(2):433-437.

## Introduction

Propofol, the most widely used anaesthetic agent for induction of anaesthesia is associated with pain at injection site, with incidence of 28% to 90% in adults [1,2,3].

Many techniques have been used to alleviate propofol-induced pain, but lignocaine (2%) premixed with propofol is most common method [4-5].

Ondansetron, a well-established agent for PONV, also blocks Na channels in rat brain neurons [6].

Fentanyl a potent opioid agonist used to attenuate laryngoscopic stress response was found to reduce pain of propofol injection [7].

We aimed to compare ondansetron and fentanyl for alleviation of pain due to propofol injection with respect to incidence and severity.

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**Received on** 14.12.2018, **Accepted on** 14.01.2019

## Material and Methods

This prospective, comparative, observational study was conducted at government medical college, Surat after approval from institutional ethical committee. A written Informed consent was taken from all the participants after explaining the study procedure.

According to purposive sampling method total 90 patients belonging to American Society of Anesthesiologist (ASA) class I to III, aged between 18 to 60 years, scheduled for surgery under GA with propofol as an induction agent were included in the study. Exclusion criteria included patient refusal, patient with history of allergy to study drugs, patient who received any analgesic before surgery and patient with communication difficulties. In our institute, to reduce the pain of Propofol injection we use propofol premixed with lignocain (2%) (9 ml Propofol + 1 ml lignocaine) as a standard therapy. We divided patients into following three equal groups:

Group O: Patients who were at increased risk for PONV (e.g middle ear surgery, laparoscopic surgery, GI surgery etc.) and received pretreatment with 4 mg ondansetron (2 ml) before inductin with inj.propofol premixed with inj.lignocaine (2%).

Group F: Patients who received fentanyl 100 µg for attenuation of sympathetic response to laryngoscopy and intubation (e.g patients with HT, IHD etc.) before induction with inj.propofol premixed with inj.lignocaine (2%).

Group P: Patients did not require any pretreatment and received only inj. Propofol premixed with inj.lignocaine 2% 20 mg I.V.

A pre anaesthesia check up was done a day before surgery and patients were explained about the procedure. They were also explained about the VRS (verbal rating scale) for assessment of pain. On the day of surgery in a preparation room, after taking vitals, patients were once again familiarized with VRS for pain. A 20 gauge cannula was placed into the largest vein on the dorsum of hand and patients were premedicated with inj.Glycopyrolate 0.004 mg/kg i.v and Inj.Midazolam 0.04 mg/kg i.v. None of the patient received any analgesic.

In operation theatre, just before induction patients of group O received Ondensetron 4mg and that of group F received Fentanyl 100 µg i.v over a period of 10 seconds while the venous drainage was occluded by placing an air-filled tourniquet inflated to 70 mm Hg on the upper arm for 20 seconds. After the release of occlusion 25% of calculated total induction dose of propofol (2 mg/kg) premixed with lignocaine 2% was injected over a period of 10 seconds. Patients of group P received 25% of total dose of propofol with lignocain 2% without any pretreatment. Immediately after injection patients were asked a standered question, "did you feel pain?" and if answer is yes "How much?" A four point categorial verbal rating scale (VRS-4) was used to quantify the pain [in which score of 0 to 3 corresponds to 0= no pain, 1= mild pain, 2= moderate pain, 3= severe pain]. Along with the verbal response, behavioral signs such as facial grimacing, arms withdrawal or tear were recorded.

*Verbal Rating Scale*

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

After recording the patient's response remaining dose of induction agent was given and anaesthetic management was continued as per schedule. Patients were assessed for swelling and redness at the injection site up to 1 hr after induction.

Data collected were presented as mean ± SD if quantitative and as percentage or number if qualitative. Data were analysed using SPSS softwere version 16.0. ANOVA test were used to compare quantitative data while chi-square test and fisher's exact test were used to compare qualitative data. p value $<0.05$ was considered as a significant.

## Results

Total 90 patients were observed from three groups.

There was no statistically significant difference observed among the groups with respect to demographic data (Table 1)

One way ANOVA between the 3 groups showed that there was no significant difference in the age

(p=0.817) or weight (p=0.634) of the participants.

The incidence of pain was significantly low in group O and group F compared to group P. The incidence of injection pain was 13.3% (4/30), 13.3% (4/30) and 100% (30/30) in group O, group F and group P respectively. Among all the patients who had pain, patients of group O and group F experienced only mild pain while patients of group P experienced moderate to severe pain. (Fig. 1)

Fisher's Exact test for comparing the grade of pain between the 3 groups showed that these was a statistically significant difference between the groups using Ondansetron or Fentanyl and the group using only Propofol (Fisher's Exact Test value = 97.298, p = 0.000). Comparison between Group O and Group F was not possible because they had similar values which show that both are equally effective in reducing pain on injection site.

Postoperatively when patients arrived at recovery room, none of them have injection site swelling or pain in any group.

## Discussion

Pain associated with propofol is well documented. The exact mechanism responsible for occurance of pain following propofol injection is not well established.

Sinharoy et al. [8] proposed one mechanism that propofol can activate the kallikrein-kinin system resulting in releases bradykinin which cause venous dilation and increased permeability there by allowing contact between propofol aqueous phase and free nerve endings, which causes pain on propofol injection. However, some studies showed that propofol injection when compares with saline did not associated with increased in plasma bradykinin concentration [9,10].

Ondansetron is a specific 5HT3 receptor antagonist, is an antiemetic commonly used along with general anaesthesia to prevent PONV. Even though its molecular structure is quite different from local anaesthetic, ondensetron blocks Na channels similar to that of local anaesthetics [6].

**Table 1:** Comparision of demographic data

| Patient characteristics | Group O (N=30) | Group F (N=30) | Group P (N=30) | P value |
|---|---|---|---|---|
| Age | 38.03 ±16.39 | 40.5 ± 16.0 | 38.9 ± 14.3 | 0.817 |
| Weight | 52.5 ± 8.58 | 54.6 ± 12.43 | 52.3 ± 9.20 | 0.634 |
| Sex (M/Fe) | 16/14 | 14/16 | 16/14 | 0.837 |

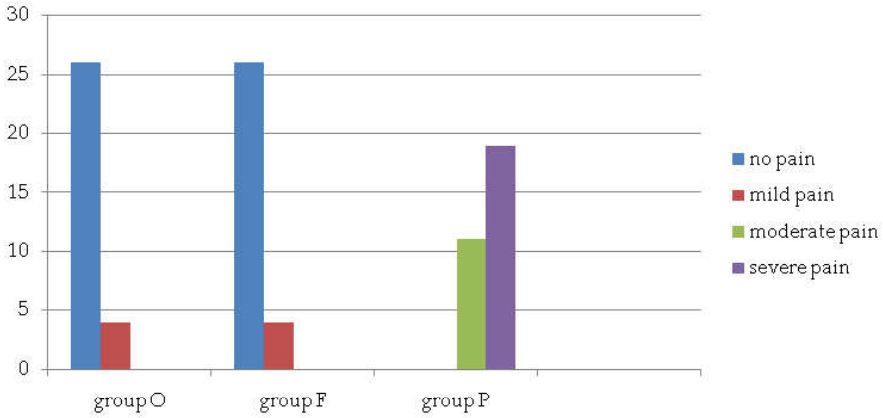


**Fig. 1:** Incidence of pain on injection of propofol:

It also blocks the opioid μ receptors and exhibits agonistic activity in human [11].

Antagonist effects on 5-HT3 receptors associated with peripheral pain pathway may be responsible for its analgesic effects.

Fentanyl a short acting opioid analgesic,is routinely used to reduced sympathetic response of laryngoscopy and intubation.

In this study we evaluated and compare the effectiveness of ondensetron and fentanyl for reduction of pain caused by propofol injection. We observed that, ondensetron and fentanyl both significantly and equally reduced the incidence and severity of pain associated with propofol injection.

Ambesh et al. [12] and H. Zahedi et al. [13] also evaluated ondensetron for alleviation of pain on propofol injection and observe that it significantly reduces the incidence and severity of propofol induced pain.

Studies evaluating the efficacy of alfentanil and remifentanil, showed that frequency and severity of pain associated with propofol injection is less as compared to normal saline [14].

In some studies fentanyl was found effective in reducing the pain on propofol injection [1,15] while in other studies [16,17] it failed to prove its effectiveness for alleviating pain on propofol injection.

There are few limitations of our study. As it was a time frame study, smaller sample size is one of the limitations of our study. Also we have not considered the impact of patient's anxiety on interpretation of pain.

## Conclusion

From the above observational study we conclude that pretreatment with either odensetron or fentanyl is equally effective in reducing the incidence and severity of pain associated with Propofol injection.

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