



Original Research Article

Comparison of intravenous granisetron and intravenous lignocaine to alleviate pain on propofol injection: A double blind, randomized, controlled trial

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ABSTRACT

Background: The objective of the study was to compare effectiveness of intravenous (IV) granisetron (2 milligram) with IV lignocaine (30 milligram) in allaying pain on propofol IV administration measured at 15 seconds after propofol administration.

Materials and Methods: 100 patients of age 18-50 years belonging to American Society of Anesthesiologists (ASA) physical status grades I and II, chosen for elective surgery were randomized to two different groups (group L and group G) of 50 each. Patients of group L received IV lignocaine 30 mg and the other group G received IV granisetron 2 mg as pretreatment, before administration of propofol. Patients were assessed for pain after 15 seconds of IV administration of propofol with McCrirk and Hunter scale.

Results: Both the pretreatments were found to prevent or decrease the pain on propofol administration. Pain assessed at the end of 15 seconds of propofol administration, showed that 76% in lignocaine group & 62% in granisetron group were not having any pain, 12% in lignocaine group and 20% in granisetron group had mild pain, and 12% in lignocaine group and 18% in granisetron group had moderate pain as assessed with McCrirk and Hunter scale. There was no significant difference in the pain scores between the groups ($\chi^2 = 2.310$, $P = 0.315$).

Conclusion: Both IV granisetron (2 mg) and IV lignocaine (30 mg) are equally effective in allaying pain on propofol injection.

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1. Introduction

Propofol is the most commonly used induction agent in day care surgery.¹ On intravenous (IV) administration it causes intense burning pain which adds to patient dissatisfaction.² Incidence of pain on IV propofol administration into a vein on dorsal aspect of hand has wide distribution ranging from 28% to 90%.³ Patient may present with pain concurrently with IV propofol administration or later.⁴ Direct irritant effect of propofol on vein causes pain on concurrent administration and kinin cascade release causes the pain 10-20 seconds later.⁵⁻⁷ The attempts to develop pain free or lesser pain causing formulations of propofol have been futile.⁴ There are many medicinal

and non medicinal ways to allay IV propofol induced pain.^{4,8,9} Some of medicinal methods are pretreatment with lignocaine, ketamine and opioids. Of these, pretreatment with IV lignocaine has proven to be most efficacious, by reducing propofol induced pain by nearly 60%.⁴ Though IV lignocaine pretreatment is better than other interventions, none of the available interventions can prevent pain on IV propofol administration in 100% of patients.⁴

In this context many new pharmacological agents including 5HT₃ receptor antagonists have been tried to prevent pain on IV propofol administration.^{4,10} Ondansetron a specific 5HT₃ receptor antagonist, has shown the property of local anesthesia, which can be used to allay propofol pain on IV administration.^{11,12} Granisetron, a higher congener of ondansetron is a specific 5HT₃ antagonist with longer period of action and has shown better antiemetic effect.¹³ The

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preliminary evidence suggests that granisetron is effective in preventing pain on IV propofol administration.^{2,14} However, replication studies are needed to gather more evidence regarding the effectiveness of granisetron. In this study the efficacy of IV granisetron 2mg in 3ml with IV lignocaine 1% (30mg in 3 ml) in allaying pain on IV propofol administration was compared.

2. Materials and Methods

Our study was a double blind randomized controlled trial and the patients were recruited after obtaining ethical committee clearance and informed consent. The sample size was calculated for the effect size of 0.3 with alpha value of 0.05 and 80% power of the study corresponding to 48 patients in each group. So, 100 patients were randomized to two groups of 50 each i.e., granisetron group (group G) and lignocaine group (group L). Patients were considered for study if they were between 18-50 years, chosen for elective surgery under general anaesthesia belonging to American Society of Anesthesiologists (ASA) physical status grades I and II. Patients with history of allergy, having received any sedatives, analgesics within 48 hours before procedure, who were pregnant and lactating, having communication disability and undergoing emergency procedures were excluded from our study. Preanaesthetic evaluation was performed one day before surgery. In the operating room, 20 G cannula was secured on the dorsal surface of hand. Standard monitors were connected, pulse rate (PR), non invasive blood pressure (BP), peripheral oxygen saturation (SpO₂) and respiratory rate (RR) were measured and recorded at 3 time intervals i.e., before administering propofol and after 1 and 3 minutes of propofol administration. Tourniquet was used to occlude the venous drainage. Patients of group G received 2mg (3ml) of granisetron IV and those of group L received 30mg lignocaine (3ml of 1% solution) IV, over a period 5 seconds about 5 minutes after cannulation. The tourniquet was released after 1 minute of premedication. Initially 20 mg bolus (2ml of 1% solution) propofol was administered over 4 seconds and 15 seconds later patient was asked to rate the pain due to propofol administration. Grading of pain was done using McCrirkick and Hunter scale (Table 1), a standardized measure of pain after IV administration of propofol (15). The author PS was blind to the randomization and evaluated the pain after propofol administration using the above-mentioned scale. Following the pain rating, patient was induced with overall dose of 2 mg/kg-body weight of propofol (including the initial bolus) & intubation with appropriate tube size was done. PR, blood pressure (BP), SpO₂ and RR was recorded at 1 and 3 minutes after induction. Routine maintenance and monitoring of anaesthesia was done. At the end of surgery, reversal of muscle relaxation (neostigmine 0.05mg/kg & glycopyrrolate 10 mcg/kg, IV) was done and the patients

were extubated. The PR, BP, SpO₂ & RR recordings before induction, at 1 & 3 min after induction were compared between Group L and G.

The data was analyzed using the R software. The data was evaluated for the normality of the distribution. The results for continuous variables were presented as mean and standard deviation and mean difference between groups was compared using independent t test. The categorical variables between the groups were compared using Chi-Square test. Repeated measure analysis of variance (RM-ANOVA) was done to compare the PR, BP, SpO₂ & RR before and after propofol induction between the groups. For all the tests probability (P) value ≤ 0.05 was considered as statistically significant.

3. Results

Patients' age, weight and ASA physical status were compared between the two groups (Table 2). The pain after propofol administration was absent in 76.0% and 62.0% patients of group L and group G respectively. Nearly 12.0% of the group L patients and 20.0% of group G patients had mild pain, while this percentage was 12.0% and 18.0% for moderate pain. None of the patients in both the groups had severe pain. The group difference was calculated using chi-square test for 2x3 table. The pain reduction between groups L and G ($\chi^2 = 2.310$, $P = 0.315$) was insignificant. There was no statistically significant mean difference between the groups in PR, RR, BP and SpO₂ at baseline and on RM-ANOVA there was no significant group time interaction for these variables at the end of 1 and 3 minutes of propofol administration compared to the baseline except for RR (Table 3). RR had significant group time interaction with granisetron group having decreased RR after induction with propofol compared to lignocaine (Table 3). The post hoc comparison of the RR across different time frames suggested that compared to the baseline, mean difference in RR at the end of 1 minute ($p = 0.006$) as well as at the end of 3 minutes (0.031) was significantly different between the groups with group G having decreased RR after induction (Table 4).

4. Discussion

The important finding of our study was that granisetron is equally effective as lignocaine for the management of pain on IV propofol administration. On comparison of two groups in pain reduction as well as in hemodynamic stability and peripheral blood oxygenation measured with PR, BP and SpO₂ respectively was insignificant.

Propofol is a fast-acting agent and its action wears off quickly making it useful for day care procedures.¹⁵ At sub hypnotic doses, it provides excellent sedation, amnesia, anxiolysis and a state of general well being in addition to its advantageous antiemetic action. As discussed earlier, its

Table 1: Mc Crirrick and Hunter scale of evaluation of propofol intravenous administration pain

Score	Description
0	None (negative response to questioning)
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)
3	Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears)

Table 2: Demographic and clinical variables of the groups

Variable	Lignocaine group	Granisetron group	P value
Mean age (mean \pm SD)	40.1 \pm 7.5	42.1 \pm 8.5	0.20
Percentage of males	64	52	0.22
Weight (mean \pm SD)	58.92 \pm 12.15	56.94 \pm 10.3	0.382
ASA physical status (percentage)			
Grade I	100	86	0.06
Grade II	0	14	
Pain scores			
0	76	62	0.315
1	12	20	
2	12	18	
3	0	0	

Table 3: Group and time interaction of the clinical variables

Clinical Variables	Lignocaine Group	Granisetron group	Group X time interaction effect (F value)	P value
Pulse rate				
Baseline	83.80 \pm 16.14	87.50 \pm 14.93	1.5	0.21
1 minute	85.40 \pm 18.05	83.94 \pm 12.60		
3 minutes	85.78 \pm 17.66	86.10 \pm 13.86		
Systolic blood pressure				
Baseline	125.32 \pm 19.62	127.52 \pm 17.38	0.47	0.62
1 minute	121.50 \pm 16.77	121.32 \pm 18.20		
3 minutes	115.70 \pm 16.76	115.64 \pm 16.96		
Diastolic blood pressure				
Baseline	73.58 \pm 12.20	74.08 \pm 9.55	1.6	0.2
1 minute	72.38 \pm 11.25	69.58 \pm 12.75		
3 minutes	71.28 \pm 15.09	66.80 \pm 13.22		
Peripheral oxygen saturation (SpO ₂)				
Baseline	99.82 \pm 0.69	99.70 \pm 0.67	1.36	0.25
1 minute	99.86 \pm 0.40	99.88 \pm 0.43		
3 minutes	99.94 \pm 0.31	100 \pm 0		
Respiratory rate				
Baseline	19.44 \pm 1.71	19.74 \pm 0.87	4.72	0.03
1 minute	20.38 \pm 1.99	18.92 \pm 2.98		
3 minutes	20.52 \pm 3.13	18.78 \pm 4.08		

Table 4: Post hoc analysis comparing the respiratory rates across time frames between groups

Time	Lignocaine group (mean \pm SD)	Granisetron group (mean \pm SD)	t value	P value
Baseline RR – 1 minute RR	0.52 \pm 2.15	-0.64 \pm 1.93	2.82	0.006
1 minute RR – 3 minute RR	0.14 \pm 1.76	-0.14 \pm 1.87	0.77	0.44
Baseline RR – 3 minute RR	0.66 \pm 3.42	-0.78 \pm 3.14	2.18	0.031

RR – Respiratory rate

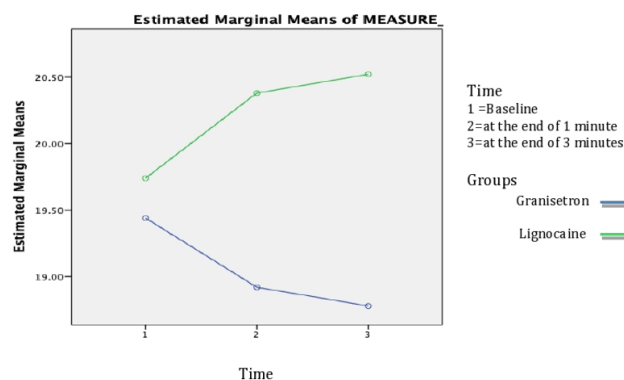


Fig. 1: Difference in respiratory rate (RR) over time after induction with propofol between lignocaine and granisetron groups

utility is constrained by pain on IV administration occurring in significant percentage of patients.⁶

When compared with placebo or normal saline, lignocaine has been shown to be significantly effective in reducing pain on IV propofol administration.¹⁶ Similar to the earlier findings, in our study also nearly three fourth of the patients did not have pain on IV propofol administration after prophylactic administration of lignocaine and it is in accordance with the earlier reports of success rates ranging between 56-87%.^{16,17} Interestingly, nearly two third of the patients (62%) did not have pain on IV propofol administration in the granisetron group and it is in line with the findings from the earlier study where 60% of the patients had no pain on IV propofol administration at the end of 15 seconds.¹⁸ In another study comparing the granisetron with placebo, nearly 90% of the patients on granisetron were reported not to have pain. But in this study after how many seconds of propofol administration pain was measured is not mentioned. We feel it is probable that the pain assessment was done immediately after (at 5 seconds) the propofol administration accounting for higher percentage of patients reporting no pain on IV propofol administration, as found in the Singh et al study.^{2,18} Overall, the findings of our study add more evidence to the role of 5HT3 receptor antagonists in general and granisetron in specific for the management of pain on IV propofol administration.

Another important aspect of our study was the absence of significant group difference between lignocaine and granisetron for the prevention of pain on IV propofol administration although numerically greater number of patients in the lignocaine group were pain free. Our findings are consistent with previous studies showing both lignocaine and granisetron being equally effective in preventing pain on IV propofol administration.^{11,19} Our study also affirms that the incidence of pain on IV propofol administration is much reduced in both the groups than patients who did not receive any pretreatment.¹⁶ Our findings suggest that the anaesthesiologist may select

either agent for the prevention of pain on IV propofol administration based on the individual profile of the patient. Of these two agents, 5HT3 antagonist granisetron carries the additional advantage of having antiemetic effect in the postoperative phase.

The PR, BP (both systolic blood pressure and diastolic blood pressure), SpO₂ and RR were compared during pre-induction, post induction at 1 minute and 3 minutes. All the parameters remained similar except for RR which decreased in the granisetron group over time. Although there was statistically significant group difference in RR, the absolute value of the mean difference was less than 2 per minute and the clinical relevance of the same may be insignificant and needs to be tested in studies with larger sample size. In addition, the confounding effect of induction dose of propofol on RR across groups has not been assessed and we could not come across any literature on pretreatment with granisetron influencing the respiratory rate. Otherwise, both lignocaine and granisetron did not cause any significant hemodynamic disturbances in our study. Even in patients who experienced pain on propofol intravenous administration, increase in heart rate was not significant enough to cause hemodynamic instability. The findings of our study should be interpreted considering the limitation of the small sample size. Although we recommend granisetron over propofol for its anti emetic action, we could not compare the postoperative nausea/vomiting between the groups.

5. Conclusion

We conclude that granisetron decreases the POPI as effectively as lignocaine and both the drugs did not differ in their effect on hemodynamic factors after the induction with propofol. Granisetron has an added advantage of decreasing postoperative nausea and vomiting. Further research is needed with larger sample size to confirm the findings.

6. Source of Funding

None.

7. Conflict of Interest

None.

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