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Original Research Article

Comparison of Lignocaine and Ondensetron on Propofol injection pain

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Abstract

Background: Propofol is widely used for induction of anesthesia, although the pain during its injection remains a concern for all anesthesiologists. The present study was undertaken to evaluate and compare the effect of lignocaine and ondansetron on propofol injection pain.
Method: Total 200 ASA grade I and II patients who underwent general anesthesia for abdominal, urosurgery, plastic surgery and orthopedic elective surgical procedures were enrolled and divided into two equal groups. Group O received ondansetron 4mg IV and group L received lignocaine 40mg IV. Mid forearm was occluded manually before injection and released after 1 min and then propofol was injected over 5 s. Patients were observed and questioned 15 s later if they had pain in the arm and pain was scored on a four-point scale and visual analogue score scale.
Results: Both the groups were comparable in respect to demographic characteristics. The incidences of no pain on injection of propofol in ondensetron and lignocaine groups were 75% and 65% respectively, ($p>0.05$). The severity of propofol induced pain was not statistically different between lignocaine and ondansetron groups. There were no side effects noted in both the groups.
Conclusion: Intravenous pretreatment with lignocaine and ondansetron with manual venous occlusion reduces propofol injection pain in adult patients but ondansetron 4mg is as effective as lignocaine 40mg. Hence, the choice of agent should be individualized with due consideration to the cost-effectiveness and benefit to the patient.
Keywords: Propofol, Anesthesia, Lignocaine, Ondansetron, Pain, Visual analogue score.

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1. Introduction

Propofol is one of the most common intravenous anesthetic drug used today for induction of general anesthesia with rapid onset and short duration of action [1]. Pain on injection of anesthetic is an important source of patient dissatisfaction and is a recognized adverse effect of propofol [2]. The pathophysiology of this pain is attributed to one of 3 proposed mechanisms. The first mechanism relates pain to the triggering of the local Kallikrein-kinin cascade. Another suggested mechanism was the stimulation of the nociceptive receptors at the free nerve endings located between the intima and the media layers of the venous wall. The third proposed mechanism relates pain to the pH and concentration of propofol [3].

A number of techniques have been tried to minimize propofol induced pain like adding lignocaine to propofol, cooling or warming propofol, diluting the propofol solution, injection of propofol into larger vein and pretreatment with IV injection of lignocaine, ondansetron, granisetron, metoclopramide, opioid, magnesium or thiopental with or without tourniquet; all have tried with variable results [4-6]. It has been demonstrated that lignocaine, a Na channel blocker and ondansetron, a specific 5-hydroxytryptamine (5HT-3) receptor antagonist provide numbness when injected under skin [6]. It has been

further demonstrated that ondansetron is 15 times more potent than lignocaine and successfully relived pain following injection propofol without any adverse effects in significant number of patients [7].

In our hospital, inj. lignocaine is routinely used prior to inj. propofol to reduce pain on inj. of propofol and inj. ondansetron is routinely administered as premedication to prevent postoperative nausea and vomiting (PONV) in patients scheduled for general anesthesia. In this observational study, the effect of pre-treatment of inj. ondansetron (PRONDEN 4MG/2ML) and inj. lignocaine (LOXICARD 2% preservative free, NEON), on propofol injection IP (1%W/V) induced pain was observed and compared amongst patients posted for various elective surgeries under general anesthesia.

2. Materials and Methods

In this prospective, randomized, observational study total200 patients of either sex aged between 18-60 years of ASA grade I and II undergoing various elective surgeries like general, orthopedic, gynecological, urological and plastic surgery under general anesthesia were enrolled. Study was approved by the Institutional Medical Ethics Committee and written informed consent was obtained from all the selected patients. Patients having communication problem, ASA grade III and IV, patients with known allergies to Inj. propofol, 5HT-3 antagonist and eggs, patients sensitive to inj. lignocaine, pregnant and lactating mothers and those patients receiving analgesics 24 hours prior to surgery were excluded from the study.

A complete pre-operative assessment was carried out and all relevant investigations were checked. The grading of the pain was explained to the patients at pre-anesthetics visit. After confirming informed consent and checking for starvation period, patient was taken on operation table and monitors were attached and baseline vital parameters were noted like ECG, blood pressure, SPO2 and heart rate. IV line was secured on dorsum of the non-dominant hand with 20 G cannula. Intravenous infusion of Ringer Lactate started @2ml/kg/hr. All the patients received premedication inj. Glycopyrrolate 0.004mg/kg and inj. midazolam 1mg intravenously. According to our institutional protocol, patients received inj. ondensetron (4mg) 2ml or inj. lignocaine 2% 2ml prior to propofol injection as pretreatment drug. Patients who received inj. ondensetron (4mg) 2ml were labeled as group O (N=100) and patients who received inj. lignocaine (40mg) 2ml were labeled as group L (N=100).

After the manual occlusion of the venous drainage at mid-forearm by an assistant inj. ondensetron 2ml or lignocaine 2% 2ml was administered intravenous slowly. The occlusion was released after a minute and anesthesia was induced with one fourth of total calculated dose of propofol over 5 sec, and 15 sec later patient was assessed for pain during injection of propofol. Assessment included standard questions asked to the patients about the comfort of the injection, verbal response, and noting down behavioral signs (such as facial grimacing, arm withdrawal, or tears). Pain was graded using a four-point scale and Visual analogue scale. Patient‘s heart rate, blood pressure and SpO2 was recorded at 1 min after propofol injection. Induction of anesthesia was achieved with inj. fentanyl 2mcg/kg and remaining dose of propofol. Tracheal intubation was facilitated with injection suxamethonium 1.5mg/kg. Patient‘s heart rate, blood pressure and SpO2 was recorded after 5mins, 10mins and 20mins after intubation. Anesthesia was maintained on oxygen, nitrous oxide and muscle relaxant with inhalational agent using closed circuit with control mechanical ventilation. Monitoring during anesthesia was continued with ECG, pulse oximetry and non-invasive blood pressure measurement. After the completion of surgical procedure, residual neuromuscular blockade was antagonized with 0.06mg/kg of neostigmine and 0.008mg/kg of glycopyrrolate. Extubation was done when the patients were fully awake and obeying commands. Adverse effects, if any were noted in post-anesthesia care unit (PACU).

2.1 Statistical Analysis

Descriptive and inferential statistical analysis has been carried out. Results on continuous variables were presented as Mean ± SD (Min-Max) and results on categorical variables were presented in Number (%). Significance was assessed at 5% level of significance.

The following assumptions on data were made,

1. Dependent variables should be normally distributed,
2. Samples drawn from the population should be random
3. Cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. $P<0.05$ is considered statistically significant. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data.

3. Observations and Results

Total 200 patients were enrolled in the study, among them 140 (70%) were males and 60 (30%) were females. Age of the cases were ranged from 18-60 years with mean age of patients was 43.03±11.52. The demographic characteristics of patients were comparable between two groups and difference was not statistically significant ($P> 0.05$) as shown in table 1.

Table 1: Demographic profile of the patients

Age in Years		Group O	Group L	Total
<20		1 (1%)	2 (2%)	3 (1.5%)
20-30		19 (19%)	23 (23%)	42 (21%)
31-40		6 (6%)	12 (12%)	18 (9%)
41-50		48 (48%)	38 (38%)	86 (43%)
51-60		25 (25%)	22 (22%)	47 (23.5%)
>60		1 (1%)	3 (3%)	4 (2%)
Gender	Male	70 (70%)	70 (70%)	140 (70%)
	Female	30 (30%)	30 (30%)	60 (30%)
ASA Grade	I	50 (50%)	47 (47%)	97 (48.5%)
	II	50 (50%)	53 (53%)	103 (51.5%)
Mean Age		44.16±10.72	41.90±12.22	43.03±11.52
Mean weight		61.5 ± 9.26	59.53 ± 8.28	-

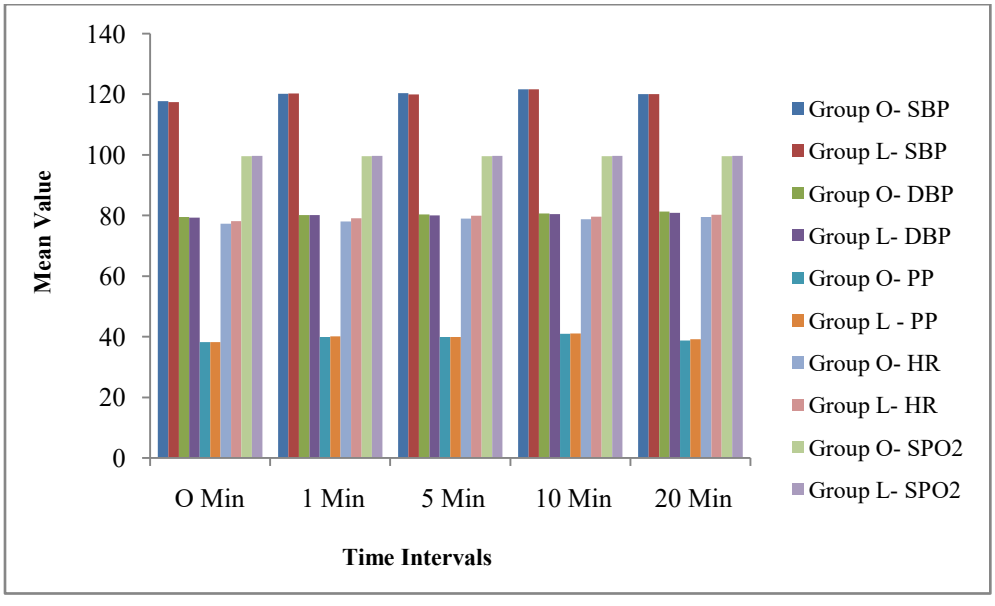
The incidences of no pain on injection of propofol in ondensetron and lignocaine groups were 75% and 65% respectively, (Table 2). Thus, the incidence of no pain was more in group O as compared to group L but difference between two groups was not statistically significant, (p>0.05).

Table 2: Distribution of patient according to Four Point Scale and Visual analogue scale (VAS) score

Four point scale	Group O	Group L	Total	P value
No pain	75 (75%)	65 (65%)	140 (70%)	0.123
Mild pain	15 (15%)	20 (20%)	35 (17.5%)	0.352
Moderate pain	6 (6%)	10 (10%)	16 (8%)	0.297
Severe pain	4 (4%)	5 (5%)	9 (4.5%)	0.733
VAS score	**Group O**	**Group L**	**Total**	**P value**
No pain	75 (75%)	65 (65%)	140 (70%)	0.123
Mild pain	15 (15%)	20 (20%)	35 (17.5%)	0.352
Moderate pain	6 (6%)	10 (10%)	16 (8%)	0.297
Severe pain	4 (4%)	5 (5%)	9 (4.5%)	0.733
Worst pain	0 (0%)	0 (0%)	0 (0%)	-
Mean VAS	0.91±2.00	1.25±2.23	1.08±2.12	-

There was no statistically significant difference noted in hemodynamic parameters like SBP, DBP, PP, BPM and SPO2 in two groups, (P>0.05) as shown in figure 1. There were no side effects noted in both the groups.

Figure 1: Comparison of hemodynamic parameters between two groups



4. Discussion

Nowadays anesthesiologists are expected to provide their services with safe, uncomplicated accepted technique of anesthesia to patient. Propofol (2, 6, di isopropyl phenol) was introduced in practice of anesthesia as an induction agent in early 1970's [8]. It has got tremendous popularity in day care surgery, pediatrics, cardiac, neuro-anaesthesia and ICU sedation for its attractive profile but it is also associated with side effects like myoclonus, apnea, hypotension and pain on injection [9]. The incidence and severity of pain on injection may be more when intravenous cannulation is performed in small veins. Hypertonic drugs, size of needle, site of injection, speed of injection and many other factors are important to produce pain on injection [8]. Several studies have shown the underlying mechanism of propofol-induced pain and claimed it due to its physical properties and chemical constituents [8, 10].

To overcome this pain on injection, McCCulloch *et al* in 1985 [11] suggested injection in large veins. Hiller *et al* in 1996 [12] suggested decreasing speed of injection, dilution in 5% dextrose or 10% intralipid or pretreatment with narcotics or thiopentone before propofol administration. All those workers have carried out their studies on various methods but no one has pointed out a single method applicable in all patients with success. Pretreatment with lignocaine with venous occlusion was found to decrease the incidence and severity of pain on injection of propofol[13-15]. Ambesh *et al* in 1999 [16] and Reddy *et al* in 2001[17] have tried pretreatment with ondansetron to alleviate pain on propofol. They claimed that ondansetron acts as $5HT_3$ antagonist and blocks sodium channels to brain neurons.

The usual dose of ondansetron in adults is 4mg. Pretreatment with the usual dose of ondansetron that could alleviate the pain produced by propofol, and one minute was allowed for its action to begin. In current study, we used 4mg ondansetron and 40 mg lignocaine and also 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. We observed that 75% patients in ondansetron group and 65% patients in lignocaine group had no pain which is comparable with the study done by Pachore *et al* [8]. Incidence of mild pain and severe pain in group O was 15% and 4% respectively and in group L 20% and 5% respectively. So, as similar to the study done by Ye *et al* [9] in present study we observed that ondansetron pre-treatment was better than lignocaine pre-treatment though the difference was statistically not significant. Thus, the pre-treatment with ondansetron 4mg and lignocaine 40 mg were equally effective and results were almost similar.

Sumalatha *et al* [18] reported the incidence of score 0 (no pain) was more as compared to present study. This may be because they used lignocaine dose 0.5mg/kg and we used fixed dose of 40mg. In their study the incidence of mild to moderate pain in groups L was 20%. In current study incidence of mild to moderate pain in groups L was 30%. This difference in incidence and severity of pain in group L could be because they used LCT propofol and we used plain propofol. We found the incidence of pain in lignocaine group was 35% but in Sunny *et al* [19] study, there was no incidence of pain in lignocaine group and this could be because of the lignocaine dose they used was 50 mg and we have used 40mg lignocaine. In their study 40% had pain in ondansetron group but in current study 25% patients complained of pain in ondansetron group, which is comparable to 24.4% as observed in study of Hamid *et al* [20].

The incidence of pain reported by Khouadja *et al* [21] in lignocaine group was 21% and in current study it was 35% using same dose of 40mg of lignocaine. The low incidence of pain in their study could be because tourniquet method of venous occlusion for two min as compared to manual method of venous occlusion for one min in our study. The incidence of adverse reaction were negligible in this study may be attributed to selection of patients of ASA grade I and II only which is comparable with the study done by Pachore *et al* [8].

5. Conclusion

From the results of present study, it can be concluded that, intravenous pretreatment with lignocaine and ondansetron with manual venous occlusion does reduces propofol injection pain in adult patients but ondansetron 4mg is as effective as lignocaine 40mg for reducing propofol injection pain. Hence, the choice of agent should be individualized with due consideration to the cost effectiveness and benefit to the patient. There is no difference in the incidence of moderate to severe pain between two groups. However, study with large sample size may be required to support our conclusion.

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