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Original Article

Comparison of Lignocaine with Ondansetron for Attenuation of Propofol-Induced Pain in Adult Patient Undergoing Laparoscopic Cholecystectomy: A Comparative Randomized Study

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ABSTRACT

Background: Propofol is a non-opioid intravenous anesthetic agent and it is most commonly used for induction of anesthesia but it has a consistent side-effect of pain when it is injected intravenously. Aim of our study was to compare lignocaine and ondansetron for attenuation of pain on propofol injection in laparoscopic cholecystectomy.

Methods: 100 patients planned for laparoscopic cholecystectomy were enrolled for this comparative randomized study. Group L (Lignocaine) – Patients received Inj. Lignocaine 0.5 mg/kg 1 minute before inducing with injection propofol. Group O (Ondansetron) – Patients received Inj. Ondansetron 0.1mg/kg 1 minute before inducing with injection propofol. The patient was evaluated for pain during injection using a four-point scale of 5 seconds and 15 seconds after the propofol injection. Chi-squared test, Fisher's exact test, and Mann-Whitney test were used for data analysis.

Result: Demographic data in group L and group O were similar. The mean± SD pain score during the first 5 seconds in group O was 0.38 ± 0.57 while in group L was 0.02 ± 0.14 ($p<0.001$). The mean± SD post-operative nausea and vomiting (PONV) score during the first hour in group O was 0.08 ± 0.27 while in group L was 1.96 ± 1.160 ($p<0.001$).

Conclusion: We concluded that lignocaine was found more effective than ondansetron for attenuation of propofol-induced pain and post-operative nausea vomiting was much lower than by ondansetron as compared to lignocaine.

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INTRODUCTION

Propofol is a non-opioid intravenous anesthetic agent and it is most commonly used for induction of anesthesia.[1] Rapid induction and rapid clear head recovery is its main advantage. [2]

Propofol is an alkyl phenol compound, hence insoluble in aqueous solutions. It requires a lipid vehicle for emulsification. The emulsion of 1% (w/v) of propofol, 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatid. [3] This emulsion when injected intravenously has a consistent effect of pain at its injection site. [4] When propofol is injected in the vein of the hand, the occurrence of pain on propofol injection is around 28-90% in adults.[5] The Propofol pain is perceived as sharp, aching, and burning in nature. Pain is not a serious complication, but is remembered as one of the most unpleasant encounters during anesthesia. Propofol pain can be categorized as immediate or late. The immediate pain occurring within 5 seconds of injection, is due to skin irritation, venous intima, and mucous membrane leading to activation of myelinated A δ fibers resulting in pain. [6] The delayed pain has a latency of 10–20s, mediated by the release of bradykinin and activation of the kallikrein–kinin system, producing hyperpermeability and venous dilatation. This increases the contact between free nerve endings, and the aqueous phase of propofol resulting in propofol pain. [7]

Pharmacological and non-pharmacological methods have been employed to reduce propofol-induced pain. Non-pharmacological methods like using a large vein for injection, decreasing the speed of propofol injection, using fast fluid as a carrier fluid, diluting propofol with either 5% glucose or 10% intra-lipids, cooling propofol to 4°C prior to injection used to decrease propofol pain.[7-9] Various drugs used to attenuate the propofol pain e.g lignocaine, tramadol, ketolac, ketoprofen, ketamin, magnesium sulfate, clonidine.[8-12] Literature shows 5

hydroxytryptamines (5-HT3) antagonists for example ondansetron, granisetron, and palonsetron are effective in allocating propofol-induced pain.[13-16]

Lignocaine has been used for a long time for abolishing propofol-induced pain and has been very effective in it.[17,18] On the other hand, Ondansetron is much more effective on Post-operative nausea and vomiting (PONV).[15] Being a 5-hydroxytryptamine-3 antagonist, it is well researched for its anti-emetic property but it also has some local anesthetic action too which is not well known.[19]

Limited studies have been done on analgesic action of ondansetron on propofol-induced pain and have conflicting results.[20,21] The aim of this study was to compare lignocaine and ondansetron for attenuation of propofol injection pain in patients undergoing laparoscopic cholecystectomy.

METHODS

This study was a prospective randomized study. The study methods were approved by the Atal Bihari Vajpayee Medical Institute and RML Hospital Ethics Committee and was registered in the Indian Clinical Trials Registry (CRTI/2019/08/020559). The inclusion criteria were American Society of Anesthesiologists (ASA) class I and II patients aged 18 to 60 years who had undergone elective laparoscopic cholecystectomy. Patients who allergic to drugs used in this study, who were suspected of having difficulty airway, and pregnant women were excluded from the study.

Sample size was calculated based on Sumalatha et al.[22] Based on the above research, the clinically relevant difference of 1 in mean propofol injection pain on a four-point scale between the two groups. With an effect size of 0.67, two followed alpha values (0.05), and beta value (0.1), 47 patients in each group were sufficient to identify a significant difference. So total sample size we have taken 100 patients.

All patients signed a consent form. Patients who met the inclusion criteria after careful pre-anesthesia screening and review were included in this study. 100 patients were divided into two groups with 50 patients in each group and different numbers were generated by the computer. The patient taken Lignocaine and Ondansetron as per group. Group L – Patients received Inj. Lignocaine 0.5 mg/kg 1 minute before inducing with injection Propofol. Group O – Patients received Inj. Ondansetron 0.1mg/kg 1 minute before inducing with injection Propofol. Both the drugs were diluted in 5 ml of normal saline. Patients were kept fasting for six hours for solids. They were given oral alprazolam 0.5 mg at night. In the operating room, intravenous access was made preferably with an 18-gauge cannula, and lactated Ringer's solution was infused. Connect the standard ASA monitor and record the baseline of heart rate, blood pressure, and oxygen saturation. Inj. midazolam 0.03mg/kg and inj. fentanyl 2µg/kg were given in all the patients. After 5 minutes, patients were given 5 ml IV lignocaine 0.5 mg/kg (Group L), or 0.1 mg/kg of ondansetron (Group O). After 5 seconds of pre- treatment in both groups, we occluded mid-arm venous drainage at 30-40 mmHg with the aid of an inflated blood pressure cuff. One minute later, the venous drainage was released. This was followed by an injection of 1% propofol just before use. 1/4 of the calculated dose of propofol is injected within 5 seconds, the remainder after 15 seconds. The patient was measured for propofol pain using a four-point scale on 5 second and 15 seconds after the propofol injection. After induction, trachea was intubated with injection vecuronium 0.1mg/kg with appropriate size endotracheal tube. Maintenance was done by injection vecuronium 0.05mg/kg with inhalation mixture of oxygen, nitrous 50%: 50% and sevoflurane titrated to reach minimum alveolar concentration (MAC) 1. At the end of the procedure, the remaining neuromuscular blocking agents were antagonized with 0.05 mg/kg neostigmine and 0.02 mg/kg glycopyrrolate. Extubation was performed while the patient was awake and following the commands.

Primary objective of the study was evaluated propofol pain during injection using a four-point scale for pain on propfol injection on 5 second and 15 seconds after the propofol. Secondary objectives of the study were assessed post-operative nausea, retching, and vomiting (Table 1).

Table 1. Four-point scale score and post-operative nausea vomiting score

Score	Four-point scale for pain on propfol injection	Post- operative nausea vomiting
0	No reaction (no pain)	No nausea/vomiting/retching
1	Grimace (mild pain)	Nausea
2	Grimace + Cry (modarate pain)	Retching
3	Cry +Withdrawal (severe pain)	Vomiting

Data were presented in mean. The study data statistically analyzed using t-test dan Mann Whitney U test for independent sample. Comparison of categorical data tested using Chi square. Statistical analysis using Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) with p-value < 0.05.

RESULT

Both Group O and Group L were similar in view of age, sex, weight, BMI, and height. Group O had 17 males (34%) and 33 females (66%) whereas Group L had 18 males (36%) and 32 females (64%). Age (years) (Mean ± SD) in Group O was 36.00 ± 14.87 whereas in Group L is 38.16 ±11.93. BMI (Mean ± SD) in Group O was 20.88 ± 2.86 whereas in Group L was 21.34 ± 4.20. Weight (kg) (Mean ± SD) in Group O was 58.62 ± 8.25 whereas in Group L was 59.56 ± 11.54. Height (cm) (Mean ± SD) in Group O was 167.56 ± 4.54 whereas in Group L was 167.20 ± 5.03 (Table 2).

Table 2. Demographic details

Characteristics	Group O	Group L
Female	33 (66.0%)	32 (64.0%)
Male	17 (34.0%)	18 (36.0%)
Age(years) Mean ± SD	36.00 ± 14.87	38.16 ± 11.93
Body mass index (Mean ± SD)	20.88 ± 2.86	21.34 ± 4.20
Weight (kg) (Mean ± SD)	58.62 ± 8.25	59.56 ± 11.54
Height (cm) (Mean ± SD)	167.56 ± 4.54	167.20 ± 5.03

Table 3. Comparison between Pain Score in Group O and Group L

Pain Score (Four-point scale for pain on propfol injection)		Group O	Group L	P-Value
		Frequency (%)	Frequency (%)	
5 second	0 (no pain)	33 (66.0%)	49 (98.0%)	<0.001
	1 (mild pain)	15 (30.0%)	1 (2.0%)	
	2 (moderate pain)	2 (4.0%)	0 (0.0%)	
	Mean± SD	0.38 ± 0.57	0.02 ± 0.14	
15 second	0 (no pain)	50 (100.0%)	50 (100.0%)	-
	Mean± SD	0.00 ± 0.00	0.00 ± 0.00	

Table 4. Comparison between Post-Operative nausea and vomiting in Group O and Group L

Post-Operative nausea and vomiting (PONV)		Group O	Group L	P-Value
		Frequency (%)	Frequency (%)	
1st Hour	0	46 (92.0%)	9 (18.0%)	<0.001
	1	4 (8.0%)	7 (14.0%)	
	2	0 (0.0%)	11 (22.0%)	
	3	0 (0.0%)	23 (46.0%)	
	Mean ± SD	0.08 ± 0.27	1.96 ± 1.16	
2nd Hour	0	50 (100.0%)	39 (78.0%)	0.006
	1	0 (0.0%)	7 (14.0%)	
	2	0 (0.0%)	1 (2.0%)	
	3	0 (0.0%)	3 (6.0%)	
	Mean ± SD	0.00 ± 0.00	0.36 ± 0.81	

Pain score in Group O during the first 5 seconds of propofol injection was zero in 66.0% of patients, 1 in 30.0%, and 2 in only 4.0% of patients. In Group L there was a pain score of zero at 98.0%, a score of 1 at only 2.0% and no patient scored 2 in Group L. No patient had pain due to propofol injection after 5 seconds in both the groups. The mean± SD pain score during the first 5 seconds in group O was 0.38 ± 0.57 while in group L was 0.02 ± 0.14 ($p<0.001$) (Table 3).

In Group O only 8% of patients experience nausea and vomiting in the first hour postoperatively whereas in Group L 14% had complaints of nausea, 22% complained of vomiting, and 46% experienced retching in the post-operative period. The mean± SD postoperative nausea and vomiting (PONV) score during the first hour in group O was 0.08 ± 0.27 while in group L was 1.96 ± 1.160 and this difference was statistically significant. ($p<0.001$) While in the second hour postoperatively no patient experienced any nausea and vomiting in Group O whereas in Group L 14.0% had complaints of nausea, 2.0% had vomiting and 6.0 % had compliant with retching. The mean± SD postoperative nausea and vomiting (PONV)score during the second hour in group O was 0.00 ± 0.00 while in group L was 0.36 ± 0.811 and this difference was statistically significant ($p=0.006$) (Table 4).

DISCUSSION

In our study mean± SD pain score during the first 5 seconds in group O was 0.38 ± 0.57 minutes while in group L was 0.02 ± 0.14 and the difference was statistically significant ($p<0.001$).

Sureshan et al [21] in 2019 showed similar results as our study. In their research, it was observed that 90% of the individuals in the lignocaine group experienced no pain. In contrast, in the Ondansetron 4 mg group, 68% of patients reported no pain, while only 13% of patients in the Ondansetron 2 mg group did not experience pain. Furthermore, the study revealed that in the Ondansetron 4 mg group, only 31% of patients had mild pain, as opposed to 75% in the Ondansetron 2 mg group and 10% in the lignocaine group. In terms of moderate pain, 11% of patients were observed in the Ondansetron 2 mg group, but there were no patients with moderate pain in the Ondansetron 4 mg group, nor were there any patients with severe pain in any of the groups. The statistical analysis yielded a p-value of less than 0.01. While Sumalatha et al [22] had coinciding similar results in their study. Compare to the ondansetron group, Propofol pain was less in the lignocaine and ramosetron group ($p= 0.001$). Mild to moderate pain was 28% (ondansetron group), 13% (ramosetron group), and 11% (lignocaine group). Severe pain was 10% in ondansetron group and 2% in ramosetron group and 2% in lignocaine group. Pain was significantly low in ramosetron group and lignocaine group compared to ondansetron group ($p=0.001$).

Abouslemah[20] in 2017 had contradictory results to our study. They found that the incidence of pain experienced in both groups was comparable (34% of patients in lignocaine and 26% in ondansetron), ($P >0.05$). Only 6% of the patient complained of

severe pain in Group O in their study which is lower than Group L which is 8%. Moderate pain was similar in both groups 6%, mild pain was less in group O than in group L ($p>0.05$).

In our study, the mean± SD postoperative nausea and vomiting (PONV) score during the first hour in group O was 0.08 ± 0.27 while in group L was 1.96 ± 1.160. ($p<0.001$) and mean± SD postoperative nausea and vomiting (PONV) score during the second hour in group O was 0.00 ± 0.00 while in group L was 0.36 ± 0.811 ($p=0.006$). Multiple authors [20-22] have commented on the effect of lignocaine and ondansetron on PONV and their results were comparable to our study. All of them suggested that ondansetron has an added advantage over lignocaine in preventing PONV.

The limitation of our study was that it was done in ASA grade 1 and 2 adult patients so extrapolation of the results of the study on geriatric and pediatric patients, and higher ASA grade individuals is not possible. The study was conducted in laparoscopic cholecystectomy, so the effect of different surgeries' pain on propofol injection was not explored.

CONCLUSION

In conclusion, lignocaine was found more effective than ondansetron for attenuation of propofol-induced pain and post-operative nausea vomiting was much lower than ondansetron as compared to lignocaine.

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CONFLICT OF INTEREST

The author declares there is no conflict of interest.

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