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Pretreatment with Ondansetron and Lignocaine for Alleviating Pain on Propofol Injection during Induction of Anaesthesia – A Comparative Study

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Abstract:
Background: *Pain on injection of anaesthetic is an important cause of patient dissatisfaction and is a recognised adverse effect of propofol, incidence varying between 28 – 90% in adults.*
Methodology: *It is a comparative study conducted on 120 patients of age 18-60 years, ASA Grade I and II, randomly allocated to two groups L and O of 60, each receiving lignocaine(L) and ondansetron(O) respectively for 3 years at Department of Anaesthesia, Osmania General Hospital using Mc Crirrick and Hunter scale.*
Results: *Both lignocaine and ondansetron were found to decrease the injection pain significantly i.e. 73% of patients in L group & 63.3% O group did not experience pain at all, 11.7% L group and 20% in O group had mild pain, 13.3% in L group and 16.7% in O group had moderate pain, severe pain was absent in both groups. 26.7% of patients in group L and 10% of patients in group O complained of nausea and vomiting within 24hr postoperative period. The incidence of Postoperative nausea and vomiting was less in ondansetron group.*
Conclusion: *Ondansetron decreases the injection pain significantly. Ondansetron has an added advantage of decreasing Postoperative nausea and vomiting.*
Keywords*: Propofol, Lignocaine, Ondansetron.*

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I. Introduction

"The relief of pain is purchased always at a price. The price in both morbidity and mortality does not greatly differ whatever the agent or agents used." - R.M.Waters.

The international association for the study of pain (IASP) defines pain as an "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" Among 33 low morbidity clinical outcomes, considering clinical importance and frequency, pain during injection of propofol was ranked as seventh most important problem of current clinical anaesthesiology Many pharmacological and non pharmacological methods have been tried to alleviate pain on propofol injection with variable success results e.g: thiopentone sodium[1],ondansetron,[2],lignocaine,[3]alfentanil,[4],tramadol,[5] magnesium sulphate,[6] ketorolac,[7] metaclopramide,[8] acetaminophen,[9] clonidine,[10] ketamine,[11] butorphanol,[12] pethidine,[13] dexamethasone[14] and other methods like site of injection, speed of injection and temperature of propofol. Ondansetron had been shown to relieve pain by its multi-faceted actions as a Na+ channel & K+ channels Block. In an experiment conducted in rats it is found that ondansetron is approximately 15 times more potent as local anaesthetic than lignocaine [15] It is found to have μ opioid agonist action, So ondansetron has been also used to decrease pain produced by propofol.

II. Aims & Objectives Of The Study

2.1 To compare the efficacy of intravenous ondansetron 4mg with intravenous lignocaine 2% (30mg) in alleviating pain on propofol injection.
2.2 To compare hemodynamic changes after pre-treatment with Lignocaine and Ondansetron.
2.3 To compare the incidence of PONV in both groups.

III. Methodology

3.1 Study Design: A comparative study was done to compare lignocaine and ondansetron as pre - treatment to reduce pain due to injection of propofol in patients posted for elective surgical procedures under general anaesthesia was undertaken at Osmania general hospital, Hyderabad.

3.2 Study Population: 120 patients were randomly allocated to two different groups of 60 each
3.2.1 Group L – received 2% (30mg) lignocaine I.V, 1 minute before injection of propofol.
3.2.2 Group O – received 4mg ondansetron I.V, 1 minute before injection of propofol.

3.3 Inclusion Criteria:
3.3.1 Patients aged between 18-60 years of both sexes posted for elective surgeries under general anaesthesia.
3.3.2 ASA (American Society of Anaesthesiologists) Grade I & II

3.4 Exclusion Criteria:
3.4.1 Patient's refusal.
3.4.2 Patients with difficulty in communication.
3.4.3 Patients with a history of allergic response to propofol or 5HT-3 receptor antagonist or lignocaine, pregnant women, patients with history of convulsions, head injury.

Patients were explained about the procedure and informed/written consent was obtained. Routine pre-anaesthetic evaluation was performed.

3.5 Anaesthetic Procedure:
On arrival in the operation room, a 20G cannula was inserted into a vein on the dorsum of patient's non dominant hand and started on Ringers lactate solution.

Patients in GROUP L received 2% (30mg) lignocaine and GROUP O received 4mg ondansetron, over a period of 5 seconds. A non- pneumatic tourniquet which was maintained for one minute duration during pre-treatment and released prior to propofol injection.Patients were induced with propofol 2mg/kg. Initially 2ml bolus of propofol was injected over 4 seconds; 15 seconds later patient was asked to rate immediately any sensation of pain during injection of propofol.

An anaesthesiologist blinded to evaluate pain during propofol injection using Mc Crirrick and Hunter scale, followed by induction & intubation with appropriate size tube. Heart rate, blood pressure, respiratory rate was recorded at 1 and 3 minute of induction.

Anaesthesia was maintained using O2 in N2O and 1-2% sevoflurane uniformly in all cases. Respiratory rate was adjusted to maintain EtCO2 between 35 – 40 mm of Hg. For muscle relaxation Inj.Vecuronium bromide 0.1 mg kg-1 was given as loading dose and one fourth of loading dose was used for maintenance.

Once the surgery was completed neuromuscular blockade was reversed with Inj.Neostigmine 0.05 mg kg^{-1} and Inj.Glycopyrrolate 0.01mg kg^{-1} both IV after ensuring adequate recovery from neuromuscular blockade. Oral cavity and throat were suctioned thoroughly prior to extubation and extubated once extubation criteria were met.

All parameters of study were recorded at following stages - before injecting propofol and at 1 and 3 minute after propofol injection. Postoperatively, patients were observed for postoperative nausea and vomiting over a period of 24 hours
Group L and O study results were compared and statistically analysed.

3.6 Mc Crirrick and Hunter scale of evaluation of propofol injection pain

0	None (negative response to questioning)
1	Mild pain (pain reported only in response to questioning without any behavioural signs)
2	Moderate pain (pain reported in response to questioning and accompanied by a behavioural sign or pain reported spontaneously without questioning)
3	Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears)

3.7 Statistical Analysis:

Data was analyzed using Chi square test, unpaired t test, descriptive statistics and frequencies. The results are presented as mean +/- standard deviation. For all the tests P value of ≤ 0.05 is considered as statistically significant.

IV Results

In both groups Drug L and Drug O, the age distribution ranged from 18 – 60 years. Maximum number of patients in 41-50 years (26.6%) in Drug L and 21-30 years (33.3%) in Drug O.

Table 1 Comparision of Heart Rate variability in two groups

BEATS PER MIN	GROUPS			
	DRUG L		DRUG O	
	1 MIN	3 MIN	1 MIN	3 MIN
0-10	50	38	52	42
11-20	9	13	4	14
21-30	1	8	3	5
31-40	0	1	1	0

The above table shows heart rate variability of 0-10 beats per minute from the values before induction, 50 patients at 1 min and 38 patients at 3 min in group-L, and 52 patients at 1 min and 42 patients at 3 min in group-O. Variability of 11-20 beats per minute from the values before induction, 9 patients at 1 min and 13 patients at 3 min in group-L, and 4 patients at 1 min and 14 patients at 3 min in group-O. p value at induction, at 1 min and 3 min was 0.436, 0.843, and 0.397 respectively. Variability of 21-30 beats per minute from the values before induction, 1 patient at 1min and 8 patients at 3min in group-L, and 3 patients at 1min and 5 patients at 3min in group-O. Variability of 31-40 beats per minute from the values before induction, 0 patients at 1min and 1 patient at 3min in group-L, and 1 patients at 1min and 0 patient at 3min in group-O.

Table 2 Comparision of Systolic Blood Pressure in Two Groups

GROUPS	SBP AT INDUCTION		SBP 1 MIN		SBP 3 MIN	
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION
DRUG L	124.60	17.009	120.95	14.837	116.05	16.547
DRUG O	127.00	16.608	120.35	18.143	113.47	16.761

In Group-L, mean systolic blood pressure decreased from 124.3 ± 17.0 mm of Hg prior to induction, to 120.95 ± 14.83 mm of Hg at 1 min and 116.705 ± 16.54 mm of Hg at 3min.In Group-O, mean systolic blood pressure decreased from 127.0 ± 16.60 mm of Hg prior to induction, to 120.35 ± 18.14 mm of Hg at 1 min and 113.64 ± 16.76 mm of Hg at 3min.The systolic blood pressure in both groups was compared before induction, during induction intra operatively at 1 min, 3 min period and it is not statistically significant.

Table 3 Comparision of Diastolic Blood Pressure in Two groups

GROUPS	DBP IND		DBP 1MIN		DBP 3MIN	
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION
DRUG L	74.20	11.459	72.90	10.876	72.73	11.464
DRUG O	73.07	12.373	68.55	12.604	65.02	13.062

In Group-L, mean diastolic blood pressure decreased from 74.20 ± 11.45 mm of Hg prior to induction, to In Group-L, mean diastolic blood pressure decreased from 74.20 ± 11.45 mm of Hg prior to induction, to 72.90± 10.87 mm of Hg at 1 min and 72.73± 11.46 mm of Hg at 3min.In Group-O, mean diastolic blood pressure decreased from 73.07 ± 12.37 mm of Hg prior to induction, to 68.55 ± 12.60 mm of Hg at 1 min and 65.02 ± 13.06 mm of Hg at 3min.The diastolic blood pressure in both groups was compared before induction, during induction intra operatively at 1 min and is not statistically significant. The changes in diastolic blood pressure at 3 min was found statistically significant.

Table 4 Comparision of Pain in Two Groups

		GROUPS				TOTAL	
		DRUG L		DRUG O			
		NUMBER OF PATIENTS	% WITHIN GROUP	NUMBER OF PATIENTS	% WITHIN GROUP	NUMBER OF PATIENTS	% WITHIN GROUP
PAIN 15 SEC – 1 MIN	NO(0)	45	75	38	63.3	83	69.2
	MILD	7	11.7	12	20	19	15.8
	MODERATE	8	13.3	10	16.7	18	15
	SEVERE	0	0	0	0	0	0
TOTAL		60	100	60	100	120	100

Comparing pain during propofol injection, 75.0% in Drug L group and 63.3% in Drug O group did not have pain, 11.7% in Drug L group and 20.0% in Drug B group had mild pain, 13.3% in Drug L group and 16.7% in Drug O group had Moderate pain and severe pain was absent in both groups. But difference between two groups is statistically insignificant.

Table 5 Comparision of PONV in two groups

PONV	GROUPS			
	DRUG L		DRUG O	
	COUNT	% WITHIN GROUP	COUNT	% WITHIN GROUP
NO	44	73.3	54	90.0
YES	16	26.7	6	10.0
TOTAL	60	100	60	100

In our study, 16 (26.7%) patients in group L and 6 (10%) patients in group O complained of nausea and vomiting within 24hrs of postoperative period.

V Discussion

Propofol has got tremendous popularity in day care surgery, paediatrics, cardiac, neuro-anaesthesia and ICU sedation for its attractive profile .But it is also associated with side effects like myoclonus, apnoea, hypotension and pain on injection.[16] The most worrying side effect which has been most extensively studied is pain on injection of propofol Propofol belongs to the group of phenols that can directly irritate the skin, mucous membrane and venous intima and could immediately stimulate nociceptors and free nerve endings.[3] Pain on injection of propofol can be immediate or delayed. Immediate pain probably results from a direct irritant effect whereas delayed pain probably results from an indirect effect via kinin cascade, delayed pain has a latency of between 10–20s.[17].Numerous studies have been done to investigate the most effective method and drug to reduce propofol-induced pain with variable results. These include site of injection, size of vein, speed of injection, propofol concentration in the aqueous solution and buffering effect of blood, other important factors include speed of intravenous carrier fluid, temperature of propofol, syringe material and concomitant use of drugs such as local anaesthetics and opiates.[17]

There are currently seven types of 5-HT3 receptor antagonists (ondansetron, granisetron, dolasetron, palonosetron, alosetron, tropisetron and ramosetron) [18] and the effect of many of these drugs has been studied in reducing propofol-induced pain. 5-HT3 receptor antagonists bind to opioid μ-receptor thus acting as agonists. In addition, 5-HT3 receptors are involved in the nociceptive pathway, and this may be the mechanism of these drugs analgesic effect.

Klement and Arndt showed that pain intensity was more with increase in concentration of propofol and was always greater with glucose than with intralipid as diluents[2]. By increasing the lipid content or decreasing the concentration in aqueous phase, the incidence of pain can be reduced. Moreover cold appears to lessen propofol induced pain through suppressing the activation of plasma kallikrein – kinin system that initiates enzymatic cascade.[19] The incidence of pain varies from 28-90% of patients and in children 28-85%.[19] Early researchers quoted that in spite of attractive properties of this drug, the high incidence of pain on injection will make it take a back seat in due course of time.

Table 6 Comparision of studies with Ondansetron as Pretreatment.

PAIN SCORE	AMBESH et al[20]	SOLTANI MOHAMMADI et al [21]	UMA [22]	Our study group
NONE (0)	30(75%)	20(90%)	40(80%)	38(63.3%)
MILD(1)	4(10%)	2(9%)	6(12%)	7(20%)
MODERATE(2)	3(7.5%)	0	2(4%)	8(16.7%)
SEVERE(3)	3(7.5%)	0	2(4%)	0

Table 7 Comparision of Studies with Lignocaine As Pretreatment

PAIN	SOLTANI MOHAMMADI etal [21]	MICHEAL H.NATHANSON[4]	OUR STUDY
NONE(0)	21(95%)	26(87%)	45(75%)
MILD(1)	1(4%)	2(6.5%)	7(11.7%)
MODERATE(2)	0	2(6.5%)	8(16.7%)
SEVERE(3)	0	0	0

VI Conclusions

6.1 Ondansetron 4mg decreases the injection pain significantly.
6.2 Ondansetron 4mg and lignocaine 30 mg are equally effective in alleviating pain of propofol injection.
6.3 Ondansetron has an added advantage of decreasing PONV.
6.4 No significant hemodynamic changes are caused by both drugs.

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