### COMPARING THE EFFECTIVENESS OF TWO DIFFERENT DOSES OF INTRAVENOUS LIGNOCAINE IN REDUCING THE INCIDENCE OF PAIN ON PROPOFOL INJECTION

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#### HOW TO CITE THIS ARTICLE:

Balaji M, Anand Subramaniam, Shalini G. Anand. "Comparing the Effectiveness of two Different Doses of Intravenous Lignocaine in Reducing the Incidence of Pain on Propofol Injection". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 19, March 05; Page: 3229-3237, DOI: 10.14260/jemds/2015/468

ABSTRACT: INTRODUCTION: Propofol in spite of its advantages as an induction agent has the drawback of pain on injection which can be very distressing to the patients. Pain on Propofol injection is estimated to be around 28-90%. Many drugs have been tried to attenuate the pain of Propofol injection. Lignocaine has been the most studied drug in varying dosages, as a mixture with Propofol, given alone and with and without venous occlusion. AIM: To compare the effectiveness of two doses of Lignocaine 25mg,50mg and a placebo in attenuating the pain of propofol injection with 60 seconds of venous occlusion using a tourniquet to a pressure of 100 mmHg. MATERIAL AND **METHODS:** a prospective randomized double blinded study of ASA I and II patients divided into three groups. Group 1(n=20) received 5 ml normal saline, group 2 (n=20) received 25 mg lignocaine diluted to 5ml, group 3 (n=20) received 50 mg lignocaine diluted to 5ml. All patients had a tourniquet applied for venous occlusion for 60 seconds at 100 mmHg. After propofol injection pain was evaluated using verbal rating scale and behavioral changes. **STATISTICAL ANALYSIS:** The obtained data was analyzed statistically using the one way analysis of variance test and the chi-square test for the pain score. **RESULTS:** Propofol produced pain on injection in 80% of patients which was reduced to 45% with 25mg of lignocaine with venous occlusion and further reduced to 25% with 50 mg lignocaine with venous occlusion. None of the lignocaine treated patients had severe pain. **CONCLUSION:** Lignocaine with venous occlusion is effective in attenuating the pain on propofol injection. 50 mg of intravenous lignocaine with venous occlusion being more effective than 25 mg of intravenous lignocaine with venous occlusion.

**KEYWORDS:** Propofol, lignocaine, pain, venous occlusion.

**INTRODUCTION:** Propofol has become the most common induction agent replacing thiopentone due to its fast induction, easy dose titration and rapid recovery profile.<sup>1</sup> It also attenuates the sympathetic response during intubation<sup>2</sup> and has antiemetic effects.<sup>3,4</sup> However one of the distressing problem with propofol during induction is pain on intravenous injection and it is estimated to be around 28-90%.<sup>5</sup> Propofol has a lipid solvent which is postulated to activate the plasma kallikrein–kinin system which results in bradykinin production which is considered to be the probable cause for pain.<sup>6</sup>

A lot of drugs have been tried as pretreatment to reduce propofol pain with varying results. Some of the most studied drugs for this purpose are ketamine,<sup>7,8</sup> flurbiprofen axetil,<sup>9,10</sup> acetaminophen,<sup>11,12</sup> metoclopramide,<sup>13</sup> remifentanil and alfentanil.<sup>14</sup> Lignocaine a amide group of local anesthetic agent is the drug which has been frequently studied for reducing propofol induced pain in different concentration, with and without occlusion of the vein and found to be useful.<sup>15-18</sup>

#### AIMS AND OBJECTIVES:

- 1. To compare the effect of two different doses of lignocaine injection and placebo with venous occlusion in reducing the incidence of pain of propofol.
- 2. To note the incidence of side effects if any.

### **MATERIALS AND METHODS:**

**Study Design:** Institutional ethical committee approval was obtained. A prospective randomized study which was double blinded was conducted on 60 patients of ASA I and II of either sex scheduled for surgery under general anesthesia.

### **INCLUSION CRITERIA:**

- 1. Patient posted for general anesthesia of either sex.
- 2. ASA I and II.

### **EXCLUSION CRITERIA:**

- 1. Patient allergic to lignocaine.
- 2. Patients with cardiac rhythm abnormalities.
- 3. Difficult intravenous line access.
- 4. Counter puncture during intravenous access.
- 5. Pain on injection with normal saline in the intravenous line.

**Pre-Operative Preparation:** Patients were premedicated with tablet alprazolam 0.5mg on the morning of surgery with sips of water. Inside the operation theater patients were started with 18 gauge venflon in the left radial vein after local infiltration with 0.5 ml of 2% lignocaine using a 26g needle. If counter puncture was made or if free flow of blood was not obtained the patients were excluded from the study. The intravenous line was flushed with 5 ml of distilled water and it was confirmed that the patient did not have any pain, if they complained of pain on injection of distilled water they were not considered for the study.

60 patients who pass the above exclusion criteria will be taken for the study and will be assigned randomly to any one of the three groups.<sup>(1,2,3)</sup> After this, the patients were started with ringer lactate infusion at a rate of 100 ml per hour. Patient's baseline vitals were noted. The tourniquet, standardized to be inflated to a pressure of 100 mmHg will be applied on the upper arm, to occlude the venous drainage. One of the test drugs corresponding to the group which the patient belongs will be given.

Group 1: Normal saline 5 ml.Group 2: 25 mg lignocaine diluted to 5 ml.Group 3: 50 mg lignocaine diluted to 5 ml.

The tourniquet is released after 60 seconds following which 50 mg of propofol is given over 20 seconds in a running drip. During the injection of propofol pain assessment was done by a person who is blinded to the different groups. Pain was assessed using a four point verbal rating scale (VRS) noting any behavioral signs associated.

VRS	PAIN RESPONSE
0 none	Does not complain of pain on questioning.
1 mild	Complains of pain on questioning
1 mmu	Without any behavioral signs.
2 modorato	Complains of pain on questioning with behavioral
2 mouerate	sign or pain reported spontaneously.
2 couoro	Strong vocal response or response accompanied
3 severe	by facial grimacing, arm withdrawal or lacrimation.

The heart rate and blood pressure was also observed during the injection. There after induction of anesthesia was continued with the remaining propofol and anesthesia maintained as per the anesthetist choice.

**RESULT:** Sixty patients were taken up for the study and divided in to three groups of twenty each. The obtained data was analyzed statistically using the one way analysis of variance test and the chisquare test for analyzing the pain score.

The groups were similar with respect to age.

						nfidence for Mean
	N	Mean	Std.	Std.	Lower	Upper
		Mean	Deviation	Error	Bound	Bound
1	20	35.70	10.271	2.297	30.89	40.51
2	20	40.60	11.600	2.594	35.17	46.03
3	20	41.25	9.210	2.059	36.94	45.56
Total	60	39.18	10.529	1.359	36.46	41.90
		Т	able 1: AGE			

	Sum of Squares	df	Mean Square	F	Sig.			
Between Groups	368.233	2	184.117	1.700	.192			
Within Groups	6172.750	57	108.294					
Total	6540.983	59						
Table 2: AGE								

The p value was 0.192 which is greater than 0.05.

The groups were comparable with respect to their weight. The p value was 0.194 which was greater than 0.05.

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					95% Co Interval	nfidence for Mean		
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound		
1	20	70.85	14.619	3.269	64.01	77.69		
2	20	63.85	11.089	2.480	58.66	69.04		
3	20	69.85	13.172	2.945	63.69	76.01		
Total	60	68.18	13.192	1.703	64.78	71.59		
	Table 3: Wt							

	Sum of Squares	df	Mean Square	F	Sig.		
Between Groups	573.333	2	286.667	1.686	.194		
Within Groups	9693.650	57	170.064				
Total	10266.983	59					
Table 4: Wt							

The change in the blood pressure both systolic, diastolic and the mean arterial pressure were comparable between the three groups and there was no statistical difference in between the groups.

The change in heart rate was significant between the groups with an increase in heart rate seen with patients who had a VRS score of 2 and 3.

	Sum of Squares	df	Mean Square	F	Sig.		
Between Groups	1524.100	2	762.050	7.746	.001		
Within Groups	5607.550	57	98.378				
Total 7131.650 59							
Table 5: Post propofol injection heart rate							

Multiple comparison tables show the post-hoc least significant difference test between the three groups.

m	m				95% Confidence Interval		
(I) Group	()) Group	Mean Difference (I-J)	Std. Error	Sig.	Lower Bound	Upper Bound	
1	2	8.350*	3.137	.010	2.07	14.63	

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2	1	-8.350*	3.137	.010	-14.63	-2.07
	3	3.700	3.137	.243	-2.58	9.98
R	1	-12.050*	3.137	.000	-18.33	-5.77
5	2	-3.700	3.137	.243	-9.98	2.58
Table 6: Post propofol injection heart rate LSD						

The mean difference is significant at the 0.05 level.

The VRS pain score between the three groups were analyzed using group cross tabulation.

			1	2	3	Total
		Count	4	11	15	30
	0	% within yrs	13.3%	36.7%	50.0%	100.0%
	Ŭ	% within group	20.0%	55.0%	75.0%	50.0%
		% of Total	6.7%	18.3%	25.0%	50.0%
		Count	6	9	5	20
	1	% within <u>yrs</u>	30.0%	45.0%	25.0%	100.0%
	1	% within group	30.0%	45.0%	25.0%	33.3%
Vre		% of Total	10.0%	15.0%	8.3%	33.3%
3463	2	Count	8	0	0	8
		% within <u>yrs</u>	100.0%	.0%	.0%	100.0%
		% within group	40.0%	.0%	.0%	13.3%
		% of Total	13.3%	.0%	.0%	13.3%
	q	Count	2	0	0	2
		% within <u>yrs</u>	100.0%	.0%	.0%	100.0%
	Ŭ	% within group	10.0%	.0%	.0%	3.3%
		% of Total	3.3%	.0%	.0%	3.3%
		Count	20	20	20	60
	Total	% within yrs	33.3%	33.3%	33.3%	100.0%
	1 otal	% within group	100.0%	100.0%	100.0%	100.0%
		% of Total	33.3%	33.3%	33.3%	100.0%
	Т	able 7: VRS pain	score cr	oss tabu	lation	

In group 1 where normal saline was injected before propofol out of 20 subjects 16 experienced pain on injection which is 80%. Of the 16 subjects 6 had mild pain 8 had moderate pain and 2 had severe pain.

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In group 2 where lignocaine 25 mg was injected before propofol out of the 20 subjects 9 experienced pain on injection which is 45%. All the 9 subjects had mild pain.

In group 3 where lignocaine 50 mg was injected before propofol out of the 20 subjects 5 experienced pain on injection which is 25%. All the 5 subjects had mild pain.

The chi-square test was done to test the null hypothesis.



	Value	df	Asymp, Sig. (2-sided)			
Pearson Chi-Square	27.500ª	6	.000			
Likelihood Ratio	30.163	6	.000			
Linear-by-Linear Association	19.219	1	.000			
N of Valid Cases	60					
Table 8: Chi-Square Tests						

The pearson chi-square value was 27.500 and the p value is 0.00 which proves that there is a statistically significant difference in reduction of pain when using lignocaine before propofol injection.

**DISCUSSION:** Propofol having a short induction time and rapid recovery with good safety profile has made it an induction agent of choice for induction replacing the age old standard thiopentone sodium. Pain on intravenous injection of propofol is one of the side effects which though not of much significance can at times be very uncomfortable to the patient.

Intravenous lignocaine is a safe and easily available drug which has been studied repeatedly in reducing the pain of intravenous propofol. Studies have premixed the drug with propofol<sup>16</sup> or given it separately before propofol injection with or without application of a tourniquet.<sup>15</sup> A meta-analysis by picard and tramer concluded that pain on propofol injection was 70 % and lignocaine was the best drug to reduce pain.<sup>19</sup>

Massad IM et al compared different duration of venous occlusion 15 sec, 30 sec and 60 sec after lignocaine injection to determine which was most effective and concluded that different duration of venous occlusion was not statistically significant in reducing pain on propofol injection.<sup>20</sup>

However Sedat kaya et al in his study was able to show that pretreatment of lignocaine with venous occlusion was more effective in reducing pain on propofol injection when comparing without venous occlusion.<sup>15</sup> We applied venous occlusion for one minute with tourniquet with a pressure of 100 mmHg.

Gehan G et al showed that the optimal dosage of lignocaine to reduce pain on propofol injection was 0.1 mg/kg and increasing the dosage did not have any benefit.<sup>21</sup> King SY et al in his study showed that lignocaine 20mg mixed with propofol was successful in decreasing the pain of propofol injection.<sup>22</sup> Halit Madenoglu etal in his study concluded that lignocaine 1 mg/kg was successful in decreasing the pain of propofol injection.<sup>23</sup>

In our study we used 25 mg and 50 mg of lignocaine pretreatment with venous occlusion. Propofol produced pain on injection in 80% which reduced to 45 % with 25 mg lignocaine and 25% with 50 mg lignocaine. None of the patient with lignocaine pretreatment had severe pain.

**CONCLUSIONS:** In this study population pretreatment of lignocaine 25 mg with one minute of venous occlusion was effective in reducing pain on propofol injection from 80% to 45%. Increasing the dosage of lignocaine to 50mg reduced the incidence of pain further to 25%.

### ACKNOWLEDGEMENT: Prof. Dr. K. Ravindran. Dean, Chettinad Hospital and Research Institute.

Prof. Dr. Lailu Mathew. HOD, Dept. of Anesthesiology and critical care, Chettinad Hospital and Research Institute. Prof Dr. K. R. Shivashankar. Senior professor, Dept. of Anesthesiology and Critical care, Chettinad Hospital and Research Institute.

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FINANCIAL OR OTHER COMPETING INTERESTS: None

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> Date of Submission: 21/02/2015. Date of Peer Review: 22/02/2015. Date of Acceptance: 25/02/2015. Date of Publishing: 03/03/2015.