ORIGINAL RESEARCH

A comparative study to assess the efficacy of ketamine, lignocaine and mixture of ketamine and lignocaine to prevent propofol induced pain

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ABSTRACT
Background: Propofol is a rapidly acting intravenous anaesthetic agent which is widely used in short cases and day care surgery as well. But pain on propofol injection can be a distressing factor and hence assessment of Pain on Propofol Injection with pretreatment of various agents being studied. **Objective:** To evaluate the efficacy of Ketamine, Lignocaine and Mixture of Ketamine and Lignocaine as pretreatment for pain on propofol injection. **Method:** A total of 150 patients of ASA I and II aged 18 – 60 years without any co morbidities were included in our study. The patients were randomly divided into 3 groups of 50 each. Group K received 0.2 mg / kg of Ketamine, group L received 40 mg of Lignocaine, whereas group KL received 0.1 mg/kg ketamine + 20 mg Lignocaine intravenously. The pain intensity was assessed among the 3 groups. **Results:** The mean pain score was significantly lower in the group having mixture of Ketamine (0.1 mg / kg)+Lignocaine (20 mg), followed by the group in which Ketamine (0.2mg/kg) was used alone .Alone use of Lignocaine was not proved to be effective in alleviating pain due to propofol injection. **Conclusion:** Present study concludes that combination of 0.1 mg/kg of Ketamine with 20 mg lignocaine is much effective followed by ketamine 0.2 mg /kg and lignocaine 40 mg alone in preventing pain from propofol injection.

Key Words – ketamine, lignocaine, propofol, tourniquet, pain

INTRODUCTION

Propofol, a rapid acting agent widely used for induction and maintenance of anesthesia, mainly for short cases and day care surgeries. It produces a good quality anesthesia with rapid recovery. Despite these positive attributes, there are many events and complications such as excitatory events during induction, tingling, numbness and pain at injection site out of which burning excruciating pain is most common.[1]

Pain on propofol injection can be immediate or delayed. Direct irritant effect can be linked with Immediate pain whereas delayed pain might be due to an indirect effect via kinin cascade. Factors contributing to pain, include the size of vein, site of injection, buffering effect of blood , speed of injection, , temperature of propofol, and concomitant use of drugs such as local anesthetics and opiates [2].

The formulation for the preparation of propofol also plays a role regarding pain during injection. Lipid emulsion propofol causes severe lipid solvent-related adverse effects. Propofol is found to be associated with lesser pain upon injection whereas microemulsion of propofol produces more intense and frequent pain during injection [3].Innumerable methods for minimizing pain have been implemented and suggested as cooling or warming, diluting the propofol solution, injecting propofol into a large vein, and prior injection of various drugs like lignocaine, fentanyl, pethidine, ketamine, ephedrine, ondansetron, metoclopramide, thiopental, etc.[4]

AIMS & OBJECTIVES

AIM

- In this study, we have compared the effectiveness of ketamine, lignocaine, and mixture of ketamine and lignocaine to alleviate the pain due to propofol injection.

OBJECTIVES

- To evaluate the efficacy of ketamine , lignocaine and mixture of ketamine and lignocaine as pretreatment for pain due to propofol. MATERIAL AND METHODS

DESIGN OF STUDY

This is a Prospective Randomized Comparative study**.**

DURATION OF STUDY

1st January 2020 to 31stAugust 2021.

SELECTION OF CASES

After obtaining approval from institutional ethics committee, this study was conducted at the N.S.C.B.Medical College and Hospital, Jabalpur.

INCLUSION CRITERIA

- Patients with Age > 18 or < 60 years of ASA physical status I and II

EXCLUSION CRITERIA

- Age < 18 or > 60 years.
- ASA physical status > II.
- History of allergy to the study drugs,
- Any chronic or systemic disease
- Pregnant or lactating mother.

METHODOLOGY

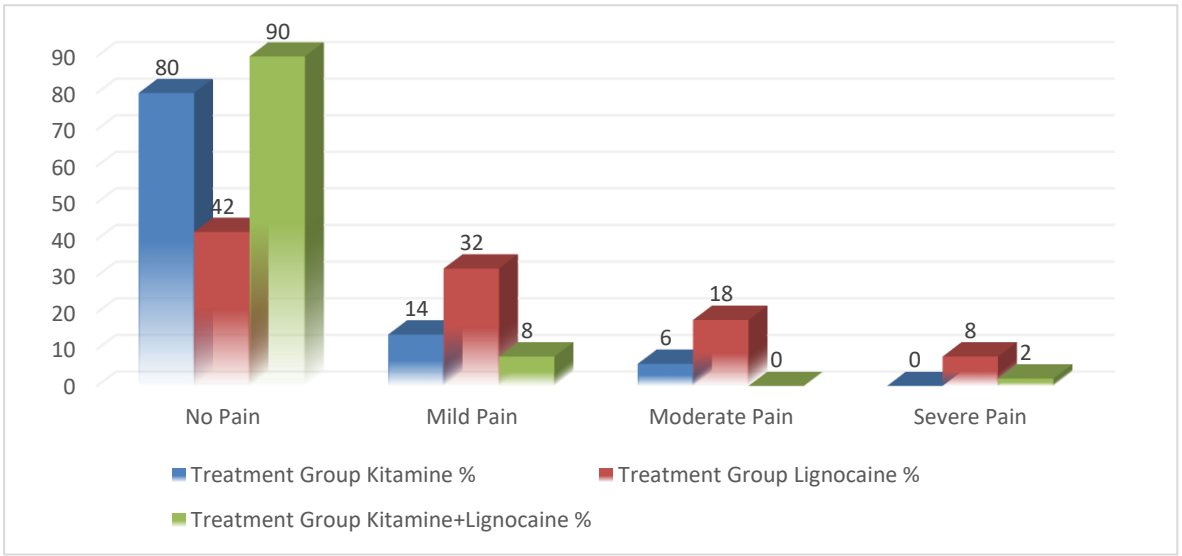
The study included 150 patients who underwent general anesthesia in various surgical sub specialities in the NSCB Medical College and Hospital Jabalpur.
The technique was explained to the patients with written informed consent and preoperative preparation was done.
Patients were then randomly allocated into 3 groups of 50 patients each as follows-
Group K – 0.2 mg /kg Ketamine i.v.
Group L –40mg Lignocaine i.v.
Group KL –0.1mg/kg Ketamine + 20mgLignocaine i.v.

TECHNIQUE

18G cannula was placed into right cephalic vein. Before induction, patients were informed that they would receive I.V. anaesthetic that may cause pain in the forearm. The patients were instructed to inform the investigators the amount of pain that they have experienced by using **4 point verbal pain scale**
0=no pain,
1= mild pain,
2=moderate pain,
3=severe pain.
Patients were monitored with routine monitoring devices. The arm with intravenous cannula in situ was elevated for 15 seconds to facilitate gravity drainage of venous blood. A manual tourniquet was placed on the upper arm to produce venous occlusion.
Study drug was diluted to10 ml with addition of normal saline.
After occluding venous drainage using pneumatic tourniquet on upper arm, the patients were treated over a period of 10 seconds with one of the pretreatment solutions. After 1 min, occlusion was released and 30% of pre calculated dose of propofol was delivered.
Patient were asked after 10 seconds of administration of propofol regarding discomfort or pain , and it was assessed using **4 point verbal pain scale-**
Assessment was done by indepenedent anaesthesiologist who was unaware of group assignment.
Heart rate, mean arterial pressure were recorded preoperatively after administration of study drugs and after propofol administration.

OBSERVATIONS AND RESULTS

GRAPH 1
VRS score for POPI



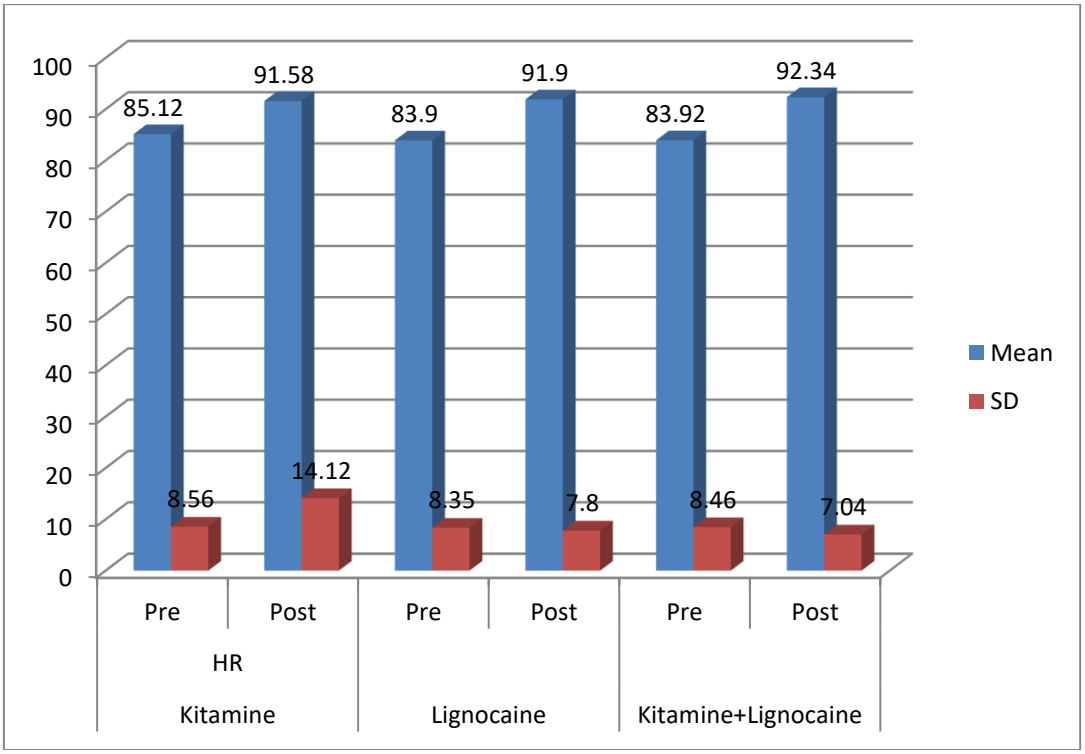
In our study no pain were experienced by 80% of the patients injected with ketamine while 14% experienced

mild pain and 6% experienced moderate pain.while on injecting with lignocaine 42% patient had no pain,mild pain was noticed in 32% of patients and moderate and severe pain was noticed in 18%, 8% of patients respectively. whereas when combination of the above 2 used no pain in 90% of the patients, mild pain in 8% and 2% had severe pain.

TABLE N0 1: EFFECT OF PROPOFOL ON BLOOD PRESSURE (SYSTOLIC AND DIASTOLIC) AND HEART RATE AFTER PRE TREATING WITH K,L,KL

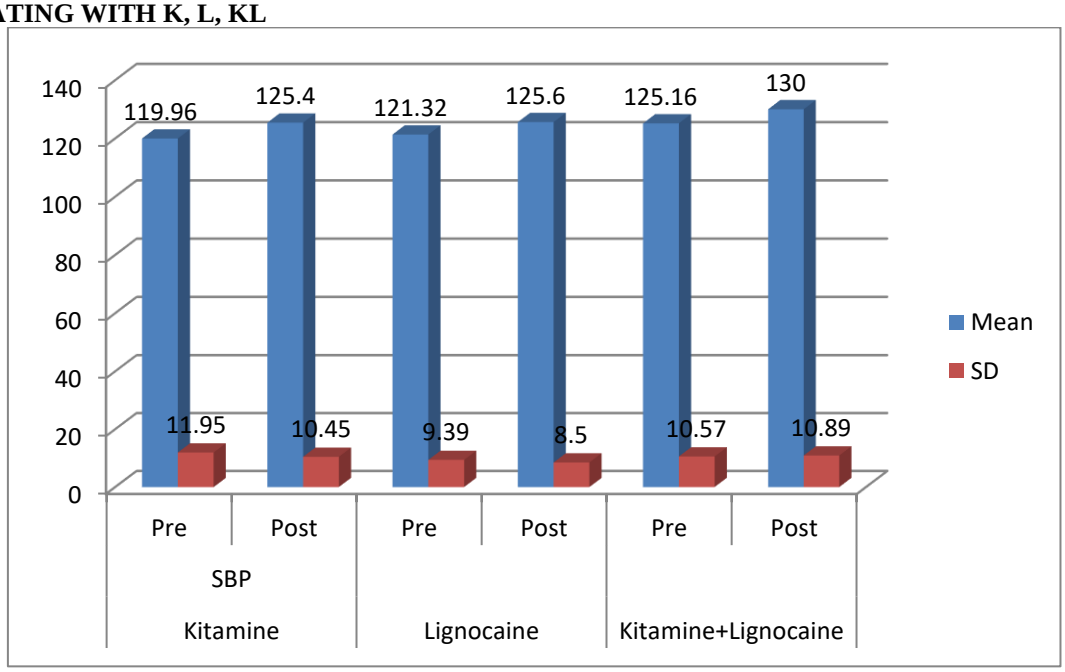
Study Group	Vitals	Follow-up time	Mean	SD	Min	Max	Paired t test	P value	Independent t test (mean changes)	P value
Ketamine	HR	Pre	85.12	8.56	68.00	100.00	3.74	0.0005	K Vs L	
		Post	91.58	14.12	10.00	106.00			0.83	0.408
Lignocaine		Pre	83.90	8.35	68.00	100.00	12.01	<0.0001	K Vs K+L	
		Post	91.90	7.80	70.00	106.00			1.06	0.289
Ketamine+Lignocaine		Pre	83.92	8.46	70.00	100.00	13.35	<0.0001	L Vs K+L	
		Post	92.34	7.04	80.00	110.00			0.46	0.648
Ketamine	SBP	Pre	119.96	11.95	100.00	144.00	10.85	<0.0001	K Vs L	
		Post	125.40	10.45	110.00	140.00			1.59	0.114
Lignocaine		Pre	121.32	9.39	100.00	140.00	8.12	<0.0001	K Vs K+L	
		Post	125.60	8.50	100.00	140.00			0.62	0.538
Ketamine+Lignocaine		Pre	125.16	10.57	106.00	144.00	5.82	<0.0001	L Vs K+L	
		Post	130.00	10.89	116.00	168.00			0.57	0.571
Ketamine	DBP	Pre	79.36	6.77	68.00	94.00	7.84	<0.0001	K Vs L	
		Post	83.44	5.27	72.00	94.00			0.69	0.489
Lignocaine		Pre	80.36	6.00	68.00	90.00	5.71	<0.0001	K Vs K+L	
		Post	83.88	5.79	68.00	96.00			1.72	0.088
Ketamine+Lignocaine		Pre	82.28	5.36	72.00	94.00	5.70	<0.0001	L Vs K+L	
		Post	85.12	4.80	76.00	94.00			0.86	0.393

GRAPH NO 2: EFFECT OF PROPOFOL ON HEART RATE AFTER PRE TREATING WITH K, L, KL

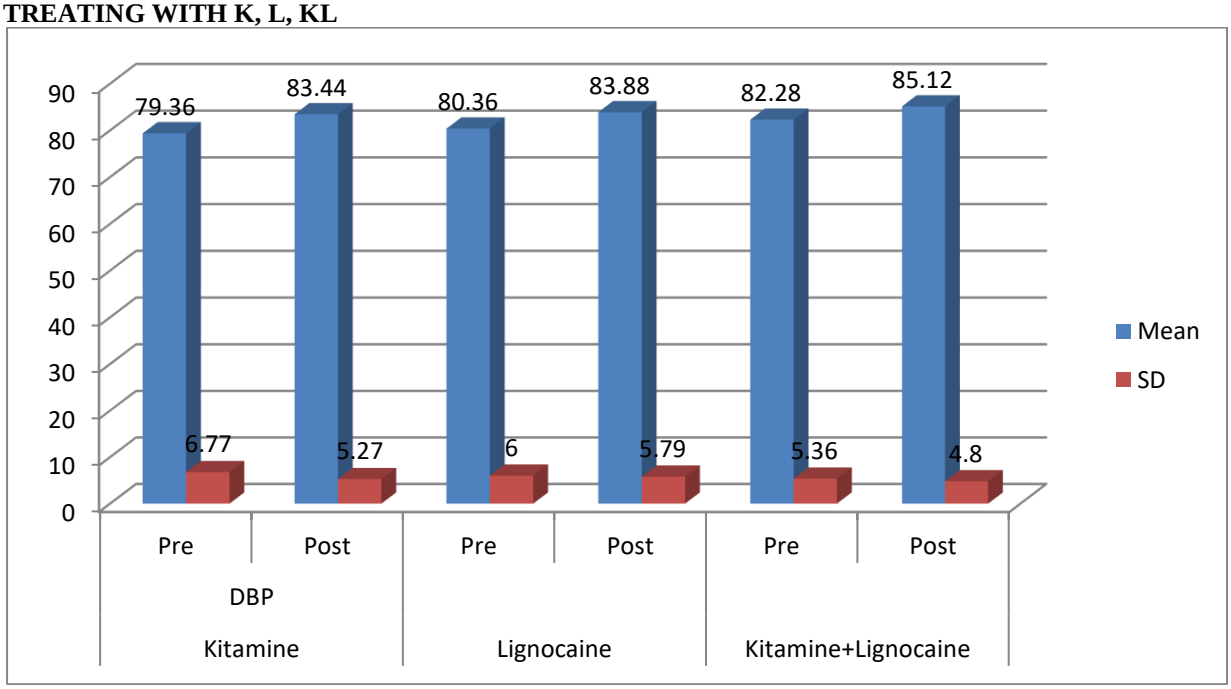


In the present study, variation in heart rate on receiving propofol was found to be minimal. There was insignificant variation on comparing before and after induction with propofol. Mild increase in heart rate was found which was similar for all 3 groups (K, L, KL).

GRAPH NO 3: EFFECT OF PROPOFOL ON DIASTOLIC BLOOD PRESSURE AFTER PRE TREATING WITH K, L, KL



GRAPH NO 4: EFFECT OF PROPOFOL ON BLOOD PRESSURE (SYSTOLIC) AFTER PRE TREATING WITH K, L, KL



In the present study no significant hemodynamic variation was reported. Change in systolic blood pressure before and after giving propofol was found to be minimal.

TABLE NO 2: Multinomial multivariate logistic regression analysis of the risk of pain and changes in vitals in the treatment groups.

Treatment Group	Independent Variables	RRR	SE	Z	P value	Lower	Upper
Ketamine		Reference (Base)					
Lignocaine							
	VRS						
	No Pain	Reference (1)					
	Mild Pain	4.86	2.65	2.9	0.004	1.67	14.14
	Moderate Pain	4.91	3.61	2.17	0.03	1.16	20.74
	Severe Pain	4.90E+07	1.19E+11	0.01	0.994	0.00	.

	Changes in HR	1.04	0.04	0.85	0.395	0.95	1.13
	Changes in SBP	0.94	0.05	-1.03	0.304	0.84	1.06
	Changes in DBP	0.98	0.06	-0.36	0.721	0.86	1.11
	Constant	0.58	0.29	-1.1	0.27	0.22	1.53
Ketamine+Lignocaine							
	VRS						
	No Pain	Reference (1)					
	Mild Pain	0.53	0.36	-0.93	0.353	0.14	2.02
	Moderate Pain	1.08E-07	0.01	-0.01	0.991	0.00	.
	Severe Pain	6150643	1.49E+10	0.01	0.995	0.00	.
	Changes in HR	1.03	0.03	1.12	0.262	0.97	1.10
	Changes in SBP	1.02	0.05	0.34	0.737	0.92	1.12
	Changes in DBP	0.88	0.06	-1.88	0.06	0.77	1.01
	Constant	1.2	0.5	0.49	0.625	0.55	2.71

DISCUSSION

Propofol, a rapidly acting intravenous agent, issued widely for induction and maintainence of anaesthesia. It has rapid onset and short duration of action which is easily titrable.

Various strategies have been tried for prevention of this pain, including variations in injection speed and carrier fluids, dilution, temperature modification [5,6] and the concomitant use of other drugs. The most common strategy is administration of lignocaine as a pretreatment to reduce pain [7] The methods of action of lignocaine in this setting are possibly related to local anaesthetic effect on the vein and stabilization of the kinin cascade.[7]

In our study, 150 patients of ASA I and II, age 18-60 years without any others co morbidities were included.

Demographical background of our study showed that maximum number of patients were in the age group of 21 to 30 years – 69 (46%) followed by 50 (33.33%) patients in the age group of 30 to 40 years. Mean age of patients for lignocaine group was 29.08 years, for ketamine It was 29.62 years and for mixture of ketamine and lignocaine it was 30.2years.

Similarly, in view of weight criteria, 67 (45%) patients lie in the weight group of 41-50 kg, followed by 51-60 kg subset.

Also, **Picardand Tramer**[7] concluded that the most effective technique for controlling POPI was when lignocaine was used with tourniquet.

Yoshitaka Fuji and M Nakayama [8] compared different doses of ketamine plus lignocaine with manual venous occlusion and concluded that pain was much less when 20 mg lignocaine combined with 5mg ketamine was used with manual venous occlusion.

Mangar and Holak [9] noticed that when lipid emulsion propofol is administered intravenously, pretreatment with lignocaine after a tourniquet is inflated to 50mmHg was more effective than when tourniquet was not used.

In accordance with above studies we assumed that venous occlusion of 60 seconds greatly helps in reducing the pain due to propopfol injection and also for ketamine to exert its peripheral effect.

King et al[10] mixed 5,10 and 20mg of lignocaine with lipid emulsion Propofol and found that a greater dose reduces pain on injection,

Jonson et al[11] showed In their study that lignocaine 40mg is more effective than 20mg in reducing pain from lipid emulsion propofol on injection.

Data from these previous clinical trials concluded that lignocaine in a dose of 30-40 mg is effective in reducing pain due to propofol injection which formed the basis of the dose of lignocaine in our present study i.e.20 mg when used in combination and 40mg when used alone.

Tweed et al [12] showed that heart rate increased from 74 to 98 beats /min (33% increase) and mean arterial pressure increased from 93 to 119 mmHg (28% increase) on administration of ketamine 2mg/kg.

In one of the studies by **Yoshitaka Fuji and M Nakayama** [8] however, patients received 10 mg of ketamine, but there were no instances of more than 20% change in heart rate and or arterial blood pressure before induction of anaesthesia .

Study done by **Furuya et al** [13] also added to the fact that ketamine 0.5 mg /kg, 1 min before propofol injection prevented not only an excessive decrease in pain prior to induction but also prevent any hemodynamic instability later. **The results of our study are also in support of these clinical studies.**

In our study, patients received 0.2mg/kg ketamine when used alone and

0.1 mg/kg when used with lignocaine; mild fluctuation of approximately 10-15% was noted in heart rate and mean arterial blood pressure,(table 1, graph 2,3,4) whereas in study done by **Tweed et al** [12] who in their study experienced a 33% increase in the heart rate and 28% increase in mean arterial pressure on administration of ketamine in a dose of 2 mg/kg.

Yoshitaka Fuji et al [8] in their study used 20 mg lignocaine either with saline or ketamine at different doses (2.5,5,10 mg) prior to propofol induction and noticed that mixture of lignocaine with 5 mg ketamine was most effective.

One of the study done by **Hwang et al**[14] on 130 patients is in concordance with our study which showed that after intravenous administration of 30 mg microemulsion propofol, 32 patients from group KL

experienced no pain (82%), while16 patients in group L (38%) and 19 patients in group K (46%) respectively experienced no pain .Whereas in our study 45 patients experienced no pain in group KL (90%), 21 patients in group L (42%) and 40 patients in group K (80%) respectively experienced no pain (graph 1).

The incidence of moderate to severe pain was significantly lower in group KL than in group L and in group K, with only 1 patient in group KL (2%) as compared to 13 (26%) in group L and 3 in group K (6%) ($p<0.05$) which further supported the results done by previous researchers concluding that mixture of lignocaine and ketamine prior to propofol injection with venous occlusion significantly reduces the pain at injection site.

CONCLUSION

From the results of present study it can be concluded that a combination of 0.1 mg/kg Ketamine and 20 mg Lignocaine with venous occlusion using a pneumatic tourniquet 1 min before the injection of propofol is more effective than lignocaine 40 mg or ketamine 0.2 mg/kg alone in preventing pain from the injection of propofol.

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