To compare the effects of pre anaesthetic single dose intravenous ketamine versus lidocaine for propofol induced pain

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Abstract

Background: Propofol is one of the most popular IV anaesthetic induction drugs use for general anaesthesia, but it causes pain when given. The aim of this randomized control study is to compare the effects of pre anaesthetic single dose intravenous ketamine 100 mcg kg^{-1} and lidocaine 1 mg kg^{-1} for propofol induced pain.

Methods: A total of sixty elective, normotensive adult patients were taken for this study. Study drugs either ketamine or lidocaine were given 15 sec before and then initially ¼ of the total calculated dose of propofol (2.5 mg kg^{-1}) administered and a blinded anaesthesiologist asked the patient to rate any sensation of pain at 5,10,15 seconds till the patient was fully induced (after abolition of eye lash reflex). Pain during induction (At 5 sec, 10 sec, 15 sec). HR, SBP, DBP, SPO2 & ECG recordings before induction, during induction, intra operatively at 5min, 10min, 15min and post operatively and any other observations and side effects or complications were recorded and a P value < 0.005 was considered as statistically significant.

Results: In our study out of 30 patients of each study group, 23 in group ketamine and 14 in group lidocaine did not have pain, 5 in group ketamine and 10 in group lidocaine had mild pain, 2 in group ketamine and 4 in group lidocaine had moderate pain, 0 in group ketamine and 2 in group lidocaine had severe pain. Median score was found 0 in group ketamine and 1 in group lidocaine.

Conclusion: Ketamine 0.5 mg/kg in volume of 2 ml pre-treatment with venous occlusion is an effective method in reducing pain and providing hemodynamic stability after propofol induction than lidocaine 2 ml of 1%.

Keywords: Propofol, ketamine, lidocaine

Introduction

Surgery is almost not possible without anaesthesia. For giving induction and sedation, there is lots of option like iv Propofol, Thiopentone, ketamine, midazolam etc. Propofol is one of the most popular IV anaesthetic induction drugs use for general anaesthesia, but it causes pain when given IV.[1] Although the mechanism of this pain following propofol injection remains obscure, the endothelium irritation, osmolality changes, non-pharmacologic pH and activation of pain cascade mediators like kinin have been suggested to be involved.[2] Several methods have been used to reduce this propofol induced pain-adding lidocaine[3,4,5], warming of propofol solution[6] or cooling the solution[7], dilution of Propofol[8], injection through large bore veins[9], using tourniquet with previous injection of lidocaine, metoclopramide[10], Tramadol[11], Ketorolac[12], magnesium sulphate[11], acetaminophen[13], clonidine[14], Ketamine[15].

Local anaesthetic like lidocaine when given intravenously prior to propofol injection has been well documented to reduce the incidence and severity of pain on injection of propofol.[3,4,5] Ketamine (a phencyclidine derivative) has potent analgesic effects and local anaesthetic properties.[1,16] It has some unique advantages notably, less cardiorespiratory depression than other anaesthetics, which makes it a good choice in specific conditions. Few studies have evaluated the advantages of ketamine to reduce propofol-induced pain suggesting the effectiveness of ketamine in adults and children.[17,18,15]

Materials and Methods

This double blinded, randomized study was conducted under the Department of Anaesthesiology and Critical Care, Guwahati Medical College and Hospital after approval from the hospital ethical committee. The study was carried out on patients aged 18 to 60 years of both sexes of ASA I and ASA II. Status, undergoing elective operation under general anaesthesia during August 2012-July 2013 in accordance with the Declaration of Helsinki. A written informed consent was taken from all the patients. Patients who refused to give consent, sensitive to study drug, sensitive to soyabean oil or egg lecithin, have significant cardiovascular and neurological disease, pregnant or lactating mothers were excluded from the study.

All patients were randomly allocated using computer-generated random numbers contained in sequentially sealed envelopes into two groups comprising of 30 patients in each group. IV ketamine 100 mcg kg^{-1} in Ketamine Group and IV lidocaine 1 mg kg^{-1} in Lidocaine Group 15secs prior to propofol injection were given.

All the patients were graded according to American Society of Anaesthesiologists classification. After explaining the anaesthetic procedure to the patients, informed written consent was taken to include them in the study. All patients were prescribed 0.5 mg of alprazolam and ranitidine 150 mg orally the previous night. Patients were

advised to be nil oral from 10 pm onwards on the previous day of surgery. On arrival of patient to operating room, a 20 gauge i.v cannula was inserted at the dorsum of hand. After that cardiac monitoring, non-invasive blood pressure and pulse oximeter monitoring were instituted. No analgesic drugs were given before induction. Drugs used for pretreatment were IV ketamine 100 mcg kg^{-1} and IV lidocaine 1 mg kg^{-1}. Patients were already informed about the scale for propofol injection pain advocated by Mc Crirrick and Hunter with 0 being no pain and 3 being severe represented by Strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears. Study drugs either ketamine or lidocaine were given 15 sec before and then initially ¼ of the total calculated dose of propofol (2.5 mg $kg^{-1)}$ administered and a blinded anaesthesiologist asked the patient to rate any sensation of pain at 5,10,15 seconds till the patient was fully induced(after abolition of eye lash reflex). The patients of both groups then induced and maintained with standard anaesthetic technique. Surgery was allowed after 15 min.

NIBP, ECG, Pulse oximeter were the intraoperative monitors used. HR,SBP,DBP, SpO2,ECG was recorded during preinduction, immediately after induction and at 5 min,10 min,15 min after induction and during postoperative period(immediate after extubation).

This study was conducted to observe Pain during induction (At 5 sec, 10 sec,15 sec). HR, SBP, DBP, SPO2 & ECG recordings before induction, during induction, intra operatively at 5min, 10min, 15min and post operatively and any other observations and side effects or complications.

All data were analysed by specific statistical methods applicable to the various sets of data. Tests employed were Student T test, Fisher's exact test which were performed on InStat3 software. Percentage of relative changes were also determined and compared between the groups. Microsoft Excel and Word have been used to generate graphs, tables etc. A probability value (P value) less than 0.05 was considered statistically significant.

Result

A total of 60 patients were recruited in this randomized control trial. It was observed that in Ketamine group out of 30 patients, 23 patients did not have pain and 7 patients had pain and in Lidocaine group out of 30 patients, 14 patients did not have pain and 16 patients had pain which was found significant between the group (P value <0.05). In ketamine group out of 7 patients, 5 patients had mild pain and 2 patients had moderate pain. None had severe pain. Median score was found 0. In lidocaine group out of 16 paitients, 10 had mild pain, 4 had moderate pain and 2 patients had severe pain. Median score was found 1.

Table 1: Demographic Data

Variables	Ketamine	Lidocaine	P-value
Age	36.167±8.465	34.167±10.557	0.421
BMI	45.733±4.963	45.267±4.731	0.627

Sex (M/F)	11/19	10/20	>0.05
ASA I/ASA II	25/5	24/6	0.739

Table 2: Comparison of Pain during Induction in Study Groups

Group	No Pain	Pain	Total
Ketamine	23(76.67%)	7(23.33%)	30
Lidocaine	14(46.66%)	16(53.33%)	30
Total	37	23	60
P-Value <0.05 Fisher`S Exact Test			

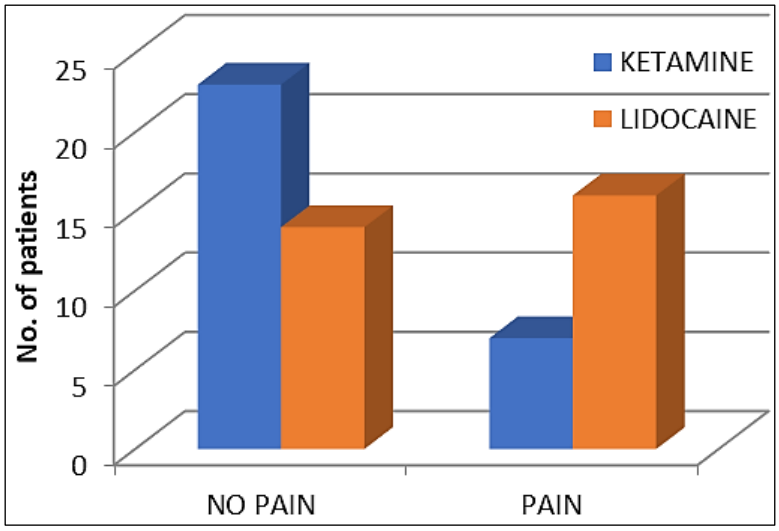

Figure 1

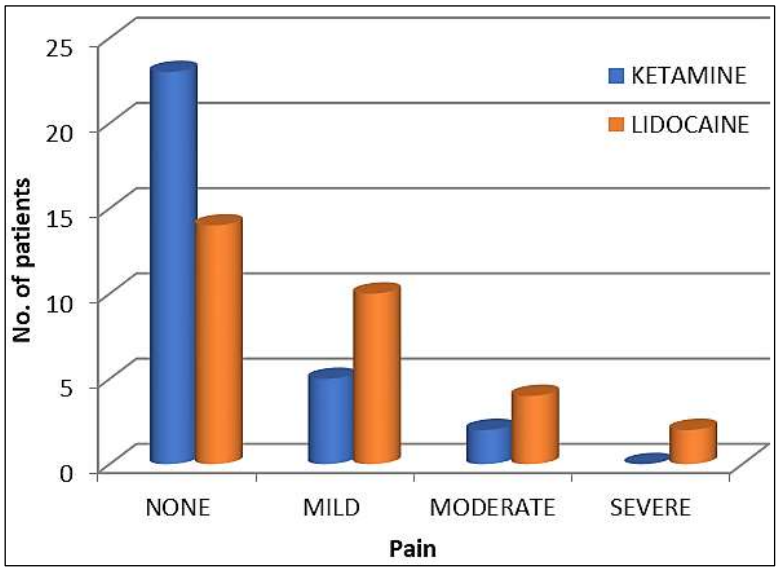

Figure 2

Table 3: Pain Score Category Wise between the Groups

Pain Score		Group			
		Ketamine		Lidocaine	
		Count	% with in Group	Count	% with in Group
Pain at Induction	None (0)	23	76.67%	14	46.66%
	Mild (1)	5	16.66%	10	33.3%
	Moderate (2)	2	6.67%	4	13.33%
	Severe (3)	0	0%	2	6.67%
	Total	30	100%	30	100%
Median Pain Score		0		1	

The two groups were comparable with regards to demographic profile and duration of surgery. The heart rate in both groups were compared before induction, during induction intraoperatively at 5min, 10min, 15min, post-operative period and which is not statistically significant (P value >0.05).

Table 4: Change of Heart rate with respect to time

Heart Rate					Within groups				Intergroup	
	Group Ketamine		Group Lidocaine		Group Ketamine		Group Lidocaine			
Time (Min)	Mean	SD	Mean	SD	P value	Inference	P value	Inference	P value	Inference
Preinduction	71.86	7.006	74.63	5.939					0.1044	P>0.05
Induction	73.26	5.669	75.77	6.564	0.1127	P>0.05	0.1762	P>0.05	0.1198	P>0.05
At 5	73.43	5.049	74.13	5.224	0.2305	P>0.05	0.6125	P>0.05	0.5997	P>0.05
At 10	72.56	4.040	72.23	4.911	0.5421	P>0.05	0.2439	P>0.05	0.5680	P>0.05
At 15	72.3	5.174	73.3	4.489	0.7908	P>0.05	0.2775	P>0.05	0.4272	P>0.05
Postop	72.17	4.713	72.43	5.569	0.8302	P>0.05	0.0584	P>0.05	0.8420	P>0.05

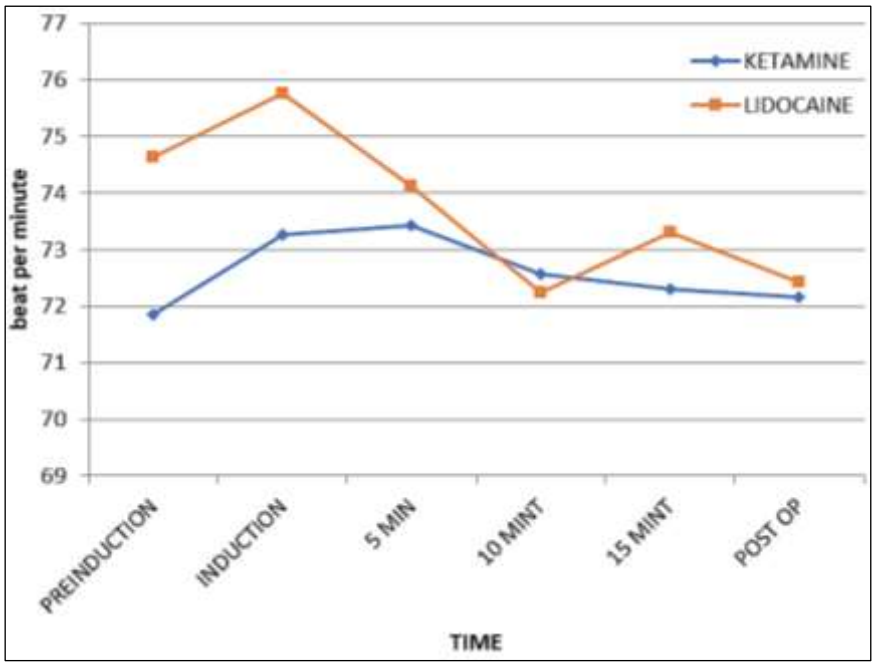

Figure 3: Change of Heart Rate with Respect to Time

It was observed that systolic blood pressure was not changed significantly in KETAMINE group at induction or at 5, 10, 15 and post op in comparison to preinduction value (P >0.05). However changes in SBP within the group lidocaine were found statistically significant difference between preinduction basal value 124.7 mmHg (mean) and at induction 118.9 mmHg (mean), 5min after induction 119.26 mmHg (mean). But at 10 min, 15 min after induction and post operatively SBP changes were not statistically significant with the preinduction basal value. Changes in DBP within the group lidocaine were found statistically significant difference between preinduction basal value 76.03 mmHg (mean) and at induction 68.93 mmHg (mean), 5 min after induction 69.43 mmHg (mean).

Table 5: Change of SYSTOLIC BLOOD PRESSURE (SBP) with respect to time

SBP					Within groups				Intergroup	
	Group Ketamine		Group Lidocaine		Group Ketamine		Group Lidocaine			
Time (Min)	Mean	SD	Mean	SD	P value	Inference	P value	Inference	P value	Inference
Preindcution	125.56	7.532	124.7	8.056					0.6685	>0.05
Induction	122.8	5.301	118.9	8.632	0.0641	>0.05	0.0008	<0.001	0.0393	<0.05
At 5	122.77	6.084	119.26	7.056	0.1339	>0.05	0.0023	<0.01	0.0441	< 0.05
At 10	122.13	7.33	121.76	6.36	0.0589	>0.05	0.0584	>0.05	0.8369	>0.05
At 15	122.766	5.770	123.96	7.467	0.1223	>0.05	0.6523	>0.05	0.4889	>0.05
Post op	123.33	7.208	121.93	5.819	0.2638	>0.05	0.0768	>0.05	0.4112	>0.05

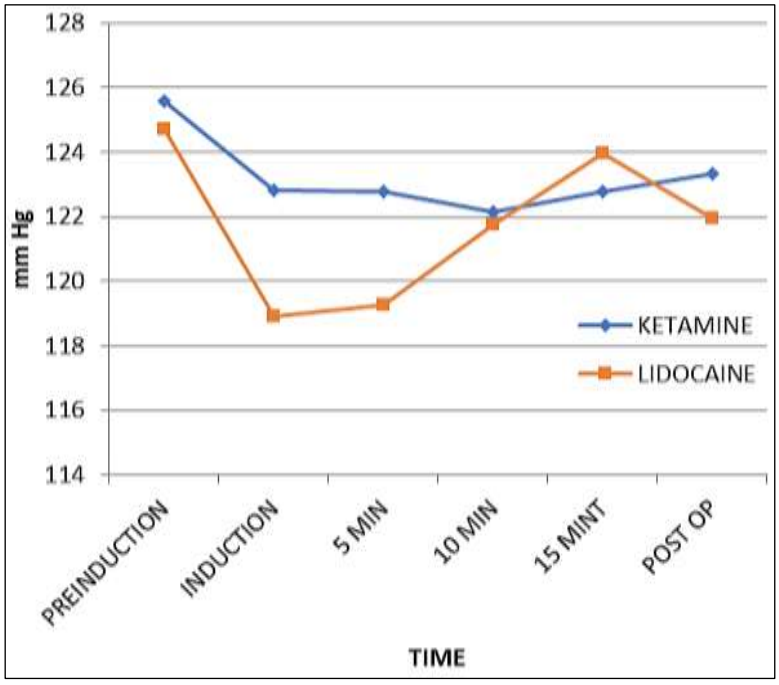

Figure 4: Change of Systolic Blood Pressure (SBP) with Respect to Time

Table 6: Change of Diastolic blood Pressure (DBP) with respect to time

DBP					Within groups				Intergroup	
	Group Ketamine		Group Lidocaine		Group Ketamine		Group Lidocaine			
Time (Min)	Mean	SD	Mean	SD	P value	Inference	P value	Inference	P value	Inference
preindcution	74.17	4.921	76.03	4.874					0.1453	>0.05
Induction	72.07	6.203	68.93	5.489	0.0804	>0.05	<0.0001	<0.0001	0.0427	<0.05
At 5	73.07	6.136	69.43	5.557	0.3480	>0.05	<0.0001	<0.0001	0.0194	<0.05
At 10	71.8	6.048	73.40	5.876	0.1265	>0.05	0.0725	>0.05	0.3030	>0.05
At 15	73.53	5.237	73.83	6.711	0.5185	>0.05	0.1237	>0.05	0.5044	>0.05
Post op	72.73	6.389	74.5	6.296	0.2461	>0.05	0.2517	>0.05	0.2852	>0.05

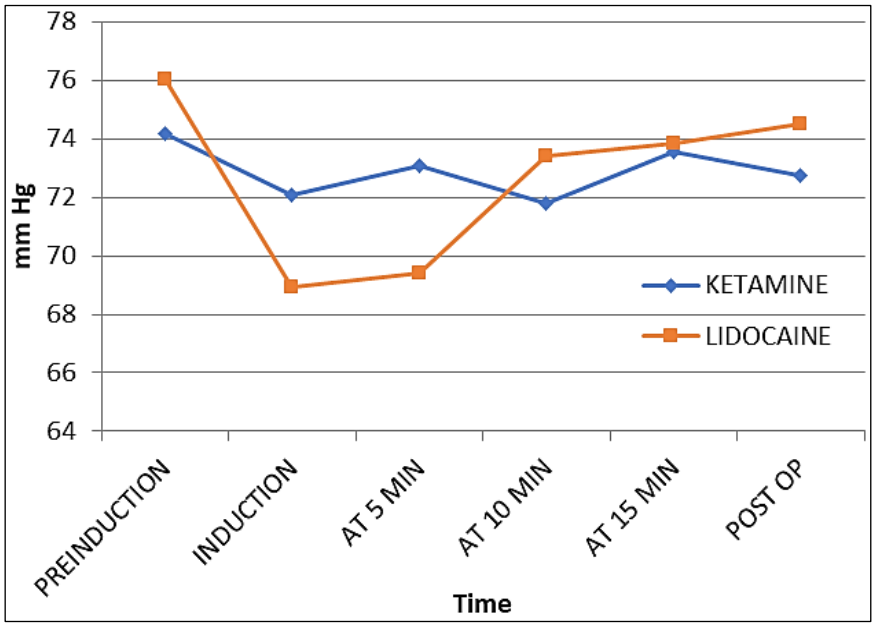

Figure 5: Change of Diastolic Blood Pressure (DBP) with Respect to TIME

It was also observed that Sp02 did not change significantly either within the group or between group (P value>0.05).

Table 7: Changes of Sp02 in relation to time

Sp02					Within groups				Intergroup	
	Group Ketamine		Group Lidocaine		Group Ketamine		Group Lidocaine			
Time (Min)	Mean	SD	Mean	SD	P value	Inference	P value	Inference	P value	Inference
Preinduction	99.63	0.7649	99.56	0.8976					0.7580	>0.05
Induction	99.7	0.5683	99.7	0.7022	0.488	>0.05	0.5461	>0.05	0.6875	>0.05
At 5	99.6	0.7701	99.63	0.7649	0.8562	>0.05	0.6553	>0.05	0.8670	>0.05
At 10	99.7	0.5960	99.66	0.6609	0.7122	>0.05	0.6203	>0.05	>0.9999	>0.05
At 15	99.67	0.6065	99.7	0.6513	0.8389	>0.05	0.4888	>0.05	0.8382	>0.05
Postop	99.3	0.9154	99.37	0.8899	0.1431	>0.05	0.3633	>0.05	0.7759	>0.05

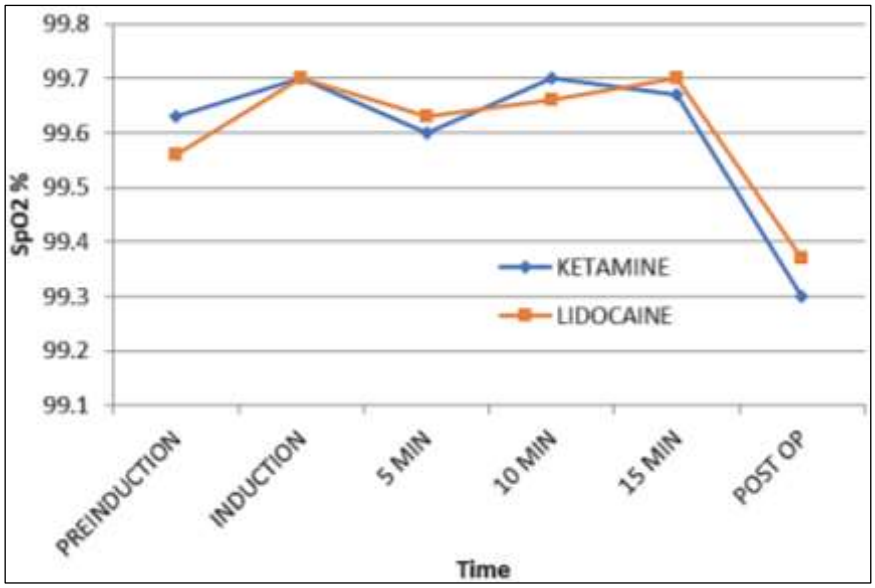

Figure 6: SpO2 Variation with Respect to Time

Discussion

Propofol is found to have many qualities of an ideal agent for induction. Propofol is useful for day care procedures because it has very rapid onset of action and early recovery. It provides excellent sedation, amnesia, anxiolysis and prevents unwanted rise of blood pressure during induction. It's antiemetic properties adds to its advantage. As a whole or in patients with hypertension, epilepsy or hyperactive airway propofol suppresses the upper airway reflexes in response to laryngoscopy and intubation.

Inspite having popularity in daycare surgery, cardiac, neuroanaesthesia and ICU sedation, propofol is also associated with side effects like myoclonus, apnoea, hypotension and pain on injection.

Propofol pain on injection has been most extensively studied. Pain incidence was found between 30-90% among the patients.[19] The high incidence of pain on injection will make it take a back seat in due course of time. Various studies have been conducted for decreasing propofol injection pain.

In our study pain induced by propofol injection has been prevented with pretreatment with ketamine or lidocaine and there efficacy in terms of reducing pain has been evaluated. Heart rate, SBP, DBP, ECG, SPO2 have been compared between each group. We have attempted to keep the variables (age, weight, sex etc.) similar as far as possible so as to standardize the results.

In our study, we preferred a larger size vein on the dorsum of hand so that elicitation of pain and hence its alleviation can be compared with respect to two agents i.e. ketamine and lidocaine**.** It is suggested that vein size is an important factor in causation of pain on injection of propofol.[9,20] In our study, before administering the drug to the patient, it was kept at room temperature. The incidence of injection pain could be significantly reduced from 46% to 23% by giving propofol at 4 °C and the

efficacy of drug was unaltered. The cold temperature caused relative inactivation of the kinin cascade.[7]

In our study, 1/4th of the induction dose of propofol (2.5mgkg-1) was given slowly in both the groups to find out the efficacy of pretreatment in alleviating the injection pain. Some researchers have shown an important determinant of pain on injection depends on speed of injection because high rate of injection causes rapid clearance of drug preventing release of kininogens from vascular endothelium.[9] Pain on propofol injection was decreased after using study drugs and on intergroup comparison it was found 77% of patients had no pain,16% of patients had mild pain, 7% of patients had moderate pain, none had severe pain in group –ketamine, however 47% of patients had no pain, 33% of patients had mild pain,13% of patients had moderate pain.7% of patients had severe pain in group-lidocaine. Hence pain incidence was lower in group-ketamine in comparison to group-lidocaine which was found statistically significant (P value <0.05).

In our study we found ketamine 100 mcg. kg^{-1} immediately before propofol injection is a safe and effective method in preventing propofol injection pain.

Similar studies have been found where different doses of ketamine were compared with lidocaine and it was found that Ketamine 100mg/Kg is safe and effective for alleviating Propofol Injection pain.

List of abbreviations

ASA: American society of anaesthesiologists.
SBP: Systolic blood pressure.
DBP: Diastolic blood pressure.
HR: Heart rate.
L kg^{-1}: Leter per kilogram.
SPO2: Oxygen saturation by pulse oximetry.

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