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Original Research Article

A COMPARATIVE STUDY OF INTRAVENOUS KETAMINE AND LIDOCAINE AS PRETREATMENT IN ATTENUATING PAIN TO PROPOFOL INJECTION DURING INDUCTION OF GENERAL ANAESTHESIA

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Abstract

Background: The commonly used intravenous anaesthetic induction agent is propofol but it is known to cause severe, sharp, stinging or burning pain on injection which is considered to be clinically unacceptable as it can cause agitation and interfere with smooth induction of anaesthesia. To prevent this pain, many methods with different results, have been suggested. The purpose of this study was to compare the analgesic effect of ketamine and lidocaine in reducing propofol induced pain at the time of induction of general anaesthesia for surgical procedures. **Materials and Methods:** This is a prospective randomized clinical study conducted on one hundred patients in the department of Anaesthesiology, Srinivas Institute of Medical Science and Hospital, Mukka, Surathkal, Mangaluru. The patients included were of age range 18-60 years, of ASA grade I and II of both sex. Using shuffle method patients were randomly allocated to one of the two groups (Group K and Group L) of 50 each. To produce venous occlusion a pneumatic rubber tourniquet was placed on upper arm with pressure inflated to 70 mm of Hg. Ketamine 0.1mg/kg and lignocaine 0.1mg/kg were the drugs used for pre-treatment to different group of patients. Tourniquet was released after 1 min of injection of drug and ¼ of the total calculated dose of propofol (2 mg/kg body weight) was administered initially and the patients were asked about the pain on injection of propofol. The behavioural signs, such as facial grimacing, arm withdrawal, or tears and verbal responses were noted. A score of 0 - 3 which corresponds to no pain, mild, moderate, and severe pain was given. Completion of induction of anaesthesia with the remaining calculated dose of propofol was done. As per surgical requirement facilitation of tracheal intubation was done with muscle relaxants and anaesthesia was maintained. If there was pain during injection of propofol in the recovery room all patients were asked to recall and grading was done as no recall and recall of pain present. **Result:** In ketamine group, majority of patients belonged to the age group of 21 to 30 years and in lidocaine group were 31 to 40 years. The association between ages was not statistically significant across both groups. Majority of patients out of 100 in both the groups were males and the association between sexes was not statistically significant across both groups. Majority of patients in both groups underwent surgical procedures related to general surgery 32 (64 %) in K group and 27 (54 %) in L group. Most of the patients in both groups were belonging to ASA I category, i.e., 37 (74 %) in K group and 40 (80 %) in L group and showed no statistically significant association between ASA grade across both groups. The difference was statistically significant in heart rate in ketamine group across the time period. However, such significant difference was not observed in lidocaine group.

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During the course of surgery there was no significant variation observed in mean heart rate between the two groups. There was a statistically significant difference in SBP across the time period in both the groups. However, in mean SBP the variation was not significant between the two groups during the course of surgery. There was a statistically significant difference in DBP across the time period in both groups. However, no significant variation was observed in mean DBP between the two groups during the course of surgery. The difference in SPO2 across the time period was statistically significant in both groups. However, in mean SPO2 no significant variation was observed between the two groups during the course of surgery. In pain score at induction, pain recall and post-operative nausea and vomiting (PONV), the difference was not statistically significant between both groups. **Conclusion:** In reducing propofol injection pain, pre-treatment with both the drugs ketamine and lidocaine are equally effective at low doses.

INTRODUCTION

Propofol (2, 6- diisopropyl phenol) is a popular induction agent, especially for short cases and daycare surgeries. Propofol, a widely used drug for induction, often causes pain when administered into a peripheral vein, the incidence of which is between 28%-90%.[1] Propofol belongs to the group of phenols, and so propofol can irritate the skin, mucous membrane, and veins.[2] It has rapid onset, short duration of action and low side effects but pain during injection of propofol is a common clinical problem during anaesthesia induction.[3-5]

There are several preparations of this agent like long chain triglyceride propofol (LCT), lipid-free microemulsion propofol etc. Commonly used preparation is LCT propofol and it is associated complications such as emulsion instability, need for antimicrobial agents, hyperlipidaemia, pancreatitis and pain during injection.[6] Many factors appear to affect the incidence of pain, which include the site of injection, size of vein, speed of injection, buffering effect of blood, temperature of propofol and concomitant use of drugs such as local anaesthetics and opiates".[7] Several methods have been described to reduce this pain, of which most effective and common are the use of a larger vein and mixing with lignocaine, the optimum dose of lignocaine was found to be 0.1 mg/kg body weight.[8-11] There are several studies on different pharmacologic and non-pharmacologic ways to avoid propofol injection-induced pain; such as premedication,[12] icing or dilution of propofol,[13,14] using concomitant drug like ketamine,[14] local anaesthesia,[15] ondansetron,[16] and opioids.[17,18] Although some of these treatments can decrease extent of pain, but none of them could eliminate the pain. Also, there are some other studies on using two concomitant drugs with propofol such as using lidocaine and remifentanil,[19] lidocaine and dexamethasone,[20] and lidocaine with metoclopramide.[21] The most common method used to decrease propofol injection pain is the usage of lidocaine.[22] However, it has a failure rate between 13 % and 32 %.[23,24] Some ideas are suggested, such as decrease in the pH of the lidocaine-propofol mixture, which decreases the concentration of propofol in aqueous phase with less pain.[25] Another mechanism is the lidocaine effect as a local anaesthetic itself.[22] It is proved that the formulation of the drug plays an important role in the incidence and severity of propofol pain. Ketamine which is N-methyl-D-aspartate (NMDA) receptor antagonist has also been recognized to reduce pain induced by propofol. Also, it acts peripherally to reduce pain. It has both anaesthetic and analgesic effects. The exact mechanism of the analgesic effect of ketamine is not clear. However, it was suggested that it may be through N-methyl-d-aspartate receptors.[26] It is also possible that ketamine acts peripherally.[25] "It is considered that ketamine when mixed with propofol can decrease the pH of the mixed solution and reduce propofol injection pain".[25] "In the sub-anaesthetic dose, it also has a local anaesthetic effect which may also reduce propofol-induced pain. However, ketamine has undesired adverse effects, including sympathetic stimulation and increased secretions".[27] The purpose of the study was to compare the effectiveness of intravenous ketamine injection with lidocaine injection in decreasing propofol-induced pain experienced during the administration of propofol injection for the induction of general anaesthesia.

MATERIALS AND METHODS

After obtaining clearance from institution ethical committee, 100 subjects posted for elective surgery, aged between 18 to 60 years, of both male and female sexes, with ASA I or II, were recruited for the study. Patients with difficulty in communication, unwilling patients, patients with vascular diseases, hypersensitivity to propofol, egg, soya bean, lignocaine, ketamine, infection on the dorsum of their left hands, patients with ASA grade III or more were exluded. With informed consent, patients were evaluated pre-operatively on the day before surgery. Using shuffle method patients were randomly allocated to one of the two groups (Group K and Group L) of 50 each. Routine monitoring with ECG leads, non-invasive blood pressure and pulse oximeter were instituted and baseline values were

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recorded on arrival of patient to operating room. Insertion of an 18-gauge IV cannula was done at the dorsum of patient's hand. No analgesic drugs were given before induction. To produce venous occlusion a pneumatic rubber tourniquet was placed on same upper arm with pressure inflated to 70 mm of Hg. Ketamine 0.1mg/kg body weight and lignocaine 0.1 mg/kg body weight were the drugs used for pre-treatment to different group of patients. Tourniquet was released after 1 min of injection of drug and ¼ of the total calculated dose of propofol (2 mg/kg body weight) was administered initially and the patients were asked about the pain on injection of propofol. The behavioural signs, such as facial grimacing, arm withdrawal, or tears and verbal responses were noted. A score of 0 - 3 which corresponds to no pain, mild, moderate, and severe pain was given. Completion of induction of anaesthesia with the remaining calculated dose of propofol was done. As per surgical requirement facilitation of tracheal intubation was done with muscle relaxants and anaesthesia was maintained. If there was pain during injection of propofol, in the recovery room all patients were asked to recall and grading was done as no recall and recall of pain present. Evaluation of propofol injection pain is done by Mc Crirrick and Hunter Scale. 0 – No pain (negative response to question). 1 – Mild pain (Reporting of pain only in response to question without any behavioural sign). 2 – Moderate pain (Reporting of pain in response to question and accompanied by behavioural sign and simultaneous reporting of pain without question). 3 – Severe pain (vocal response that is strong or response accompanied by arm withdrawal, facial grimacing, and tears). Data was collected and entered in the pre-designed excel spreadsheet. Statistical Package for Social Sciences (SPSS) program for Windows, version 23.0 was used for performing statistical analysis. Analysis was done by descriptive statistics. Student's t test was used for comparison. Expression of categorical variables was done as frequencies and percentages and Chi square test or Fisher's exact test was done for comparison as appropriate. Mann–Whitney U test was used for comparing non normal distribution continuous variables. $P < 0.05$ was taken to indicate a significant difference for all statistical tests.

RESULTS

A total of one hundred patients were recruited to the study. 50 patients were present in each group - ketamine (K) and lidocaine (L) group. In ketamine group, majority of patients were in the age group of 21 to 30 years and in lidocaine group were 31 to 40 years. The association between ages was not statistically significant across both groups. Majority of patients out of 100 in both groups were males. The association between sexes was not statistically significant across both groups. Mean weight of patients in ketamine group was 51.04kg and in lignocaine group was 51.40Kg. The difference was not statistically significant in weight across both groups. Majority of patients in both groups underwent surgical procedures related to general surgery 32 (64 %) in K group and 27 (54 %) in L group. The association between the type of surgery was not statistically significant across both groups. Out of 100 patients, majority of patients in both groups were belonging to ASA I category, i.e., 37 (74 %) in K group and 40 (80 %) in L group. The association between ASA grade was not statistically significant across both groups.

The difference in mean heart rate across the time period in ketamine and lidocaine group is not significant. Also, the variation in mean heart rate between the two groups was not significant during the course of surgery. [Table 1]

The difference was statistically significant in SBP across the time period in both the groups. However, in mean SBP, there was no significant variation observed between the two groups during the course of surgery. [Table 2]

There was a statistically significant difference in DBP across the time period in both the groups. However, in mean DBP, there was no significant variation observed between the two groups during the course of surgery. [Table 3]

The difference was statistically significant in SPO2 across the time period in both groups. However, the variation in mean SPO2 was not significant between the two groups during the course of surgery. [Table 4]

The difference was not statistically significant in pain score at induction between both the groups. [Table 5, Figure 5]

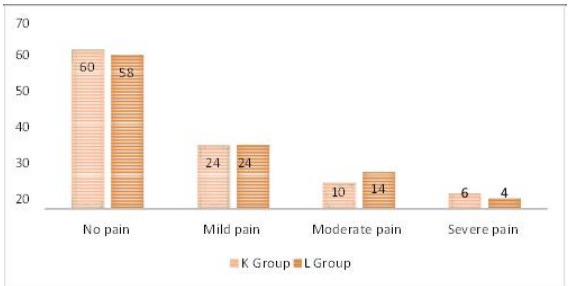

Figure 1: Comparison of Pain Score at Induction between Both Groups (%)

The difference was not statistically significant in pain recall between both the groups. [Table 6]

The difference in post-operative nausea and vomiting (PONV) was not statistically significant between both the groups. [Table 7]

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Table 1: Distribution of Study Patients Based on Heart Rate

Heart Rate/Min	N	Ketamine		Lidocaine		p
		Mean	SD	Mean	SD	
Pre induction	50	74.58	5.429	74.90	5.744	0.775
Induction	50	72.08	3.922	74.72	4.603	0.003
5 mins	50	73.54	4.450	73.66	5.173	0.877
10 mins	50	75.00	2.893	75.16	3.377	0.901
15 mins	50	75.04	6.328	74.84	6.604	0.800
Post Operative	50	75.10	3.960	73.78	9.475	0.366
		p= 0.006		p=0.756		

Table 2: Distribution of Study Patients Based on SBP

SBP (mmHg)	N	Ketamine		Lidocaine		p
		Mean	SD	Mean	SD	
Pre induction	50	126.56	7.296	126.72	8.038	0.917
Induction	50	116.20	7.001	118.62	6.449	0.075
5 mins	50	116.32	7.084	116.40	7.384	0.782
10 mins	50	122.84	7.161	124.26	5.371	0.956
15 mins	50	121.14	7.762	121.58	8.107	0.265
Post Operative	50	119.48	6.348	118.84	6.529	0.620
		p= 0.001		p=0.001		

Table 3: Distribution of Study Patients Based on DBP

DBP (mmHg)	N	Ketamine		Lidocaine		p
		Mean	SD	Mean	SD	
Pre induction	50	76.20	4.101	76.24	4.922	0.965
Induction	50	74.54	4.320	75.66	5.228	0.246
5 mins	50	72.60	3.709	72.46	4.795	0.741
10 mins	50	76.46	4.301	76.14	4.041	0.871
15 mins	50	76.70	3.940	76.42	4.482	0.702
Post Operative	50	75.98	4.583	76.26	5.287	0.778
		p= 0.001		p=0.001		

Table 4: Distribution of Study Patients Based on SPO2

SPO2	N	Ketamine		Lidocaine		p
		Mean	SD	Mean	SD	
Pre induction	50	99.44	.611	99.38	.602	0.622
Induction	50	100.00	.000	100.00	.000	1.000
5 mins	50	99.88	.385	99.96	.198	1.000
10 mins	50	100.00	.000	100.00	.000	0.195
15 mins	50	99.92	.274	99.92	.274	1.000
Post Operative	50	98.92	.804	98.88	.824	0.806
		p= 0.001		p=0.001		

Table 5: Comparison of Pain Score at Induction between Both Groups

Pain score	Group		Total	X2	p
	Ketamine	Lidocaine			
No pain	30 (60.0)	29 (58.0)	59 (59.0)	0.550	0.908
Mild pain	12 (24.0)	12 (24.0)	24 (24.0)		
Moderate pain	5 (10.0)	7 (14.0)	12 (12.0)		
Severe pain	3 (6.0)	2 (4.0)	5 (5.0)		
Total	50	50	100		

Table 6: Comparison of Pain Recall between Both Groups

Pain recall	Group		Total	X2	p
	Ketamine	Lidocaine			
No	37 (74.0)	36 (72.0)	73 (73.0)	0.051	0.822
Yes	13 (26.0)	14 (28.0)	27 (27.0)		
Total	50	50	100		

Table 7: Comparison of PONV between Both Groups

PONV	Group		Total	X2	p
	Ketamine	Lidocaine			
No	46 (92.0)	47 (94.0)	93 (93.0)	0.154	0.695
Yes	4 (8.0)	3 (6.0)	7 (7.0)		
Total	50	50	100		

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DISCUSSION

In our study, there was no significant variation was observed in mean heart rate between the two groups during the course of surgery. Our study results are in concordance with the study of Ayatollahi et al. and Mehra et al. Ayatollahi et al. observed that there was no significant difference in heart rate between K group, L group and control groups of heart rate. Mehra et al,[28] also did not find any statistically significant difference in heart rate after administration of propofol between ketamine group and control.

In both groups, there was a statistically significant difference in SBP, DBP and SPO2 across the time period. However, no significant variation was observed in mean SBP, DBP and SPO2 between the two groups during the course of surgery. This is in contrast with the study of Ayman et al. study regarding hypotension, there was significant differences between L, and the K group. This may be attributed to the activation of the sympathetic nervous system by ketamine".[29]

There was no statistically significant difference in pain score and pain recall between both the groups. Pang et al. administrated 60 mg intravenous lidocaine and the pain incidence was 11 % whereas we used a low dose of 0.1 mg/kg body weight thus the incidence of pain was 24% (mild pain), 10 % (moderate pain) and 6 % had severe pain in K group.[30] Whereas in L group, the incidence of pain was 24 % (mild pain), 14 % of the patients had moderate pain and 6 % had severe pain and found higher rate of pain incidence in our study after propofol injection respectively, but no statistically significant difference was found. Turan et al. who administered 0.5 mg/kg intravenous lidocaine, had also a higher incidence of the pain of 33.3 % which is similar to our study finding.[31] Picard and Tramèr study also had a higher incidence of pain i.e., 40% following 0.5 mg/kg of lignocaine similar to our study".[32]

Propofol injection pain after pre-treatment with ketamine was ranged from 6 to 24 % in ketamine group and this was proved by the current study. Other previous reports using only a 30-s interval with smaller doses of ketamine (0.1 – 0.5 mg/ kg) did not eliminate the pain completely. However, the usage of a larger dose of ketamine 1 mg/kg could eliminate the pain completely".[33] In the elimination of propofol pain, a study conducted by Wang et al,[34] found that ketamine at 0.3 mg/kg was effective. 100 mcg/kg ketamine given just before propofol injection decreased the possibility and the intensity of pain more than smaller doses (10 and 50 mcg/kg) and this was proved by Koo et al.[35] In treatment and attenuation of propofol pain, lidocaine 40 mg and ketamine (100 mcg/kg) are equally effective as proved by Polat et al.[36] This result is in accordance with our result that proved that ketamine and lidocaine were both efficacious in the treatment of propofol pain.

In our study, post anaesthesia nausea and vomiting were observed in 4 (8 %) in K group and 3 (6 %) in L group. There was no statistically significant difference in PONV between both the groups. Ayman et al. observed that only two patients in group K experienced emergence agitation".[29]

CONCLUSION

We observed that in reducing the pain caused by propofol, pre-treatment with ketamine at the dose of 0.1 mg/kg body weight and lidocaine at the dose of 0.1 mg/kg body weight was effective. However, the difference between ketamine and lidocaine was not significant. Incidences of complications were not significant between both the study drugs.

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