

EFFECTIVENESS OF LOW DOSE KETAMINE AND LIGNOCAINE IN PREVENTION OF PROPOFOL INDUCED PAIN

Umbrin Naz, Fazal Wadood, Aurangzeb, Muhammad Ilyas, Ambareen Sifat Ullah, Rubina Bangash

Department of Anaesthesiology and Critical Care, Khyber Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To prove that low dose ketamine is more effective than lignocaine in prevention of propofol injection pain.

Materials and Methods: This randomized controlled trial study was conducted in the central operation theatre of Khyber Teaching Hospital, Peshawar-Pakistan, from July 2018 to December 2018. A total of 174 patients were randomly allocated in two groups by lottery method. Patients in group A (n=87) received Ketamine 0.5 mg/kg and patients in group B (n=87) received 0.5 mg/kg of 2% Lignocaine for prevention of propofol induced pain. Pain scores were calculated through visual analogue scale (VAS).

Results: The mean VAS score in group A was 2.264 ± 0.990 and in group B was 4.540 ± 1.070 . There was statistical difference between the two groups ($p < 0.05$).

Conclusion: Ketamine is more efficacious than lignocaine in reducing injection site pain caused by propofol.

Keywords: Pain, Lignocaine, Propofol, Ketamine.

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INTRODUCTION

Propofol is a renowned intravenous anesthetic that is used to induce general anesthesia. It has fast, smooth induction with fast recovery and antiemetic properties.¹ However 70% of patients complain that propofol is used to induce sharp and burning pain at the injection site during anesthesia.² Propofol (2,6-diisopropylphenol) is available in 1% aqueous solution as an oil in water emulsion containing soybean oil, glycerol and egg lecithin. This formulation often causes pain during injection. The initial vascular pain may be due to the direct irritation of skin, mucous membrane and venous intima, while the delayed pain which occurs after 10-20 seconds is supposed to be because of the indirect effect of kallikrein-kinin cascade activation.^{3,4}

Pain is defined by International Association for study of pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue

damage, or described in terms of such damage." Numerous methods have been used to ease the pain of propofol injection, such as choosing a larger vein, increasing the injection speed, cooling the propofol solution, diluting it with 5% dextrose, and occluding the vein before injection.^{5,6} In addition to these many drugs have also been tried to reduce this pain with different successes, such as lignocaine, tramadol, dexamethasone, butorphenol, ketorolac, ondansetron, magnesium sulfate, metoclopramide, thiopentone.^{7,8,9}

In our study, the efficacy of lignocaine is compared with ketamine. Lignocaine is commonly used for propofol caused pain and acts by its local anaesthetic action and stabilization of kinin cascade. Ketamine (a phencyclidine derivative) can be used as a general anaesthetic in a dose of 1-2 mg/kg intravenously. Ketamine has analgesic and local anaesthetic effects. Ketamine given as pretreatment acts as preemptive analgesic preventing sensitization of local nerve endings by noxious inputs. By antagonism of N-methyl-D-aspartate receptors it acts as a local anesthetic and therefore can prevent propofol induced pain.¹⁰

MATERIAL AND METHODS

After approval from hospital's ethical and research committee this randomized, single-blind, controlled trial study was conducted in Khyber Teaching Hospital Peshawar.

Correspondence

Dr. Umbrin Naz

Assistant Professor, Anesthesia Department Khyber Teaching Hospital, Peshawar Pakistan.

Email: umbrinnaz1@yahoo.com

Cell: +92-333-9116410

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war, Pakistan from July 2018 to December 2018. A total of 174 patients were included who underwent elective surgery using propofol for induction of general anesthesia. There was no gender discrimination between the American society of anesthesiologists (ASA) grade 1 and grade 2, 15-60 years age groups. Patients allergic to the study drugs, suspected of having difficult intubations, requiring rapid sequence induction or belonging to ASA grade 3 and 4 were excluded from the study.

A pre-operative evaluation of the patients was performed to assess their fitness for anesthesia. The process explained to patients and they were educated about how to label the VAS scale and written informed consent obtained. Each patient received the same standard pre-operative protocol and data were collected in proformas. Patients advised to remain nil orally for 6 to 8 hours before surgery.

After reaching the operating room monitoring of baseline pulse, blood pressure, and oxygen saturation were performed before induction. The study drug was prepared by a non-participating anesthesiologist in a volume of 2 ml in identical syringes. A 20G cannula was placed in the dorsum of the patient's non-dominant hand without local anesthesia and flushed with normal saline. All patients were randomly divided into two groups by lottery. Inj. Ketamine (0.5mg / kg) 2ml was given to patients in group A and patients in group B received 2ml 2% lignocaine (0.5mg/kg). Venous blockage was achieved by

using a rubber tourniquet on the upper arm which was raised by systolic pressure above about 50 mm Hg for 60 seconds. After 60 s occlusion was released and 2 mg per kg of propofol was administered through the same cannula at a rate of 0.5 ml / sec. Anesthesia resident physician who did not know the assigned patient group asked the patient about the injection pain 15 seconds after 25% dose of propofol was injected. Induction anesthesia was completed with the remaining calculated dose of propofol (2 mg / kg). Any adverse effects were noted. Visual analogue scale is a tool to assess pain. It consists of a straight line with a length of 0-10 cm (zero indicates no pain and 10 indicates maximum pain). The patient was educated to mark his or her pain level on the line between the two endpoints. This distance from zero (considered no pain) to the length marked by the patients were taken as the patients pain intensities and recorded in form.

RESULTS

Data were analyzed using SPSS version 10.0. Categorical variables like gender were described in terms of frequencies and percentages while quantitative variables such as age and pain were described as mean \pm SD. Regarding pain, it was significant to use independent student t-tests to keep p values ≤ 0.05 . The average pain score was calculated. The results were presented in the form of tables, and the two groups compared for any statistical differences with each other. Student's t-test was applied. The calculated p-value was < 0.001 . The results were statistically significant, suggesting that ketamine is superior to lignocaine and can reduce pain caused by propofol.

Table 1: Sex Distribution

Group	Male n(%)	Female n(%)	Total n(%)	p-Value
A(Ketamine)	49(56)	38(44)	87(100)	0.18
B(Lignocaine)	48(55)	39(45)	87(100)	
P > 0.05 (not significant)				

Table 2: Age Distribution

Age	Group A n(%)	Group B n(%)	p- Value
15-20	16(18.4)	18(20.7)	>0.01
20-30	24(27.6)	22(25.3)	>0.01
31-40	25(28.7)	23(26.5)	>0.01
41-50	14(16.1)	15(17.2)	>0.01
51-60	8(9.2)	9(10.3)	>0.01
Total	87(100)	87(100)	>0.01
Mean \pm SD	34.56 \pm 9.81	32.36 \pm 8.63	>0.05
Range	17-60	18-59	

Note: As p-Value is > 0.05 therefore the difference in age is not significant.

Table 3: Incidence and Intensity of Pain on Injection of Propofol in Ketamine and Lignocaine groups along with VAS score

Pain Score	Ketamine group		Lignocaine group	
	Number (n)	Frequency (%)	Number (n)	Frequency (%)
No Pain (0)	53	60.91%	25	28.79%
Mild (1,2,3)	3	3.49%	3	3.49%
Moderate (4,5,6)	20	22.99%	23	26.44%
Severe (7,8,9,10)	11	12.64%	35	40.23%
Distribution of patients by visual analogue score (n=174)				
VAS	Group A (Ketamine)		Group B (Lignocaine)	
Mean±SD	2.264±0.990		4.540±1.070	
P.Value<0.001				

DISCUSSION

The most common drawback of propofol that causes distress to patients is pain on injection. It is ranked as the seventh most important clinical problem by anesthesiologists worldwide.¹¹ Propofol is one of the most common intravenous anesthetic agent, especially for short-term surgery, total intravenous anaesthesia (TIVA), when the laryngeal mask airway (LMA) is used and sedation in the intensive care unit.¹² Lignocaine reduces pain due to propofol injection by its local anaesthetic action and stabilization of kinin cascade and is mostly used for this purpose, but it has a failure rate of 13 to 32%.¹³ According to recent researches ketamine pretreatment is more effective at reducing propofol pain than lignocaine pretreatment.¹⁴

Our study found that 60.91% patients were pain-free with ketamine pretreatment (average VAS score 2.264 ± 0.990) and with lignocaine 28.75% did not complain of pain (average VAS score 4.540 ± 1.070) demonstrating the superiority of ketamine over lignocaine to prevent propofol-induced pain. Further it was observed that intensity of pain was severe 12.64% with ketamine pretreatment while it was 40.23% with lignocaine pretreatment. There were no adverse hemodynamic effects as we have used sub-anaesthetic dose of ketamine. In a study performed by OzKocak I et al. the average pain score with low-dose ketamine (0.5 mg / kg) was 2.1 ± 3.1 . They used VAS like we did in our study.¹⁵ Mohsin and associates evaluated the effect of low-dose ketamine (0.25 mg / kg) to reduce pain from propofol injections in 130 female patients undergoing cesarian section. They observed that 83.1% of women were painfree and only 16.9% women suffered from pain with ketamine pretreatment which is supportive for our study.¹⁶

A study conducted by Elsayed and Rayan com-

pared ketamine 0.5 mg / kg, 1% lignocaine 0.5 mg / kg and acetaminophen 2 mg / kg and found that the incidence of pain was 16% with the use of ketamine and 40% with lignocaine for propofol associated injection pain. None of the patients had severe pain in the ketamine group, while 8% of patients had severe pain in pretreatment with lignocaine thus favoring the current study.¹⁷ A single sub-anaesthetic dose of ketamine was used in our study, Zahedi H and colleagues conducted a research to determine the correct dose of ketamine that can alleviate pain caused by propofol. They concluded that ketamine is better than lignocaine and that increasing the dose of ketamine reduces the frequency of pain because in their study the incidence of pain was 60% with 50mcg / kg, 55% with 75mcg / kg, and 45% with 100mcg / kg. Although it was 65% with lignocaine.¹⁸

Mahmood and Yasmin used a 4-point verbal scale instead of visual analog scale to compare lignocaine and ketamine, and observed that 4% patients complained of severe pain with use of ketamine and 12% with lignocaine, but 40% of patients had no pain with ketamine while 60% were pain free with lignocaine. So they proved that ketamine reduces the intensity, but not the frequency of propofol induced pain.¹⁹ Bano and associates while studying the effects of 1% lignocaine 20mg and ketamine 0.5mg / kg pretreatment on injection pain found that the intensity and incidence of pain after propofol administration was lower in the ketamine group in accordance with our research.²⁰

In another study completed by Patilbuwa and Yarramalle an average VAS score was investigated for lignocaine, ketamine and metoclopramide, and it was observed to be 1.560 ± 0.712 for lignocaine and 2.320 ± 0.945 for ketamine, metoclopramide was 3.120 ± 1.666 .

This implements that lignocaine is better than ketamine in reducing pain (p value < 0.01). Similarly P value (p value < 0.05) between ketamine and metoclopramide indicates that ketamine is better than metoclopramide, contradicting our study. This may be due to the small dose of ketamine in their study, and also a small number of patients in each group were $n = 25$, which they have taken to cause different result.²¹ Polat and Aktay demonstrated that 100 mcg / kg of ketamine, 40 mg of lignocaine, 10 mg of metoclopramide, and remifentanil were equally effective for pain caused with propofol. It may be that the small dose of ketamine (100 micrograms / kg) used by them in contrast to our study dose (500 micrograms / kg) of ketamine was responsible for the difference from our study.²²

Visual analogue scale is a useful clinical tool which reflects human response, experience and perception. It's simple to use and seems sensitive to smaller changes in effect over time than are categorical measures.²³ That is the reason for using VAS in our study, some researchers have preferred to use the verbal rating scale which is based on subjective feelings. The patients respond to pain as mild, moderate and severe varying from patient to patient.²⁴

LIMITATIONS

It was not a double blind study. Moreover we did not include control group in our study which could give us the exact incidence of propofol induced pain without any pretreatment in our setup.

CONCLUSION

For prevention of pain during injection of propofol the use of ketamine could significantly reduce pain score compared to lignocaine. Pretreatment with low dose ketamine should be administered at the time of induction of anaesthesia with propofol.

RECOMMENDATIONS

Multicenter trials should be performed in large populations to recommend their use in routine settings.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Naz U: Planning of Study

Wadood F: Data Analysis

Auranzeb: Manuscript writing

Ilyas M: Data management

Ullah AS: Statistics

Bangash R: Supervision

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.