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ORIGINAL ARTICLE

RANDOMISED CLINICAL TRIAL TO COMPARE THE EFFECT OF PRETREATMENT OF KETAMINE AND LIGNOCAINE ON PROPOFOL INJECTION PAIN

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ABSTRACT: BACKGROUND: Pain following injection of Propofol occurs in 28-90 % of patients. Various methods have been used to reduced the pain on intravenous injection of propofol namely administration of drugs like alfentanil, metoclopramide, pretreatment with intravenous lignocaine, pretreatment with intravenous ketamine etc., **AIMS:** In this study, we aimed to evaluate and compare the effect of pretreatment of ketamine and lignocaine on propofol injection pain. **STUDY DESIGN:** Randomised controlled study. **METHODS:** 120 patients of ASA grade I and II of both sexes between 18-60 years of age group scheduled for various elective surgical procedures, were randomly allocated into three groups of 40 each by envelope method using random number table. Patients of Group K (n=40) received ketamine 10 mgs (1 ml), Patients of Group L (n=40) received lignocaine 10 mgs (1 ml) and patients of Group S (n=40) received 0.9% normal saline (1 ml). In all these patients injection propofol (1%) was administered intravenously over a period of 5 seconds. 15 seconds later patients were asked about the presence of injection pain. **RESULTS:** Pain on Injection of propofol was assessed using the "Verbal categorical scoring system." Asked the patient to grade pain as no pain, mild pain or severe pain. They were score as 0, 1, or 2 respectively. The overall incidence of pain in control group (normal saline group) was 80%, Incidence of pain in ketamine group was 20 %, incidence of pain in lignocaine group was 30%. When compared between these two groups, ketamine significantly reduces pain as compared to lignocaine, which was not statistically significant (P>0.05). **CONCLUSION:** We conclude that both ketamine and lignocaine are effective in reducing the pain of intravenous injection of propofol, However ketamine is superior to lignocaine.

KEYWORDS: Propofol, ketamine, Lignocaine, Injection pain.

INTRODUCTION: "It is easier to find men who will volunteer to die, than to find those who are willing to endure pain with patience". - Julius caesur.

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. This definition recognizes the interplay between the objective, physiological sensory aspects of pain and its subjective, emotional and psychological components.[1]

Pain relief is regarded as one of the prime duties of an anaesthesiologist. Pain relief should be extended not only in the postoperative period but also in the preoperative period especially the procedural pain. (i.e, the one associated with procedures like intravenous cannulation, lumbar puncture) and pain on injection, which was not thought in the previous days.

Modern anaesthesiologists are now concerned about alleviating pain on injection also.

Propofol is a popular anaesthetic induction agent with rapid onset of action and rapid recovery. However its main disadvantage is that of pain during intravenous injection.[2,3]

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Pain on injection occurs in 28-90% of patients, which may be severe.[4]

Various methods have been used to reduce this pain viz, administration of drugs like alfentanil, ondansetron, metoclopramide and local anaesthetics etc., addition of lignocaine, pretreatment with intravenous ketamine, application of nitroglycerin ointment to the skin, chilling of the propofol to 4^0C, injection of propofol into large antecubital veins or into a freely flowing intravenous line.[5,6,7,8]

Since propofol is being widely used with distinct adventages, the minor side effects like pain on injection need to be alleviated by the anaesthesiologist using these drugs.

Hence this study is proposed to evaluate and compare two methods of alleviation of pain on propofol injection.

MATERIALS AND METHODS: A randomized, prospective study was carried out in one hundred and twenty patients between 18 to 60 years of age of both sexes, belonging to ASA Grade I and II, who were scheduled to undergo various elective surgical procedures.

After institutional ethical committee approval, informed consent was taken from all the patients.

INCLUSION CRITERIA:

- Patients belonging to ASA Grade I and II.
- Patients between 18 to 60 years of age of both sexes.
- Patients posted for various elective surgical procedures under general anaesthesia with or without intubation.

EXCLUSION CRITERIA:

- Patients with history of known allergy to drugs.
- Patients with history of epilepsy, hypertension, diabetes mellitus.
- Patients who were taking sedatives and analgesics.
- Pregnant women.

Routine investigations like haemoglobin and urine routine examination were obtained.

Patient height and weight were recorded. Airway assessment was done for all the patients and nil by mouth history was confirmed.

All the patients were premedicated with injection Atropine 0.02 mg/ kg body weight intramuscularly, 30 minutes prior to the surgery.

Patients were randomly allotted into three groups of 40 each by envelop method using random number table. Patients of Group K (n=40) will receive ketamine 10 mgs (1 ml), patients of Group L (n=40) will receive 0.9% lignocaine 10 mgs (1 ml), and patients of Group S (n=40) will receive 0.9% normal saline (1 ml).

Patients were taken in the operating table; baseline heart rate and blood pressure were recorded. Intravenous access was secured with 18G cannula into a vein on the dorsum of the hand in all the patients.

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1ml of ketamine containing 10mgs was prepared by taking 2ml of injection ketamine (5%) in a syringe and diluting it upto 10 ml with 0.9% normal saline. Out of that 1 ml was taken which contained 10 mgs.

1 ml of lignocaine containing 10 mgs was prepared by taking 1 ml of preservative free lignocaine I.e., xylocard 2% in a syringe diluted it with 1 ml of 0.9% normal saline. Out of that 1 ml was taken which contained 10 mgs.

Above prepared injection ketamine 10 mgs (1 ml) in Group K or injection lignocaine 10 mgs (1 ml) in Group L or injection 0.9% normal saline 1 ml in Group S was injected into the vein on the dorsum of the hand; 30 seconds after this, bolus injection of 3 ml of propofol (1%) was given to the patients weighing less than 70kg body weight. 4ml of propofol (1%) was given as bolus dose to the patients weighing more than 70 kg body weight. In all these patients propofol (1%) was administered over a period of 5 seconds. 15 seconds later patients were asked about the presence of injection pain. Pain was assessed using the "verbal categorical scoring system".[9] Asked the patient to grade pain as no pain, mild pain or severe pain. These were scored as 0, 1 or 2 respectively.

Mild pain was defined as discomfort in the arm or hand, acceptable to the patients; severe pain was defined as grimacing or limb withdrawl, which was not acceptable to the patient.

Following this, patients were induced with injection propofol (1%) at the dose of 1.5 mgs – 2mgs/kg body weight and anaesthesia was continued as per the requirement of the surgery. Haemodynamic parameters were monitored throughout the surgical procedure.

OBSERVATION AND RESULTS: Effects of ketamine pretreatment (Group K) on propofol injection pain was compared with effect of lignocaine pretreatment (Group L) and also with normal saline pretreatment (control group i.e., Group S).

	No. of Patients	Age (in years) Mean values (SD)	Weight (in kgs) Mean values(SD)	Sex		ASA distribution	
				Male	Female	I	II
Group S	40	31.03 (+ 11.55)	55.80 (+ 4.70)	7	33	33	7
Group K	40	32.73 (+ 11.47)	53.47(+ 7.30)	4	36	37	3
Group L	40	31.85(+ 9.78)	56.63(+ 7.32)	7	33	37	3

Table 1

Table 1 shows the distribution of patients in three groups 40 each and shows mean age and mean weight with standard deviation in each groups. Age and weight of the patients were comparable between the three groups. There were no statistically significant differences between the groups, Table 1 also shows sex distribution, maximum patients were female and ASA distribution, maximum patients belonged to ASA Grade I.

Surgical procedures	Group S	Group K	Group L
Gynaecological	29	34	32
Surgical	9	5	6
Orthopaedics	2	1	2

Table 2: Surgical procedures

Table 2 shows surgical procedures, maximum patients underwent gynaecological procedures.

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Showing pain scores following propofol injection in patients receiving normal saline, ketamine and lignocaine.

Allocation	Pain score		
	'0' (%)	1(%)	2(%)
Group S (n=40)	8 (20)	12 (30)	20(50)
Group K (n=40)	32 (80)	8(20)	0(0)
Group L (n=40)	28(70)	10(25)	2(5)

Table 3

Pain score: 0- No pain, 1 - Mild pain, 2 - Severe pain

Assessment of pain score was done using a "Chi square test".

The overall incidence of pain in control group (normal saline group) was 80%. In that 50% of patients felt severe pain and 30% of patients felt mild pain. Incidence of pain in ketamine group was 20%. All the 20% patients felt mild pain, no patients felt severe pain. Incidence of pain in lignocaine group was 30%, In that 25% patients felt mild pain and only 5% patients felt severe pain.

Looking at the results both ketamine and lignocaine were effective in reducing pain on propofol injection, when compared between these two drugs ketamine significantly reduces pain (incidence of pain was 20%) as compared to lignocaine (incidence of pain was 30%), but this is not statistically significant ($p>0.05$). However when compared with control group (incidence of pain 80%), both drugs i.e., ketamine (Incidence of pain -20%) and lignocaine (incidence of pain – 30%) significantly reduces pain on propofol injection, which is statistically significant ($P>0.05$).

DISCUSSION: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. This definition recognizes the interplay between the objective, physiological sensory aspects of pain and its subjective, emotional and psychological components.[1]

Pain relief is regarded as one of the prime duties of an anaesthesiologist. Pain relief should be extended not only in the postoperative period but also in the preoperative period especially the procedural pain (i.e., the one associated with procedures like intravenous cannulation, lumbar puncture) and pain on injection, which was not thought in the previous days.

Modern anaesthesiologists are now concerned about alleviating pain on injection also.

Propofol is a popular anaesthetic induction agent with rapid onset of action and rapid recovery. However its main disadvantage is that it causes pain during intravenous injection.

Pain on injection occurs in 28-90% of patients, which may be severe.[5]

The present study was conducted to compare the efficacy of prior intravenous administration of ketamine and lignocaine in reducing the incidence and severity of the pain associated with propofol injection.

120 patients scheduled to undergo various elective surgical procedures were studied. They were distributed in to 40 for each three groups i.e., n=40 for Group S (control group – normal saline group), n=40 for Group K (ketamine group), n= 40 for Group L (Lignocaine group).

The age and weight of the patients were comparable between the groups.

In our study, in sex distribution maximum patients were female, in ASA distribution maximum patients belonged to ASA grade I and in surgical procedures maximum patients underwent gynaecological procedures.

Assessment of the pain score was done using a "Chi square test".

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In control group (Normal saline) 8 patients have not felt pain, 12 patients felt mild pain and 20 patients felt severe pain.

In ketamine group 32 patients did not feel any pain, 8 patients felt mild pain and no patients felt severe pain.

In lignocaine group 28 patients did not feel any pain. 10 patient's felts mild pain and only 2 patients felt severe pain.

The overall incidence of pain in control group was 80%. Overall incidence of pain in ketamine group was 20%, and that of lignocaine group was 30%.

Looking at the results both ketamine and lignocaine are effective in reducing pain on propofol injection pain. When compared between these two drugs, Ketamine significantly reduces pain (incidence of pain – 20%) as compared to lignocaine (incidence of pain – 30%), but this is not statistically significant. However when compared with control group, both the drugs significantly reduces pain on injection of propofol, which is statistically significant, more so in ketamine group.

Tan C.H. et al during 1998[5] conducted a study to compare the prior intravenous administration of ketamine 10 mgs (1mg) or 0.9% saline (1ml) on propofol injection pain. Showed that incidence of pain was 26% in the ketamine group compared with 84 % in the control group. The results of our present study closely correlate with the results of this study.

Nicol M. E. et al, 1990 [10] conducted a study to compared the prior intravenous administration of lignocaine 10 mgs, procaine 10mgs or isotonic saline 0.5ml, 15 seconds before the injection of propofol into a vein on the back of the hand. The incidence of pain on injection in the control group (51 %) was compared with other studies. Lignocaine and procaine both significantly reduced the pain (35% and 34% respectively) but there was no statistical difference between these two groups. These results are also comparable with those of our study.

Ganta R. and fee J. P. H., 1992[11] conducted a study to compare the efficacy of lignocaine (10mg) and metoclopramide (5mg) in minimising the pain of injection of intravenous propofol. They have shown that both lignocaine and metoclopramide significantly reduced pain on injection compared with saline group.

Mechanism of pain of intravenous injection of propofol may be due to its endothelial irritation, osmolality differences, unphysiological pH and activation of pain mediators such as kininogens.[5]

Ketamine has been shown to have a local anaesthesia action when administered intravenously for regional anaesthesia. As a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, ketamine may activate N-methyl-D-aspartate (NMDA) receptors either in the vascular endothelium or in the central nervous system. This explains the mechanism of ketamine in reducing the pain on propofol injection.[5]

Lignocaine being local anaesthetic agent apart from its direct effect on vascular endothelium it stabilizes the pain mediator such as kininogens.[10,12]

From this study we confirm that both ketamine and lignocaine are effective in reducing the pain on propofol injection, However ketamine is superior to lignocaine.

CONCLUSION: From this study we conclude that both ketamine and lignocaine are effective in reducing the pain of intravenous injection of propofol, however ketamine is superior to lignocaine.

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