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Original Research Article

Evaluation of Efficacy of Low Dose IV Ketamine for Prevention of Pain Associated with IV Propofol Injection

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Abstract:

Background: Propofol is the intravenous (IV) anaesthetic that is used the most frequently for induction and maintenance of anaesthesia as well as for sedation both inside and outside of the operating room. Propofol is very close to being the perfect IV anaesthetic agent; however, there is still a problem with pain during its injection. A low dose of ketamine may be useful because of its peripheral local anaesthetic impact, whereas a high dose of ketamine may be effective because of its central analgesic and sedative action.

Objective: To study the efficacy of low dose IV ketamine for prevention of pain associated with IV propofol injection.

Materials and Method: Prospective, randomised and was conducted in Department of Anaesthesia GGH, Guntur. 60 ASA 1 and 2 patients ranging in age from 18 to 65 years old who were scheduled for surgery under complete intravenous anaesthesia were randomly assigned to one of two groups (A or B). Patients in group A were given ketamine as the pre-treatment before they were given propofol.. Those who were in group B were given saline prior to having propofol administered to them. Pain scores were measured by the investigator immediately following injection of propofol. A verbal pain score was assigned to each patient's response to the questionnaire.

Results: The comparison of pain score as per McCrirrick and Hunter evaluation scale between group A and group B at P5, P10 and P15 intervals were statistically highly significant (p value < 0.0001).The incidence of propofol injection discomfort was reduced from 95% in the group that received saline to 63% in the group that received ketamine pre-treatment.

Conclusion: Pre-treatment with low-dose ketamine greatly reduces pain after propofol injection. The short-term preservation of hemodynamics after propofol injection was more effective than placebo. Low doses of ketamine do not cause any negative effects.

Keywords: Propofol, Low dose Ketamine, Pain associated with Propofol, Placebo.

Introduction

Propofol is a substituted isopropyl phenol chemically 2, 6-diisopropyl phenol. It is administered intravenously as a 1% solution in an aqueous solution of 10% soybean oil, 1.2% purified egg phosphatide and 2.25% glycerol. [1] A quick intravenous administration of 1.5 to 2.5 mg/Kg propofol (<15 seconds) causes loss of consciousness in around 30 seconds.

This medication induces a faster and more complete awakening than other medicines. The quick return of consciousness with minimal central nervous system effects is a significant benefit of propofol. [2] Propofol's sedative and hypnotic effects are thought to be caused by its interaction with GABA, the primary inhibitory neurotransmitter in the CNS. Activation of GABA receptors leads to increased transmembrane chloride conductance, hyperpolarizing post-synaptic cell membranes and inhibiting neuron activity. Propofol's interaction with GABA receptor complex components may slow GABA dissociation, prolong chloride channel opening, and cause cell membrane hyperpolarization. [3]

By 1970, ketamine was marketed as a “rapidly acting, non-barbiturate general anaesthetic” for brief procedures. Due to its unique pharmacological features and newly discovered favourable clinical properties, ketamine has survived the test of time and has many clinical applications. New neuroprotective, anti-

inflammatory and anticancer effects and low-dose ketamine regimens have expanded its therapeutic use. [4]

Lipid-soluble ketamine breaks down quickly and distributes to peripheral tissues. N-demethylation and ring hydroxylation mechanisms extensively metabolize it in the liver. [5] The major metabolite, nor ketamine, is one-third to one-fifth as powerful as ketamine as an anaesthetic. Nor ketamine and its hydroxylated derivatives are eliminated in urine and faeces. The effect builds. Repeated administration increases resistance. Ketamine binds non-competitively to the allosteric phencyclidine recognition site on NMDA receptors. Inhibition of NMDA receptors can diminish pain perception and produce drowsiness due to their role in central sensitization. Ketamine may affect muscarinic, monoaminergic, voltage-sensitive sodium, L-type calcium, and opioid receptors. [6]

Ketamine is a unique medication that can provide significant analgesia at sub anaesthetic levels.

Ketamine's analgesic effects derive from its impact in the thalamic and limbic circuits, which process painful impulses.

- Small dosages of ketamine can enhance opioid analgesia. - Spinal cord sensitization may cause pain when touching or moving an affected portion. Ketamine regulates spinal cord sensitization in the dorsal horn, causing analgesia.[7]

For healthy individuals, the intravenous induction dose is 1.5 to 2.5mg/kg, with blood levels of 2 to 6mcg/mL causing loss of consciousness, depending on age and medicines. Typically, awakening occurs at plasma concentrations of 1 to 1.5mcg/mL. [8]

The normal IV dose for maintaining anaesthesia is 50-200mcg/kg/minute, often with a short-acting opioid. General anaesthesia with propofol often causes minimal post-operative nausea and vomiting. Quick awakening with minimal sedation. [8]

This study aimed to assess the effectiveness of low-dose ketamine in reducing propofol injection discomfort in the dorsal hand vein, as well as the haemodynamic effects and potential side effects, such as emergence phenomena.

Materials and Method

Prospective, randomised and was conducted in Department of Anesthesia GGH, Guntur. After obtaining approval from the Ethics Committee, 60 ASA 1 and 2 patients ranging in age from 18 to 65 years old who were scheduled for surgery under complete intravenous anaesthesia were randomly assigned to one of two groups (A or B). Patients in group A were given ketamine as the pre-treatment before they were given propofol.. Those who were in group B were given saline prior to having propofol administered to them. Pain scores were measured immediately following injection of propofol. A verbal pain score was assigned to each patient's response to the questionnaire.

Inclusion Criteria:

- ASA I and II adult patients between the ages of 18 and 40 who were scheduled operation while under general anaesthesia.
- A verbal reaction scale with four points was used to determine the level of discomfort caused by the injection.

Exclusion Criteria:

- Individuals with ASA physical status III or IV,
- Patients younger than 18 or older than 40,
- BMI greater than 30, and
- Patients with a history of epilepsy were also disqualified.

Patients who have received parenteral or oral analgesics during the last twenty-four hours prior to the beginning of the operation, or patients who have allergy medications.

A pneumatic tourniquet at 70 mmHg was applied on the same arm with the intravenous catheter. The study drug was given intravenously over 10 seconds, i.e., 1 ml of Inj. Ketamine 100mcg/kg in Group A and 1 ml of 0.9% of Normal Saline in Group B. 60 seconds after pre-treatment bolus, tourniquet was released and the first 25% of the calculated dose (2.5mg/kg) of Propofol was injected immediately intravenously over 20 seconds. Pain assessment was done 15 seconds after injection of 25% of calculated dose.

The pain score was assessed every 5 seconds till 15 seconds by an anaesthetist who has been blinded to the study using the verbal rating scale (VRS) during injection of Propofol and graded it as 0 to 3 in accordance with scale advocated by McCrirrick and Hunter (1990).9

At the conclusion of the procedure, the patients were sent to the recovery area, where the isoflurane was turned off, the laryngeal mask was removed, and they were given oxygen.

As a premedication, the patients were given an intravenous dose of metoclopramide calculated at 0.15 milligrams per kilogram. NiBP and HR readings were taken at 0 (the baseline), 1, 2, and 3 minutes following the administration of propofol.

Statistical analysis

Continuous data was reported as mean ± standard deviation. Comparison of age, sex, weight and ASA between the groups was obtained by Student’s t-test. Categorical data was reported as numbers and percentages and analysed using Chi-

square test or Fisher's exact test as appropriate. P <0.05 were considered as statistically significant.

Results

Table 1: Comparison between saline group and ketamine group regarding Age and BMI

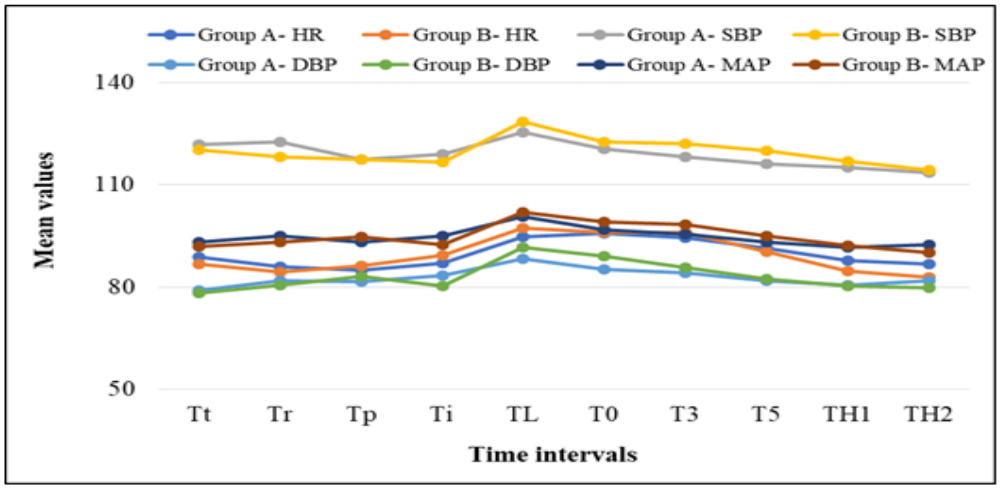
	Age Mean±SD	**BMI** Mean±SD
Saline group	**28.32±3.05**	**27.26±3.65**
Ketamine group	**29.25±2.32**	**29.56±5.23**
Test value Independent t-test	**1.72**	**2.73**
P-value	**0.9**	**0.9**
Sig.	**NS**	**NS**

Table 2: Comparison between saline group and ketamine group regarding pain score

Pain score	**No pain**	**Mild pain**	**Moderate pain**	**Severe pain**
Saline group	**3**	**6**	23	**28**
Ketamine group	**38**	**12**	9	**1**
Independent t-test	**43.21**			
P-value	< 0.001			
Sig.	**HS**			

Table 3: Comparison between saline group and ketamine group regarding heart rate

	Pulse rate 0	**Pulse rate 1**	**Pulse rate 2**	**Pulse rate 3**
Saline group	78.52± 12.35	83.25± 12.30	78.23± 11.23	78.23 ± 12.
Ketamine group	78.32± 8.36	84.32± 7.98	79.65 ± 7.56	82.36 ± 11.560.
Independent t-test	0.10	0.5	0.6	1.9
P-value	0.9	0.5	0.5	0.9
Sig.	NS	NS	NS	NS



Graph 1: Comparison of hemodynamic parameters between saline group and ketamine group

During the study period, a total of 60 patients were included and randomly divided into two groups of patients in each group. Both the groups were comparable with respect to demographic profile of the patients and preoperative vitals.

The comparison of pain score as per McCrirrick and Hunter evaluation scale between group A and group B at P5, P10 and P15 intervals were statistically highly significant (p value < 0.0001). Both the groups were comparable and found no significant difference with respect to hemodynamic profile.

Discussion

The intravenous anaesthetic propofol is versatile. Local injection site pain from propofol is uncertain, however it may be caused by: 1). direct irritation. 2) kinin cascade indirect impact. Bradykinin causes local vasodilation. Increased permeability may promote free nerve ending contact (3). Propofol injection pain depends on place, vein size, injection speed, aqueous concentration, and syringe material temperature. If a vein on the dorsum of the hand is used, propofol injection can cause 90% pain. [10]

Various strategies have been employed to reduce propofol injection pain. In their investigation, Sadawy et al. [11] utilized various medications, including ketamine, thiopental, meperidine,

lidocaine, and saline Ketamine was determined to be the most efficient pain reliever when paired with venous occlusion. We found that most medications evaluated for reducing propofol injection discomfort did not provide any haemodynamic benefits. Therefore, we investigated ketamine, which has opposite effects to propofol. Additionally, its local anesthetic action can reduce pain during propofol injections.

Anesthesia quality is judged by patients' memory of operation pain and discomfort. When Propofol alone is used for induction, 70% of patients suffer pain. Avoiding discomfort on Propofol injection is desirable because pain limits an otherwise helpful medicine.

In the current study, the incidence of propofol injection discomfort was reduced from 95% in the group that received saline to 63% in the group that received ketamine pre-treatment. The use of ketamine resulted in a total elimination of the occurrence of severe pain.

The findings of Tan et al [12] who discovered that ketamine pre-treatment reduced the occurrence of pain from 84% to 26%,and The incidence of propofol injection pain in the Naglaa Mohammad et al. [13] Study was reduced from 93.2% in saline group to 55% in ketamine group. Sangawar et al [14] found that total patients who experienced pain were 28 patients in group B (77.78%) as compared to 5 patients (13.89%) in group A, which was statistically highly significant, (p value <0.0001).

During the perioperative period, the hemodynamic parameters (SBP, DBP, HR, and SpO2) were monitored and recorded at a number of different time intervals. It was determined that the differences in heart rate between the two groups were not statistically significant. This is correlated with other studies Sangawar et al, Sadawy et al. Tan et al. Naglaa Mohammad et al, A comparable temporary spike in mean systolic blood pressure was noted in both groups at laryngoscopy and intubation, and it was maintained till 5 minutes post intubation.

This phenomenon, which can be related to the stress response of laryngoscopy and intubation, was observed in both groups at laryngoscopy and intubation.

After giving 25% of the total dose of Propofol and the full dose, both groups' systolic blood pressure dropped sequentially, this was statistically insignificant. Both groups' systolic blood pressure variations were not clinically significant and did not require treatment. Propofol lowers arterial blood pressure following anesthesia. This reduces peripheral vascular resistance, inhibiting sympathetic activity and cardiac contractility.

During laryngoscopy and intubation, there was a momentary increase in diastolic blood pressure in both group A and group B, but it was not statistically significant. This is correlated with other studies Sangawar et al, Sadawy et al. Tan et al. Naglaa Mohammad et al

Conclusion

Pre-treatment with low-dose ketamine greatly reduces pain after propofol injection. After receiving an injection of propofol, the short-term preservation of hemodynamics was more effective than when receiving a placebo. The usage of ketamine at low doses does not result in any adverse consequences. It would appear that administering a low dosage of ketamine followed by propofol is the most effective way to manage the pain associated with medication injections.

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