

ADMINISTRATION OF LOW DOSE KETAMINE FOR REDUCTION OF PROPOFOL INJECTION PAIN- A PROSPECTIVE STUDY

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ABSTRACT

Background: The intravenous administration of propofol often leads to significant pain. Previous studies have indicated that ketamine can effectively alleviate this pain. Aims: This study aimed to evaluate the effectiveness of low-dose ketamine in reducing propofol injection pain. **Material & Methods:** Conducted at a tertiary care hospital's Department of Anesthesiology from February 2019 to November 2019, the randomized controlled clinical trial enrolled 70 patients aged 18-65 years undergoing surgical procedures under general anesthesia (GA) with ASA physical status I or II. Participants were randomly assigned to two groups: Group K received ketamine 100µg/kg pre-treatment, while Group S received 0.9% normal saline. Ketamine or saline was injected over 10 seconds with a forearm tourniquet, followed by propofol injection. Pain was assessed using a Verbal Rating Scale (VRS) graded from 0 to 3, and hemodynamic parameters were recorded peri-operatively. **Results:** In Group K, 81.5% of subjects experienced no pain, 15.6% had mild pain, and 2.9% experienced moderate pain. In Group S, 34.6% experienced no pain, 28.5% had mild pain, 25.2% experienced moderate pain, and 11.7% reported severe pain. Additionally, no statistically significant differences in mean heart rate and mean arterial pressure were observed between the groups ($p>0.05$). **Conclusion:** Pretreatment with ketamine 100 µg/kg before propofol injection resulted in a reduction in propofol-induced injection pain. This suggests the potential of low-dose ketamine as an effective strategy for managing propofol injection pain. **Keywords:** ketamine, injection pain, propofol.

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INTRODUCTION

Propofol is a popular intravenous induction agent, administered for short surgeries, day surgery & when usage of laryngeal mask is required. It produces intense burning pain on injection, in around 28–90% of the patients. (1) Etiological factors behind this may be attributed to size & site of vein, speed of injection, pH of the agent, iv fluid rate, temperature & concentration. Various techniques have been used to reduce this pain , including metoclopramide, local anesthetics (2,3) pretreatment with iv lignocaine, preparation of skin with nitroglycerin ointment (4), chilling of the propofol to 4 °C (5), addition of lignocaine to the propofol emulsion , injection into large antecubital veins or into a freely flowing intravenous line (6) and the

dilution of the propofol emulsion with intra-lipid.(7) Also usage of novel propofol emulsions, modified emulsions and micro-emulsions formulations have been introduced .

Ketamine has potent analgesic and local anesthetic properties. In sub-anesthetic doses, it attenuates the afferent pain pathway, reduces the injection pain of propofol. Ketamine has less marked cardiorespiratory depressant effects than other drugs.

Thus, this prospective randomized study was undertaken to assess the efficacy of low dose ketamine in reduction of propofol injection pain. (8)

MATERIALS AND METHODS

This randomized controlled clinical trial was conducted in the Department of Anesthesiology of our tertiary care hospital from February 2019 to Nov 2019. The study recruited 70 patients aged 18-65 years who were admitted for surgical procedures under general anesthesia (GA) with American Society of Anesthesiologists (ASA) physical status I or II.

Patients with diabetes, hypertension, cardiovascular, respiratory diseases, neurological deficits, allergy to the study drug and propofol were excluded from the study. Institutional ethical consent was sought & a written informed consent was taken from the study subjects.

The study subjects were randomly divided into two groups:

Group K- pre-treatment with ketamine 100µg/kg. (1ml)

Group S- pre-treatment with 0.9% normal saline (1ml)

The study drug was prepared by an experienced anesthesiologist who was not a part of the study by diluting the drug with normal saline. A tourniquet was applied over the forearm & ketamine was injected over 10 seconds, after which tourniquet was removed. The first 25% of the dose of propofol (2.5 mg/kg) was injected over 20 seconds. The pain was assessed using verbal rating scale for every 5 seconds & graded as 0 to 3. Remaining dose of propofol was given for the induction of anesthesia following standard protocol. The hemodynamic parameters were recorded in the peri-operative period at various time intervals viz. baseline, after test drug, after induction, after intubation, after 3 & 5 minutes of intubation.

Statistical analysis

The tabulated data was statistically analyzed using SPSS version 22.0 for Windows (IBM Corp, India). Quantitative data are presented as mean \pm SD or proportions. Intergroup comparisons were made using Student's paired t-test. P-value 0.05 at a 90% confidence interval was considered to be statistically significant. Values were expressed as number (n) and percentage (%).

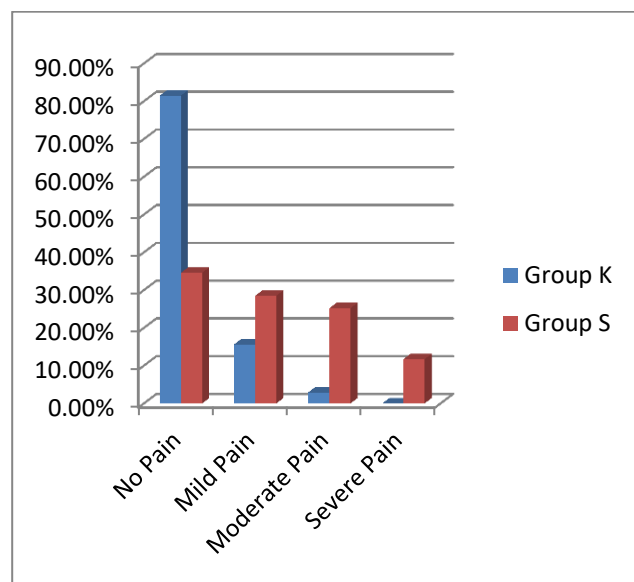
RESULTS

Both the groups were comparable with respect to baseline demographic parameters ($p>0.05$). The average age of study subjects in Group K was 38.34

\pm 2.81 years while in Group S it was 37.17 \pm 3.22 years. The average weight of the study subjects was 64.27 \pm 3.92 kg while in Group S it was 65.26 \pm 3.76 kg. Gender and ASA physical status did not show any statistically significant difference between the groups ($p>0.05$).

In Group K, 81.5% of the study subjects experienced no pain, 15.6% experienced mild pain & 2.9% experienced moderate pain. In Group S, 34.6% of the study subjects experienced no pain, 28.5% experienced mild pain, 25.2% experienced moderate pain & severe pain in 11.7%. (Fig 1) Also, the mean heart rate and mean arterial pressure (MAP) at different time intervals showed no statistically significant difference between the groups ($p>0.05$).

Fig 1 shows the pain experienced by study subjects in Group K & Group S



DISCUSSION

Propofol is the most commonly used IV anesthetic. It has short duration of onset, excellent recovery profile but its use is associated with pain on injection, increased triglyceride levels & potential for microbial contamination. In about 30%-90% of cases intense pain occurs after propofol injection. (9)

In the present randomized, double blinded controlled study, the demographic profiles, weight, height and ASA physical status of the patients, were comparable between the study and the control groups ($p>0.05$). In Group K, 81.5% of the study subjects experienced no pain, 15.6% experienced mild pain & 2.9% experienced moderate pain. In

Group S, 34.6% of the study subjects experienced no pain, 28.5% experienced mild pain, and 25.2% experienced moderate pain & severe pain in 11.7%. Similarly, Taloh Y et al 2018 observed no pain in 80% patients in ketamine group & 2% in saline group. (8) Other similar studies were conducted by Shriyan et al (10), Qattan et al (11). Ommid M et al 2019 evaluated low dose Ketamine and Fentanyl as a pre medication for reduction of pain due to propofol infection. (12)

Iman et al concluded that pretreatment with ketamine 0.4 mg/kg was effective in elimination of pain. Seung WK et al concluded administration of ketamine 100 µg/kg before propofol injection. (13)

In the present study, On pretreatment with ketamine, pain reduction was observed which may be attributed to analgesic properties of ketamine in sub-anesthetic doses mediated via the μ or δ receptors, and it may also be a μ antagonist and κ -agonist. (15) Such observations have also been noted by Qattan et al (11), Taloh Y et al (8) & Saadawy et al. (7)

In the present study, the mean heart rate and mean arterial pressure at different time intervals showed no statistically significant difference between the groups ($p > 0.05$). Accordingly, Tan C H et al (14) study observed hypotension in 58% of the patients in ketamine group and 60% in the control group. No incidence of heart rate of < 50 beat/min was observed. This may be attributed to the fact that the cardio-stimulant effects of ketamine balanced the cardio-depressant effects of propofol. (15) Propofol induces a fall in the mean arterial blood pressure after Induction of anesthesia. This is caused by the reduction in peripheral vascular resistance, inhibition of both the sympathetic activity and myocardial contractility. Pretreatment with ketamine is advantageous with non-significant decrease in the arterial pressure compared to preoperative level. This could be explained by the positive effect of ketamine on sympathetic stimulation leading to increase in myocardial contractility and vascular resistance, which in turn leads to increase arterial pressure. (16)

Applying a tourniquet, helped in achieving local action of the ketamine at the peripheries. (16) This can be a useful method for studying the peripheral actions of the drug by excluding its central effects. In the present study, a tourniquet was applied briefly before injection of pretreatment drug, which was released during propofol induction.

CONCLUSION

The present study concludes prior administration of low dose ketamine before propofol injection with a tourniquet, statistically significantly reduced pain due to propofol injection without any significant adverse hemodynamic effects. Further large scale randomized clinical trials should be conducted to come to a definite conclusion.

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