

Original Article



Effect of Low Dose Ketamine on Propofol Injection Pain: A Double-Blind Clinical Trial

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Abstract

Background: Propofol, most frequently used intravenous anesthetic for induction of routine elective surgical procedure. Pain on propofol injection (POPI) still remains a considerable concern for the anesthesiologist. A number of techniques has been tried to minimize propofol-induced pain with variable results. **Objective:** This study was performed to determine the effect of ketamine on reducing pain on propofol injection (POPI) at the onset of anesthesia. **Materials and Methods:** A total of 80 adult healthy patients were selected in this study of either sex, scheduled for routine elective ENT surgery under general anesthesia. The patients enrolled were divided randomly into two groups of 40 patients each. Group I (ketamine group) received 10 mg intravenous ketamine in 10 ml normal saline. Group II (placebo group) received 10 ml of 0.9% intravenous normal saline. Then the patients were induced with propofol and asked to report their pain during injection of propofol and recorded according to the Mc Cririck and Hunter scale. **Results:** The incidence of pain experienced in ketamine group was 10% patients and in saline group was 60% patients, which is statistically significant $p < 0.05$. The severity of POPI was also lower in ketamine group than the saline group ($p < 0.05$). The incidence of mild and moderate pain in ketamine group versus saline group was 7.5% versus 45% and 2.5% versus 15% respectively $p < 0.05$. There was no severe pain recorded in any groups. **Conclusion:** Intravenous ketamine in low dose before induction of general anesthesia can be effective medication in reducing pain on propofol injection.

Key words: Ketamine, Propofol, Pain on propofol injection (POPI).

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Introduction

Propofol is a popular anesthetic induction drug that can cause considerable discomfort or pain at the site of injection.¹⁻³ During induction of anesthesia, 37.5% to 90.0% of patients experience pain on propofol injection when a vein on the dorsum of the hand is used.⁴ Many methods have been proposed to reduce the incidence of pain on propofol injection, including varying injection speed and carrier fluid, an adding other concomitant drugs, including the injection of low doses of narcotics such as pethidine, sufentanil and butorphanol, lignocaine injection together with tourniquet closure, cold-warm propofol, magnesium, beta blocker, 5-HT₃ receptor

antagonists, Alpha 2 agonists like dexmedetomidine.⁵⁻¹⁷

Ketamine is a drug with analgesic effects, used in induction of anesthesia. It is an N-methyl-D-aspartate (NMDA) receptor antagonist with strong analgesic effects, even at low concentrations. Some studies have revealed that ketamine can significantly reduce the pain caused by propofol injection.^{18,19}

The present study was conducted to determine the efficacy of intravenous ketamine 10 mg in comparison with placebo (normal saline) on incidence and severity of pain on propofol injection (POPI).

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Materials and Methods

After obtaining written informed consent, the study was conducted on 80 normal healthy adult patients, who were scheduled for elective ENT surgery in National Institute of ENT Dhaka during the period of July 2018 to September 2018. Patients taking regular analgesics or sedatives, suffering from acute or chronic pain syndromes, or any neurological or cardiovascular diseases, thrombophlebitis, known allergy to propofol or ketamine were excluded. All patients had routine examination for fitness of general anesthesia.

When the patient arrived in the operating room, routine monitoring was applied and values were recorded then a 20-G IV cannula was inserted on the dorsum of the non-dominant hand and Ringer's Lactate was started. No other solution was injected before the induction of anesthesia with propofol. Patients were randomly assigned into two groups: Group I (ketamine group) received ketamine 10 mg in 10 ml saline with venous occlusion for 1 min and Group II (saline group) received 10 ml saline with venous occlusion for 1 min. Venous occlusion was performed using a rubber tourniquet placed on the upper arm after elevating the arm for 30 seconds for gravity drainage of venous blood. Before induction of anesthesia, the patients were informed that they would be receiving an intravenous (IV) anesthetic that may cause pain in the forearm. Sixty seconds after the pretreatment bolus, the occlusion was released and propofol 2.5 mg/ kg was administered through the same 20-G catheter at the rate of 1 ml/second. Fifteen seconds after injection of 25% of the dose of propofol, patients were asked by an independent, second anesthesiologist to grade their pain as per McCririck and Hunter scale.10After assessment of the pain intensity, the rest of the dose of propofol was given and anesthesia was continued as planned.

Grading of pain: As per Mc Cririck and Hunter scale 20

0= No pain

1=Mild pain (pain reported only in response to questioning without any behavioral signs)

2=Moderate pain (pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning).

3=Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears).

For comparison of quantitative variables between the two groups, the unpaired t-test and for qualitative variables the Chi-squared test was used. The statistically significant level was P<0.05.

Results

There was no significant demographic difference between the groups (Table I).

Basal Mean arterial pressure (MAP) and Heart rate (HR) were comparable in both groups. There was no significant difference of MAP and HR between ketamine and saline groups during pre-intubation or three minutes post-intubation period (p>0.05) (Table II).

The incidence of pain experienced in ketamine group (group I) was 10% patients and in group II (saline group) was 60% patients, which was statistically significant p<0.05 (Table III). The severity of POPI was also lower in ketamine group than the saline group (p<0.05) (Table III). The incidence of mild and moderate pain in groups I versus group II was 7.5% versus 45% and 2.5% versus 15% respectively p<0.05. There was no severe pain recorded in any groups.

Table I: Comparison of demographic data between the two groups

Parameters	Group I (Ketamine group) n=40.	Group I (Saline group) n=40.	p value
Age in years (mean±SD)	34.23±8.48	35.32±9.63	p>0.05
Weight in kg (mean±SD)	64.23±8.56	65.86±7.93	p>0.05
Sex (male/female)	23/17	22/18	p>0.05
ASA Physical status I/II	37/3	36/4	p>0.05

Table II: Changes of mean arterial pressure and heart rate between two groups

Hemodynamic parameter	Basal		Post intubation	
	Group I / Group II			
Mean arterial pressure (MAP) mm Hg	94/96	92/90	105/102	
Heart rate per minute	78/82	75/73	91/87	

Table III: Incidence and severity of pain following propofol injection between two groups

Characteristics of pain	Group I (Ketamine group) n=40. Number and %	Group II (Saline group) n=40. Number and %	p value
No pain	36 (90%)	16 (40%)	p <0.05
Pain	4 (10%)	24 (60%)	p <0.05
Mild pain	3 (7.5%)	18 (45%)	p <0.05
Moderate pain	1(2.5%)	6 (15%)	p <0.05
Severe pain	0	0	-

Discussion

Pain on propofol injection is a common problem, can be immediate or delayed. The immediate pain could be the result of a direct irritant effect, but the kinin cascade is probably the cause of delayed pain. The lipid solvent for propofol activates the plasma kallikrein-kinin system which results in bradykinin production that increases local vein permeability and dilation. The aqueous-phase propofol diffuses into more free nerve endings outside the endothelial layer of the vessel which is more permeable and dilated because of bradykinin effect, thereby intensifying pain on injection.²⁰

In present study, the overall incidence and severity of pain were significantly less in ketamine group compared to placebo group.

The incidence of no pain was significantly higher in ketamine group (90%) than placebo group (40%). The incidence of mild pain in ketamine group and placebo group were 7.5% and 45% respectively and incidence of moderate pain in those groups were 2.5% and 15% respectively. A study on prevention of pain induced by intravenous injection of propofol using ketamine, magnesium sulfate and lignocaine and they found POPI in 16% patients in ketamine group.²¹

Batra et al.¹⁸ had a study on attenuation of propofol injection pain using ketamine pretreatment with venous occlusion and they observed 12% patients experienced POPI.

An investigator compared the effect of ketamine, magnesium sulfate and sodium-thiopental on propofol injection pain. Their observation was 4% patients complained pain during propofol injection.²²

Another study done on preventing POPI using ketamine and found 8% patients had pain during propofol injection.²³

The results of present study are comparable to those of Khoshfehrat et al. and Batra et al. These studies were done using the same dose (0.1 mg/kg) of ketamine. But the results of Akbariet al.²² and Saadawy et al.²³ are lower because they used larger dose of ketamine (0.5 mg/kg and 0.4 mg/kg respectively).

Conclusion

According to the result of present study, it can be concluded that pretreatment with low dose of intravenous ketamine with venous occlusion attenuates pain on propofol injection.

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