ORIGINAL ARTICLE

Use of Dexmedetomidine for Preventing Pain on Propofol Injection: A Double Blinded Placebo Controlled Study

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ABSTRACT

Background and aim of study: Propofol is a commonly used drug for general anesthesia. It can irritate the skin, mucous membrane and venous intima. The main drawback is the pain during intravenous injection. Aim of this prospective randomized study is to observe the efficacy of intravenous dexmedetomidine as pretreatment for the prevention of pain caused by the propofol injection.

Methods: A total of 80 adult patients were selected in this study with either sex, ASA (American Society of Anesthesiologists) grade I and II, scheduled for routine elective surgical procedure under general anesthesia. The patients enrolled were divided randomly into two groups of 40 patients each. Group I received 0.25 mcg of intravenous dexmedetomidine in 5 ml. Group II (placebo group) received 5 ml of 0.9% intravenous normal saline one minute before injection of propofol. The patients were asked to report their pain during injection of propofol according to the McCririck and Hunter scale.

Results: The incidence of pain experienced in dexmedetomidine group was 35% patients and in saline group was 70% patients ($p < 0.05$). The severity of POPI was also lower in dexmedetomidine group than the saline group ($p < 0.05$). The incidence of mild and moderate pain in dexmedetomidine groups versus saline group was 20% versus 45% and 15% versus 25% respectively $p < 0.05$. There was no severe pain recorded in any groups.

Conclusion: Pretreatment with 0.25 mcg/kg of dexmedetomidine with venous occlusion for one minute, effectively reduces pain on propofol injection.

Key Words: Dexmedetomidine, propofol, general anesthesia, pain on propofol injection (POPI).

Introduction

Propofol (2, 6-diisopropylphenol) is a widely used intravenous anesthetic agent to induce general anesthesia.[1] However, pain following propofol injection is one of the adverse effects of propofol, which occurs in 60% to 80% of patients receiving propofol via peripheral vein on the dorsum of hand.[2-4] Several methods including pretreatment with lignocaine with venous occlusion or premixed lignocaine with propofol have been tried to attenuate pain on propofol injection (POPI). Among these methods, pretreatment with lignocaine with venous occlusion is the most effective method in preventing pain following propofol injection.[5,6] However, unfortunately this treatment could not abolish the pain. It is reported that the amount of free propofol in the aqueous phase of the emulsion is positively

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associated with injection pain. Therefore, propofol long-chain triglycerides (LCT)/medium-chain triglycerides (MCT) was introduced in attempts to prevent injection pain by reducing the concentration of aqueous-free propofol.[7] However, pain can occur up to 47% during injection of propofol-LCT/MCT.[8] It was demonstrated that pretreatment with lignocaine with venous retention before injection of propofol LCT or lignocaine premixed in propofol LCT were more effective in reducing pain than a more expensive reformulation of propofol-LCT/MCT.[8,9] Other studies have suggested methods for controlling POPI, including the injection of low doses of narcotics such as sufentanil and butorphanol,[10,11] injection in large vessels, cold-warm propofol.[12] Some researcher used magnesium,[13] beta blocker,[14] 5-HT3 receptor antagonists,[15] $Alpha_2$ agonists like dexmedetomidine[16] and metoclopramide injection as a premedication for prevention of POPI.

The possible mechanism involved in decreasing propofol injection pain by dexmedetomidine is not fully understood. The possible mechanism might be due to $alpha_1$ and $alpha_2$ stimulation causing release of vasodilator prostaglandins that antagonize the vasoconstrictor response. This modulation of the sympathetic response of the venous smooth muscle might be important in endothelial dysfunction causedby propofol.[17] It may be due to hyperpolarization-activated conductance in the peripherally mediated antinociception, but the peripheral analgesic effects of dexmedetomidine have not yet been fully elucidated. But as dexmedetomidine is more potent $alpha_2$ adrenergic agonist compared to clonidine, the peripheral antinociception produced by clonidine-like drugs mediating the local release of enkephalin-like substances is also possible.[18,19] The present study was conducted to determine the efficacy of intravenous dexmedetomidine 0.25mcg/kg, in comparison with placebo (normal saline) on incidence and severity of pain on propofol injection (POPI).

Materials & Methods

The present double-blind clinical study was conducted on 80 adult patients undergoing elective ENT surgeries in National Institute of ENT, Dhaka during the period of July to October 2018 after receiving informed consent from the patients.The inclusion criteria were ages 20-50 years, Class I and II American Society of Anesthesiology (ASA), no history of known skin disease and severe burns in the organs, lack of diabetes or heart, liver and kidney disorders, no history of known allergy to used drugs, no history of addiction to alcohol and oral or injectable drugs.

The patients were randomly divided into two equal groups of 40 after enrolment in the study. Group I which was scheduled to receive 0.25 mcg/kg intravenous dexmedetomidine in 5 ml normal saline and Group II which was scheduled to receive 5 ml intravenous normal saline before induction of general anesthesia. On arrival to the operation room, standard monitoring was applied to all patients including pulse oximeter, electrocardiogram and noninvasive arterial blood pressure. A 20-gauge intravenous cannula was placed on the dorsum of non-dominant hand of the patient and Ringer's solution was started. Patients received no premedication. While the venous drainage was occluded by placing an air-filled tourniquet (pressure inflated to 70 mm Hg) on the upper arm by an assistant; a blinded anesthesiologist injected prepared study drug or saline according to the allocation. The occlusion was released after one minute. First one-fourth of induction dose (2 mg/kg) of propofol was injected slowly over 10 seconds. The pain intensity was measured based on McCririck and Hunter scale.[20] After the assessment of pain, induction of anesthesia was completed with the remaining dose of propofol then tracheal intubation was facilitated with the injection of succinylcholine. Anesthesia was maintained with injection of fentanyl, vecuronium, oxygen, nitrous oxide (66%) and halothane. When surgery was completed general anesthesia was reversed as usual.

Grading of pain: As per McCririck 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).

Statistical analysis: 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 MAP and HR were comparable in both groups. There were no significant differences of MAP and HR between dexmedetomidine and saline groups during pre-intubation or three minutes post-intubation period ($p > 0.05$) (Table II). The incidence of pain experienced in dexmedetomidine group (group I) was 35% patients and in group II (saline group) was 70% patients, which was statistically significant $p < 0.05$ (Table III). The severity of POPI was also lower in dexmedetomidine group than the saline group ($p < 0.05$) (Table III). The incidence of mild and moderate pain in groups I versus group II were 20% versus 45% and 15% versus 25% 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 (Dexmedetomid-inegroup) n=40	Group II (Saline group) n=40	p value
Age in years (mean±SD)	38.23±8.12	37.65±9.32	p>0.05
Weight in kg (mean±SD)	64.86±8.72	65.28±9.36	p>0.05
Sex (male/female)	25/15	26/14	p>0.05
ASA Physical status I/II	36/4	37/3	p>0.05

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

Hemodynamic parameter	Basal Group I/Group II	Pre intubation Group I/Group II	Post intubation Group I/Group II
Mean arterial pressure (MAP) mm Hg	94/97	90/92	105/108
Heart rate per minute	78/81	73/77	91/93

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

Characteristics of pain	Group I (Dexmedetomidine group) n=40 Number and %	Group II (Saline group) n=40 Number and %	p value
No pain	26 (65%)	12 (30%)	p <0.05
Pain	14 (35%)	28 (70%)	p <0.05
Mild pain	8 (20%)	18 (45%)	p <0.05
Moderate pain	6 (15%)	10 (25%)	p <0.05
Severe pain	0	0	-

Discussion

Propofol, an excellent IV anesthetic belonging to the phenol group, can irritate the skin, the mucous membrane and the venous intima. The mechanism of pain is attributed to the activation of the kinin-kallikrein system that releases bradykinin, causing vasodilatation and hyper-permeability, thereby increasing contact between the aqueous phase propofol and the free nerve endings. A number of drugs were tried for attenuation of propofol injection pain.

In the present study, the overall incidence and severity of pain were significantly less in dexmeditomidine group compared to placebo group. The incidence of pain experienced in dexmedetomidine group (group I) was 35% patients and in group II (saline group) was 70% patients ($p < 0.05$). The severity of POPI was also lower in dexmedetomidine group than the saline group ($p < 0.05$). The incidence of mild and moderate pain in groups I versus group II were 20% versus 45% and 15 % versus 25% respectively $p < 0.05$. There was no severe pain recorded in any groups. The study done by Singh *et al.*[21] in alleviating propofol

injection pain using 0.25 mcg/kg of dexmedetomidine and 0.5 mg/kg lignocaine and recorded POPI in 37.14% and 20% patients respectively. Debnath *et al.*[22] had a comparative study of effects of dexmedetomidine and lignocaine in alleviating propfol injection pain in a tertiary care center, their result showed 34% patients experienced pain on propofol injection. Another study on attenuation of POPI by Turan *et al.*[23] comparing the effect of dexmedetomidine and lignocaine and found 33.34% complained pain during propofol injection in dexmedetomidine group. Uzan *et al.*[18] also had a study on prevention of POPI using dexmedetomidine and pain recorded 43% patients during injection of propofol. The result of present study is nearly similar to the above studies except that of Uzan *et al.*[18] which is a bit higher.

Conclusion

Pretreatment with a dose of 0.25mcg/kg dexmedetomidine intravenously administered with mid-arm occlusion applied for one minute before propofol administration can effectively reduce the incidence and severity of pain on propofol injection.

Conflict of interest: None.

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