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Original Article

Effect of Intravenous Dexamethasone on Propofol Injection Pain: A Randomized Placebo Controlled Study

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Abstract:

Background and aim of study: *Pain on propofol injection (POPI) is a common problem. None of the commonly used methods completely attenuate the pain. Inflammatory response to propofol contributes to the pain. This study was conducted to compare the efficacy of dexamethasone in attenuation of pain following intravenous injection of propofol.*

Materials and methods: *A total of 80 adult patients were scheduled in this study with either sex, ASA (American Society of Anesthesiologists) grade I and II, for routine elective surgical procedure under general anesthesia. The patients enrolled were divided randomly into two groups of 40 patients each. Group I received 0.15 mg/kg of intravenous dexamethasone in 5 ml normal saline and Group II (placebo group) received 5 ml of 0.9% intravenous normal saline, following exsanguination and occlusion of the vein of the arm. This was followed by 0.5 mg/kg of propofol intravenously.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 dexamethasone group was 45% patients and in saline group was 70% patients ($p<0.05$). The severity of POPI was also lower in dexamethasone group than the saline group ($p<0.05$). The incidence of mild and moderate pain in dexamethasone groups versus saline group was 30% versus 45% and 15% versus 25% respectively $p<0.05$. There was no severe pain recorded in any groups.*

Conclusion: *Pretreatment with intravenous dexamethasone (0.15 mg/kg) before injection of propofol is effective and safe in reducing the incidence and severity of pain on propofol injection (POPI).*

Key words: *Dexamethasone, propofol, general anesthesia, pain on propofol injection (POPI).*

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Introduction:

Propofol is a popular intravenous general anesthetic agent because of its rapidity and reliability in causing loss of consciousness associated with quick and smooth recovery. However, pain onpropofol injection (POPI), which has been reported to occur in 40-86%.[1] The need to treat propofol-induced nociception is essential not only because it is unpleasant, but also because it can lead to serious sequelae such as myocardial ischemia when hemodynamic changes occur in response to the pain associated with injection.[2]

The mechanism of pain from vascular tissues following propofol injection are multifactorial in origin. Propofol has been demonstrated in vitro to stimulate nitric oxide (NO) release.[3] Nociceptive nerve endings have been found in the endothelium of veins in humans, a well-known source of NO, suggesting a role of NO in nociception.[4,5] In addition, NO from the vascular endothelium binds to guanylcyclase which catalyzes the conversion of guanosine triphosphate to guanosine monophosphate, which facilitates PGE2-induced hyperalgesia.[6] It has been found that pain following intravenous injection of bradykinin and hyperosmolar solutions can be blocked by pretreatment with NO synthase (NOS) inhibitor, suggesting that an intact NOS pathway is needed to elicit vascular nociception.[7]

Several methods for prevention of pain have been tried with varying degrees of success like addition of lignocaine,[8-10] cooling[11,12] or warming[13] of the drug, diluting propofol solution,[14] pretreatment with ondansetron,[15] metoclopramide,[16] opioids,[17] thiopentone,[18] paracetamol,[19] dexamethasone[20] and dexmedetomidine.[21]

Recent studies have shown that dexamethasone reduces postoperative pain, nausea and vomiting.[22,23] It is known that propofol releases nitric oxide (NO) from the vessels animal and human models and causes pain in vein.[24,25] The effect of corticosteroids such as dexamethasone has been shown to reduce the production of NO,thereby reducing pain on propofol injection (POPI).[26,27]

The present study was conducted to determine the efficacy of intravenous dexamethasone 0.15mg/kg, in comparison with placebo (normal saline) on incidence and severity of pain on propofol injection (POPI).

Materials and methods:

The present prospective, randomized study was conducted in National Institute of ENT Dhaka, during the period of September to November 2018. After obtaining written informed consent, a total of 80 patients, ASA grade I and II were taken up in the study with the age group of 20 to 50 years of either sex scheduled for routine elective surgical procedure under general anesthesia with endotracheal intubation. Patients excluded were those who had history of adverse effects to study drugs, presence of hepatic or renal dysfunction, patients with seizure disorder, history of drug abuse and uncontrolled hypertension. Pre-anesthetic check-up was done a day before surgery including a detailed history, a thorough physical and systemic examination. Routine investigations included CBC, routine urine test, electrocardiogram, serum urea, serum creatinine, blood sugar and chest radiograph. The patients were fasted for 8 hours preoperatively.

In the operating room, monitors including non-invasive arterial pressure, electro-cardiography and pulse oximetry were applied. The patients enrolled were divided randomly into two groups of 40 patients each.

Group I was selected for pretreatment with 0.15 mg/kg of intravenous dexamethasone in 5 ml normal saline and group II was selected for pretreatment with 5 ml of intravenous normal saline. A 20 G intravenous cannula was placed in a vein on the dorsum of the no-dominant hand and Ringer's Lactate solution was started 100 ml/ hour. The mid arm of the side on which cannula was placed on the dorsum of hand was occluded by a BP cuff. The study drug was then injected and maintained in the vein for 1 minute. After 1 minute, the occlusion was released and one fourth of total calculated dose (0.5 mg/kg) of propofol was injected over 5 seconds. Then the patients were asked by a blinded investigator to any sensation of pain during injection of propofol as per the McCririck and Huntescale.[12]

After the assessment of pain, induction of anesthesia was completed with the remaining dose of propofol, and 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.[12]

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 mean arterial pressure (MAP) and heart rate (HR) were comparable in both groups. There were no significant differences of MAP and HR between dexamethasone and saline groups during pre-intubation or three minutes post-intubation period ($p>0.05$) (Table II).

The incidence of pain experienced in dexamethasone group (group I) was 45% 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 dexamethasone group than the saline group ($p<0.05$) (Table III). The incidence of mild and moderate pain in groups I versus group II were 30% 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 (Dexamethasone group) n=40	Group II (Saline group) n=40	p value
Age in years (mean±SD)	34.92±5.42	35.83±4.17	p>0.05
Weight in kg (mean±SD)	64.36±6.34	65.72±5.58	p>0.05
Sex (male/female)	25/15	26/14	p>0.05
ASA Physical status I/II	37/3	38/2	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 after 3 minutes Group I / Group II
Mean arterial pressure (MAP) mm Hg	92/94	84/82	102/105
Heart rate per minute	78/80	72/70	88/90

Table III :

Incidence and severity of pain following propofol injection between two groups

Characteristics of pain	Group I (Dexamethasone group) n=40	Group II (Saline group) n=40	p value
No pain	22 (55%)	12(30%)	p <0.05
Pain	18 (45%)	28 (70%)	p <0.05
Mild pain	12 (30%)	18 (45%)	p <0.05
Moderate pain	6 (15%)	10 (25%)	p <0.05
Severe pain	-	-	-

Discussion

The most important finding of this study was the reduction in the number of subjects that reported pain following propofol injection when pretreated with dexamethasone compared to saline. Systemic dexamethasone has been commonly used perioperatively to minimize postoperative nausea and vomiting and to improve overall quality of recovery. In addition, dexamethasone has been shown to decrease nitric oxide production which has been shown to mediate propofol-induced vascular pain.[6] The present study suggests that the preoperative administration of dexamethasone also diminishes pain on propofol injection.

In present study, the overall incidence of pain on propofol injection experienced in dexamethasone group (group I) was 45% patients and in group II (saline group) was 70% patients, which was statistically significant p<0.05. The severity of POPI was also lower in dexamethasone group than the saline group (p<0.05). The incidence of mild and moderate pain in groups I versus group II were 30% versus 45% and 15 % versus 25% respectively p<0.05.

Adinehmehr et al.[28] had a study to evaluate the effect of pretreatment on reducing the pain by the injection of propofol. The first group received 1 mg granisetron in 5 ml, the second group received 0.15mg/kg dexamethasone in 5 ml normal saline. The incidence of pain following the injection of propofol was significantly decreased with both granisetron and dexamethasone (50.7% and 49.4%).

Ahmad et al.[29] compared the effect of dexamethasone and intravenous lignocaine on intravenous propofol pain along with saline. The results of that study indicated the

effect of dexamethasone on reducing the pain by intravenous injection of propofol. The incidence of pain after the injection of propofol was 60% in the saline group, 26% in the lignocaine group, and 41% in the dexamethasone group. They used dexamethasone in a dose of 0.25 mg/kg.

Present study showed that 45% patient experienced pain following propfol injection which is nearly similar to the above studies.

Conclusion

It can be concluded that, venous priming with a dose of 0.15mg/kg dexamethasone administered with mid-arm tourniquet applied for one minute before propofol administration can reduce the incidence and severity of pain on propofol injection without significant adverse effects.

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