

ORIGINAL
ARTICLE**The Effect of Dexamethasone in Reducing Propofol Injection
Pain in 6 to 13-Year-Old Children Undergoing
Adenotonsillectomy Surgery: A Double-Blind Clinical Trial**Seyyed Hassan Karbasi¹, Pooya Derakhshan², Hossein Hashemi^{3*}¹ Associate Professor, Department of Anesthesiology, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran.² Assistant Professor, Department of Anesthesiology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran.³ Bachelor of Anesthesiology, Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran

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Abstract

Introduction: Propofol is a popular intravenous anesthetic and a quick inducer of anesthesia with quick recovery. However, its downside lies with pain and discomfort during intravenous injections when injected in small blood vessels in the back of the hand, which prevails in 85% of children. This study investigates the effect of Dexamethasone in reducing propofol injection pain in children.

Methods: In this double-blind clinical trial, 50 children aged from 6 to 13 years undergoing elective Adenotonsillectomy in Birjand-based Valiasr Hospital were randomly assigned into case and control groups. Intravenous cannulation was performed with intravenous cannula No. 22 on hands of all participants. Under similar conditions, 0.2 mg (oral) Midazolam as premedication and 20 ml of juice were administered for all the patients two hours before surgery. The same volume of Dexamethasone and normal saline (0.15 mg/Kg) was injected in the case and control groups, respectively. Immediately after, 20% of anesthesia induction dose of propofol (1%) was injected on all patients following which injection pain severity was measured using the Face Pain Scale (FPS) on a scale from 0 to 10. The remaining doses of propofol, Atracurium, and Fentanyl were subsequently injected whereby the anesthesia process was completed. The collected data were analyzed in SPSS-17 using t-test, Mann-Whitney, Fisher, and McNemar's tests. The significance level was set at $P < 0.05$.

Results: Half of the participants were female. Pain severity rates were 4.32 ± 4.89 and 6.48 ± 1.76 in case and control groups, respectively. The results showed that pain severity was significantly greater in the controls than the cases. Heart rate increased in both groups after intervention ($p < 0.001$). In terms of drug injection complication, three cases were reported in the control group, while there was only one patient in the cases with a significant difference between the groups according to Fisher and McNemar tests.

Conclusions: Dexamethasone can be used as an effective and routine drug in the operating room to reduce propofol injection pain in children before the induction dose of propofol, hence increased satisfaction of children from anesthesia.

Key Words: Propofol; Pain; Dexamethasone; Child; Tonsillectomy

Introduction

Propofol is fast-acting intravenous anesthetic

used

for induction and maintenance of anesthesia and for sedation purposes (1). Intravenous (IV)

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propofol is a popular anesthetic and a quick inducer of anesthesia with quick recovery. However, its downside lies with pain and discomfort during intravenous injection when injected in small blood vessels in the back of the hand, which prevails in 85% of children (2).

Propofol has a white milky appearance with a PH of about 7. The injection pain is a common complaint and can be reduced by using an opioid as the premedication or by concurrent administration of lidocaine (50 to 100 mg IV). Dilution of propofol and injection in larger veins can reduce the incidence and severity of injection pain (3).

Although different drugs like ketamine, lidocaine, alfentanil and remifentanil are used for reducing propofol injection pain, it is still considered as a clinical problem in children, especially in younger children due to the smaller size of accessible vessels. The common pain relief method involves mixing propofol with lidocaine immediately before injection. However, lidocaine is not effective in all 9 to 11-year-old children (4).

Propofol-induced pain is divided into immediate and delayed categories. The etiology and mechanisms responsible for propofol injection pain still remains unknown. It is suggested that phenol can cause immediate pain by local irritation. Delayed pain (after 10 to 20 seconds) is caused by an indirect effect of the endothelium via the release of kininogens. The prevalence of pain is about 50 to 100 percent (4).

The mechanism of analgesia by dexamethasone is unknown. However, it is likely that dexamethasone, as a powerful anti-inflammatory, can reduce inflammation in controlling the delayed phase caused by propofol injection in which the mediators of pain such as kinin system are activated (4, 5). On the other hand, Karimetal showed that subcutaneous injection of dexamethasone can cause prolonged analgesia in rats (6).

Adenotonsillectomy is the most common surgery in children; hence, effective pain relief in children seems necessary (7). Although this surgical procedure is technically easy, it may be associated with serious complications such as spasm of the larynx, laryngitis and hemorrhage. The mortality rate after adenotonsillectomy varies from 0.5 to 1 per 10 thousand cases (8).

Thus, it seems that dexamethasone can be considered as an alternative in reducing propofol injection pain. So far, several studies have evaluated the effects of corticosteroids in increasing the duration of analgesia. Nevertheless, no such study has been carried out on children. In this double-

blind clinical trial, we have investigated the efficacy of dexamethasone in reducing propofol injection pain.

Methods

In this double-blind clinical trial (patient and injector), 50 children aged from 6 to 13 years undergoing elective adenotonsillectomy in Birjand-based Valiasr Hospital were randomly assigned into case and control groups. After describing the project to all patients entering the study and justifying them, written consent was obtained from their parents. This study was performed in the framework of a research project conducted in Birjand University of Medical Sciences which was approved under plan code No.1103, the ethics code of Ir.bums.1394.45, and the RCT code IRCT2016011325992N1 from the Iranian Registry of Clinical Trials.

The children who were crying while entering the operating room, the emergency cases, children with liver and kidney impairments or musculoskeletal disorders, those allergic to propofol or dexamethasone, and children for whom it was not possible to insert an intravenous line to the back of the hand were excluded from the study. In both groups, intravenous cannulation was performed on the hands of the patients with venous cannula No. 22 (blue). Under similar conditions, 0.2 mg (oral) Midazolam as premedication and 20 ml of juice were administered for all the patients. Then, 6 ml per kg of IV sugar solution was administered. The same volume of Dexamethasone and normal saline (0.15 mg/Kg) was injected in the case and control groups, respectively, such that neither the pain severity registrar nor the patients were aware of the nature of the given dose. Immediately after, 20% of anesthesia induction dose of propofol 1% (induction dose being 2 mg/kg) was injected on all patients at a rate of 1 ml/s, following which injection pain severity was measured and recorded on the basis of the Face Pain Scale (FPS) (a simple pictorial scale with 0 to 10 degrees for assessment of the pain in patients who do not have verbal communication). The patient's heart rate was recorded before the injection of dexamethasone and normal saline and after completion of the anesthesia process.

In both groups, the remaining doses of Propofol, atracurium, and Fentanyl were subsequently injected where by the anesthesia process was completed. Maintenance of anesthesia was performed using isoflurane. The propofol injection site was examined in recovery in terms of phlebitis,

redness and pain. The collected data were analyzed in SPSS-17 using pair t-test, Mann-Whitney, and Fisher exact tests. According to the obtained data and using Kolmogorov-Smirnov test, the assumption of normality of pain variable was rejected. However, in the case of heart rate, according to the Kolmogorov-Smirnov test, both groups had a normal distribution ($P>0.40$).

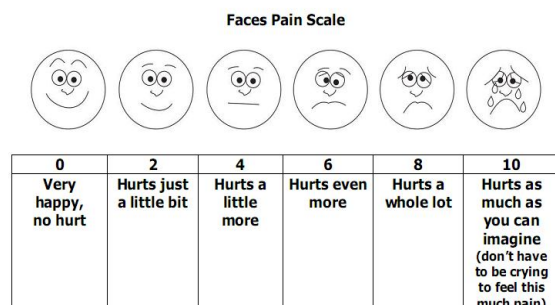


Figure 1: Faces pain scale

Results

Half of the participants were female. According to Table (1), pain severity rates were 4.32 ± 4.89 and 6.48 ± 1.76 in case and control groups, respectively. The results showed that pain severity was significantly greater in the controls than the cases. Heart rate increased in both groups after intervention ($p<0.001$). In terms of drug injection complications, three cases were reported in the control group, while there was only one patient in the cases with a significant difference between the groups according to Fisher exact test. No cases of phlebitis or pain were observed in the samples.

Table 1. Comparison of pain severity in children in the case and control groups after intervention

Variable	Group	
	Case (SD±Mean)	Control (SD±Mean)
Pain severity	4.32±4.89	6.48±1.76
Statistical Test	Mann- Whitney: Z=-3.29, P=0.001	

Table 2: Comparison of heart rate in children in the case and control groups before and after intervention

Group	Intervention phase	SD±Mean	Statistical Test
Case	Before	112.08±16.9	t = - 4.37 P < 0.001
	After	127.4±17.13	-
Control	Before	107.48±14.1	t = - 4.65 P < 0.001
	After	128.96±21.4	-

Table 3: Comparison of pain severity in children in the case and control groups after intervention

Group	Without complications N (%)	With complications N (%)	Statistical Test
Case	24 (96%)	1 (4%)	Fisher exact: P=0.305
Control	22 (88%)	3 (12%)	

Discussion

For many years, several studies have been conducted to evaluate the effects of different methods for reducing propofol injection pain (9, 10, 11, 12). The most common drug to prevent propofol-induced pain is lidocaine (13). Nonetheless, 32-48% of the patients who receive lidocaine still suffer from propofol injection pain (16-15).

The present study showed that intravenous injection of dexamethasone is effective in reducing propofol injection pain in children (6 to 13 years) undergoing adenotonsillectomy surgery.

In a study by Liu et al., the effect of opioid along with oral dexamethasone was compared with opioid alone in 480 patients undergoing Tonsillectomy where the results revealed that postoperative tissue edema and pain were lower in the steroid group (17).

Kim EM. evaluated the analgesic effect of dexamethasone along with Ropivacaine in caudal anesthesia in children and suggested that dexamethasone improved the analgesic effect of ropivacaine (18).

Ahmad S studied the effect of intravenous dexamethasone and lidocaine on Propofol-induced vascular pain and showed that premedication with dexamethasone was conducive to reduced propofol injection pain and that its efficacy was similar to premedication with lidocaine (19). The results of their study are consistent with the results of the present study.

Shoabi studied the effect of dexamethasone in reducing intravenous propofol injection pain, found similar results, and proved the effectiveness of Dexamethasone on propofol injection pain (14). This study also confirms the results of our study.

However, what is special in the current study, making it more reliable than and eliminating weaknesses of previous studies, is the fact that all patients in the present study underwent the same elective surgery (Adenotonsillectomy). The reason for this choice was to prevent the impact of the side effects of various diseases that can affect the patients' pain before implementation of the project; thus, all patients underwent a similar surgery under similar conditions in order

to eliminate the confounding variable of type of surgery. Also, the reason for choosing the same age range was to prevent bias in the analysis of the results. The number of boys and girls in both groups were the same and this also has not been considered in previous studies. Using Mann-Whitney test, results of the present study showed a significant difference between the two sexes in terms of pain severity.

On the other hand, the novelty of this study is that it was carried out on children who are within the sensitive age range of society and reducing the pain in these patients is more important. In order to prevent the effect of children's worry about being away from parents and their fear of the operating room, oral midazolam was administered to all of them in admission to the operating room.

Comparing the heart rate one minute after injection of 20% anesthesia induction dose of propofol (1%) with its rate before injection of dexamethasone showed an increased rate in both groups. While the rate of increase was higher in the control group, the difference was not significant.

Moreover, according to Safari et al. dexamethasone is effective in preventing postoperative nausea and vomiting after adenotonsillectomy, and this effect has been more visible in the late stage (4-24 hours after surgery) (20). Accordingly, in addition to reducing the propofol injection pain, dexamethasone is also effective in reducing the postoperative nausea and vomiting. This can be more important in children, with less ability to control their airways after surgery.

Conclusions

In all, the results of this study revealed that dexamethasone can be categorized as a drug which reduces propofol injection pain. In addition, another advantage of dexamethasone is reducing inflammation in the surgical regionals well as reducing postoperative nausea and vomiting, and this can induce anesthesiologists to make use of this drug.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Borazan H, Sahin O, Kecicioglu A, Uluer MS, Et T, Otelcioglu S. Prevention of propofol injection pain in children: A comparison of pretreatment with tramadol and propofol-lidocaine mixture. *Int J Med Sci*. 2012 Jan 1;9(6):492-7.
2. Yu J, Zhang Y, Lu Y, Dong C. Preemptive dexmedetomidine to prevent propofol injection pain in children. *Ir J Med Sci*(1971-). 2015 Jun 1;184(2):375-8.
3. Ronald D. Miller, Manuel C. Pardo, Jr. Basic of anedthesia. Tehran: ghazal; 2011.
4. Afhami MR, Naghipour B, Hassan zadeh Salmasi P. Effect of Ephedrine on Reducing Pain Induced by Intravenous Injection of Propofol at the Time of Anesthesia Induction. *Arak University Medical Journal*. 2006 Jan 15;10(4):1-1.
5. Karim F, Kanui TI, Mbugua S. Effects of codeine, naproxen and dexamethasone on formalin-induced pain in the naked mole-rat. *Neuroreport*. 1993 Jan 1;4(1):25-8.
6. Kolahdouzan k, ghorbanian n, eydi m, dadashzadeh s. Evaluation of the remifentanyl effect in prevention of propofol intravenous injection pain. *Pharmaceutical sciences*. 2008summer; (2):21-26.
7. Amani S, Rasti BM, Abedinzadeh M. Effects of local injection of bupivacaine and dexamethasone on postoperative pain of adenotonsillectomy. *Shahrekord University of medical sciences journal*. 2006 Spring; 8(1): 76-81.
8. Barash P, Cullen B, Stoelting R. editors. Management of Acute Postoperative Pain. In: *Clinical Anesthesia*. Lippincott: Williams &Wilkins; 2006.
9. Hassani E, Abbaszadeh R, Aghdashi MM, Shirvani M. Ephedrine Reduces the Pain from Propofol Injection. *Zanjan Arak University Medical Journal*. 2012 May 1;20(79):55-60.
10. Shoaybi G, Soltani mohammadi S, Rajabi M. The effect of Magnesium sulfate on reducing Propofol injection pain in elective surgeries. *Tehran University Medical Journal TUMS Publications*. 2008 Mar 15;65(2):30-4.
11. Zahedi H, Maleki A, Rostami G. Ondansetron pretreatment reduces pain on injection of propofol. *Acta Med Iran*. 2012 Apr 1;50(4):239.

12. Yu J, Zhang Y, Lu Y, Dong C. Preemptive dexmedetomidine to prevent propofol injection pain in children. *Irish Journal of Medical Science* (1971-). 2015 Jun 1;184(2):375-8.
13. Desousa KA. Pain on propofol injection: Causes and remedies. *Indian J Pharmacol*. 2016 Nov;48(6):617.
14. O'hara JF, Sprung J, Laseter JT, Maurer WG, Carpenter T, Beven M, Mascha E. Effects of topical nitroglycerin and intravenous lidocaine on propofol-induced pain on injection. *AnesthAnalg*. 1997 Apr 1;84(4):865-9.
15. King SY, Davis MF, Wells EJ, Murchison DJ, Pryor PJ. Lidocaine for the prevention of pain due to injection of propofol. *AnesthAnalg*. 1992 Feb 1;74(2):246-9.
16. Liu K, Hsu CC, Chia YY. Effect of dexamethasone on postoperative emesis and pain. *Br J Anaesth*. 1998 Jan 1;80(1):85-6.
17. EM, Lee JR, Koo BN, Im YJ, Oh HJ, Lee JH. Analgesic efficacy of caudal dexamethasone combined with ropivacaine in children undergoing orchiopexy. *Br J Anaesth*. 2014 Feb 2:aet484.
18. Ahmad S, De Oliveira GS, Fitzgerald PC, McCarthy RJ. The effect of intravenous dexamethasone and lidocaine on propofol-induced vascular pain: a randomized double-blinded placebo-controlled trial. *Pain Res Treat*. 2013 Jul 15;2013.
19. Shoeibi G, Khajavi Khan J, Movafegh A. Assessment And Comparing The Efficacy Of Propofol Pretreatment With Dexamethasone In Prevalence And Severity Of Its Pain On Injection. *Tehran University Medical Journal TUMS Publications*. 2005 May 15;63(1):55-60.
20. Safari f, aghighi k, salimi a, rahmanian a. Comparison of dexamethasone and metoclopramide on prevention of post adenotonsilectomy nausea and vomiting. *Journal of iranian society anaesthesiology and intensive care*. 2004; 25(46):57-62.