Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Research Article

Comparison of the Emergence Agitation in Children Undergoing Nasolacrimal Duct Probing Between Isoflurane and Propofol

*Majid Razavi, Hamideh Zarezadeh, Ahmad Bagheri Moghaddam, Mehryar Taghavi Gilani**

Lung Diseases Research Center, Imam-Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran.

ARTICLE INFO

Article history:
Received 01 March 2025
Revised 21 March 2025
Accepted 05 April 2025

Keywords:
Emergence agitation;
Propofol;
Isoflurane;
Sevoflurane

ABSTRACT

Background: Postoperative emergence agitation in children is so common. Isoflurane and propofol are evaluated for agitation, but results were contradictory. This study aimed to compare the effect of isoflurane and propofol for emergence agitation in children under three years old.

Methods: This double-blinded, randomized clinical trial was performed on 104 children under three years' old who were candidates for nasolacrimal probing. The children were anesthetized by sevoflurane and then were divided into isoflurane and propofol groups. After transfer to the recovery room, at first, 4 and 8 minutes, the degree of agitation of the child was measured according to the Watcha sedation criteria.

Results: The demographic parameters were not different. The mean duration of anesthesia (from LMA insertion to extubation) in isoflurane was significantly shorter than in propofol (p = 0.001). Also, the recovery time in the isoflurane group was significantly shorter than that of the propofol group (P=0.02). The prevalence of agitation was 7.69% in the propofol and 59.61% in the isoflurane, and the difference was significant (P = 0.001). Agitation scores at first, 4 and 8 minutes in the recovery room, showed less agitation in the propofol group (P=0.001).

Conclusion: Our study showed that propofol in children reduces the incidence of emergence agitation compared to isoflurane. But emergence and recovery time in the isoflurane group was less than in the propofol group.

Introduction

Emergence agitation (EA) is a complication with confusion, agitation, and restlessness that occurs during the recovery process following general anesthesia [1]. These events may be accompanied by altered levels of consciousness and irritable or strange behaviors, especially in young people. The incidence of EA varies considerably, ranging from 10 to 80% [2-3]. Multiple factors affect the development of EA, including the characteristics of the patient, the anesthesia method, and the type of operation. The symptoms of EA commonly manifest during the initial stages of recovery, around 14 minutes after the general anesthesia; sometimes, it has been observed up to 45 minutes later [4]. It is commonly a self-limiting condition and rarely needs to be treated. However, the complications, such as venous catheter or drainage tube loss, patient or staff harm, and greater recovery time and cost, remain significant [5]. Long-term effects, such as cognitive disturbance following general anesthesia in children and their relations, are unknown.

Sevoflurane is an inhalation anesthetic for pediatric and outpatient anesthesia. Sevoflurane has hemodynamic stability, low blood solubility, rapid emergence and recovery on general anesthesia. But, due to the unknown mechanism, sevoflurane-induced emergence agitation,

The authors declare no conflicts of interest.
*Corresponding author.
E-mail address: taghavim@mums.ac.ir

particularly in young patients, is common [6]. Also, the incidence and severity of EA in children were the same between desflurane and sevoflurane anesthesia [7]. Various agents can be used in the EA control, such as dexmedetomidine, fentanyl, ketamine, clonidine, and propofol bolus at the end of sevoflurane-based anesthesia [8-12].

However, the studies that have been conducted to compare the effects of isoflurane and propofol, especially in children, are limited. This study aimed to compare the effect of isoflurane with propofol on postoperative agitation in children under three years of age after nasolacrimal tract probing anesthesia.

Methods

This double-blinded, randomized clinical trial was done on 104 children with American Society of Anesthesiologists physi-cal status class I (ASA I) candidates for nasolacrimal probing. The children less than three years old referred to the ophthalmologic hospital in Mashhad in 2021-2022 were chosen. The present study was approved by the Ethics Committee of the Mashhad University of Medical Sciences with the ethics code of IR.MUMS.MEDICAL.REC.1400.083 and registered in the Iranian Registration Clinical Trial Center NO: IRCT20210525051394N1.

The research procedure was described to the patients' parents, and the written informed consent was obtained. In this study, 104 patients were recruited and fulfilled all the criteria and participated in the study. Each patient was allocated to a group using a sealed envelope. The parents and recovery nurses that evaluated the agitation scale and also the data analyzer were blinded from the groups. Children with a history of recent upper respiratory tract infection and comorbidity disorders were excluded.

After induction with sevoflurane 8% and O2-N2O 2-2 lit/min on the parents' arms, a venous catheter was inserted, and then, with a suitable depth of anesthesia, an LMA was inserted for the patients. Then the patients were separated into two groups utilizing the blocking system on www.sealedenvelop.com. Anesthesia was maintained with 2.5 percent isoflurane in the isoflurane group, whereas in the propofol group, propofol was infused at 50–100 mcg/kg intravenously. Fentanyl (1 μg/kg) was administered intravenously for postoperative pain control. Muscle relaxant was not administered during the surgery. Superficial peripheral oxygen saturation (SpO2), electrocardiography, and non-invasive blood pressure were monitored at 5-minute intervals during surgery and the recovery time. At the end of surgery, isoflurane and propofol were discontinued, and the fresh gas flow was changed to O_2 100% and 10 L/min until the return of airway reflexes and mild movement. LMA was exerted when the child had a cough or a gag reflex, a grimace, and purposeful movement. The children were transported to the postanesthetic care unit and monitored. After the eyes opening, crying, and no agitation, the child was transferred to the ward.

The induction time (from beginning to LMA insertion) and surgery time were recorded. The time from discontinuation of anesthetics to extubation (emergence time) as well as the duration of recovery stay were compared. After transfer to recovery, 5th and 10th minutes, the child's level of agitation was assessed using WATCHA sedation criteria (Table 1). If the WATCHA score was four, midazolam 0.1 mg/kg was administered, and if agitation was not better, propofol 20 μg/kg was injected.

Table 1- WATCHA sedation scale

Scale	Definition
one	Calm
two	Crying, can be consoled
Three	Crying, cannot be consoled
four	Agitated, thrashing around

Statistical analysis

According to a study in 2014 [13], the incidence of agitation in the control group was 47.2% and in the case group was 19.5%. By considering 80% power and a 95% confidence interval, the sample size for each group was 51 participants. With probable of 5% dropout in the samples, 104 patients were included. SPSS software version 26 was used to analyze the data. The central and dispersion indices were used to describe the variables. The student's t-test was used to compare quantitative data between the two groups, and the Mann-Whitney test was used in noncontinuous parameters with the normal distribution. The chi-square test was used to compare qualitative variables. All tests were considered bilateral, and the significance level was determined to be less than 0.05.

Results

A hundred and four patients were included and divided into two groups: propofol (N = 52) and isoflurane (N = 52). There was no significant difference in age, sex, and weight of patients in the two study groups (Table 2).

The induction time, duration of surgery, anesthesia time (from discontinuation of anesthetics to extubation), and recovery time are shown in (Table 3). The induction time and the duration of surgery were not significantly different in the two groups. The duration of emergence of anesthesia in the isoflurane group was significantly shorter than in the propofol group (P=0.001). Also, the time of recovery in the isoflurane group was significantly shorter than in the propofol group, despite more midazolam and propofol administration (P = 0.02). None of the subjects in the propofol group needed midazolam,

while 18 patients (34.6%) in the isoflurane group needed midazolam to reduce agitation (p = 0.001) (Table 3).

The prevalence of agitation (score > 2) in recovery was 7.69% in the propofol group and 59.61% in the isoflurane group, and the difference was significant (P = 0.001). The agitation scores at first, 5th and 10th minutes were shown in table 4. Accordingly, the number of calm patients in the propofol group was significantly higher than in the isoflurane group (P = 0.001). Similarly, agitation scores after 5 and 10 minutes were less in the propofol group compared to the isoflurane group (P = 0.001).

Discussion

Postoperative emergence agitation is the most common complication especially in pediatric surgeries after general anesthesia. Child agitation is distressing for the parents and nurses, difficult for management, and also can result in self-harm, venous catheter loss, ulcer bleeding, and bed falling.

According to our study, the incidence of EA was lower with propofol (7.69%) than isoflurane (59.61%). There are conflicting results regarding the impact of isoflurane on the incidence of EA. Voepel-Lewis et al. evaluated the incidence of EA between isoflurane and sevoflurane, and indicated that isoflurane is an independent risk factor for the development of EA [4]. On the contrary, Bortone et al. evaluated the use of sevoflurane and isoflurane as anesthetic maintenance in preschool children receiving regional anesthesia during subumbilical surgery in 2006, and they showed isoflurane dramatically reduced postoperative pain and discomfort [14]. Several studies demonstrated that the incidence of EA was not significantly different between isoflurane, sevoflurane, and desflurane [15-16]. A meta-analysis study compared the effects of sevoflurane and other inhalation anesthetics on children and revealed that the evidence for the beneficial effects of isoflurane on the incidence of EA is inadequate, and the effectiveness of this drug cannot be determined with certainty [13].

The numerous trials have demonstrated that propofol reduces postoperative EA in children. Based on their systematic review and meta-analysis of EA in children following propofol and sevoflurane administration, Kanaya et al. concluded that propofol significantly decreased the EA in children [17]. In another cohort study, 1 mg/kg propofol at the end of surgery in pediatric ENT & ophthalmic procedures is reduced the incidence & severity of emergence agitation [18]. In contrast, in Jin Lee et al.'s study, 1 mg/kg propofol at the end of surgery was not effective in the incidence of emergence agitation [19]. In one adult study, on closed reduction of distal radius fracture, propofol decreased the incidence of emergence agitation compared to isoflurane [20].

Table 2- The demographic parameters, mean±sd.

Characteristic	Propofol group (N=52)	Isoflurane group (N=52)	P value
Age (months)	19.7±7.4	19.3±7.9	0.79
Sex (male/female)	29/23	31/21	0.69
Weight (kg)	12.2±2.0	12.2±2.2	0.83

Table 3- The induction time for isoflurane, anesthesia duration, maintenance time, recovery, and time of emergence in the recovery, mean±sd.

Times (minutes)	Propofol group (N=52)	Isoflurane group (N=52)	P value
Induction time	4.00±1.76	3.96±1.53	0.90
Surgery time	12.02±7.04	11.28±4.57	0.06
emergence time	4.36±3.94	1.19±0.58	0.001
Recovery time	17.13±8.85	12.36±3.94	0.02

Table 4- Comparison of the agitation scores between study groups at recovery, 5, and 10 minutes after recovery transfer, mean±sd.

Times	Groups	Calm	Crying, can be consoled	Crying, cannot be consoled	Agitated, thrashing around	P value
recovery	Propofol	31 (59.6%)	17 (32.7%)	4 (7.7%)	0 (0.0%)	0.001
	Isoflurane	5 (9.6%)	16 (30.8%)	13 (25.0%)	18 (34.6%)	
5th minute	Propofol	24 (72.7%)	9 (27.3%)	0 (0.0)	0 (0.0)	0.001
	Isoflurane	5 (15.6%)	11 (34.4%)	8 (25.0%)	8 (25.0%)	
10th minute	Propofol	7 (36.8%)	8 (4.21%)	4 (21.1%)	0 (0.0)	0.001
	Isoflurane	0 (0.0)	5 (25.0%)	4 (25.0%)	10 (50.0%)	

Isoflurane's poor efficacy in reducing postoperative EA is likely a results of several factors. First, isoflurane causes a rapid return to consciousness. On the other hand, propofol can delayed recovery, the same as in our study.

Isoflurane has a smaller solubility than propofol and is eliminated from the body more rapidly [21-22]. Second, the long-lasting hypnotic effects of propofol may contribute to a reduction in EA during the early stages of recovery [23]. In our study, patients who received propofol did not require midazolam after regaining consciousness; however, 34.6% of those who received isoflurane did. As a result, propofol is a safer alternative to isoflurane since midazolam can cause paradoxical adverse effects such as agitation, disorientation, delirium, and hysteria. Third, isoflurane-induced EA is caused by GABA receptors and changes in the central nervous system and also decreased inhibitory impulses from the internal globus pallidus and substantia nigra [24].

The present study had limitations. First, the level of preoperative anxiety in patients was not measured. Past studies have shown that preoperative anxiety increases EA [25]. Second, all patients studied underwent NLD probing; therefore, the results of this study cannot be generalized to other surgeries. Finally, the WATCHA sedation criterion was used to evaluate agitation in this study. The standard method for diagnosing agitation has not been reported so far; however, a review study in 2010 recommended that all studies use the PAED criterion to evaluate EA [26]. We recommend that future studies perform on a larger sample size, compare EA between different surgeries, compare EA development in propofol and other anesthetic drugs, and finally, assess EA while considering the predisposing factors.

Conclusion

Our study showed that propofol compared to isoflurane in children following sevoflurane induction of anesthesia lowers the incidence of emergence agitation. The patients receiving propofol did not require the midazolam, but isoflurane significantly increased midazolam usage. In the isoflurane group, the time to wake up was faster and the recovery time was shorter.

Ethics approval and consent to participate

This study was taken from thesis no. 991742 with the ethics code of IR.MUMS.MEDICAL.REC.1400.083 and registered in the Iranian Registration Clinical Trial Center NO: IRCT20210525051394N1.

Acknowledgment

We sincerely thank the Research Council of Mashhad University of Medical Sciences for providing the funds for this study. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

[1] Stamper MJ, Hawks SJ, Taicher BM, Bonta J, Brandon DH. Identifying pediatric emergence delirium by using the PAED Scale: a quality improvement project. Aorn J. 2014;99(4):480-94.

[2] Dahmani S, Stany I, Brasher C, Lejeune C, Bruneau B, Wood C, et al. Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies. Br J Anaesth. 2010;104(2):216-23.

[3] Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology. 2004;100(5):1138-45.

[4] Voepel-Lewis T, Malviya S, Tait AR. A prospective cohort study of emergence agitation in the pediatric postanesthesia care unit. Anesth Analg. 2003;96(6):1625-30.

[5] Banchs RJ, Lerman J. Preoperative anxiety management, emergence delirium, and postoperative behavior. Anesthesiol Clin. 2014;32(1):1-23.

[6] Kim JH. Mechanism of emergence agitation induced by sevoflurane anesthesia. Korean J Anesthesiol. 2011;60(2):73-4.

[7] Lim BG, Lee IO, Ahn H, Lee DK, Won YJ, Kim HJ, Kim H. Comparison of the incidence of emergence agitation and emergence times between desflurane and sevoflurane anesthesia in children: A systematic review and meta-analysis. Medicine (Baltimore). 2016; 95(38):e4927.

[8] Moore AD, Anghelescu DL. Emergence Delirium in Pediatric Anesthesia. Paediatr Drugs. 2017; 19(1):11-20.

[9] Malviya S, Voepel-Lewis T, Ramamurthi RJ, Burke C, Tait AR. Clonidine for the prevention of emergence agitation in young children: efficacy and recovery profile. Paediatr Anaesth. 2006;16(5):554-9.

[10] Jiang S, Liu J, Li M, Ji W, Liang J. The efficacy of propofol on emergence agitation--a meta-analysis of randomized controlled trials. Acta Anaesthesiol Scand. 2015; 59(10):1232-45.

[11] Wu X, Cao J, Shan C, Peng B, Zhang R, Cao J, et al. Efficacy and safety of propofol in preventing emergence agitation after sevoflurane anesthesia for children. Exp Ther Med. 2019;17(4):3136-40.

[12] Valley RD, Freid EB, Bailey AG, Kopp VJ, Georges LS, Fletcher J, et al. Tracheal extubation of deeply anesthetized pediatric patients: a comparison of desflurane and sevoflurane. Anesth Analg. 2003;96(5):1320-4.

[13] Costi D, Cyna AM, Ahmed S, Stephens K, Strickland P, Ellwood J, et al. Effects of sevoflurane versus other general anaesthesia on emergence agitation in children. Cochrane Database Syst Rev. 2014(9):Cd007084.

[14] Bortone L, Ingelmo P, Grossi S, Grattagliano C, Bricchi C, Barantani D, et al. Emergence agitation in preschool children: double-blind, randomized, controlled trial comparing sevoflurane and isoflurane anesthesia. Paediatr Anaesth. 2006;16(11):1138-43.

[15] Meyer RR, Münster P, Werner C, Brambrink AM. Isoflurane is associated with a similar incidence of emergence agitation/delirium as sevoflurane in young children--a randomized controlled study. Paediatr Anaesth. 2007;17(1):56-60.

[16] Singh R, Kharbanda M, Sood N, Mahajan V, Chatterji C. Comparative evaluation of incidence of emergence agitation and postoperative recovery profile in paediatric patients after isoflurane, sevoflurane and desflurane anaesthesia. Indian J Anaesth. 2012;56(2):156-61.

[17] Kanaya A, Kuratani N, Satoh D, Kurosawa S. Lower incidence of emergence agitation in children after propofol anesthesia compared with sevoflurane: a meta-analysis of randomized controlled trials. Journal of Anesthesia. 2014;28(1):4-11.

[18] Haile S, Girma T, Akalu L. Effectiveness of propofol on incidence and severity of emergence agitation on pediatric patients undergo ENT and ophthalmic surgery: Prospective cohort study design. Ann Med Surg (Lond). 2021 Aug 24;69:102765.

[19] Lee CJ, Lee SE, Oh MK, Shin CM, Kim YJ, Choe YK, et al. The effect of propofol on emergence agitation in children receiving sevoflurane for adenotonsillectomy. Korean J Anesthesiol. 2010 Aug;59(2):75-81. Liu GY, Chen ZQ, Zhang ZW. Comparative study of emergence agitation between isoflurane and propofol anesthesia in adults after closed reduction of distal radius fracture. Genet Mol Res. 2014; 13(4):9285-91.

[20] Nakayama S, Furukawa H, Yanai H. Propofol reduces the incidence of emergence agitation in preschool-aged children as well as in school-aged children: a comparison with sevoflurane. Journal of Anesthesia. 2007;21(1):19-23.

[21] Lindenmayer JP. The pathophysiology of agitation. J Clin Psychiatry. 2000;61 Suppl 14:5-10.

[22] Smith I, Ding Y, White PF. Comparison of induction, maintenance, and recovery characteristics of sevoflurane-N2O and propofol-sevoflurane-N2O with propofol-isoflurane-N2O anesthesia. Anesth Analg. 1992;74(2):253-9.

[23] Ghouri AF, Bodner M, White PF. Recovery profile after desflurane-nitrous oxide versus isoflurane-nitrous oxide in outpatients. Anesthesiology. 1991;74(3):419-24.

[24] Lepousé C, Lautner CA, Liu L, Gomis P, Leon A. Emergence delirium in adults in the post-anaesthesia care unit. Br J Anaesth. 2006;96(6):747-53.

[25] Key KL, Rich C, DeCristofaro C, Collins S. Use of propofol and emergence agitation in children: a literature review. Aana J. 2010;78(6):468-73.