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Original Research Article **Pediatric Anesthesia**

Low Dose Propofol at the End of Sevoflurane Anesthesia Reduces Emergence Agitation in Children: A Prospective Observational Study

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Abstract

***Introduction*:** EA is characterized by agitation, inconsolable sobbing, disorientation, delusions, and hallucinations, decreased cognition and memory. Sevoflurane is widely used as an anesthetic agent for children because of its less pungent nature, lower solubility but it has a greater incidence of EA in preschool aged children. Propofol is a hypnotic amnestic agent with a short duration of action, commonly used for sedation, induction, and maintaining anesthesia and it has been used to prevent Emergence agitation. ***Aim of the Study*:** The aim of this study was to determine the efficacy of low dose propofol in reducing the incidence of EA at the end of face-mask sedation with sevoflurane. ***Methods*:** This was a prospective observational study and was conducted in the Department of Pediatric Anesthesia of Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh during the period from July, 2021 to December, 2021.In our study we took 220 children operated for hernia were randomized into two groups – Group A (Control group, n=110) and Group B (Propofol group, n= 110). ***Result*:** In total 220 patients from both the groups completed the study. In our study we found the mean age in group A & B was 6.3 ± 1.6 & 6.1 ± 1.9 years respectively. The mean PAED score was 14.41 ± 2.59 & 9.83 ± 3.51, the mean emergence time was 7.1 ± 2.0 & 13.4 ± 2.5, time in PACU was 44.5 ± 5.9 & 46.6 ± 7.6 mins in control & propofol group respectively. In contrast to the control group, no patient in the propofol group experienced EA beyond 15 or 20 minutes of emergence. ***Conclusion*:** In our study, we found that 0.5mg,/kg propofol was effective in preventing Emergence Agitation in children underwent herniotomy with caudal block and who's sedation were maintained with sevoflurane.

Keywords: Emergence agitation, Children, Sevoflurane, Propofol.

INTRODUCTION

Sevoflurane anesthesia in young infants has been associated with behavioral alterations, characterized as Emergence agitation (EA) or emergence delirium (ED) following recovery [1, 2]. EA is characterized by agitation, inconsolable sobbing, disorientation, delusions, and hallucinations, as well as decreased cognition and memory [3]. ED is sometimes defined as a type of EA occurring in a few patients who experience delirium with psychomotor agitation [1, 2]. The incidence of EA varies between 10% to 80%, with the highest incidence found in patients aged 2 to 5 years [4, 5]. A previous study by Aktara showed that the incidence of EA in our population was 39.7% [6]. The incidence of EA depends on the definition of EA used and the duration of monitoring after emergence from anesthesia. Sevoflurane and desflurane anesthesia have been shown to be risk factors for EA in children [7, 8]. However, the precise etiology is still unclear. Sevoflurane is widely used as an anesthetic agent for children because of its less pungent nature and lower solubility and greater hemodynamic stability than other potent inhaled anesthetics [9]. However, sevoflurane may have a greater incidence of EA in preschool-aged children [10]. As anatomical and physiological functions of children change rapidly and are different from adults, physiological characteristics of children should be carefully considered for the determination of anesthesia dosage, methods, and equipment. In addition, drug metabolism should also be considered [11, 12]. Sevoflurane is commonly used for the induction and maintenance of general anesthesia through inhalation [13].

It can also be used as sedative agent. To avoid intubation and general anesthesia it has been used through face mask in children for inguinal hernia

operated with caudal block. Sevoflurane has the advantages of quick recovery, low distribution coefficient, and less damage to the respiratory system [14]. However, sevoflurane also causes a restless reaction and unstable mood [15], leading to increased difficulties in post-operative care [16]. Propofol is a new type of short-acting intravenous anesthetic that is commonly used in the induction and maintenance of general anesthesia. It has a sedative effect and is often used with other narcotic drugs [17, 18]. Propofol is a hypnotic amnestic agent with a short duration of action, commonly used for sedation, induction, and maintaining anesthesia. Studies show that administration of intravenous (IV) propofol 1–3 mg/kg at the end of inhalation anesthesia may reduce the incidence of EA. However, it is also associated with a prolonged time for extubation, time to transport to the Postanesthesia Care Unit (PACU), and return to consciousness, hindering the readiness of patient turnover in the operating room [19-21]. There is a paucity of literature on the effectiveness of doses less than 1 mg/kg of propofol given at the end of inhalation anesthesia to decrease the incidence of EA [22]. Although EA is a temporary and self-limiting condition, it potentially endangers patients and threatens patient safety. Many studies have been performed to reveal possible causes, prevention, and treatment of EA, but no definite guidelines have been established. We anticipated that a lower dose of propofol as low as 0.5mg/kg can effectively reduce incidence of EA when sevoflurane used for sedation in children with caudal block.

Therefore, this study aimed to ascertain if administering 0.5mg/kg of propofol at the conclusion of sevoflurane sedation lowers the incidence of EA following herniotomy operation under caudal block.

OBJECTIVE OF THE STUDY

The main objective of the study was to determine the efficacy of low dose propofol reduces the incidence of postoperative EA at the end of general anesthesia with sevoflurane.

METHODOLOGY & MATERIALS

This prospective observational study was conducted at the Department of Pediatric Anesthesia, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh. The study duration was 6 months, from July 2022 to December 2022. During this period, a total of 220 patients who had undergone Herniotomy operation under caudal anesthesia with sedation maintained with Sevoflurane were selected for the study. The children were randomized into two groups – Group A, or the control group who didn't receive propofol, (n=110) and Group B, or the Propofol group who received propofol, (n= 110). Children between the ages of 1 and 12 years who were admitted to the Pediatric Anesthesia department, and belonged to American Society of Anesthesiology class I or II, were included in the study after proper consent was obtained. However, children with malignant hyperthermia, operating time longer than 60 minutes, neurological or psychiatric illness, known allergy to study drugs, or any history of acute illness (such as renal or pancreatic diseases or ischemic heart disease) were excluded from the study. In the study, anesthesia was induced using sevoflurane and oxygen, and a caudal epidural block was performed using 1ml/kg of 0.25% bupivacaine for supplemental analgesia. Patients randomized to the propofol group received propofol 0.5mg/kg intravenously at the end of operation after discontinuation of sevoflurane anesthesia. Children in the control group did not receive propofol. The primary outcome of the study was the incidence of emergence agitation (EA), which was assessed using two different scales: the Pediatric Emergence Anesthesia Delirium (PAED) scale and the Watcha scale.[23] EA on the PAED scale was defined as a PAED score > 12 throughout the first 30 minutes after emergence. EA was diagnosed by a score of ≥ 3 on the Watcha scale at any point during the first 30 minutes after emergence. The secondary outcomes included peak PAED scores, emergence time, and the time spent in the post-anesthesia care unit (PACU). A blinded researcher monitored the patient from the time of arrival in the PACU until 30 minutes after emergence. The time to emergence was defined as the duration of time from the termination of anesthesia until the onset of eye-opening or purposeful movement. All data were recorded systematically, and the statistical analysis was performed using SPSS 23. The study was approved by the Ethical Review Committee of Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh.

RESULT

Table 1: Baseline characteristics of our study participants

Baseline characteristics	**Group A (Control group)**		**Group B (Propofol group)**		**P-value**
	N=110	**P(%)**	**N=110**	**P(%)**	
Mean Age (years)	6.3 ± 1.6		6.1 ± 1.9		**0.210**
Gender					
Male	104	94.54	99	90	**0.742**
Female	6	5.46	11	10	
Body weight (kg)	14.8±4.9		13.9±5.0		0.454
Duration of surgery (min)	34.8 ± 9.2		36.7 ± 11.6		0.157
Duration of sevoflurane administration (min)	42.8 ± 10.8		43.6 ± 11.2		0.574

We found that the mean age of patients in group A and B was 6.3 ± 1.6 and 6.1 ± 1.9 years, respectively. The majority of patients were male, comprising 94.54% and 90% of both groups, while females accounted for 5.46% and 10%. The prevalence of ASA 2 was 70.91% in group A and 73.64% in group B. The duration of surgery was 34.8 ± 9.2 and 36.7 ± 11.6 mins for groups A and B, respectively, while the duration of sevoflurane administration was 42.8 ± 10.8 and 43.6 ± 11.2 mins, respectively. The duration of extubation was 12.6 ± 5.1 and 13.7 ± 3.6 mins in control and propofol groups, respectively.

Table 2: Emergence Agitation and Emergence Time

Emergence Agitation and Emergence Time	Group A (Control group)		Group B (Propofol group)		P-value
	N=110	P(%)	N=110	P(%)	
Emergence agitation (all patients)					
Using the PAED scale	51	46.36	26	23.64	**0.524**
Using the Watcha scale	53	48.18	29	26.36	
Peak PAED scores	14.41 ± 2.59		9.83 ± 3.51		0.694
Emergence time (min)	7.1 ± 2.0		13.4 ± 2.5		0.194
Time in PACU (min)	44.5 ± 5.9		46.6 ± 7.6		0.212

Abbreviation: PAED: Pediatric Anesthesia Emergence Delirium, PACU: post-anesthesia care unit.

Based on the PAED scale, 46.36% of patients in the control group and 23.64% in the propofol group experienced EA. Using the Watcha scale; we found that 48.18% of patients in the control group and 26.36% in the propofol group had EA. The mean PAED score was 14.41 ± 2.59 and 9.83 ± 3.51 in the control and propofol groups, respectively. The mean emergence time was 7.1 ± 2.0 and 13.4 ± 2.5 mins, and the time spent in PACU was 44.5 ± 5.9 and 46.6 ± 7.6 mins in groups A and B, respectively.

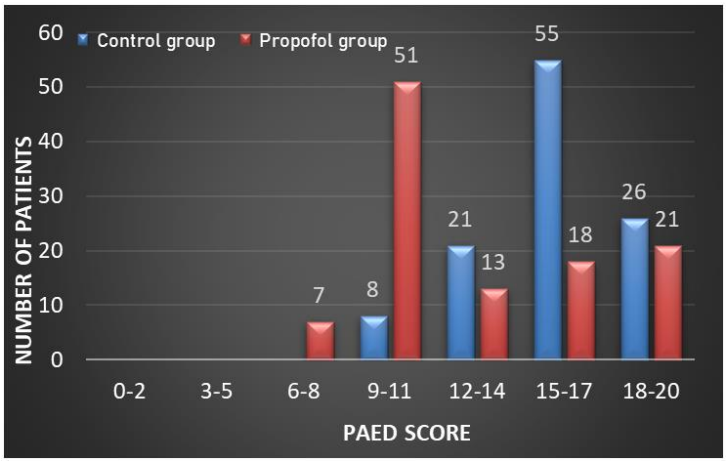

Figure 1: Comparison of PAED score between control and propofol group

The majority (51) of patients in the propofol group had PAED scores ranging from 9 to 11, while most (55) of the patients in the control group had PAED scores between 15 to 17.

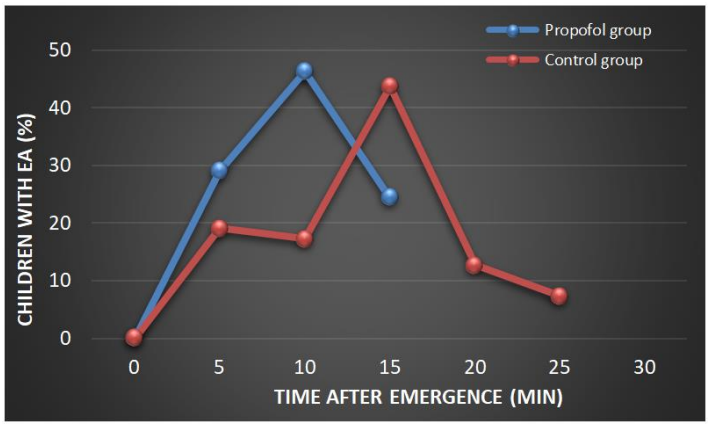

Figure 2: Proportion of children with emergence agitation (PAED score > 12) against time after emergence

Figure 2 represents the percentage of children who experienced EA (PAED score > 12) during the first 30 minutes after emergence. No patient in the propofol group experienced EA beyond 15 minutes of emergence, unlike the control group.

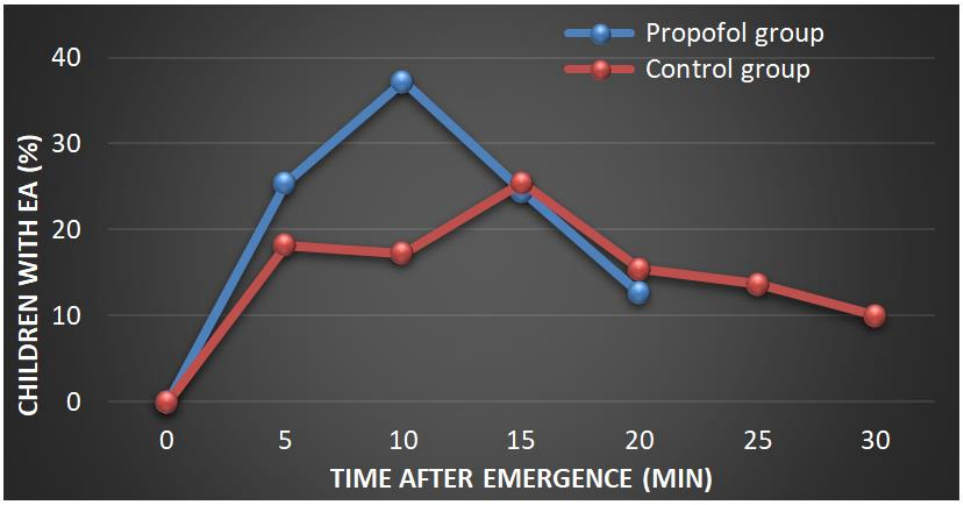

Figure 3: Proportion of children with emergence agitation (Watcha score ≥ 3) against time after emergence

Figure 3 represents the percentage of children who experienced EA (Watcha score ≥ 3) during the first 30 minutes after emergence. No patient in the propofol group experienced EA beyond 20 minutes of emergence, unlike the control group.

DISCUSSION

The present study linked a simple transition from sevoflurane sedation to propofol sedation for short duration with a dose of 0.5mg/kg of drug resulting in significant reduction in the incidence, severity, and duration of EA. Previous studies have reported a higher incidence of EA in children anesthetized with sevoflurane, with a 67% incidence of postoperative agitation reported in one study compared to 29.2% in the halothane group [25]. Although the etiology of EA is not clearly understood, possible factors include post-anesthesia, surgery, rapid emergence, postoperative pain, age, preoperative anxiety, child temperament, and adjuvant medication. The causes of the higher incidence of EA after sevoflurane are not fully understood, but inhalational anesthetics with low blood solubility, such as sevoflurane, generally tend to cause a higher incidence of EA. Rapid awakening in an unfamiliar environment has also been suggested as a cause for this phenomenon [26]. Yasui *et al.*, described an increase in noradrenaline release following sevoflurane exposure in the preoptic area of the brain in rats, especially in the locus coeruleus [27]. This may lead to disorientation in the early stages of recovery, resulting in the agitation component of EA. EA may also occur due to the rapid elimination of inhalational agents, including sevoflurane, desflurane, and isoflurane, or due to postoperative pain, which transition to propofol may offset and prevent [28, 29]. Propofol enables quick recovery from general anesthesia and has a low incidence of EA in infants and young children [30]. Propofol anesthesia is associated with a reduced incidence of EA compared to sevoflurane anesthesia because recovery is smooth and delayed [31]. The lingering hypnotic and euphoric effects of propofol in the initial stages of recovery could be the cause of the lower prevalence of EA [32]. Propofol appears to be useful in preventing EA based on prior research and is reliant on the timing of delivery [33]. Despite this fact, pediatric anesthesiologists frequently choose sevoflurane as the preferred medication for inducing and maintaining anesthesia in children. During sevoflurane anesthesia, the incidence of EA could be reduced with a single dosage of propofol given at the conclusion of the procedure to postpone or modify emergence. Abu-Shahwan's study showed that the administration of sub-hypnotic doses of propofol at the end of sevoflurane general anesthesia was effective in decreasing the incidence and severity of EA in children undergoing MRI [34]. Aouad *et al.*, reported that the administration of a single dose of propofol 1 mg/kg after discontinuation of sevoflurane at the end of surgery in children undergoing strabismus surgery significantly decreased the incidence of EA and improved patient satisfaction. They concluded that the delayed emergence from anesthesia reduced PAED scales without delaying discharge from the PACU [35]. Several clinical studies have shown that emergence agitation (EA) is a common problem in children following sevoflurane anesthesia and is significantly more frequent than with other inhalational anesthetics or propofol-based anesthesia. For instance, the incidence of EA after total intravenous anesthesia with propofol ranges from 0% to 9% compared to 23% to 46% after sevoflurane anesthesia, as reported in several studies [30, 31, 36]. Previously, propofol 2 mg/kg was administered at the beginning of surgery during sevoflurane anesthesia to reduce the incidence of EA, but this technique did not result in a decrease in EA incidence [37]. However, a preliminary trial with

propofol 3 mg/kg administered over 3 minutes after cessation of sevoflurane anesthesia demonstrated a decrease in the incidence of EA based on the PAED and Watcha scales, although this study was performed in children undergoing magnetic resonance imaging scan [19]. In our study, we investigated the percentage of children who experienced EA during the first 30 minutes after emergence. We observed that none of the patients in the propofol group experienced EA beyond 15 or 20 minutes of emergence, unlike the control group [see Figure 2 & 3]. Using a cut off of 12 on the PAED scale and 3 on the Watcha scale for the assessment of EA after switching to propofol 0.5mg/kg, we found a decreased incidence of EA in the propofol group. We used the Watcha scale in addition to the PAED scale due to its ease of measurement and potential to improve evaluation accuracy overall.

Limitations of the Study

The present study was conducted at a single center with a small sample size due to the short study period and limited resources. Several limitations were identified, including the lack of assessment of propofol safety, including airway complications and apnea. Our results require validation in different surgical settings, and additional etiologies of EA need to be evaluated. Additionally, after the initial evaluation, the patients were not followed up, and possible long-term interferences were not investigated.

CONCLUSION

The present study suggests that the use of propofol as low as 0.5mg/kg may reduce the incidence of EA in children after inhalation anesthesia with sevoflurane. Our findings indicate that a dose 0.5 mg/kg of propofol at the end of sevoflurane anesthesia can effectively prevent EA and decrease its severity and reduces stay time in PACU.

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