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ORIGINAL ARTICLE

The Effect of Dexmedetomidine on Emergence Agitation in Children After Desflurane Anesthesia

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ABSTRACT

Objective: To evaluate the effect of dexmedetomidine on the emergence agitation in children after desflurane anesthesia.

Materials and Methods: In this prospective randomized comparative study, 50 children between the age group 2-10 years of American Society of Anesthesiologists physical status I or II, who were scheduled for infrainguinal urologic surgery were enrolled and randomly divided into two groups. Group dexmedetomidine (Group B) (n=25) received 0.2 µg/kg dexmedetomidine in 10 ml saline intravenously over 10 minutes after induction and group control (Group A) (n=25) received only 10 ml saline infusion after induction. The emergence agitation levels of the children were evaluated according to the Pediatric Anesthesia Emergence Delirium Scale in the recovery room and postoperative pain scores were evaluated using Children's and Infants' Postoperative Pain Scale at the 10th and 30th minutes after extubation. Age, gender, weight, hemodynamic parameters, duration of anesthesia, duration of surgery and side effects were recorded.

Results: There was no significant difference in Pediatric Anesthesia Emergence Delirium scores at the 10th and 30th minutes after extubation between dexmedetomidine and saline groups. The decrease in emergence agitation at the 30th minute compared to the 10th minute was independent from sex, age and anesthesia duration in both groups. Incidence of hypotension and bradycardia was higher in the dexmedetomidine group compared to the saline group.

Conclusion: In children aged from two to 10 who undergo surgery with desflurane anesthesia, dexmedetomidine administration was not effective in preventing postoperative emergence agitation and caused increased side effects, such as hypotension and bradycardia.

Key words: Dexmedetomidine, desflurane, anxiety, emergence agitiation

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INTRODUCTION

Emergence agitation, which is frequently seen in children between 2 and 5 years of age, is defined as unintentional discomfort characterized with disorientation, confusion, prolonged crying, self-bashing, screaming and prolonged emergence [1,2]. It usually takes 30 minutes and resolves spontaneously [3]. The incidence of emergence agitation varies between 25 % and 80 % in children [4,5]. Several factors like sudden awakening of child in an unfamiliar environment, duration of anesthesia, pain (wounds, sore throat, bladder distention, etc.), stress during induction, hypoxemia, airway obstruction, environmental noise, child's personality, premedication, and type of anesthesia have been suggested to contribute this situation, which has not been precisely explained yet [6].

Several prior studies investigated effects of prophylactic and postoperative treatments to reduce the problems caused by emergence agitation and ensure the use of appropriate agent [1]. Desflurane has the lowest blood/gas partition coefficient among inhaled anesthetics and thus has particularly rapid onset and offset of effect. Emergence agitation was observed in 50 % - 80 % of children who receive desflurane, and this high prevalence of emergence agitation was attributed to the above mentioned features of desflurane [7, 8].

The aim of this study was to evaluate the effect of dexmedetomidine administration after induction on the emergence agitation in children who

underwent infrainguinal urologic surgeries under desflurane anesthesia

MATERIALS and METHODS

This study was conducted between March-July 2011 with the approval of the Human Research Ethics Committee of the Hacettepe University Faculty of Medicine (Project No: LUT 11/05 Decree No: LUT 11/05 Date: 03.02.2011). 50 children between the age group 2-10 years of American Society of Anesthesiologists physical status (ASA) I or II, who underwent elective infrainguinal urologic surgery were included after obtaining written informed consents from parents. The children who had history of any drug/food allergies, asthma, sleep apnea syndrome, cardiovascular disease, neurological disorders, mental and/or growth retardation, risk of malign hyperthermia, and psychological disorders were excluded from the study.

Patients were randomly divided into two groups. Children were orally premedicated with 0.5 mg/kg midazolam mixed in fruit juice with a limited total volume of 10 ml 30 minutes before anesthesia induction. Afterwards; they were taken to the operating theatre. Patients were monitored in terms of electrochocardiography (ECG), noninvasive blood pressure (NIBP), peripheral oxygen saturation, and end-tidal carbon dioxide pressure. Hemodynamic variables were recorded every 5 minutes. Anesthesia induction was performed using intravenous propofol (2.5 mg/kg) and fentanyl (2 µg/kg). Endotracheal intubation was performed after administration of rocuronium bromide (0.6 mg/kg). The patients in group A (control group, n=25) received only 10 ml saline infusion over 10 minutes after induction while the patients in group B (dexmedetomidine group) (n=25) received 0.2 mcg / kg dexmedetomidine infusion in 10 ml saline over 10 minutes after induction. Anesthesia was maintained using 6% desflurane in a mixture of 50% O2 and 50% N2O.

The time from induction of anesthesia to extubation was considered as the "duration of anesthesia." The time from the incision till the end of last suture was considered as the "duration of surgery". Pulse rate and blood pressure were measured before the administration of dexmedetomidine. >20% of decrease in normal pediatric heart rate after dexmedetomidine infusion was considered as bradycardia and >20% of decrease than normal pediatric blood pressure was considered hypotension. Children with bradycardia and hypotension were treated with appropriate doses and volumes of fluid support along with ephedrine and atropine.

Once the surgery was completed, neostigmine (0.05 mg/kg) and atropine (0.01 mg/kg) were administered for the reversal of neuromuscular blockade. Postoperative analgesic method was determined according to age, weight, accompanying diseases and type of surgical procedure, and multimodal treatment method was preferred unless contraindicated. The patients were taken to the post-anesthesia care unit (PACU) after extubation. A PACU nurse, who was blind to the intervention (dexmedetomidine or saline), evaluated the agitation levels of children at the 10th and 30th minutes after extubation using The Pediatric Anesthesia Emergence Delirium (PAED) Scale (Table 1). PAED score 10 was selected as the cut-off, which was shown to be sensitive and specific in prior studies [9,10].

Table 1. Pediatric Anesthesia Emergence Delirium Scale (PAEDS)

	Score
Makes eye contact with caregiver	4 = not at all
Actions are purposeful	3 = just a little
Aware of surroundings	2 = quite a bit
	1 = very much
	0 = extremely
Restless	0 = not at all
Inconsolable	1 = just a little
	2 = quite a bit
	3 = very much
	4 = extremely

The number of the children with PAEDS ≥ 10 and PAEDS < 10 were recorded in both groups at different times. PAED scores of the groups were recorded and compared regarding to preschoolers (between 2 and 5 years of age) and school - age children (between 6 and 10 years of age) and anesthesia duration (≤60 and >60 min).

Postoperative pain levels of the children were assessed in the PACU at the 10th and 30th min after extubation using the Children's and Infants' Postoperative Pain Scale (CHIPPS) by a physician, who was blind to the intervention [11](Table 2).

Table 2. Children's and Infants' Postoperative Pain Scale (CHIPPS)

Item	Score 0	Score 1	Score 2
Crying	None	Moaning	Screaming
Facial expression	Relaxed smiling	Wry mouth	Grimacing
Posture of the trunk	Neutral	Variable	Rear up
Posture of the legs	Neutral	Kicking	
Tightened			
Motor restlessness	None	Moderate	Restless

Analyses were carried out using the SPSS 15.0 (Statistical Package for Social Sciences, SPSS Inc. Chicago, IL, USA) software. The variables were analyzed using Kolmogorov-Smirnov/Shapiro-Wilks test to determine whether they were distributed normally. Mean ± standard deviation was used for the variables with normal distribution. Median (minimum -maximum) was used for non-normally distributed variables. Results were defined as numbers and percentages for categorical variables. Two-way Analysis of Variance was used in repeated measures to analyze the significance of time - related effects and interaction effects related to other factors. While comparing the two groups, we used the t-test for normally distributed variables in independent groups, and the Mann Whitney U test for non-normally distributed variables. The Chi-square (Pearson's Chi-square, Yates' Correction for Continuity, Chi-square and Fisher's exact test) test was used for comparison of categorical variables between the groups. $p < 0.05$ was accepted statistically significant.

RESULTS

There was no statistically significant difference between the groups regarding the demographic characteristics. Demographic data and perioperative variables of the patients in groups are listed in Table 3.

Table 3. Demographic data and perioperative variables of the patients in groups

	Group A	GroupB B (Dexmedetomidine)	p value
Age	(Control)	7 (range 2-10)	0,129
Weight	4,5 (range 2-10)	20 (range 10-70)	0,240
Duration of operation	17 (range 8,5-43)	70 (range 35-180)	0,884
Duration of anesthesia	70 (range 40-530)	90 (range 60-225)	0,641
Number of malegender	90 (range 55-570)	16 (64%)	0.765
	17 (68%)		

Numbers presented are medians (with ranges) except male gender variable

While the incidence of emergence agitation was found 40 % in the dexmedetomidine group, it was 52 % in the saline group.

The highest incidence of emergence agitation is seen in preschoolers from two to five years [4,12].Regarding this, we also compared preschoolers (from two to five years) and school - age children (from six to 10 years). The number of the children getting PAED scores ≥ 10 and < 10 at the 10th and 30th minutes after extubation were summarized in Table 4. There was no statistically significant difference in the patient number who have PAED scores<10 compared to ≥10between control and dexmedetomidine groups at the 10th ($p=0.395$) and 30th minutes ($p = 0.702$) after extubation. PAED scores at the 30th minutes after extubation were significantly lower than the 10th minutes after extubation in both groups ($p<0.001$).

Table 4. The number of the children getting Pediatric Anesthesia Emergence Delirium Scale (PAEDS) ≥10 and <10 at the 10th and 30th minutes after extubation (A=control, B=dexmedetomidine)

Time	Group	PAEDS ≥10 n (%)	PAEDS<10 n (%)
	A	13(52)	12(48)
10th minutes after extubation	B	10(40)	15(60)
	Total	23(46)	27(54)
	A	5(20)	20(80)
30th minutes after extubation	B	3(12)	22(88)
	Total	8(16)	42(84)

When the incidence of emergence agitation at the 10th and 30th minutes was compared considering group and sex factors at once, the decrease in emergence agitation incidence at the 30th minutes was found statistically significant (p<0.001). Both groups had similar PAUDS score at the 10th and 30 th min after extubation. PAEDS score significantly decreased at the 30th minutes after extubation compared to the 10th min after extubation in both groups, (p<0.001).

Pediatric Anesthesia Emergence Delirium Scale (PAEDS) scores at the 10th and 30th minutes after extubation by age groups were listed in Table 5.There was no significant difference in both groups regarding the PAED scores in the preschool (between the ages of 2 and 5) and school-age children (between the ages of 6 and 10) at the 10th and 30th minutes after extubation (Table 5).

Table 5. Pediatric Anesthesia Emergence Delirium Scale (PAEDS) scores at the 10th and 30th minutes after extubation-by age groups (A=control, B=dexmedetomidine)

Time	Age	GROUP A		GROUP B		p value
	Group	n	Mean±SD	n	Mean±SD	
10th minutes after extubation	≤5	15	9.87±5.74	11	9.27±3.04	0,728
	6-10	10	7.90±5.04	14	6.21±2.94	0,669
30th minutes after extubation	≤5	15	6.93±5.64	11	6.00±3.87	0,556
	6-10	10	2.70±4.30	14	2.43±2.62	0,564

PAEDS scores presented aremean±SD

Table 6.Pediatric Anesthesia Emergence Delirium Scale (PAEDS) scores at the 10th and 30th minutes after extubation by the anesthesia durations (≤ 60 min and > 60 min) of the groups (A=control, B=dexmedetomidine)

Duration of Anesthesia	Time (n A/B)	PAEDS Group A	PAEDS Group B	P value
≤60 min	10th min (5/2)	8.40±5.59	8.00±4.24	0,918
	30th min (5/2)	5.20±5.81	7.00±4.24	0,648
>60 min	10th min (20/23)	9.25±5.55	7.52±3.33	0,225
	30th min (20/23)	5.25±5.54	3.74±3.57	0,299

PAEDS scores presented are mean±SD

All patients in both groups were administered a standard analgesic method based on their pain levels and age. None of children had a postoperative pain score >3 and no additional analgesic application was required the PACU.
No hemodynamic side effects were observed in the control group since hypotension (5 children), bradycardia (2 children), and hypotension+bradycardia (1 child) were observed in dexmedetomidine group. The incidence of hypotension and bradycardia was significantly higher in the group B (p=0.004).

DISCUSSION

Emergence agitation is a common clinical condition for pediatric patients undergoing general anesthesia. Several prior studies investigated ways of preventing and treating emergence agitation by using various agents [3]. Alpha-2 agonists (dexmedetomidine, clonidine) have been used commonly for different indications such as premedication, adjuvant for central and peripheral blocks, and infusion in intrathecal analgesia as well as for treatment of sedation-induced withdrawal syndromes. Prevention and treatment of emergence agitation may be also added to the list of indications [13,14]. Dexmedetomidine has analgesic, anxiolytic and sedative effects and may be effective against emergence agitation [15]. However our data showed that dexmedetomidine administration (0,2 µg/kg) in children receiving desflurane anesthesia did not cause any significant decreases in incidence of emergence agitation.

Although there are contradictory results in the literature, short-acting premedication such as midazolam may be useful to reduce preoperative anxiety, which is an independent risk factor for emergence agitation [16]. It has been shown that midazolam reduces separation anxiety from parents and anxiety, since other studies reported that midazolam delays emergence and does not reduce the incidence of agitation [17,18]. While Özcengiz et al. reported that midazolam premedication was very effective in decreasing the incidence of agitation, Schmidt et al. indicated that the α2 agonists, dexmedetomidine and clonidine, were more effective than midazolam when used as premedication in children [19,20]. In this study, all children scheduled for surgery were premedicated with 0,5 mg/kg oral midazolam and this might be a reason why we could not find any significant effects of dexmedotimidine on emergence agitation since use of midazolam might also have decreased emergence agitation in both saline and dexmedetomidine-treated groups.

Isik et al. administered 1 µg/kg dexmedetomidine after induction in the pediatric patients, who had sedation for magnetic resonance imaging, and found the incidence of emergence agitation 4%; while the incidence was found 47,6 % in the patients receiving placebo. There were no difference in the time of emergence or intraoperative hemodyamic disturbances [21]. Mohanad et al stated that continuous infusion of 0,2 µg/kg/hr dexmedetomidine infusion decreased the incidence of emergence agitation compared to placebo in pediatric patients having sevoflurane anesthesia for general anesthesia [22].

Ibacache et al. also compared different dexmedetomidine bolus doses (0,15 vs 0,3 µg/kg) and found that 0,3 µg/kg dexmedetomidine bolus dose was more effective in reduction of emergence agitation [23]. Guler et al. reported that infusion of 0,5 µg/kg/hr dexmedetomidine was effective decreasing the incidence of emergence agitation [24]. Our data showed that dexmedetomidine administration did not provide reduction in incidence of emergence agitation in children.

In children, it is difficult to distinguish agitation from pain. Weldon et al. Also observed agitation in patients provided sufficient analgesia via caudal block. On the other hand, both Isik et al. and Crevero et al. reported that pediatric patients who are scheduled for painless radiological or noninvasive procedures also developed emergence agitation [5,21,25]. Therefore, the analgesic modality was determined according to age, weight, accompanying diseases and type of surgical procedure, and multimodal treatment method was preferred unless contraindicated. None of the patient had Children's and Infants' Postoperative Pain (CHIPP) score more than 3 in the follow-up.

Although slow infusion of low dose dexmedetomidine has not been reported to lead to hemodynamic instability in blood pressure; rapid infusion, especially bolus dose, can cause sudden increase in blood pressure, reflex bradycardia, and eventually hypotension [15]. Therefore, bolus application must be given over ten minutes. The transient increase in blood pressure is followed by 10% to 20 % decrease in basal blood pressure [15]. Despite using the low dose of dexmedetomidine, the patients experienced side-effects, such as hypotension and bradycardia, in our study. Dyck et al. Shoed that administration of 2 µg/kg dexmedetomidine for 5 minutes may cause biphasic response while in Jaakol et al. and Arai et al. showed that preoperative administration of 1 µg/kg dexmedetomidine for 10 minutes can cause 20% decrease in heart rate and mean arterial pressure [26,27,28]. Administration of the same dose after induction for 10 minutes did not cause hemodynamic instability in blood pressure. Hypotension and bradycardia may have resulted from potentiated pharmacological properties of other anesthetic agents and sympatholytic effect.

CONCLUSION

This study indicated that administration of 0,2 µg / kg dexmedetomidine after induction did not have any effect on agitation developing after desflurane anesthesia. However, further studies should

be carried out to investigate the effects of the administered dose, time of administration, duration of administration, rapidity, and application with similar and different peroperative infusion doses on the postoperative agitation.

ETHICS

This study was conducted with the approval of the Human Research Ethics Committee of the Faculty of Medicine of Hacettepe University (Project No: LUT 11/05 Decree No: LUT 11/05 Date: 03.02.2011).

FUNDING

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CONFLICT OF INTEREST

None

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