Original Article

Comparative Study of the Effect of Two Different Doses of Dexmedetomidine to Prevent Emergence Agitation in Tonsillectomy in Children Aged 2 to 12 Years Old

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Abstract

Background: Emergence agitation (EA) is one of the complications following anesthesia in pediatric surgery. Various drugs are used to prevent this complication, and one of them is dexmedetomidine. Choosing the right dose of this drug for the best efficiency is an important issue due to this complication.The main purpose of this study is to evaluate the prophylactic effect of intravenous dexmedetomidine in different doses in preventing EA after tonsillectomy in children.

Materials and Methods: Our study was a double-blind clinical trial performed on 75 children ASAI, II candidates for tonsillectomy. Patients were divided into three groups. The group 1 received a dose of 0.6 μg/kg per hour and group 2 received a dose of 0.3 μg/kg per hour and group 3 was the control group. Then vital signs and observational pain score (OPS) and pediatric anesthesia emergence delirium (PAEDS) criteria were measured in patients. The collected data were analyzed by using SPSS software version 23 and non-parametric tests such as Friedman, Mann-Whitney.

Results: According to the data analysis, mean blood pressure, mean heart rate, OPS and PAEDS score in group 1 were lower than other groups. Also, the average time of staying in recovery and extubation in group 1 was less than other groups.

Conclusion: A dose of 0.6 μg/kg dexmedetomidine has a better effect on reducing EA (emergence agitation) after pediatric tonsillectomy.

Keywords: Dexmedetomidine, emergence delirium, pain, tonsillectomy

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Introduction

Emergence agitation (EA), also known as emergence delirium and emergence excitement, is a condition in which a person experiences restlessness, agitation, crying, and disorientation and lack of coordination after anesthesia.[1] This complication often occurs in anesthesia with Sevoflurane and desflurane[2] and its prevalence in children is 80%.[3] EA usually occurs within 30 to 45 min of recovery and can be self-limiting or last for two days. EA causes complications such as self-injury, increased bleeding from the surgical incision site and catheter, thereby increasing the need for serious nursing and parental care and the length of stay in recovery[4] and the dissatisfaction of parents and health care providers.[5]

These complications can affect the complications of tonsillectomy surgery in which the risk of bleeding is significant. EA is a lesser known phenomenon. Etiologies such as pain, induction of anesthesia with stress, hypoxemia,

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and rapid recovery of the patient, physical stimulation such as sound, age of anesthesia, intraoperative drugs, and type of operation are involved in its development.[4,6]

Many drugs are used to prevent EA, including propofol,[7] midazolam, ketamine,[8] and an alpha-2 agonist such as clonidine[9] and dexmedetomidine.[10] Despite reducing the risk of EA, these drugs also have side effects such as increased drowsiness after anesthesia, slow recovery, and nausea and vomiting.[11] Dexmedetomidine is a selective alpha-2 receptor agonist that was first approved by the Food and Drug Administration as a short-term sedative in less than 24 hours.[12] It exerts its sympathetic effect by reducing the secretion of noradrenaline from the sympathetic nerve terminals (central and peripheral) where there is a large amount of alpha-2 adrenoceptors.

Dexmedetomidine is a more selective alpha-2 adrenoceptor agonist than clonidine. Research has also shown that it has a more postoperative morphine-like effect and a shorter half-life than clonidine.

Dexmedetomidine also has an effect on the cardiovascular system, which in low doses leads to hypotension and bradycardia, and in high doses leads to hypertension and reduced bradycardia. It is used in adult anesthesia, ICU, and pediatrics[6,13] and is used to prevent EA from detaching from the ventilator. Its analgesic and sedative properties are suitable for controlling EA.

A study of 72 samples by Garg *et al.* in 2018 examined the effectiveness of dexmedetomidine in preventing EA and concluded that it inhibits EA but has side effects such as prolonged extrusion time and retention of sedation. Moreover, prolong the stay in the PACU.[4,14]

However, there is debate about the dosage used to prevent EA.[10] A dose of 0.5 μg/kg of body weight adequately prevents EA, but it is associated with side effects such as decreased heart rate, blood pressure, delayed emergence, and delayed extubation.[14] In this study, we tried to evaluate the effect of two different doses of this drug to prevent EA in tonsillectomy surgery in children aged 2 to 12 years old of Isfahan Imam Hossein Hospital.

Materials and Methods

This study is a double-blind randomized clinical trial with a control group that was performed on 75 children aged 2 to 12 years who were candidates for tonsillectomy in Imam Hossein Hospital during year 1399 (2020).

The patients in the age group of 2–12 and ASA 1, 2 were included.

The patients with previous use of beta-blocker, Sensitivity to the drugs used in the study, History of ADHD (Attention-deficit hyperactivity disorder), History of severe cardiovascular disease, Kidney disease, Liver disease, Asthma, drug allergies, Bradycardia, Hypotension Heart blocks were not included in the study.

Patients who have severe hemodynamic changes after induction of anesthesia and need intervention**.**

Then, the sample size required for the study is calculated using the formula

$$\frac{\left(z_{\alpha}+z_{\beta}\right)^{2}\left[p1(1-p1)+(p21-p2)\right]}{d^{2}}$$

As a result, at least 25 people were placed in each group. After approving the plan and obtaining a license from the Medical Ethics Committee of Isfahan University of Medical Sciences (1399.278), 75 patients with tonsillectomy surgery were selected on the basis of inclusion criteria (available) and divided into three groups using random allocation software.[15] Informed consent was assessed from parents of all study groups.

Children eligible to study as pre-med and to control the etiology of agitation before the patient enters the operating room and preparation room and in the presence of parents received midazolam 0.01 mg/kg intravenously and were given an oxygen mask. They were then brought to the operating room. Standard monitoring devices including electrocardiogram, noninvasive blood pressure manometer, pulse oximeter, and capnogram was attached to them and their basic vital signs were recorded.

After induction of patients with fentanyl 2mcg/kg, propofol 2 mg/kg, atracurium 0.5 mg/kg they were received face mask oxygen and 3 minutes later they were intubated.

After that patients in groups 1and 2 received dexmedetomidine 1 μg/kg bolus for 10 min, then dexmedetomidine was infused in dose of 0.6 μg/kg per hour in group 1 and 0.3 μg/kg per hour in group 2. for group 3 patients the equivalent of normal bolus saline was injected and infused for 10 min. Normal saline was established for them. Vital signs were recorded in the first minute after intubation and 10 mins after induction and the moment of surgical incision.

Continued anesthesia of the patient during surgery was provided with 0.8% isoflurane.

At the end of anesthesia, dexmedetomidine and isoflurane were discontinued and after reaching TOF = 0.4 train-of-four (TOF) ratio (, a measurement of ratio/fade between first and last of four consecutive electrical stimuli) as the standard of acceptable recovery, postoperative residual paralysis is a frequent occurrence in postanesthesia care units), which is a measure of muscle relaxation, the combination of neostigmine and atropine was injected as reverse and the time spent to extubation (from drug discontinuation to excision endotracheal tube) was recorded in both groups.

The method of blinding was such that the nurse who collected the information did not know the groups. The drugs were prepared in three forms, A, B, and C, and the injector and evaluator were unaware of the type of drugs. In case of agitation in each group, propofol, 1–2 mg/kg was used (which

cannot lead to apnea and is injected under a respiratory and cardiac monitor).

The patient was transferred to recovery room once the patient is able to sustain spontaneous breathing. During recovery, observational pain score (OPS) and pediatric anesthesia emergence delirium (PAEDS) criteria and heart rate (HR), mean arterial pressure (MAP) and SPO2 were measured and recorded at minutes 1, 15, 30, 45 and 60 from the time of arrival.

Agitation during awakening can be associated with hemodynamic changes but is not a measure of exclusion. In this study, the control group was not exposed to any particular complication because their anesthesia method was the usual method for tonsillectomy surgery and was mentioned in textbooks. At the end of the study, the values of the variables were analyzed with SPSS version 23 software (IBM company, Armonk, New York) and the results were reviewed and interpreted.

Results

In this study, all incoming members were divided into three groups, group 1 received a dose of 0.6, and group 2 received a dose of 0.3 μg of the drug and group 3 received normal saline And these data Was obtained:

Analysis of the data showed that there was no significant difference between the groups in terms of demographic characteristics) *P* value >0.05) [Table 1]. The mean MAP in all three groups decreased from the time after intubation to 60 min after transfer to recovery. It also had its highest amount after intubation, which could be due to the painful process of intubation. The mean blood pressure in group 1 was significant lower than the other two groups (*P* value < 0.001).

The mean heart rate in all three groups decreased from the time of intubation to 60 min after transfer to recovery and in all three groups had the highest amount during intubation and surgical incision. Compared between the three groups, group 1 had the lowest heart rate compared to the other two groups (*P* value < 0.001) [Tables 2 and 3].

The OPS[16] criterion was ascending in all three groups from 0 min to 30 min, which could be due to the disappearance of anesthesia drugs. The results of the intergroup test were meaningful for comparing the mean OPS in the three groups, with group 1 having the least amount of pain and group 3 having the highest amount of pain (*P* Value = 0.026) [Tables 2 and 3].

Table 1: Demography

Variable	A	B	C	*P*
Age (mean±SD)	9±2	9±2	9±2	0.236*
Sex				
Men	11 (44)	16	8 (32)	0.072**
Women	14 (56)	9	17 (68)	

*Kruskal Wallis Test **Chi-squared test

PAEDS[17] criteria in all three groups increased from 0 min to 30 min, which could be due to the loss of anesthetic drugs. This increase was more in group 3 than other groups. The result of intergroup test to compare the mean of PAEDS was meaningful in three groups, group 1 had the lowest agitation rate, and group 3 had the highest agitation rate (*P* Value = 0.026) [Tables 2 and 3].

The average length of stay in recovery and extubation time in group 1 was less than other groups [Table 4].

Discussion

EA is known as a set of psychomotor disorders as a disorder of perception and delusion following sedation and general anesthesia.[18]

The mechanism of this disorder is unknown. According to some studies, the prevalence of this complication in school-age children is 80%, which can lead to postoperative complications such as self-injury, increased recovery time, and dissatisfaction of parents and treatment staff.[3]

EA depends on a number of factors, including age, type of surgery, pain, personality, rapid awakening, and preoperative agitation.[19] There are several ways to prevent these complications, including topical block, premedication, propofol, opioid, and alpha 2 agonists. One of the alpha-blockers is dexmedetomidine.[20]

Dexmedetomidine is an alpha-2 adrenoceptor that has sedative and analgesic properties and can prevent EA.[10] There have been several studies on the effectiveness of this drug in preventing EA.

The aim of this study is to compare the effect of two different doses of dexmedetomidine to prevent EA in tonsillectomy in children aged 2 to 12 years. The pain of this procedure (OPS), the average heart rate, and blood pressure decreased from the time of intubation to 60 min in recovery, which is a trend in all three groups. Mean blood pressure and heart rate in group 1 are lower than other groups.

The OPS and PAEDS criteria in all three groups increased from 0 to 30 min over time, which could be due to lowering levels of anesthetics and analgesia drugs and becoming more alert. These two criteria are lower in group 1 than the other groups, which could indicate a better effect of 0.6 μg/kg on pain relief and agitation.

The mean length of stay in recovery and extubation time in group 1 was less than other groups. The above findings show a better effect of 0.6 dose than 0.4 dose in preventing EA. Different studies have been performed comparing different drugs with different doses of dexmedetomidine in the prevention of EA, but no study was found on two different doses of this drug.

In 2018, like our study, Mathur *et al.* studied 70 patients aged 2 to 10 years and concluded that dexmedetomidine at

Table 2: Difference between mean heart rate, mean blood pressure, pain rate (OPS), and PAEDS between measurement times

Variable	Time	(mean±SEM)			*P**
		A	B	C	
HR (beats per minute)	After intubation-during surgery cut	4.64±1.43	6.28±1.56	6.12±1.64	0.01
	During surgery cut-0 min	5.92±2.90	2.04±1.71	6.60±2.10	<0.001
	0 min-15 min	0.76±0.70	-0.12±0.55	0.44±1.69	0.674
	15 min-30 min	1.12±0.65	1.56±0.46	0.08±2.06	0.775
	30 min-45 min	0.04±0.72	0.28±0.71	1.64±1.45	0.340
	45 min-60 min	0.72±0.98	-0.44±0.44	0.36±0.54	0.237
MAP (mmHg)	After intubation-during surgery cut	4±1.48	-70.36±49.59	4.44±1.14	0.114
	During surgery cut-0 min	2.6±1.54	74.28±49.78	2.44±2.01	0.123
	0 min-15 min	0.16±0.60	-0.32±0.89	0.48±0.51	0.543
	15 min-30 min	-0.16±0.61	0.08±0.66	0.44±0.72	0.970
	30 min-45 min	1.96±0.57	-0.48±0.69	1.52±1.03	0.109
	45 min-60 min	1.76±0.78	0.96±0.55	8.04±5.54	0.294
OPS	0 min-15 min	-0.64±0.14	-1.92±0.31	-5.80±0.61	<0.001
	15 min-30 min	0.001±0.14	-1.12±0.28	0.52±0.56	0.009
	30 min-45 min	-0.04±0.20	0.52±0.31	0.40±0.45	0.337
	45 min-60 min	0.16±0.23	0.72±0.33	0.92±0.39	0.561
PAEDS	0 min-15 min	2.04±0.45	0.52±3.02	-4.44±0.88	<0.001
	15 min-30 min	1.52±0.52	-1.56±0.45	-0.84±0.62	<0.001
	30 min-45 min	0.64±0.43	1.96±0.47	1.08±0.89	0.334
	45 min-60 min	1.32±0.21	1.08±0.43	1.52±0.84	0.856

*Kruskal Wallis Test

Table 3: Mean heart rate, mean blood pressure, pain rate (OPS), and PAEDS at measurement times in three groups

Variable	Time	(mean±SD)			*P* (inter group)	*P* (intra group)[a]
		A	B	C		
MAP (mmHg)	After intubation	91.80±7.71	104.28±8.99	110.40±4.94	<0.001	<0.001
	During surgery cut	87.80±7.48	174.64±249.38	105.96±4.28		
	0 min	85.20±7.79	100.36±11.95	103.52±9.82		
	15 min	85.04±6.44	100.68±9.36	103.04±853		
	30 min	85.20±7.21	100.60±9.37	102.60±7.78		
	45 min	83.24±7.96	101.08±8.43	101.08±8.50		
	60 min	81.48±8.27	100.12±7.90	93.04±25.64		
HR (beats per minute)	After intubation	89.88±14.17	109.04±6.01	121.52±957	<0.001	<0.001
	During surgery cut	85.24±15.85	102.76±10.72	115.40±13.75		
	0 min	79.32±10.66	100.72±9.08	108.80±7.30		
	15 min	78.56±9.90	100.84±9.15	108.36±7.10		
	30 min	77.44±9.63	99.28±10.31	108.28±9.20		
	45 min	77.40±9.50	99.00±8.48	106.64±7.02		
	60 min	76.68±9.97	99.44±7.27	106.28±8.06		
OPS	0 min	0.04±0.200	1.28±1.14	1.96±2.49	<0.001	<0.001
	15 min	0.68±0.63	3.20±1.53	7.76±2.35		
	30 min	0.68±0.63	4.32±1.38	7.24±2.20		
	45 min	0.72±0.89	3.80±1.47	6.84±1.99		
	60 min	0.56±0.92	3.08±1.50	5.92±1.60		
PAEDS	0 min	10.20±1.04	11.28±2.37	10.92±2.72	<0.001	<0.001
	15 min	8.16±2.37	10.76±1.94	15.36±3.55		
	30 min	6.64±1.95	12.32±2.17	16.20±3.97		
	45 min	6.00±1.87	10.36±3.07	15.12±3.93		
	60 min	4.68±1.70	9.28±3.12	13.60±2.65		

P value: based on repeated measures test by adjusting before intubation

Table 4: Recovery and extubation time				
Recovery time (mean±SD)	50±9	67±8	75±7	<0.001
Extubation time (mean±SD)	10±3	14±3	19±3	<0.001

a dose of 0.3 μg/kg intravenously before intubation could be beneficial for EA after sevoflurane anesthesia in tonsillectomy with or without adenotonsillectomy surgery.[20] In 2017, Ahmed Ezz *et al.* examined 90 patients and concluded that in children undergoing myringotomy, both nasal dexmedetomidine and nasal ketamine administered 20 min before induction had beneficial effects in preventing EA and there is no significant difference in the effect of these two drugs in reducing this complication.[21]

Another study conducted in 2019 by Uzma Begum concluded that bolus dose and dexmedetomidine infusion could prevent EA, but bolus dose had a better effect.[5]

In a study conducted by Ashraf Elsayed Elagamy *et al*.[22] in 2020 on 80 patients, they examined the effect of 0.1 μg/kg dexmedetomidine and nalbuphine on the prevention of EA and found the superiority of dexmedetomidine in the prevention of EA.

Conclusion

According to the statistical analysis of the obtained data, in tonsillectomy surgery, the mean heart rate and mean blood pressure in group 1 are lower than other groups. Also, the severity of pain and agitation (PAEDS) and time of stay in recovery and extubation in group 1 are less than the other two groups, which indicates a better effect of 0.6 μg/kg dose.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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