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Effect of Dexmedetomidine Infusion on Emergence Agitation in Patient Undergoing Adenotonsillectomy under Sevoflurane Anesthesia

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Summary

Emergence agitation (EA) is one of postoperative problems after adenotonsillectomy , this study aimed to assess the effect of dexmedetomidine infusion on emergence agitation in patient undergoing adenotonsillectomy under sevoflurane anesthesia. Therefore, a comparative study was conducted included 40 children who under-went elective outpatient either tonsillectomy or adenotonsillectomy durig the period January 2020– April 2020. Findings of the study showed that Intravenous infusion of DEX is effective for reducing EA after sevoflurane anesthesia in children undergoing adenotonsillectomy surgery without producing sever adverse side effects. Therefore we recommend further studies with larger sample size to get more precise results and confirm effectiveness of DEX on EA, and to identify an optimal doses.

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1 INTRODUCTION

Emergence agitation (EA) is one of postoperative problems after adenotonsillectomy (1), the incidence of EA is wide ranging in the literature from 10% to 80% in adenotonsillectomy (2) the patients exhibits non-purposeful movement, restlessness, agitation, thrashing, crying or moaning, disorientation, and incoherence during early recovery from general anesthesia (3). The incidence of EA varies, with age, tools used in assessment, techniques of anesthesia, definitions, type of surgery, and time of EA assessment postoperativly (4). The clinical consequences of EA are varied. It is typically short duration and resolves spontaneously, and its clinical sequelae are often considered minimal (5). However, it may have clinically significant consequences, such as injury to the affected patient or their medical staff, falling out of bed, bleeding from wound side, accidental removal of drains or intravenous lines, unintended extubation, respiratory depression, and increasing medical care costs (6).

Sevoflurane

Sevoflurane belongs to a group of medicines called inhaled general anesthetics. These are acting by temporarily reducing the activity of the body's central nervous system. This causes a complete loss of sensation in the body, including loss of consciousness allowing surgery to be achieved without pain. Sevoflurane is a clear colorless liquid, that when put into a special anesthetic machine (vaporiser) becomes a gas. This mixes with the oxygen when the patient will be breathing in. Once breathed in (inhaled), Sevoflurane will induce and maintain a deep, pain-free sleep (general anesthesia) in adults and children. As with all anesthetics, Sevoflurane can cause side effects (7). These can occur both during and after surgey. The following side effects with Sevoflurane are serious:

Slow heart rate (bradycardia), agitation, decreased blood pressure (hypotension), cough, nausea, vomiting, drowsiness (somnolence), dizziness, slow shallow breathing (respiratory depression), watering mouth (salivary hypersecretion), chills, fever (pyrexia), low body temperature (hypothermia), delirium. (7, 8)

Dexmedetomidine (Precedex)

Centrally acting alpha2-adrenoceptor agonist that has sedative and anesthetic properties possibly by activating G-proteins in the brainstem, which results in the inhibition of norepinephrine release. Usage of precedex is indicated for sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting. Precedex should be administered by continuous infusion not to exceed 24 hours (9). Precedex has been continuously infused in mechanically ventilated patients prior to extubation, during extubation, and post-extubation. It is not necessary to discontinue Precedex prior to extubation (10).Precedex is indicated for sedation of non-intubated patients prior to and/or during surgical and other procedures. The clinical significant adverse reactions are Hypotension, bradycardia, transient hypertension sinus arrest (10). Various doses (0.15–2.0 μg/kg) of dexmedetomidine have been reported to prevent pediatric EA after sevoflurane anesthesia, but the optimal dose of dexmedetomidine is not known. Dexmedetomidine does not cause respiratory depression, but it does have cardiovascular effects, so use of the drug requires monitoring, especially for children (11). Thus, we sought to identify an optimal dose of dexmedetomidine to prevent EA without significant adverse effects during tonsillectomy and adenotonsillectomy.

Table 1. Pediatric anesthesia emergence delirium scale (12)

Clinical Status	Not at all	Just a little	Quite a bit	Very much	Extremely
1.The child makes eye contact with the caregiver	4	3	2	1	0
2.The child's actions are purposeful	4	3	2	1	0
3.The child is aware of his/her surroundings	4	3	2	1	0
4.The child is restless	0	1	2	3	4
5.The child is inconsolable	0	1	2	3	4

2 PATIENTS AND METHODS

A cross sectional study carried at our hospital, this study included 40 children who underwent elective outpatient either tonsillectomy or adenotonsillectomy (January 2020–April 2020).

Inclusion Criteria

- Age 4–10 year.
- ASA I–II.
- Elective outpatient tonsillectomy or adenotonsillectomy.

Exclusion Criteria

- Allergy to the study medications.
- Developmental delay.
- Mental retardation.
- Psychological disorders.
- Liver, renal and cardiac diseases.

All patients fasted for at least 6 hours, and the patients presented to operative room with intravenous line was already inserted. The patients did not premedicated. Patient was attached to monitors, monitoring include: ECG, noninvasive blood pressure, SpO2, end tidal carbon dioxide after intubation.

These parameters were recorded from time of induction of anesthesia (time zero) and every 5 minutes during surgery. Most of surgeries lasted for about 30 minutes. After attaching the monitors to patients, intravenous anesthetic induction was done by fentanyl (2µg/kg), anesthetic dose of propofol (1–2 mg/kg), and rocuronium (0.6 mg/kg); after tracheal intubation, the patients were ventilated mechanically with minute ventilation adjusted to maintain normal end-tidal carbon dioxide. All patients were maintained on 1–3% sevoflurane then the patients were randomly allocated (using simple randomization) into 2 equal groups.

Group A (control group N=20): the patients received equivalent volume of normal saline in 50 ml syringe using syringe pump.

Group B (dexmedetomidine group N=20): the patients received dexmedetomidine 0.1–0.3 µg /kg /h in 50 ml syringe using syringe pump.

Those infusions were started immediately after induction and continue until discontinuation of sevoflurane. The dose of study medications (sevoflurane and dexmedetomidine) was adjusted to maintain hemodynamics of the patient (heart rate and mean arterial blood pressure) within 20% of pre-induction readings. To all patients intravenous dexamethasone 0.25 mg/kg and paracetamol suppository was given after induction of anesthesia, at the end of the surgical intervention the anesthetics were discontinued; suctioning of the oropharynx and muscle relaxants were reversed with neostigmine and atropine when spontaneous breathing was adequate, and extubating was done in lateral position when patient recovered well and then the patients were transferred to the recovery room, where the observer was blinded about the study medications.

In the recovery room, the required monitors were observed in addition to PAED Scale to assess the EA (minimal score is 0 and maximal is 20) Table (1.1). The degree of EA is directly increases with the total score. The scale was assessed at times 0, 5, 15, 30 minutes after extubating.

In PAED of more than 12, the child was considered agitated. The patients were transferred to the ward according to modified Aldrete score criteria.

The following time intervals were (Extubation time) from the discontinuation of sevoflurane to the removal of endotracheal tube. (Emergence time) from discontinuation of sevoflurane to the first verbal response. Adverse events such as, laryngospasm, oxygen desaturation, and bradycardia were also noted and was treated accordingly. The cases with any adverse events were dropped out of study.

Statistical Analysis

Microsoft Excel 2010 and SPSS programs were used for data entry and analysis. For normally distributed data; mean of two groups was compared using T – test and for skewed data Mann Whitney test was used. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using Chi-square or Fisher's exact test whichever is applicable. All statistical tests were two sided and were performed at a significance level of P = 0.05.

3 | RESULTS

However statistically significant reduction was observed in the mean of Diastolic BP of Group B at time interval (10 to 25) minutes of surgery in comparison to group A, there was no significant difference that required medical intervention ; (Figure 1). PR mean also shows statistically significant reduction at zero minute of surgery among group B in comparison to group A, P=0.021, but with no significant difference that required medical intervention; (Figure 2). SpO2 mean was decreased at all-time intervals among group B in comparison to group A, but without significances, P>0.05; (Figure 3). SpO2 mean was decreased at all-time intervals among group B in comparison to group A, but without significances, P>0.05; (Figure 4).

PAED score >12 is a criteria to define Emergence Agitation (EA). PAED scores were statistically significantly reduced in Group B as compared to Group A with P < 0.05 at all-time intervals. As shown in Table 3.1; there was a dramatically decrease in emergence agitation among Group B, (Figure 5).

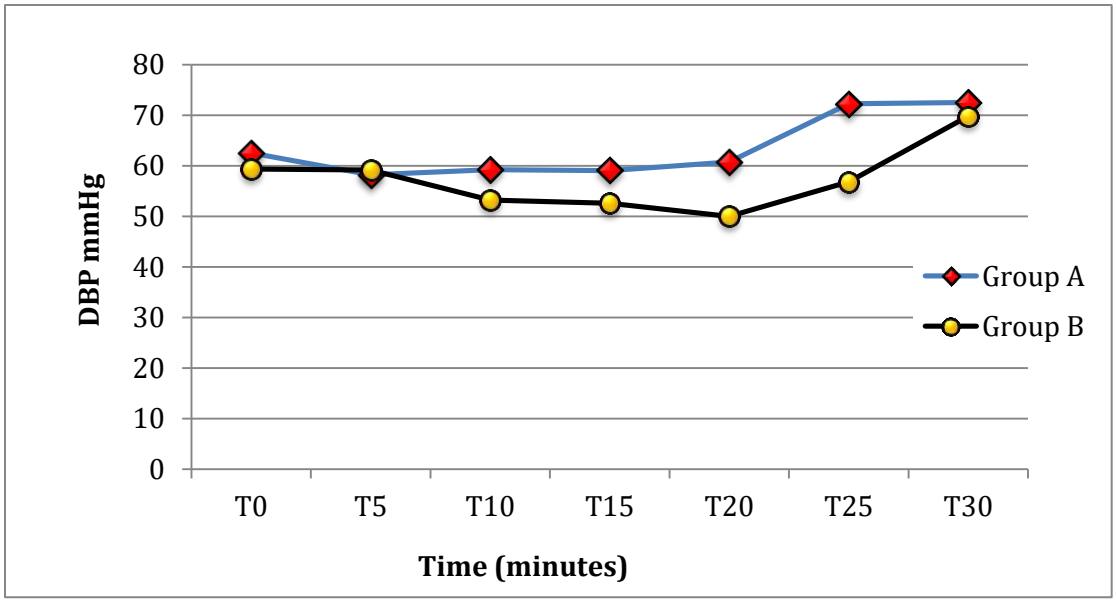

Figure 1: Changes in diastolic blood pressure (DBP)of pediatric patients in the studied groups. (Group A=control group, Group B=dexmedetomidine group).

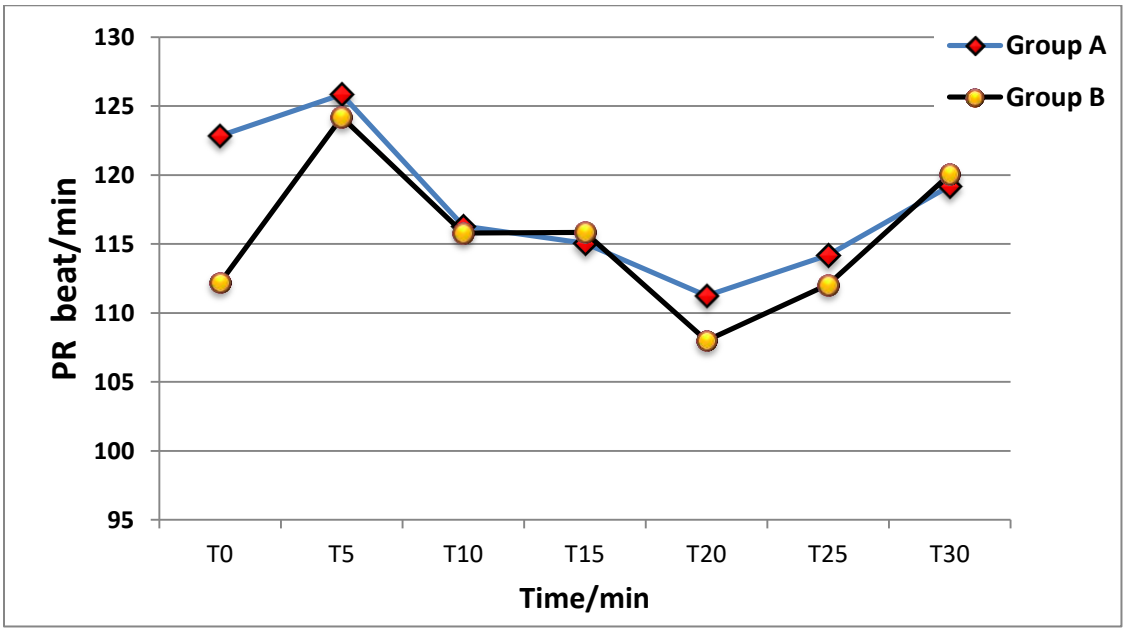

Figure 2: PR changes of pediatric patients in the two groups.
(Group A=control group, Group B=dexmedetomidine group).

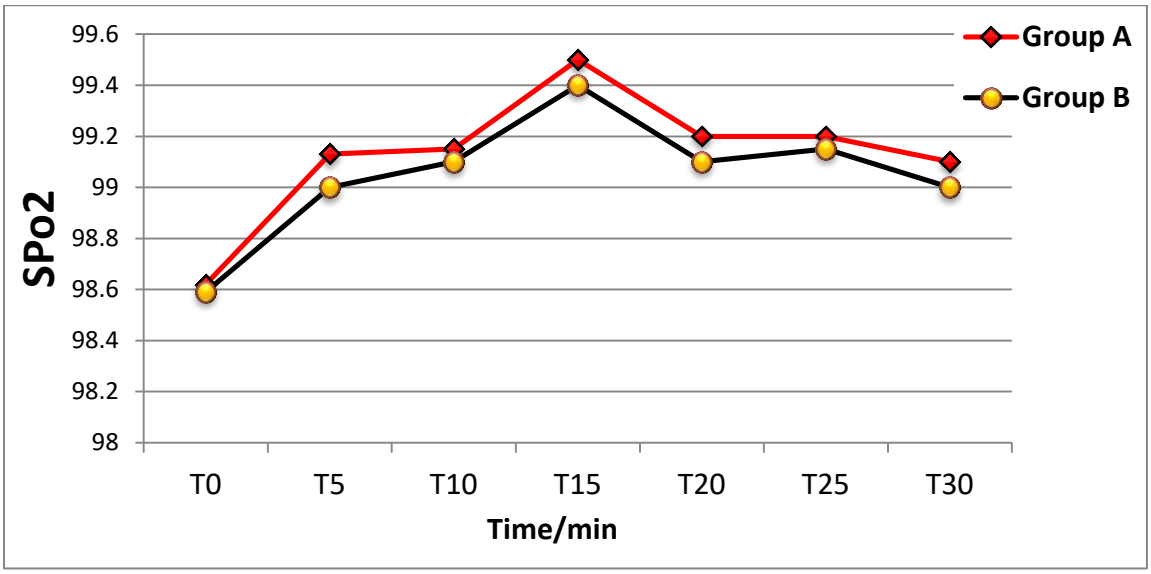

Figure 3: SPo2 changes of pediatric patients in the two groups.
(Group A=control group, Group B=dexmedetomidine group).

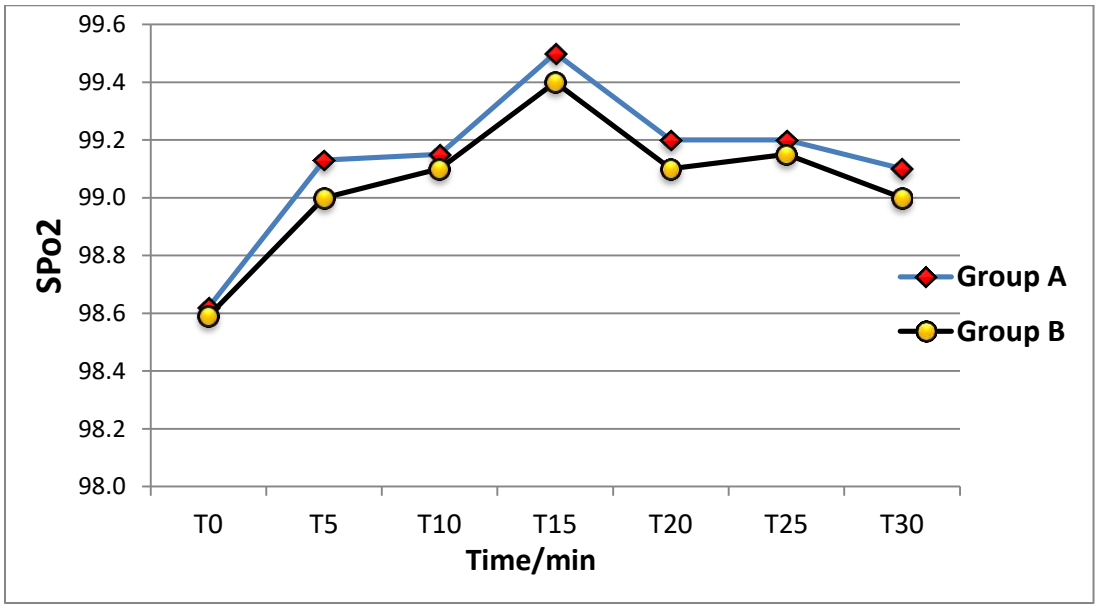

Figure 4: SPo2 changes of pediatric patients in the two groups. (Group A=control group, Group B=dexmedetomidine group).

Table 2. Pediatric Anesthesia Emergence Delirium score according to the time for study groups

Time/minute	PAED score	Groups				P*
		Group A		Group B		
		N	%	N	%	
T0	≤12	3	15.0	15	75.0	<0.001
	>12	17	85.0	5	25.0	
T5	≤12	10	50.0	18	90.0	0.014
	>12	10	50.0	2	10.0	
T15	≤12	12	60.0	19	95.0	0.02
	>12	8	40.0	1	5.0	
T30	≤12	13	65.0	19	95.0	0.044
	>12	7	35.0	1	5.0	
*Fisher's exact test						

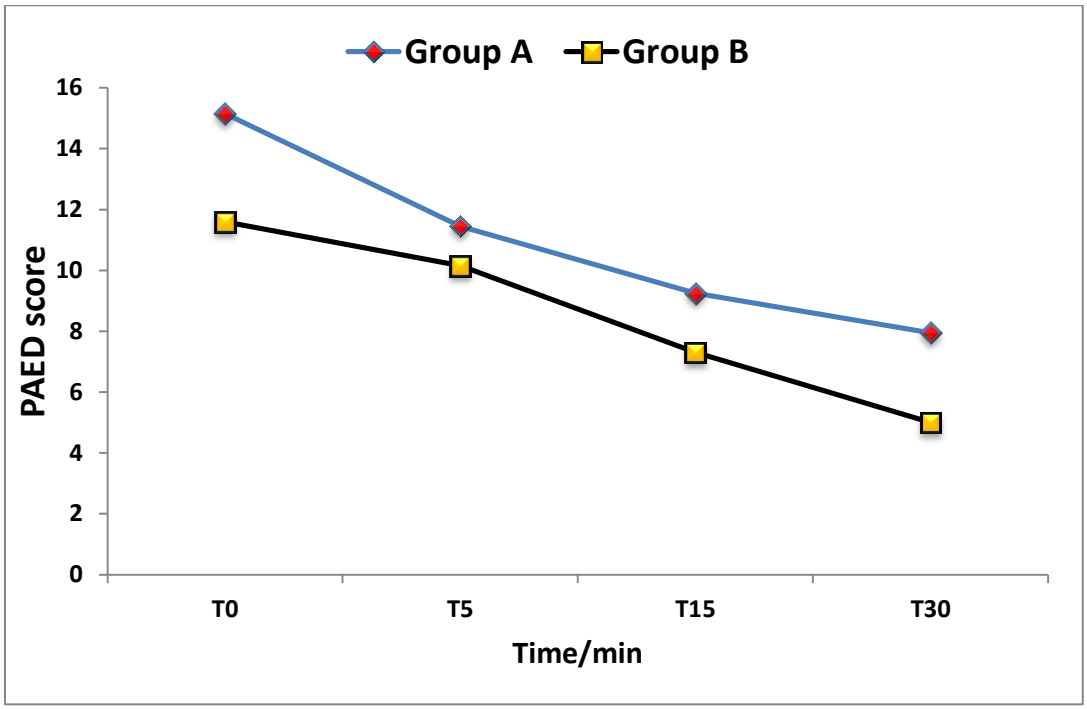

Figure 5: PAED score of pediatric patients in the two groups (Group A=control group, Group B=dexmedetomidine group, PAED=pediatric anesthesia emergence delirium)

4 DISCUSSION

Sevoflurane, a day care anesthetic agent, causes rapid emergence and recovery from GA. However, its beneficial effects are decreased by the high incidence of EA, especially in pediatric age group (13). In this study, we assess the effectiveness of intravenous infusion DEX in reducing Sevoflurane EA in children, undergoing elective adenotonsillectomy or tonsillectomy surgery. This study included 40 pediatric patients divided randomly in to 2 groups; Group A (control) that received normal saline and Group B (dexmedetomidine group) that received DEX. The mean age group was about 8 years. The study found prolongation in extubation time, and emergence time among dexmedetomidine study group, with no significant p value differences among both groups. It has been known that patient in the age group of 1–6 years have the highest incidence of EA (14). Notably, in our study, extubation time and emergence time prolonged in dexmedetomidine group. This is differed from a study of Shukry et al. (15) who studied the effects of a perioperative infusion of DEX on the incidence of EA in 50 children aged 1–10 years planned for anesthesia under sevoflurane . They found significant reduction in the incidence of

EA with DEX, but no prolongation in emergence time and extubation time. Also, Jin-hui et al. (16), did a meta-analysis study included 27 trials and found the incidence of emergence agitation was decrease in DEX group in compared to control group as what resulted in our study. However, on the other hand, Bong et al. (17), failed to demonstrate any effect of 0.3 mcg/kg dexmedetomidine on the incidence of emergence delirium in children undergoing general anesthesia for magnetic resonance imaging, this may be related to lower total dose and the way of administration was used in this study in compare to the current study. Several factors may have influenced these results; the difference in results among those mentioned studies could be attributed to the lack of premedication, the comparable age range, and the type of surgery (adenotonsillectomy). Of the limited studies performed to assess the effect of various drugs on emergence time and emergence agitation following the use of sevoflurane, Shi et al found that neither propofol nor midazolam was effective in reducing the instance of EA nor emergence time in children undergoing adenotonsillectomy (18). Regarding intraoperative hemodynamic changes, our study reported a reduction in mean of systolic BP among children received dexmedetomidine IV infusion. While a significant reduction was observed in the mean of diastolic BP of the same group at time intervals (10 to 25) minutes of surgery. PR, SpO2 mean was decreased. Similarly, EtCO2 mean was reduced all-time intervals among group B in comparison to the control group. This could be understood as the most common adverse reactions from dexmedetomidine use are hypotension and bradycardia. These effects have occurred mainly with the use of IV rapid bolus dose instead of infusion (19). However, this is differed from a study of Makkar et al (20) which found no significant reduction of heart rate, blood pressure, respiratory rate, and oxygen saturation between the groups of children who received dexmedetomidine medication . None of the children recruited in the study developed bradycardia, hypotension, or desaturation throughout the study time (20). In this study noted that the PAED score was significantly reduced in dexmedetomidine studied group as compared to control group, there was a dramatically decrease in emergence agitation among studied group.

Studies reported that delirium generally begins when the child recovered from general anesthesia and can take up to 45 minutes to recover, so in this study, it was assessed within the first thirty minutes after surgery. The pediatric anesthesia emergence delirium (PAED) scale has

been used as it is the only validated scale in the pediatric population. A PAED value above 12 is considered agitated (21). At the same time, many clinical trials found that administration of Dexmedetomidine at the end of surgery or as continuous infusion has better results in preventing postoperative delirium than bolus propofol at the end of surgery or the use of continuous intraoperative ketamine administration (22). This had been found also by Rao et al when they studied the effect of different medications on PEAD, they found that dexmedetomidine significantly decreased the incidence of post-anesthesia EA or ED compared with placebo, opioids and midazolam, in pediatric patients (23). It is worth to mention that rapid awakening in a hostile environment might frighten the children and may play a role in provoking agitation. In order to eliminate this, we allowed parental presence in a warm and quiet post anesthesia care unit. It is difficult to completely differentiate between pain related agitated behavior and emergence delirium specially in toddlers and preschool children as there is some overlap of categories in scales assessing pain and ED(24).

Limitation of the Study

Numbers of patients was restricted due to episode of Covid 19 infection that lead to restriction in numbers of admission of elective adenotonsillectomy surgery.

5 CONCLUSIONS

Intravenous infusion of DEX is effective for reducing EA after sevoflurane anesthesia in children undergoing adenotonsillectomy surgery without producing sever adverse side effects.

However, we recommend further studies with larger sample size to get more precise results and confirm effectiveness of DEX on EA, and to identify an optimal doses.

Ethical Issue:

All ethical issues were approved by the author, in accordance with Ethical Principles of Declaration of Helsinki of the world Medical Association, 2013, for research involving human subjects

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