INTRODUCTION

Emergence agitation (EA) is an abnormal mental state that develops in the early postoperative period during the transition from unconsciousness to complete wakefulness which can last up to 2 days.[1] There is a disturbance in the child's awareness, perception, cognition, physical agitation and hypersensitivity to external stimulus. Though self-limiting, it creates a disturbance to the parents and recovery room attendants. It can lead to self-harm, inadvertent removal of intravenous (IV) cannulas and dressings, and injure the surgical repair and drains.[2] Adenotonsillectomy is one of the independent risk factors for EA.[3] Sevoflurane is a pleasant-smelling
Dexmedetomidine, a selective alpha 2 agonist, has been shown to reduce the incidence of postoperative agitation with sevoflurane anaesthesia. It also reduces the requirement of anaesthetic agents. However, it has the property to cause dose-dependent hypotension and bradycardia. A detailed review of literature has not given one particular dose of dexmedetomidine for the prevention of EA. Various doses have been studied for this purpose. Larger doses produced haemodynamic disturbances. Hence, we aimed to compare 0.3 μg/kg/h versus 0.5 μg/kg/h infusion following a bolus dose of 0.5 μg/kg dexmedetomidine in reducing emergence delirium in children undergoing adenotonsillectomy/tonsillectomy. The secondary objectives were to compare the perioperative haemodynamics and postoperative pain between the two groups.

Methods

After getting institutional ethical committee approval and an informed written consent from the parents, eighty children aged 5 to 14 years belonging to American Society of Anesthesiologists physical status I and II undergoing adenotonsillectomy/tonsillectomy under sevoflurane anaesthesia were included in the study. The study was registered with the Clinical Trials Registry of India. Children with hypersensitivity to the study medication, medications known to interact with dexmedetomidine, developmental delay and mental retardation, liver, renal or respiratory disorders were excluded from the study.

All the children had fasted for solids for 6 hours preoperatively. Premedication was omitted for the study requirements and an intravenous cannula was secured in the preoperative holding area with parental presence. The patients were transferred to the operating room and baseline parameters like heart rate (HR), peripheral oxygen saturation and blood pressure (BP) were noted.

In both groups, anaesthesia was induced with inj. glycopyrrolate 5 μg/kg, inj. fentanyl 1 μg/kg, inj. propofol 1.5 mg/kg, sevoflurane 2% and inj. vecuronium 0.1 mg/Kg. Patients were intubated with appropriately sized endotracheal tubes and tube position was confirmed by bilateral air entry and end tidal carbon dioxide. The patients were mechanically ventilated and anaesthesia was maintained with oxygen, nitrous oxide (FiO 0.5) and sevoflurane at one minimum alveolar concentration (MAC) intraoperatively. Loading dose of 0.5 μg/kg of dexmedetomidine was given to all the children after intubation for 10 minutes using an infusion pump.

Patients were then randomly allocated into 2 groups by a computer-generated randomisation chart with 40 children in each group. An anaesthesiologist not involved in the study loaded the drugs as per the randomisation chart. Subsequently, the patients in group A received dexmedetomidine 0.3 μg/kg/h infusion and group B 0.5 μg/kg/h infusion till surgical haemostasis was achieved. The blinded of the anaesthesiologists for the rate of infusion administered was achieved by covering the syringe with the non-transparent plaster. Sevoflurane concentration was adjusted to maintain the haemodynamics (HR and BP) within 20% from baseline. Reduction in sevoflurane concentration was done and rescue medications (ephedrine 0.5 mg/kg and atropine 20 μg/kg) were administered in case the BP and HR dropped to <20% of baseline, respectively. Intraoperative haemodynamics such as HR and mean arterial BP were monitored at 0, 1, 3, 5, 10, 15, 30 minutes and every 15 minutes thereafter till surgical closure was achieved and the patient was extubated. Inj. dexamethasone 0.1 mg/kg was given after intubation as an antiemetic and to reduce the airway edema. Paracetamol suppository 30 mg/kg was given at the end of the procedure and the anaesthetics were discontinued. After thorough oral suctioning and demonstrating a partial muscle reversal, muscle paralysis was reversed with inj. neostigmine 50 μg/kg and inj. atropine 20 μg/kg and the patients were extubated in a fully awake state.

In the postoperative care unit, the children were observed by the anaesthesiologist blinded to the study for EA using paediatric anaesthesia emergence delirium scale (PAED scale) [Table 1] and postoperative pain using objective pain scale [Table 2].

Rescue medication Inj. fentanyl 1 μg/kg was given to those patients who complained of pain or had an objective pain score of more than 4. The patients were...
transferred to the ward when the modified Aldrete score was more than 9.

The sample size was calculated with emergence delirium as the primary outcome. The sample size was calculated for a non-inferiority trial with the binary outcome at a power of 80% and 5% significance level with an expected 90% successful outcome using standard therapy (0.5 μg/kg/h dexmedetomidine) and a non-inferiority margin, not more than 10%, using alternative therapy (0.3 μg/kg/h). The calculated sample size was a total of 78 patients (39 in each group). To account for dropout of 2%, the sample size was increased to 80 (40 in each group). Data were statistically described in terms of mean ± standard deviation (± SD), percentage, median and frequency.

Age, body mass index (BMI), duration of surgery and anaesthesia were compared using Student’s unpaired t-test. Categorical variables were analysed using Chi-square test and Fisher’s Exact test. Mann-Whitney U test was used to compare the PAED scores, objective pain score and time of onset of pain. Repeated measures Analysis of Variance (ANOVA) and pairwise comparison were used for haemodynamic parameters over various time intervals. P value < 0.05 was considered as statistically significant.

**RESULTS**

A total of 80 children were enroled in the study with 40 in each group [Figure 1]. The two groups were comparable in demographic details such as age, gender, BMI and ASA grade. The surgical procedures (adenotonsillectomy/tonsillectomy) were equally distributed between both the groups (P = 0.133). The mean duration of surgery in group A was 67.2 and in group B was 67.4 minutes, respectively (P = 0.970). The mean duration of anaesthesia was 76.1 in group A and 78.9 minutes in group B, respectively (P = 0.575). There was no statistically significant difference in time for extubation in group B compared to group A.

The mean PAED score was comparable in both groups A and B at varied time intervals [Figure 2]. Similarly, the mean objective pain score was similar in both groups A and B [Figure 3].

The mean HR and mean arterial pressure (MAP) showed no significant difference between both the groups (P value > 0.05) [Figure 4].

**DISCUSSION**

EA in a paediatric age group is one of the most common postoperative problems encountered in the recovery room (Incidence 80%). Hospitalisation, anaesthesia and surgery result in postoperative behavioural alterations which can cause substantial psychological impact. A number of non-pharmacological techniques like parental presence during induction (PPIA), playing animated videos on a smartphone, operating room tours are advocated to prevent this. Drugs like opioids, benzodiazepines, clonidine, ketamine, propofol, gabapentin, magnesium and hydroxyzine have been used to reduce the incidence of EA.

| Parameter | Finding | Point |
|-----------|---------|-------|
| Crying    | Not crying | 0     |
|           | Responds to age-appropriate nurturing (tender loving care) | 1     |
|           | Does not respond to nurturing | 2     |
| Movements | No movements relaxed | 0     |
|           | Restless (moving about in bed constantly) | 1     |
|           | Thrashing (moving wildly) | 2     |
|           | Rigid (stiff) | 2     |
| Agitation | Asleep or calm | 0     |
|           | Can be comforted to lessen the agitation (mild) | 1     |
|           | Cannot be comforted (hysterical) | 2     |
| Complaints of pain | Asleep | 0     |
|           | States no pain | 0     |
|           | Cannot localise | 1     |
|           | Localises pain | 2     |
| Systolic Blood Pressure | Increase <20% of preoperative blood pressure | 0     |
|           | Increase 20%-30% of preoperative blood pressure | 1     |
|           | Increase >30% of preoperative blood pressure | 2     |

1-3: none/insignificant pain. 4-6: moderate pain. 7-10: severe pain.
Even now there is no consensus regarding any specific intervention. Dexmedetomidine is used in different routes and doses to reduce the incidence of EA and improve the wake-up scores in children.\textsuperscript{[19,20]}

The EA was recorded by using PAED scale at 0, 5, 10, 15, 30 minutes after extubation. A score of 1–15 suggested no agitation and ≥16 showed the presence of agitation. At 0 minute, i.e., extubation, 6 patients in both group A and group B had a score ≥16 suggesting a 15% incidence of EA with the mean score of 7.5. Since extubation is considered a stressful stimulus, this was considered normal.\textsuperscript{[21,22]} At 5 minutes after extubation, only 3 patients (7.5%) from group A had a PAED score ≥16. No patients in group B had score ≥16 at 5 minutes. At 10\textsuperscript{th} minute, only 1 patient (2.5%) from group A had a score of ≥16 suggesting agitation and none in group B. All the 4 patients were treated with fentanyl 1 μg/kg. At 15 and 30 minutes following extubation, none of the patients’ scores were higher and none showed agitation.

Guler et al.\textsuperscript{[23]} found that administration of single dose of dexmedetomidine 0.5 μg/kg IV 5 minutes
before the end of surgery prevented the incidence and severity of EA as well as pain. Begum et al.\(^2\)\(^{[24]}\) found both bolus (0.4 µg/kg/h) and infusion (0.4 µg/kg/h) of dexmedetomidine to be equally effective in preventing EA in children undergoing ambulatory surgeries. However, the bolus dose was more effective and it did not produce any haemodynamic instability.

In order to differentiate EA from pain, as pain is one of the confounding factors, we used an objective pain score to quantify pain. There was no statistically significant difference in the pain score in both the groups up to the 15-minute period. At 30 minutes, 4 patients in group B showed a mean pain score of 0.18 compared to 0.00 of group A and this difference was statistically significant. This discrepancy probably occurred because fentanyl 1 µg/kg was administered if the patient complained of pain even if the pain score was less than 4.

Twelve patients (30%) in group A complained of pain and received rescue medication with the mean time of onset of pain being 2.08 and 14 patients (35%) in group B had pain and received Inj. fentanyl with the mean time of onset of pain being 2.50 minutes. However, there was no statistically significant difference in the onset of pain between the 2 groups (\(P = 0.817\)).

In another study by Ghai et al.\(^2\)\(^{[25]}\) dexmedetomidine was compared in dosages of 0.15 µg/kg and 0.3 µg/kg to prevent EA in midazolam premedicated children undergoing cataract surgeries. They concluded that both 0.15 µg/kg and 0.3 µg/kg prevented EA in comparison with normal saline group without any significant variation in the haemodynamic parameters which could be possibly attributed to midazolam premedication, paracetamol and sub tenon’s block.

Haemodynamic parameters over time were studied in each of the groups individually and it was found that both the HR and MAP remained within 20% of the baseline values.

Patel et al.\(^2\)\(^{[26]}\) compared dexmedetomidine 2 µg/kg over 10 minutes followed by 0.7 µg/kg/h against inj. fentanyl 1 µg/kg bolus in 122 children aged 2–10 years undergoing adenotonsillectomy. Though the incidence of EA was lower in dexmedetomidine group than the fentanyl group, the mean HR and systolic blood pressure were significantly lower in the dexmedetomidine group (\(P > 0.05\)). This could be probably explained by the higher dose of dexmedetomidine (0.7 µg/kg/h) in their study.

In another study by Kim et al.\(^2\)\(^{[27]}\) 1 µg/kg bolus followed by 0.1 µg/kg/h dexmedetomidine infusion was compared with volume matched normal saline in children undergoing ambulatory surgeries. Incidence of emergence was lower in the dexmedetomidine group (5% vs 55%). However, MAP and HR were reduced by 22%–28% in the dexmedetomidine group. Atropine was given to 6 children who developed bradycardia with or without hypotension. They concluded that dexmedetomidine reduced the intraoperative requirement of sevoflurane and incidence of EA without delaying discharge from the recovery room.

Garg et al.\(^2\)\(^{[28]}\) studied the efficacy of dexmedetomidine 1 µg/kg bolus followed by 0.4 µg/kg/h infusion with placebo in 72 patients undergoing nasal surgeries under desflurane anaesthesia. Though dexmedetomidine reduced the incidence of EA (5.6% in dexmedetomidine group vs 52.8% in placebo), it was associated with delayed extubation, residual sedation and prolonged post-anaesthesia care unit (PACU) stay.

In order to prevent the occurrence of bradycardia, hypotension and delayed extubation, we reduced the loading and the maintenance dose of dexmedetomidine in our study. Despite the relatively lower dose, we were able to reduce the incidence of EA and maintain haemodynamic stability without causing any untoward effects.

Our study had some limitations. Postoperative monitoring for haemodynamics as well as pain scores was done only for 30 minutes and 54/80 patients did not receive postoperative analgesia in the recovery room and we did not chart when the first dose of rescue analgesia was given in the ward. Subgroup analysis regarding the incidence of EA according to age was not done due to the relatively smaller sample size...

**CONCLUSION**

From our study, we conclude that intraoperative dexmedetomidine infusion of 0.3 µg/kg/h and 0.5 µg/kg/h following an initial bolus dose of 0.5 µg/kg is equally effective. Hence, we recommend a smaller dose of dexmedetomidine as sufficient to provide adequate relief from emergence agitation without having to resort to a higher dose.
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients' parents have given their consent for their children images and other clinical information to be reported in the journal. The parents understand that their children's 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.

REFERENCES
1. Wong DD, Bailey CR. Emergence delirium in children. Anaesthesia 2015;70:383-7.
2. Voepel-Lewis T, Malviya S, Tait AR. A prospective cohort study of emergence agitation in the pediatric postanesthesia care unit. Anesth Analg 2003;96:1625-30.
3. Whitman TM. Emergence delirium in children: Review and rationale for the use of dexmedetomidine for prevention. J Pediatr Surg Nurs 2018;7:41-6.
4. Beskow A, Westrin P. Sevoflurane causes more postoperative agitation in children than does halothane. Acta Anaesthesiol Scand 1999;43:336-41.
5. Mehrrota S. Postoperative anaesthetic concerns in children: Postoperative pain, emergence delirium and postoperative nausea and vomiting. Indian J Anaesth 2019;63:763-70.
6. Soliman R, Alshehri A. Effect of dexmedetomidine on emergence agitation in children undergoing adenotonsillectomy under sevoflurane anesthesia: A randomized controlled study. Egypt J Anaesth 2015;31:283-9.
7. Mason KP, O'Mahony E, Zurakowski D, Libenson MH. Effects of dexmedetomidine sedation on the EEG in children. Paediatr Anaesth 2009;19:1175-83.
8. Shi M, Mao S, Gu T, Wang D, Zhang H, Liu J. Dexmedetomidine for the prevention of emergence delirium and postoperative behavioral changes in pediatric patients with sevoflurane anesthesia: A double-blind, randomized trial. Drug Des Devel Ther 2019;13:897-905.
9. Ibacache ME, Muñoz HR, Brandes V, Morales AL. Single-dose dexmedetomidine reduces agitation after sevoflurane anesthesia in children. Anesth Analg 2004;98:60-3.
10. Ali WA, Mohammed AK, Elshorbagy HM. Dexmedetomidine versus ketolol effect on the incidence of emergence agitation associated with sevoflurane-based anesthesia in children undergoing orthopedic surgery. Egypt J Anaesth 2016;32:277-84.
11. Phan H, Nahata MC. Clinical uses of dexmedetomidine in pediatric patients. Paediatr Drugs 2008;10:49-69.
12. Su F, Hammer GB. Dexmedetomidine: Pediatric pharmacology, clinical uses and safety. Expert Opin Drug Saf 2011;10:55-66.
13. Aouad MT, Nasr VG. Emergence agitation in children: An update. Curr Opin Anaesthesiol 2005;18:814-9.
14. Mason KP. Paediatric emergence delirium: A comprehensive review and interpretation of the literature. Br J Anaesth 2017;118:335-43.
15. Yip P, Middleton P, Cyna AM, Carlyle AV. Non-pharmacological interventions for assisting the induction of anaesthesia in children. Cochrane Database Syst Rev 2009;CD006447. doi: 10.1002/14651858.CD006447.pub2.
16. 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. J Anesth 2014;28:1-11.
17. Zhang C, Li J, Zhao D, Wang Y. Propylactic midazolam and clonidine for emergence from agitation in children after emergence from sevoflurane anesthesia: A meta-analysis. Clin Ther 2013;35:1622-31.
18. 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;104:216-23.
19. Kumar L, Kumar A, Panikkevastil R, Vus BK, Rajan S, Nair SG. Efficacy of intranasal dexmedetomidine versus oral midazolam for paediatric premedication. Indian J Anaesth 2017;61:125-30.
20. Prabhu MK, Mehandale SG. Comparison of oral dexmedetomidine versus oral midazolam as premedication to prevent emergence agitation after sevoflurane anaesthesia in paediatric patients. Indian J Anaesth 2017;61:131-6.
21. Karmarkar S, Varshney S. Tracheal extubation. Continuing Educ: AnaesthCrit Care Pain 2008;1:214-20.
22. Pal S, Ghosh TR, Pahari S. Haemodynamic changes and recovery response after intravenous dexmedetomidine during tracheal extubation after general anaesthesia. J Evolution Med Dent Sci 2019;8:3171-6.
23. Guler G, Akin A, Tosun Z, Ors S, Esmaooglu A, Boyaci A. Single-dose dexmedetomidine reduces agitation and provides smooth extubation after pediatric adenotonsillectomy. Paediatr Anaesth 2005;15:762-6.
24. Begum U, Singh PR, Naithani B, Singh V, Singh GP, Tiwari T. Dexmedetomidine as bolus or low-dose infusion for the prevention of emergence agitation with sevoflurane anesthesia in pediatric patients. Anesth Essays Res 2019;13:57-62.
25. Ghaib B, Jain D, Coutinho P, Wig J. Effect of low dose dexmedetomidine on emergence delirium and recovery profile following sevoflurane induction in pediatric cataract surgeries. J Anesthesiol 2015;2015. doi: 10.1155/2015/617074.
26. Patel A, Davidson M, Tran MC, Quraishi H, Schoenberg C, Sant M, et al. Dexmedetomidine infusion for analgesia and prevention of emergence agitation in children with obstructive sleep apnea syndrome undergoing tonsillectomy and adenoidectomy. Anesth Analg 2010;111:1004-10.
27. Kim NY, Kim SY, Yoon HJ, Kil HK. Effect of dexmedetomidine on sevoflurane requirements and emergence agitation in children undergoing ambulatory surgery. Yonsei Med J 2014;55:209-15.
28. Garg A, Kamal M, Mohammed S, Singariya G, Chouhan DS, Biyani G. Efficacy of dexmedetomidine for prevention of emergence agitation in patients posted for nasal surgery under desflurane anaesthesia: A prospective double-blinded randomised controlled trial. Indian J Anaesth 2018;62:524-30.