ORIGINAL ARTICLE

Prevention of sevoflurane related emergence agitation in children undergoing adenotonsillectomy: A comparison of dexmedetomidine and propofol

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ABSTRACT

Background: Emergence agitation (EA) in children is increased after sevoflurane anesthesia. Propofol and dexmedetomidine have been used for prophylactic treatment with controversial results. The aim of the present study was to compare the effect of a single dose of propofol or dexmedetomidine prior to termination of sevoflurane-based anesthesia on the incidence and severity of EA in children. **Methods:** One hundred and twenty children, American Society of Anesthesiologists I-II, 2-6 years old undergoing adenotonsillectomy under sevoflurane based anesthesia were enrolled in the study. Children were randomly allocated to one of the three equal groups: (Group C) received 10 ml saline 0.9%, (Group P) received propofol 1 mg/kg or (group D) received dexmedetomidine 0.3 ug/kg^{-1}. The study drugs were administered 5 min before the end of surgery. In post anesthesia care unit (PACU), the incidence of EA was assessed with Aonos four point scale and the severity of EA was assessed with pediatric anesthesia emergence delirium scale upon admission (T0), after 5 min (T5), 15 min (T15) and 30 min (T30). Extubation time, emergence time, duration of PACU stay and pain were assessed. **Results:** The incidence and severity of EA were lower in group P and group D compared to group C at T0, T5 and T15. The incidence and severity of EA in group P were significantly higher than group D at the same times. The incidence and severity of EA decreased significantly over time in all groups. The modified Children's Hospital of Eastern Ontario Pain Scale was significantly lower in group D compared to group C and group P. **Conclusions:** Dexmedetomidine 0.3 ug/kg^{1} was more effective than propofol 1 mg/kg in decreasing the incidence and severity of EA, when administered 5 min before the end of surgery in children undergoing adenotonsillectomy under sevoflurane anesthesia.

Key words: *Children, dexmedetomidine, emergence agitation, propofol, sevoflurane*

INTRODUCTION

The occurrence of emergence agitation (EA) in children after sevoflurane anesthesia is common, with a reported incidence up to 80%.[1] EA is characterized by a period of restlessness, agitation, inconsolable crying, disorientation, delusion, hallucination and cognitive changes plus memory impairment.[2] EA in children is generally short-lived with no after-effect, however, it is a troublesome phenomenon, because it can result in injury to the patient or damage to the surgical site, leads to dissatisfaction and anxiety for the parents, and requires extra nursing care with associated costs.[3]

Different drugs such as propofol, α2-adrenoreceptor agonists, midazolam, and ketamine have been used to allow a smooth emergence from sevoflurane anesthesia.[4] However, their efficacy remains the subject of debate. Propofol is a short-acting sedative and hypnotic agent. Generally, propofol is used in children for its sedative action as well as for induction and maintenance of general anesthesia.[5] Based on previous studies,[6,7] propofol seems to be effective in preventing EA and is dependent on the timing of administration.[4]

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Dexmedetomidine, is a more highly specific α2-adrenoreceptor agonist (α2/α1=1620/1) than clonidine (α2/α1=220/1), has sedative and analgesic properties without significant respiratory depression at clinical dosages.[8,9] Dexmedetomidine is reported to significantly reduce EA frequency after sevoflurane anesthesia in pediatric surgery and non-surgical procedures in inpatient[10,11] and outpatient settings.[12,13]

This double-blinded randomized prospective study was conducted to compare the effect of administration of a single dose of propofol or dexmedetomidine prior to the termination of sevoflurane-based anesthesia on the incidence and severity of EA as well as emergence and discharge time in children undergoing adenotonsillectomy.

METHODS

After institutional review board (Menoufiya University hospital, Menoufiya City, Egypt) approval and written informed consent from parents, 120 healthy children aged 2-6 years, with American Society of Anesthesiologists (ASA) physical status I or II, scheduled to undergo adenotonsillectomy were prospectively enrolled in this double blind, randomized prospective controlled study. The patients were then randomized to one of three equal groups using a computer generated randomization table. The control group (Group C), propofol group (Group P) and dexmedetomidine group (Group D). Exclusion criteria included mental disease, neurologic disease, and treatment with sedatives, full stomach, or indication for rapid sequence induction.

Children fasted for 8 h and received 0.5 mg/kg^{1} oral midazolam approximately 30 min before separation from the parents. The number of children who were agitated or combative during induction of anesthesia despite premedication with midazolam was recorded in each group. An electrocardiogram, pulse oximeter and noninvasive arterial blood pressure monitor were attached. General anesthesia was induced with 8% sevoflurane in 70% nitrous oxide in oxygen, via a facemask. After establishing a venous access, rocuronium 0.6 mg/kg^{1} was given. Orotracheal intubation was performed and anesthesia was maintained with 60% nitrous oxide in oxygen, supplemented by an end-tidal concentration of 2-3% sevoflurane with controlled ventilation, to maintain an end-tidal CO_2 of 4.6±0.5 kPa (35±4 mmHg). All patients received 15 mg/kg^{1} i.v. paracetamol (Perfalgan; UPSA Laboratories, Agen, France) for the control of postoperative pain and 1 mg/kg^{1} i.v. dexamethasone (maximum 16 mg) for the control of postoperative pain, nausea, and vomiting. About 5 min before the end of surgery, patients in (Group C) received 10 ml NaCI 0.9%, patients in (Group P) received propofol 1 mg/kg^{1} and patients in (Group D) received dexmedetomidine 0.3 ug/kg^{1} diluted in 10 ml NaCI 0.9%. Experimental drugs were administered intravenously over 5 min. At the conclusion of the procedure, following the discontinuation of sevoflurane and nitrous oxide, residual muscle relaxation was reversed with neostigmine 0.05 mg/kg^{1} and atropine 0.02 mg/kg^{1} i.v. Extubation was performed when the patients' gag reflex was restored and they showed facial grimaces or purposeful appearing motor movements, and the rate of train of four (TOF) was higher than 0.8 by a nerve stimulator (TOF-Watch®, Organon, Ireland). Children were transferred to the post anesthesia care unit (PACU). Upon arrival to the PACU, all children were received by one of their parents, who stayed with them until discharge.

The incidence of EA was evaluated using Aonos four point scale;[14] 1=calm; 2=not calm but could be easily consoled; 3=moderately agitated or restless and not easily calmed; 4=combative, excited, or disoriented, thrashing around. Scores of one and two were considered as absence of EA, and scores of three and four were analyzed as presence of EA. The severity of EA was evaluated using pediatric anesthesia emergence delirium (PAED) scale devised by Sikich *et al.*[2] [Table 1], a five-point rating scale with five grades for each item. The incidence and severity of EA were measured upon admission to the PACU (T0) and in the PACU at 5 min (T5), at 15 min (T15) and at 30 min (T30). Children were considered severely agitated if they had a PAED scale of 15/20 or higher.

Postoperative pain was assessed using the modified Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) in the PACU at (T0), (T5), (T15) and (T30). Vomiting was treated with metoclopramide 0.15 mg/kg^{1} i.v. and the incidence of vomiting was recorded. Nausea was not recorded as it was difficult to assess in children. The incidence of adverse events such as hypotension, bradycardia, laryngospasm, bronchospasm and oxygen desaturation, were noted.

The following time intervals were recorded: The duration of surgery (from the time of mouth opening to the completion of the procedure), duration of sevoflurane anesthesia (from

Table 1: Pediatric anesthesia emergence delirium scale

Behavior	Not at all	Just a little	Quite a bit	Very much	Extremely
Make eye contact with caregiver	4	3	2	1	0
Actions are purposeful	4	3	2	1	0
Aware of surrounding	4	3	2	1	0
Restless	0	1	2	3	4
Inconsolable	0	1	2	3	4

1 – Calm; 2 – Not calm but could be easily consoled; 3 – Moderately agitated or restless and not easily calmed; 4 – Combative, excited, thrashing around

mask induction to the discontinuation of the inhaled anesthetic), duration of extubation (from the discontinuation of sevoflurane to the removal of endotracheal tube), time of emergence (from discontinuation of sevoflurane to the first response to a simple verbal command), and duration of PACU stay (from arrival to the PACU until discharge). Children were discharged from the PACU to a ward when the modified aldrete score was more than nine without agitation and vomiting.

Two anesthesiologists were involved in the study. All above i.v. agents were prepared and hidden behind drapes and administered by the first anesthesiologist according to the group to which the patient was randomized. The recordings of all variables were collected by the second anesthesiologist who was blinded to the group to which the patient was assigned.

Statistical analysis

Distribution of baseline variables was assessed by the Shapiro-Wilk W tests. Assuming an incidence of postoperative agitation of 30% or more after sevoflurane anesthesia was previously reported,[15,16] and a 50% reduction in EA was considered to be clinically significant, we calculated that 40 patients were required in each group (for a level of significance of 0.05 and a power of 0.80). By using Statistical program for social science (SPSS) software for Windows, version 11(SPSS Inc, Chicago, IL, USA), arithmetic mean and standard deviation values for different variables were calculated and statistical analyses were performed for each group. Independent sample *t*-test was used to compare continuous variables exhibiting normal distribution, and Chi-squared or Fisher exact test for non-continuous variables. Serial measurements such as Aonos four point scale, PAED scale and modified CHEOPS were analyzed by repeated measures analysis of variance. $P<0.05$ is considered significant.

RESULTS

There were no significant differences among the three studied groups in patient characteristics, incidence of agitation before induction of anesthesia as well as the different durations of anesthesia and surgery [Table 2].

The incidence and severity of EA were significantly lower in group P and group D compared to group C at T0, T5, T15 but not at T30. Compared to group D, the incidence and severity of EA in group P were significantly higher at T0, T5, and T15 but not at T30. The number of patients who developed severe EA (PAED >15) was significantly lower in group D and group P compared to group C. Compared to group D, group P showed no statistically significant difference. Modified CHEOPS was significantly lower in group D compared to group P and group C at T0 and T5 but not at T15 and T30. There was no significant difference between group P and group C at any time of measurement. Aonos four point scale, PAED scale and modified CHEOPS decreased significantly over time in each group. Regarding the incidence of vomiting, there was no statistically significant difference among the studied groups. Times to emergence and extubation in group P were significantly longer compared to group C and group D. Time to discharge from the PACU was not significantly different among the studied groups [Table 3].

Table 2: Patients' criteria and anesthetic details

	Group C (*N*=40)	Group P (*N*=40)	Group D (*N*=40)
Age (years) (mean±SD)	3.9±1.6	4.2±1.4	4.3±1.3
Weight (kg) (mean±SD)	18.7±4.5	19.8±4.6	19.5±4.8
Sex (M:F) (*N*)	22/18	24/16	23/17
Duration of surgery (min) (mean±SD)	35±9.8	38.6±12.2	36.7±10.8
Duration of anesthesia (min) (mean±SD)	43.6±13.6	46.3±10.5	45.0±11.3
Incidence of agitation before induction (%)	12.5	10	7.5

Data are presented as mean±SD, number or percent; *Significant difference between group C and group P or group D; ΔSignificant difference between group P and group D; $P<0.05$ is significant

Table 3: Incidence of emergence agitation, pediatric anesthesia emergence delirium scale, modified children's hospital of eastern ontario pain scale and recovery characteristics

	Group C (*N*=40)	Group P (*N*=40)	Group D (*N*=40)
Incidence of emergence agitation (*N*)			
T0	22†	13*†	5*Δ†
T5	18	9*	2*Δ
T15	11	4*	1*Δ
T30	2	1	0
PAED (mean±SD)			
T0	13.7±5.2†	11.6±3.8*†	9.8±3.5*Δ†
T5	8.4±4.5	6.6±3.2*	5.2±2.9*Δ
T15	5.7±3.8	5.2±2.3*	4.2±1.9*Δ
T30	4.2±1.5	4.1±2.6	3.5±1.7
Patients with PAED score>15 (*N*)	7	3*	2*
Modified CHEOPS (mean±SD)			
T0	5.5±1.8†	5.3±1.4†	4.7+1.2*Δ†
T5	4.4±1.5	4.3±1.7	3.6±1.3*Δ
T15	3.6±1.8	3.4±2.0	2.8±1.9
T30	2.2±1.6	2.3±1.4	2.1±1.1
Duration of extubation (min)	7.2±2.3	8.6±2.5*	7.47±2.1Δ
Time of emergence (min)	10.7±2.5	12.3±3.4*	10.9±2.8Δ
Duration of PACU stay (min)	37.9±5.5	38.5±5.3	40.1±6.1
Vomiting in PACU (*N*)	3	5	4

Data are presented as mean±SD, number or percent; *Significant difference between group C and group P or group D; ΔSignificant difference between group P and group D; †Intragroup significant difference; $P<0.05$ is significant; PAED – Pediatric anesthesia emergence delirium; CHEOPS – Children's hospital of eastern ontario pain scale; PACU – Post anesthesia care unit

No adverse events such as laryngospasm, bronchospasm, hypotension, bradycardia and oxygen desaturation episodes were recorded in any of the children.

DISCUSSION

The etiology of EA in children is not fully understood but possible risk factors are intrinsic characteristics of an anesthetic, rapid emergence from anesthesia, postoperative pain, preschool age, otolaryngologic surgical procedures, preoperative anxiety, and child temperament.[1] Meta-analysis of 23 randomized controlled trials revealed that EA occurred more frequently with sevoflurane than halothane.[17] Rapid awakening after sevoflurane anesthesia has been assumed to be a cause for the phenomenon. However, it is currently thought that rapid emergence is not the only cause of EA, because recovery from propofol anesthesia, which also has rapid emergence properties, is associated with low incidence of EA.[18]

In our study, the incidence and severity of EA were significantly lower in group D compared to group P and group C. Previous studies[10,13,19] showed that dexmedetomidine reduces the incidence of EA after sevoflurane anesthesia in children because of their sedative and analgesic effects. In a study by Guler *et al.*[11] 1.5-2% sevoflurane in 60% N_2O in Oxygen and muscle relaxants were used in children undergoing adenotonsillectomy. They reported that dexmedetomidine given 5 min before the end of surgery, was effective in reducing the agitation with prolongation of extubation and emergence times. Ibacache *et al.*[10] found patients undergoing lower abdominal surgery anesthetized with 1-3% sevoflurane in 50% N_2O in oxygen and a single i.v. dose of dexmedetomidine after induction, resulted in a reduction of postoperative agitation from 37% in the control group to 17% and 10% with 0.15 and 0.3 μg/kg^1, respectively.

Recovery from propofol anesthesia is smooth and delayed, so propofol anesthesia is associated with a lower incidence of EA compared to sevoflurane.[20] The decreased incidence of EA could be accounted for the residual sedative effect and euphoric effect of propofol in the early recovery period.[21] Due to rapid pharmacokinetics of propofol, a bolus of 1 mg/kg^1 given at the end of the procedure or continuous infusion used during maintenance of anesthesia results in increased concentrations during emergence and decreased incidence of EA.[4] Abu-Shahwan's study[6] 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 magnetic resonance imaging (MRI). Aouad *et al.*[7] reported that the administration of a single dose of propofol 1 mg/kg^1 after discontinuation of sevoflurane at the end of surgery in children undergoing strabismus surgery significantly decreased the incidence of EA and improved patient satisfaction. On the other hand, Lee *et al.*[22] reported that administration of a single dose of 1 mg/kg^1 propofol at the end of surgery in children undergoing adenotonsillectomy under sevoflurane anesthesia did not decrease the incidence and severity of EA.

The presence of pain is thought to be one of the major causes of EA, but painless treatment does not guarantee calm emergence from sevoflurane anesthesia.[1] Isik *et al.*[12] reported that EA was seen in 48% of pediatric patients after sevoflurane anesthesia for MRI. A recent meta-analysis shows no correlation of the efficacy of ketamine, α2-agonists, or fentanyl in postoperative pain relief and EA reduction.[4] These results suggest that the analgesic properties alone of these compounds are unlikely to be involved in their preventive effects for EA. Nevertheless, the properties to induce emergence sedation could explain their preventive effect.

The modified CHEOPS was significantly lower in group D compared to group P and group C at T0 and T5. Modified CHEOPS in each group decreased significantly over time. Modified CHEOPS was not influenced by propofol because propofol is not an analgesic agent. Kim *et al.*[23] reported that propofol 1 mg/kg^1 at the strabismus surgery under sevoflurane anesthesia did not reduce EA in children, and they emphasized the importance of pain control.

Many studies have shown that EA is self-limited and is resolved without pharmacologic intervention over time.[1,24] Our data also demonstrated that the incidence and severity of EA and pain intensity are improved over time without analgesic or sedative drugs. Our study allowed children to stay with one of parents in the PACU and this seemed to help them to acclimate themselves to a strange and naive environment.

Time of extubation and emergence time were significantly longer in group P compared to group C. This is consistent with previous studies[6,7] showing that the time to awakening correlates negatively with EA scores. The statistically significant difference between group P and group D is of small magnitude and is not clinically significant. The delayed extubation time and emergence from anesthesia in group P did not delay discharge; children in all groups had comparable durations of PACU stay.

Dexmedetomidine produces dose-dependent HR and BP decrease.[9,25] Ibacache *et al.*[10] and Guler *et al.*[11] reported no hemodynamic effects at a 0.3-0.5 ug/kg^1 bolus dose. Similarly, there was no significant hemodynamic effect

in our study. Administering dexmedetomidine before extubation may contribute to hemodynamic stability.

Despite the fact that adenotonsillectomy surgery is well known to be associated with a high incidence of postoperative nausea and vomiting[26] the incidence of vomiting in our study is lower than previous studies.[26] This finding may be explained by the following facts: Only paracetamol, a nonopioid analgesic was administered, in addition to dexamethasone that possesses both analgesic[27] and antiemetic properties. Also, children stayed for approximately half an hour in the PACU. Discharge from the PACU coincided with the end of the study period. Therefore, the occurrence of delayed vomiting may have not been recorded by the investigators.

In our study dexmedetomidine 0.3 ug/kg[1] was more effective than propofol 1 mg/kg[1] in decreasing the incidence and severity of EA, when they administered 5 min. before the end of surgery in children undergoing adenotonsillectomy under sevoflurane anesthesia. Dexmedetomidine decreased postoperative pain, extubation time and emergence time compared to propofol without affecting the length of stay in PACU.

REFERENCES

1. Vlajkovic GP, Sindjelic RP. Emergence delirium in children: Many questions, few answers. Anesth Analg 2007;104:84-91.
2. Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology 2004;100:1138-45.
3. Silva LM, Braz LG, Módolo NS. Emergence agitation in pediatric anesthesia: Current features. J Pediatr (Rio J) 2008;84:107-13.
4. 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.
5. De Grood PM, Coenen LG, van Egmond J, Booij LH, Crul JF. Propofol emulsion for induction and maintenance of anaesthesia. A combined technique of general and regional anaesthesia. Acta Anaesthesiol Scand 1987;31:219-23.
6. Abu-Shahwan I. Effect of propofol on emergence behavior in children after sevoflurane general anesthesia. Paediatr Anaesth 2008;18:55-9.
7. Aouad MT, Yazbeck-Karam VG, Nasr VG, El-Khatib MF, Kanazi GE, Bleik JH. A single dose of propofol at the end of surgery for the prevention of emergence agitation in children undergoing strabismus surgery during sevoflurane anesthesia. Anesthesiology 2007;107:733-8.
8. Kamibayashi T, Maze M. Clinical uses of alpha2 -adrenergic agonists. Anesthesiology 2000;93:1345-9.
9. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263-8.
10. Ibacache ME, Muñoz HR, Brandes V, Morales AL. Single-dose dexmedetomidine reduces agitation after sevoflurane anesthesia in children. Anesth Analg 2004;98:60-3.
11. Guler G, Akin A, Tosun Z, Ors S, Esmaoglu A, Boyaci A. Single-dose dexmedetomidine reduces agitation and provides smooth extubation after pediatric adenotonsillectomy. Paediatr Anaesth 2005;15:762-6.
12. Isik B, Arslan M, Tunga AD, Kurtipek O. Dexmedetomidine decreases emergence agitation in pediatric patients after sevoflurane anesthesia without surgery. Paediatr Anaesth 2006;16:748-53.
13. Shukry M, Clyde MC, Kalarickal PL, Ramadhyani U. Does dexmedetomidine prevent emergence delirium in children after sevoflurane-based general anesthesia? Paediatr Anaesth 2005;15:1098-104.
14. Aono J, Ueda W, Mamiya K, Takimoto E, Manabe M. Greater incidence of delirium during recovery from sevoflurane anesthesia in preschool boys. Anesthesiology 1997;87:1298-300.
15. 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.
16. Welborn LG, Hannallah RS, Norden JM, Ruttimann UE, Callan CM. Comparison of emergence and recovery characteristics of sevoflurane, desflurane, and halothane in pediatric ambulatory patients. Anesth Analg 1996;83:917-20.
17. Kuratani N, Oi Y. Greater incidence of emergence agitation in children after sevoflurane anesthesia as compared with halothane: A meta-analysis of randomized controlled trials. Anesthesiology 2008;109:225-32.
18. Cohen IT, Finkel JC, Hannallah RS, Hummer KA, Patel KM. Rapid emergence does not explain agitation following sevoflurane anaesthesia in infants and children: A comparison with propofol. Paediatr Anaesth 2003;13:63-7.
19. Sato M, Shirakami G, Tazuke-Nishimura M, Matsuura S, Tanimoto K, Fukuda K. Effect of single-dose dexmedetomidine on emergence agitation and recovery profiles after sevoflurane anesthesia in pediatric ambulatory surgery. J Anesth 2010;24:675-82.
20. Uezono S, Goto T, Terui K, Ichinose F, Ishguro Y, Nakata Y, *et al*. Emergence agitation after sevoflurane versus propofol in pediatric patients. Anesth Analg 2000;91:563-6.
21. Nakayama S, Furukawa H, Yanai H. Propofol reduces the incidence of emergence agitation in preschool-aged children as well as in school-aged children: A comparison with sevoflurane. J Anesth 2007;21:19-23.
22. Lee CJ, Lee SE, Oh MK, Shin CM, Kim YJ, Choe YK, *et al*. The effect of propofol on emergence agitation in children receiving sevoflurane for adenotonsillectomy. Korean J Anesthesiol 2010;59:75-81.
23. Kim HJ, Kim HS, Kim SD, Kim CS, Kim JT, Lee KJ, *et al*. Effects of propofol and nalbuphine on emergence agitation after sevoflurane anesthesia in children for strabismus surgery. Korean J Anesthesiol 2008;55:575-8.
24. Cole JW, Murray DJ, McAllister JD, Hirshberg GE. Emergence behaviour in children: Defining the incidence of excitement and agitation following anaesthesia. Paediatr Anaesth 2002;12:442-7.
25. Coursin DB, Coursin DB, Maccioli GA. Dexmedetomidine. Curr Opin Crit Care 2001;7:221-6.
26. Furst SR, Rodarte A. Prophylactic antiemetic treatment with ondansetron in children undergoing tonsillectomy. Anesthesiology 1994;81:799-803.
27. Afman CE, Welge JA, Steward DL. Steroids for post-tonsillectomy pain reduction: Meta-analysis of randomized controlled trials. Otolaryngol Head Neck Surg 2006; 134:181-6.

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