

Dexmedetomidine Infusion for Analgesia and Prevention of Emergence Agitation in Children with Obstructive Sleep Apnea Syndrome Undergoing Tonsillectomy and Adenoidectomy

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BACKGROUND: Dexmedetomidine, a specific α_2 agonist, has an analgesic-sparing effect and reduces emergence agitation. We compared an intraoperative dexmedetomidine infusion with bolus fentanyl to reduce perioperative opioid use and decrease emergence agitation in children with obstructive sleep apnea syndrome undergoing adenotonsillectomy (T&A).

METHODS: One hundred twenty-two patients with obstructive sleep apnea syndrome undergoing T&A, ages 2 to 10 years, completed this prospective, randomized, U.S. Food and Drug Administration–approved study. After mask induction with sevoflurane, group D received IV dexmedetomidine $2 \mu\text{g} \cdot \text{kg}^{-1}$ over 10 minutes, followed by $0.7 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$, and group F received IV fentanyl bolus $1 \mu\text{g} \cdot \text{kg}^{-1}$. Anesthesia was maintained with sevoflurane, oxygen, and nitrous oxide. Fentanyl 0.5 to $1 \mu\text{g} \cdot \text{kg}^{-1}$ was given to subjects in both groups for an increase in heart rate or systolic blood pressure 30% above preincision values that continued for 5 minutes. Observers in the postanesthesia care unit (PACU) were blinded to treatment groups. Pain was evaluated using the objective pain score in the PACU on arrival, at 5 minutes, at 15 minutes, then every 15 minutes for 120 minutes. Emergence agitation was evaluated at the same intervals by 2 scales: the Pediatric Anesthesia Emergence Delirium scale and a 5-point scale described by Cole. Morphine (0.05 to $0.1 \text{ mg} \cdot \text{kg}^{-1}$) was given for pain (score >4) or severe agitation (score 4 or 5) lasting more than 5 minutes.

RESULTS: In group D, 9.8% patients needed intraoperative rescue fentanyl in comparison with 36% in group F ($P = 0.001$). Mean systolic blood pressure and heart rate were significantly lower in group D ($P < 0.05$). Minimum alveolar concentration values were significantly different between the 2 groups ($P = 0.015$). The median objective pain score was 3 for group D and 5 for group F ($P = 0.001$). In group D, 10 (16.3%) patients required rescue morphine, in comparison with 29 (47.5%) in group F ($P = 0.002$). The frequency of severe emergence agitation on arrival in the PACU was 18% in group D and 45.9% in group F ($P = 0.004$); at 5 minutes and at 15 minutes, it was lower in group D ($P = 0.028$). The duration of agitation on the Cole scale was statistically lower in group D ($P = 0.004$). In group D, 18% of patients and 40.9% in group F had an episode of SpO_2 below 95% ($P = 0.01$).

CONCLUSIONS: An intraoperative infusion of dexmedetomidine combined with inhalation anesthetics provided satisfactory intraoperative conditions for T&A without adverse hemodynamic effects. Postoperative opioid requirements were significantly reduced, and the incidence and duration of severe emergence agitation was lower with fewer patients having desaturation episodes. (Anesth Analg 2010;X:●●●–●●●)

Adenotonsillectomy (T&A) is one of the most common surgical procedures performed in children. The presence of obstructive symptoms is replacing recurrent tonsillitis as the primary indication for T&A. The prevalence of obstructive sleep apnea syndrome (OSAS) in children, also referred to as *sleep disordered breathing*, is

estimated to be 1%–3%.¹ Postoperative pain can be severe after T&A, and providing effective and safe perioperative analgesia in this group of patients is challenging. Not only are children with OSAS undergoing T&A at significant risk of respiratory and cardiovascular complications,² they also have enhanced analgesic sensitivity to opiates and reduced morphine requirements after T&A.³ A high incidence of emergence agitation (EA) in patients having otolaryngologic procedures adds another challenge.⁴ Dexmedetomidine (Dex) (Precedex, Hospira Worldwide, Lake Forest, Illinois), a specific α_2 -adrenergic receptor agonist, has sedative, anxiolytic, and analgesic properties⁵ and is very effective in prevention of EA in children.^{6,7} An intraoperative infusion of Dex used as a substitute for fentanyl has been shown to reduce opiate use in the postoperative period in adult patients undergoing bariatric surgery,⁸ but clinical data on the analgesic-sparing effect of Dex in children are conflicting. The present study was performed to evaluate whether

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Accepted for publication June 10, 2010.

Financial support was provided by an Institutional Cost of Drug support grant from Hospira Worldwide, Lake Forest, Illinois.

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DOI: 10.1213/ANE.0b013e3181ee82fa

an intraoperative infusion of Dex combined with general anesthesia would be a safe and effective substitute to opiates intraoperatively, reduce opiate requirements postoperatively, and also be effective in reducing the incidence and severity of EA in children with OSAS undergoing T&A.

METHODS

An Investigational New Drug number (76,041) was obtained from the U.S. Food and Drug Administration. The study was registered at www.clinicaltrials.gov (registration number NCT00468052) and approved by the IRB of the University of Medicine and Dentistry of New Jersey. One hundred thirty-seven children ages 2 to 10 years, ASA physical status II–III, undergoing elective T&A, were enrolled in this investigator-initiated, prospective, randomized, blinded, controlled study. Informed, written consent to participate in the study was obtained from the parent or legal guardian and assent from children older than 7 years of age. All patients had OSAS on the basis of clinical symptoms or diagnostic polysomnography. Clinical grading of OSAS was done by the surgeon on the basis of severity of symptoms such as restless sleep, severe snoring, apnea witnessed by the parents, nocturnal enuresis, stertor, hyperactivity, or failure to thrive. Exclusion criteria were known allergy to α_2 agonists, developmental delay, cardiac and craniofacial abnormalities, anxiety disorder, chronic disabilities or pain syndrome, and use of psychotherapeutic medications, β blockers, digoxin, cimetidine, α_2 agonists, anticonvulsants, or psychotropic medications. A random number table was used to assign subjects into 1 of 2 treatment groups: Dex infusion (group D) or IV fentanyl (group F). The anesthesiologists and data collectors in the operating room (OR) were not blinded; the subjects, their parents, and observers in the postanesthesia care unit (PACU) were blinded to treatment group.

No premedication was given. Monitoring included pulse oximetry, electrocardiogram, noninvasive arterial blood pressure (NIBP), end-tidal CO_2 (ETCO_2), and a depth of anesthesia monitor, the Bispectral Index (BIS; Aspect Medical Systems, Natick, Massachusetts). Anesthesia was induced with 8% inspired sevoflurane and 60% nitrous oxide (N_2O) in oxygen by facemask. Group D received IV Dex ($2 \mu\text{g} \cdot \text{kg}^{-1}$ over 10 minutes, followed by $0.7 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ until 5 minutes before the end of the surgery), and group F received IV fentanyl ($1 \mu\text{g} \cdot \text{kg}^{-1}$) as a bolus, as soon as IV access was obtained. A balanced salt solution was administered according to standard fluid administration guidelines. Rocuronium $0.6 \text{ mg} \cdot \text{kg}^{-1}$ was used to facilitate tracheal intubation. End-tidal sevoflurane concentration was maintained at 1 minimum alveolar concentration (MAC) with 60% N_2O as long as the BIS remained below 60 during surgery. If the BIS reached 60 or more, the sevoflurane concentration was increased to reduce the BIS below 60. All patients received IV dexamethasone $0.5 \text{ mg} \cdot \text{kg}^{-1}$ (maximum 10 mg) and rectal acetaminophen 30 to 40 $\text{mg} \cdot \text{kg}^{-1}$ up to a maximum of 1000 mg before the start of surgery. The data collector recorded the heart rate (HR), systolic and diastolic blood pressures (NIBP), hemoglobin oxygen saturation (SpO_2), ETCO_2 tension, MAC, and BIS every 5 minutes during the anesthetic. The values in the

holding area for HR and systolic blood pressure were used as baseline. Both groups received fentanyl 0.5 to $1 \mu\text{g} \cdot \text{kg}^{-1}$ for an increase in HR or systolic NIBP 30% above the value before start of surgery and sustained for 5 minutes. Lactated Ringer's solution 15 mL/kg was administered as a fluid bolus for a 30% decrease of systolic blood pressure from baseline, which continued for 2 readings and glycopyrrolate $0.01 \text{ mg} \cdot \text{kg}^{-1}$ for a 30% decrease in HR. Sevoflurane was discontinued once hemostasis was achieved and muscle relaxation was reversed with neostigmine $0.05 \text{ mg} \cdot \text{kg}^{-1}$ and glycopyrrolate $0.01 \text{ mg} \cdot \text{kg}^{-1}$. The time to awakening (TA), defined as spontaneous eye opening or on command from end of surgery, and the time to extubation (TE), defined as time from end of surgery to tracheal extubation, were recorded. All patients were observed continuously in the PACU for 2 hours by observers blinded to study group. Pain was evaluated using the objective pain score (OPS)⁹ in the PACU on arrival and at 5 minutes, at 15 minutes, and then every 15 minutes for 120 minutes. EA was evaluated at the same intervals by 2 scales: the Pediatric Anesthesia Emergence Delirium (PAED) scale¹⁰ and a 5-point agitation scale described by Cole.¹¹ Duration of severe EA was noted on the Cole scale. Morphine (0.05 to $0.1 \text{ mg} \cdot \text{kg}^{-1}$) was given for pain (score >4) or severe agitation (score 4 or 5) lasting more than 5 minutes. HR, systolic and diastolic NIBP, respiratory rate (RR), and SpO_2 were recorded in the PACU every 5 minutes for the first 15 minutes, then at 15-minute intervals for the next 2 hours. Any desaturation episode with SpO_2 below 95% was noted.

Statistical Methods

A power analysis indicated that 60 subjects were required per group to show that the number of patients needing intraoperative rescue fentanyl and rescue morphine in the PACU would be 50% lower in the subjects receiving Dex. Sixty subjects were also required per group to determine that treatment with Dex would decrease the incidence of severe EA after surgery by 50% with 80% power ($\alpha = 0.05$) in comparison with the control group.

Data were analyzed using SPSS software (version 16, Chicago, Illinois), and are presented as number (*n*) or percentage (%), mean \pm SD, or median as appropriate. Student *t* test was used to compare the mean value of quantitative data between the 2 groups. Two-way repeated-measures analysis of variance (ANOVA) was used for NIBP, HR, SpO_2 , MAC, and BIS. Student *t* test was used for the comparisons of intragroup values of intraoperative and postoperative systolic blood pressure and HR. Nonparametric data such as pain score, PAED score, and EA score on the Cole scale were compared between groups with Mann–Whitney *U* test. Fischer exact test was used for comparison of gender; percentage of patients in each group with a preoperative diagnosis of mild, moderate, or severe OSAS; and number of patients rescued with fentanyl or morphine and those with episodes of severe EA. *P* value of 0.05 or less was considered statistically significant.

RESULTS

Results are presented for 122 patients. One hundred thirty-seven subjects were enrolled in this study; 15 subjects were eliminated from data analysis for the following reasons:

Table 1. Demographic Data			
	Group F (n = 61)	Group D (n = 61)	P value
Age (years)	3.8 ± 1.5	4.2 ± 2.1	0.16
2–3 years old (%)	26 (42.6)	26 (42.6)	1
Gender (M/F)	35/26	35/26	1
Weight (kg)	18.3 ± 5.7	20.4 ± 8.6	0.12
Baseline HR (beats/minute)	105 ± 18	104 ± 15	0.77
Baseline systolic NIBP (mm Hg)	101 ± 13.7	104 ± 12.6	0.29
OSAS (% patients)			
Mild	30	26	
Moderate	50	60	
Severe	20	14	0.55

Data are expressed as n (%) and mean ± SD.

Group D = dexmedetomidine group; group F = fentanyl group; HR = heart rate; NIBP = noninvasive arterial blood pressure; OSAS = obstructive sleep apnea syndrome.

Table 2. Intraoperative Data			
	Group F (n = 61)	Group D (n = 61)	P value
Rescue by fentanyl, n (%)	22 (36.1)	6 (9.8)	0.001*
Fentanyl rescue dosage (μg/kg)	1.04 ± 0.67	0.73 ± 0.25	0.312
Time of rescue (minutes)	10.82 ± 12.5	17.6 ± 6.77	0.256
Acetaminophen dosage (mg/kg)	31.51 ± 4.96	28.30 ± 6.59	0.02*
Dexamethasone dosage (mg/kg)	0.30 ± 0.12	0.30 ± 0.14	0.847
Duration of surgery (minutes)	43.33 ± 17.36	37.54 ± 13.33	0.041*
Duration of anesthesia (minutes)	75.08 ± 24.73	69.80 ± 16.82	0.175
Time to awake (minutes)	8.75 ± 4.06	7.18 ± 4.05	0.03*
Time to extubate (minutes)	10.44 ± 4.15	8.59 ± 4.51	0.02*

Data are expressed as n, mean ± SD, and percentage.

Group D = dexmedetomidine group; group F = fentanyl group; HR = heart rate; NIBP = noninvasive arterial blood pressure.

* $P < 0.05$.

surgery was cancelled for 2 patients, 1 refused to participate after enrolling, and 1 patient had an intraoperative complication. Eleven subjects who completed the study had deviation from this strictly controlled protocol or incomplete data and were also removed before data analysis.

The 2 groups were comparable in age, gender, baseline HR, systolic NIBP, and diagnosis of OSAS (Table 1). The age range of patients in the study was 2 to 10 years, 90% of patients were 6 years or younger, and 26 patients (46.2%) in each group were 2 to 3 years old.

Intraoperative data are presented in Table 2. In group D, 6 patients (9.8%) needed rescue fentanyl in comparison with 22 (36%) in group F ($P = 0.001$). Mean HR ($P = 0.001$) (Fig. 1A) and mean systolic NIBP (Fig. 1B) were significantly lower in group D during the first 60 minutes ($P = 0.019$). Mean diastolic NIBP was not statistically different in the 2 groups ($P = 0.29$). During the first 60 minutes of the anesthetic, MAC values of sevoflurane were significantly

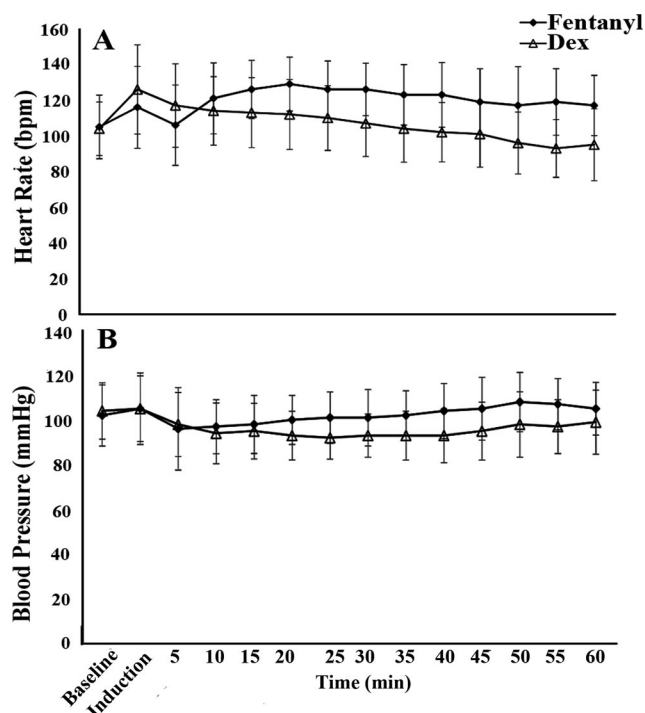


Figure 1. A, Heart rate and B, systolic blood pressure during the first 60 minutes of the procedure. Both variables were statistically lower in the dexmedetomidine group ($P < 0.05$).

different between the 2 groups ($P = 0.015$); MAC was lower in group D, ranging from 5.7% to 41.6%. There was a statistical difference in TA and TE, both lower in group D than in group F ($P < 0.05$). Duration of surgery was statistically lower in group D ($P = 0.041$). There was no difference in the average dose of intraoperative fentanyl and dexamethasone between the 2 groups. The dose of acetaminophen was lower in group D. None of the subjects needed glycopyrrolate for bradycardia or fluid bolus for hypotension in the OR.

The variables measured in the PACU are shown in Table 3. In group D 10 (16.3%) patients required rescue morphine, in comparison with 29 (47.5%) in group F ($P = 0.002$). The median of the maximum OPS was 3 for group D and 5 for group F ($P = 0.001$). The percentage of patients with an OPS score of 4 and above (Fig. 2A) from arrival ($P = 0.001$) and at 5 and 15 minutes was statistically lower in group D ($P < 0.05$). On the Cole scale (5-point scale), severe EA was defined as a score of 4 to 5. The frequency of severe EA is shown in Figure 2B. On arrival in the PACU it was statistically lower, 18% in group D and 45.9% in group F ($P = 0.004$). At 5 and 15 minutes it was statistically lower in group D ($P = 0.028$). At 30 minutes none of the patients had severe EA in group D, and 1.6% of patients in group F had severe EA. The duration of agitation on the Cole scale showed statistical significance; it was 6.59 ± 7.4 minutes (mean ± SD) for group D and 11.85 ± 12.0 minutes (mean ± SD) for group F ($P = 0.004$). There was a statistical difference in the median of the highest score on the Cole scale, 3 for group D and 4 for group F ($P = 0.001$). The percentage of patients with a score of 10 and above for the PAED (Fig. 2C) was statistically lower in group D at arrival ($P = 0.004$).

Table 3. Postanesthesia Recovery Unit Data

	Group F (n = 61)	Group D (n = 61)	P value
OPS maximum (range)	5 (0–10)	3 (0–10)	0.001*
EA score maximum (range)	4 (1–5)	3 (1–5)	0.001*
Duration of severe EA (minutes)	11.85 ± 12.02	6.59 ± 7.42	0.004*
PAED score maximum (range)	14 (0–20)	10 (0–20)	0.051
Rescue by morphine, n (%)	29 (48)	10 (17)	0.0003*
Morphine dosage (mg/kg)	0.073 ± 0.033	0.074 ± 0.033	0.928
SpO ₂ below 95%, n (%)	25 (41)	11 (18)	0.01*

OPS, PAED, and EA (Cole scale) are expressed as median values of the maximum score.

Other data are expressed as n (%) and mean ± SD.

Group D = dexmedetomidine group; group F = fentanyl group; OPS = objective pain score; EA = emergence agitation; PAED = pediatric anesthesia emergence delirium.

* $P < 0.05$.

and at 5 and 15 minutes ($P < 0.05$). The median of the highest score on the PAED scale did not show a statistical difference, 10 for group D and 14 for group F ($P = 0.051$).

On arrival in the PACU until 90 minutes, HR was statistically lower in group D ($P = 0.001$) than in group F. There was no statistical difference in mean systolic NIBP, respiratory rate, and SpO₂ in the PACU. There was a statistically significant difference in the number of patients with SpO₂ below 95% between the 2 groups, 11 (18%) in group D and 25 (40.9%) in group F ($P = 0.01$).

DISCUSSION

In this study of children undergoing T&A, an intraoperative initial loading dose of $2 \mu\text{g} \cdot \text{kg}^{-1}$ Dex followed by an infusion at $0.7 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ decreased intraoperative opiate and anesthetic requirements and decreased opiate requirements in the PACU, in comparison with a control group receiving intraoperative IV fentanyl. Additionally, there was a significantly lower incidence and duration of severe EA in children who received Dex.

We are reporting on the use of a high initial loading dose of Dex ($2 \mu\text{g} \cdot \text{kg}^{-1}$) followed by a relatively high dose continuous intraoperative infusion, because T&A is a procedure with an intense surgical stimulus, and surgery starts immediately with no preparation time. An analgesic-sparing effect of Dex has been shown,⁵ and when combined with N₂O there is an additive interaction to enhance analgesia.¹² We aimed to use the analgesic-sparing effect of Dex and evaluated whether a continuous infusion could be used as a substitute for bolus fentanyl. In our study, 90% of patients in group D did not require any other intraoperative analgesics. Because there are no studies using a high-dose continuous infusion of Dex combined with inhalation anesthetics, the U.S. Food and Drug Administration mandated reporting hemodynamic changes as a safety concern.

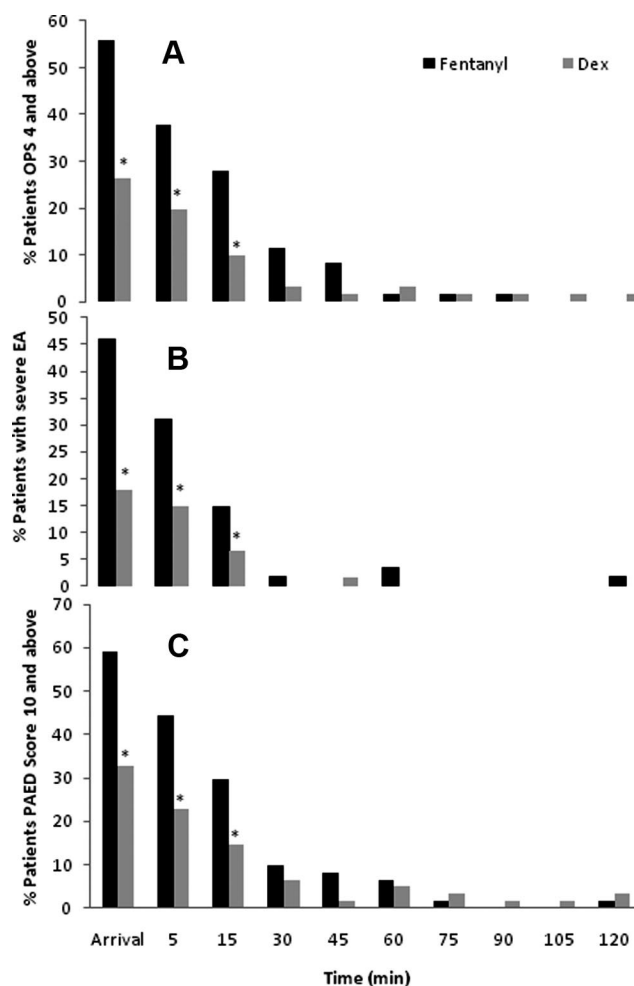


Figure 2. A, Percentage of patients with an objective pain score (OPS) of 4 and above. Score 4 and above lasting more than 5 minutes was treated. Statistically lower in group D (dexmedetomidine) at arrival ($P = 0.001$), at 5 minutes ($P = 0.028$), and at 15 minutes ($P = 0.011$). B, Percentage of patients with severe emergence agitation (EA), defined as a score of 4 or 5 on the 5-point scale. Lower in group D at arrival ($P = 0.001$), at 5 minutes ($P = 0.028$), and at 15 minutes ($P = 0.028$). C, Percentage of patients with Pediatric Anesthesia Emergence Delirium (PAED) score of 10 and above. Statistically lower in group D at arrival ($P = 0.001$), at 5 minutes ($P = 0.028$), and at 15 minutes ($P = 0.011$).

Children in group D had statistically lower systolic blood pressure and HR, almost the entire duration of the anesthetic (Fig. 1), but none of the patients needed intervention for bradycardia or hypotension on the basis of study criteria. Hemodynamic data are consistent with reports by other investigators. Mason et al.¹³ used higher doses of Dex (2 to $3 \mu\text{g} \cdot \text{kg}^{-1}$ loading dose and infusion of 1.5 to $2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) as the sole drug for sedation in children and observed a decrease in HR and blood pressure, which were within 20% of awake normal range. In children anesthetized with one MAC sevoflurane or desflurane and given a single, lower dose of Dex ($0.5 \mu\text{g} \cdot \text{kg}^{-1}$), Deutsch et al.¹⁴ found a significant decrease in HR, but neither the systolic nor diastolic blood pressure was statistically lower. The biphasic response usually seen in adults, with an initial increase in systolic blood pressure and a reflex decrease in

HR followed by stabilization of these variables below baseline, is not observed in children.¹⁵

On the basis of routine clinical practice, fentanyl was given in a dose of $1 \mu\text{g} \cdot \text{kg}^{-1}$ as a bolus to the control group. This lower dose is based on the enhanced analgesic sensitivity to opiates in children with OSAS.³ It is noteworthy that in the control group only 36% of patients needed rescue fentanyl, indicating that our technique of low-dose fentanyl is effective in almost two thirds of patients. HR and systolic blood pressure increase was used as the trigger for rescue fentanyl in both groups in response to surgical stimulation. The BIS monitor was used to ensure that patients in group D had an adequate depth of anesthesia because they may not display hemodynamic changes due to the inherent sympatholytic properties of Dex. In an attempt to maintain equivalent depth of anesthesia in both groups, the sevoflurane concentration was titrated to maintain a BIS value below 60. Consistent with studies in adult patients, the concentration of sevoflurane required to maintain the BIS below 60 was smaller in patients receiving Dex (MAC in group D was 5.7% to 41.6% lower). Tufanogullari et al.⁸ found reductions in the average end-tidal desflurane concentration of 19%–22%, depending on the rate of Dex infusion, which ranged from 0.2 to $0.8 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. The anesthetic-sparing effect of Dex appears to have an added advantage in facilitating earlier awakening and tracheal extubation. In the present study, TA and TE were statistically lower in group D, despite the high dose used. Most investigators using Dex as a low-dose intraoperative infusion or as a single bolus reported no difference in TA and TE in comparison with placebo.^{6,16} Only 1 study reported that a single dose of $0.5 \mu\text{g} \cdot \text{kg}^{-1}$ Dex, 5 minutes before the end of surgery significantly prolonged TA and TE in comparison with placebo in patients having T&A.⁷

Evaluation of postoperative pain is complicated by the difficulty in assessing pain in younger children and by the occurrence of EA. It is often difficult to distinguish between pain and EA because of the overlapping clinical picture, and pain itself can be the source of agitation.¹⁷ Most investigators have used different assessment tools to try and separate the two, but there is generally overlap in the scales, because a child who is restless or thrashing will score high on both scales. We did find a positive correlation between agitation and pain; group F had higher pain and EA scores than did group D. Results on the OPS, Cole scale, and PAED showed a very similar trend in both groups; scores were highest on arrival in the PACU and decreased over time (Fig. 2, A–C). A significantly smaller number of patients needed rescue morphine in group D, 18% in comparison with 44% in group F. Because it is difficult to separate pain and EA, and the fact that the rescue drug for both agitation and pain in our study was morphine, it is not possible to determine whether the morphine was given for pain or for agitation. On the basis of the effectiveness of smaller doses of intraoperative Dex in adult patients for reducing postoperative morphine consumption for 24 hours,^{8,18} we could assume that an analgesic effect would be present in our study patients in the immediate postoperative period. In children, Guler et al.⁷ found that 23% patients who received a single dose of $0.5 \mu\text{g}/\text{kg}$ Dex before the end of the procedure (T&A) required opioids for

analgesia in the PACU in comparison with 53% in the placebo group. Erdil et al.¹⁹ compared a single dose of $0.5 \mu\text{g} \cdot \text{kg}^{-1}$ Dex with $2.5 \mu\text{g} \cdot \text{kg}^{-1}$ fentanyl in patients undergoing adenoidectomy and concluded that Dex provided residual analgesia similar to that of fentanyl.

Pain can be severe after T&A, and it is commonly treated with opioids, despite a known sensitivity of patients with OSAS and recurrent hypoxemia to opiates. Brown et al.³ reported enhanced analgesic morphine sensitivity in children with OSAS during T&A and reduced morphine requirements after T&A. Therefore, several nonopioid analgesics such as ketorolac, ketamine, and tramadol have been evaluated for pain management after T&A,^{20–22} but none have gained widespread use or acceptance because of concerns with side effects or inadequate analgesia. A morphine-sparing effect of acetaminophen has been demonstrated in pediatric day-case surgery,²³ and dexamethasone also reduces post-tonsillectomy pain.²⁴ In the present study, all patients were given 30 to $40 \text{ mg} \cdot \text{kg}^{-1}$ of acetaminophen rectally before start of surgery and intraoperative IV dexamethasone. A multimodal, opioid-sparing, analgesic approach including Dex, such as the one used in our study, is worth considering in this patient population with a high potential for adverse respiratory events. The incidence of nausea or vomiting was extremely low in this study. Only 1 patient needed an antiemetic in the PACU, probably because of the antiemetic effect of dexamethasone.

EA is a complex phenomenon, the etiology of which is multifactorial. The wide variability in the incidence of agitation in the different studies on EA may be due to the criteria used to define this phenomenon and the time in the PACU when EA was measured.¹⁷ We did repeated measurements at frequent time intervals, because a single measurement may not reflect the true incidence of EA.¹¹ Group D had a statistically lower frequency of severe EA than did group F until 30 minutes (Fig. 2B). At 30 minutes there was no incidence of severe EA in group D, and in group F it was 1.6%. Severe EA lasting more than 5 minutes was treated. The incidence of severe EA on arrival in the PACU in group D (18%) was similar to that reported by Guler et al.⁷ (17%), who used a single dose of Dex 5 minutes before the end of the procedure in children undergoing T&A. The occurrence of EA in younger patients and otolaryngologic procedures is reported to be high, although the exact reason for this is not known.⁴ Ninety percent of patients in our study were 6 years old or younger, and 26 patients (46.2%) in each group were 2 to 3 years old. Hyperactivity and attention deficit disorder are frequently seen in children with OSAS, possibly explaining or contributing to a high incidence of EA in our T&A patients. Dexmedetomidine has been used successfully as an infusion ($0.2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) continued into the postoperative period for 15 minutes or single dose at the end of surgery ($0.5 \mu\text{g} \cdot \text{kg}^{-1}$) to prevent or reduce emergence delirium in children.^{6,7,16} It must be noted that these studies compared Dex with placebo, whereas our control group received fentanyl $1 \mu\text{g} \cdot \text{kg}^{-1}$, which also reduces EA. However, a higher dose is reported to be effective in patients having painful procedures.²⁵ From our study and others, it remains difficult to discern whether the analgesic or sedative effects of α_2 agonists are responsible for reducing EA in

children; regardless of the mechanism, Dex appears to be effective in a wide range of doses. The half-life of Dex is reported to be 1.8 hours in children,¹⁵ but there are no data on duration of sedative or analgesic effects after discontinuation of Dex infusion. The HRs were significantly slower in group D until 90 minutes in the PACU. The residual effects on HR of an intraoperative Dex infusion and the potential for an attenuated response to postoperative bleeding in T&A patients may be a concern and a disadvantage of using a Dex infusion.

The risk of respiratory morbidity after T&A in children with OSAS is reported to be about 20%.² Sanders et al.²⁶ reported that although the patients with OSAS were more likely to require supplemental oxygen, oral airway use, or assisted ventilation on emergence, severe complications such as laryngospasm and bronchospasm were uncommon. In the present study, there were no instances of laryngospasm or bronchospasm after extubation. One patient developed intraoperative pulmonary edema and was excluded from the study because she remained intubated overnight. Although not a study variable, we noted that extubation was much smoother with less coughing and breath-holding in patients given Dex. All patients were observed continuously in the PACU for 2 hours, and the observers were asked to record the lowest SpO₂ during this period. There was a statistically significant difference in the number of patients with SpO₂ below 95% in the PACU between the 2 groups, 11 in group D and 25 in group F. This could be related to the smaller requirement for opiates in the PACU in group D or to the lower incidence and duration of severe EA in group D. The goal of having a child who was settled, comfortable, and less restless, with application of monitors and administration of supplemental oxygen in the PACU, was easier to achieve in patients who received Dex.

A few methodological considerations of this study need to be mentioned. The anesthesiologist and the data recorder in the OR were not blinded to the study group. We believe that knowledge of study group assignment did not bias the conduct of the anesthetic, because the study protocol was tightly controlled, with specific criteria regarding intraoperative rescue fentanyl, sevoflurane concentration, the time to discontinue sevoflurane, extubation criteria, and use of rescue morphine in the PACU.

The PAED is the only validated rating scale for emergence delirium.¹⁰ The investigators who developed the PAED scale rated emergence behavior 10 minutes after the child awakened and remained awake (did not fall back to sleep). Early in the present study, we found this to be a potential problem because children who were asleep were receiving ratings of 4 on the first 3 items of the scale because they could not make eye contact, their actions were not purposeful, and they were not aware of their surroundings. Therefore we had to modify the scoring on the scale and rate these items as zero. Clearly, the children were not agitated if they were sleeping. Because we used a modified version of the PAED, we used a second scale (Cole) to run concomitantly to support the findings with the modified version of the PAED. The 1 to 5 scale described by Cole et al.¹¹ has been used in several studies of EA. It is not a

validated scale, but is easy to use, and defining the categories of mild or severe is clear.

The OPS is not a validated scale, but this scale or some modification of it has been used in several studies in children. Although 2 other studies on EA^{6,19} have used the OPS, it is perhaps not the best scale to use in a study on EA because of considerable overlap on the items being scored.

We did not follow patients once they were discharged from the PACU. A future study with overnight pulse oximetry data and use of postoperative analgesics would be worthwhile to perform.

CONCLUSION

In children undergoing T&A, the goal is to minimize respiratory and airway compromise and have an awake, settled, comfortable child after the surgery. An opioid-sparing technique is particularly appealing in children with OSAS, when airway obstruction is known to preexist and may persist on the night after surgery. An intraoperative infusion of Dex combined with sevoflurane and N₂O provided satisfactory intraoperative conditions for T&A without adverse hemodynamic effects. TA and TE were shorter than they were for the patients receiving fentanyl. Postoperative opioid requirements were significantly reduced, and the incidence and duration of severe EA was lower, resulting in a smooth recovery. We have described a practical, effective, and safe technique for using Dex infusion. A multimodal, opioid-sparing, analgesic approach including Dex, such as the one used in our study, can be useful in children with OSAS undergoing other surgical procedures besides T&A, wherein the advantages of decreased perioperative opioid requirements and a reduced occurrence of EA will be beneficial. ■■

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