

A Comparison of Intranasal Dexmedetomidine and Oral Midazolam for Premedication in Pediatric Anesthesia: A Double-Blinded Randomized Controlled Trial

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BACKGROUND: Midazolam is the most commonly used premedication in children. It has been shown to be more effective than parental presence or placebo in reducing anxiety and improving compliance at induction of anesthesia. Clonidine, an α_2 agonist, has been suggested as an alternative. Dexmedetomidine is a more α_2 selective drug with more favorable pharmacokinetic properties than clonidine. We designed this prospective, randomized, double-blind, controlled trial to evaluate whether intranasal dexmedetomidine is as effective as oral midazolam for premedication in children.

METHODS: Ninety-six children of ASA physical status I or II scheduled for elective minor surgery were randomly assigned to one of three groups. Group M received midazolam 0.5 mg/kg in acetaminophen syrup and intranasal placebo. Group D0.5 and Group D1 received intranasal dexmedetomidine 0.5 or 1 μ g/kg, respectively, and acetaminophen syrup. Patients' sedation status, behavior scores, blood pressure, heart rate, and oxygen saturation were recorded by an observer until induction of anesthesia. Recovery characteristics were also recorded.

RESULTS: There were no significant differences in parental separation acceptance, behavior score at induction and wake-up behavior score. When compared with group M, patients in group D0.5 and D1 were significantly more sedated when they were separated from their parents ($P < 0.001$). Patients from group D1 were significantly more sedated at induction of anesthesia when compared with group M ($P = 0.016$).

CONCLUSIONS: Intranasal dexmedetomidine produces more sedation than oral midazolam, but with similar and acceptable cooperation.

(Anesth Analg 2008;106:1715-21)

One of the challenges for pediatric anesthesiologists is to minimize distress for children in the operating room (OR) environment and to facilitate a smooth induction of anesthesia. This is often accomplished by prior administration of a sedative drug before transfer to the OR. Midazolam is the most commonly used drug for this purpose.^{1,2} Premedication with midazolam has shown to be more effective than parental presence or placebo in reducing anxiety and improving compliance at induction of anesthesia.^{3,4} The beneficial effects of midazolam include sedation, anxiolysis, and reduction of postoperative vomiting.⁴⁻⁹ A recent evidence-based clinical update has shown that oral

midazolam 0.5 mg/kg is effective in reducing both separation and induction anxiety in children, with minimal effect on recovery time.¹⁰ However, the acceptability of oral midazolam by pediatric patients is only 70%.¹¹ Other undesirable effects including restlessness, paradoxical reaction, and negative postoperative behavioral changes have made it a less than ideal premedication.¹²⁻¹⁴ Although amnesia is considered an advantage by some authorities, it has also been regarded as a possible disadvantage by others.¹⁵ Clonidine, an α_2 -agonist, has been suggested as another option for premedication in children¹⁶ and previous studies have shown it to be equally as effective as midazolam.¹⁷⁻¹⁹ Oral clonidine premedication has also been shown to reduce the incidence of sevoflurane-induced emergence agitation.²⁰ Dexmedetomidine is a newer α_2 -agonist with a more selective action on the α_2 -adrenoceptor and a shorter half-life. Its bioavailability is 81.8% (72.6-92.1%) when administered via the buccal mucosa.²¹ Yuen et al., in a randomized, crossover evaluation of healthy adult volunteers, demonstrated that intranasal 1 and 1.5 μ g/kg dexmedetomidine produces sedation in 45-60 min and peaks in 90-105 min. In addition, they observed only a modest reduction of heart rate (HR) and arterial blood pressure (BP).²²

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Accepted for publication January 23, 2008.

Presented at the "Gilbert Brown Prize Session" of the 2007 Annual Scientific Meeting of the Australian and New Zealand College of Anaesthetists.

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DOI: 10.1213/ane.0b013e31816c8929

The purpose of this investigation was to test the hypothesis that intranasal dexmedetomidine is as effective as oral midazolam for preoperative anxiety and sedation in children before induction of anesthesia.

METHODS

Subjects and Study Protocol

After approval from the our local IRB and written informed consent from the patients' parents or legal guardian, 96 children of ASA physical status I or II, aged between 2 and 12 years, scheduled to undergo elective minor surgery, were enrolled in this prospective, randomized, double-blind, controlled trial. In appropriate instances when the child was mature enough to understand and discuss the need for premedication, patient assent was also obtained. Exclusion criteria included known allergy or hypersensitive reaction to dexmedetomidine or midazolam, organ dysfunction, cardiac arrhythmia or congenital heart disease, and mental retardation.

Children were randomly allocated to one of the three groups by drawing lots. Since previous study of healthy adults has shown that the mean onset time for significant sedation after 1 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine was approximately 45–60 min,²² all children received intranasal medication or placebo at approximately 60 min before induction of anesthesia. Oral medication or placebo was given at 30 min before induction of anesthesia. Group M received 0.5 mg/kg oral midazolam, up to a maximum 15 mg (5 mg/mL parenteral preparation) in 20 mg/kg acetaminophen syrup, and up to 1 g and 0.4 mL intranasal placebo (normal saline). Group D0.5 and Group D1 received intranasal dexmedetomidine at 0.5 $\mu\text{g}/\text{kg}$ and 1 $\mu\text{g}/\text{kg}$, respectively, and 20 mg/kg oral acetaminophen syrup. Intranasal dexmedetomidine was prepared from the 100 $\mu\text{g}/\text{mL}$ parenteral preparation (Hospira®) in a 1-mL syringe; 0.9% saline was added to make a final volume of 0.4 mL. All study drugs were prepared by an independent investigator not involved in the observation or administration of anesthesia for the children. Observers and attending anesthesiologists were blinded to the study drug given.

Children had premedication in the preoperative holding area in the presence of one parent. All children received EMLA® cream unless contraindicated. Baseline HR, oxygen saturation (SpO_2), and BP were measured before any drug administration. Intranasal drug was dripped into both nostrils using a 1-mL syringe with the child in the recumbent position. HR, SpO_2 , and BP were measured before and every 15 min after intranasal drug administration until transfer to the OR. Sedation status was assessed by a blinded observer every 5 min with a 6-point sedation scale, which was modified from the Observer Assessment of Alertness and Sedation Scale (Table 1). Behavior was evaluated every 5 min with a 4-point behavior score

Table 1. Evaluation Scale

Sedation scores	
1	Does not respond to mild prodding or shaking
2	Responds only mild prodding or shaking
3	Responds only after name is called loudly or repeatedly
4	Lethargic response to name spoken in normal tone
5	Appear asleep but respond readily to name spoken in normal tone
6	Appear alert and awake, response readily to name spoken in normal tone
Behavior scores	
1	Calm and cooperative
2	Anxious but reassuring
3	Anxious and not reassuring
4	Crying, or resisting
Wake-up behavior scores	
1	Calm and cooperative
2	Not calm but could be easily calmed
3	Not easily calmed, moderately agitated or restless
4	Combative, excited, disoriented

(Table 1). A parent was allowed to accompany the child at induction if the child refused to be separated from his/her parent. The duration of premedication was approximately 60 min; however, it could be longer or shorter depending on the schedule of the OR.

Sedation status and behavior were evaluated by the attending anesthesiologist at induction using the same scale. Mode of induction (IV versus inhalation) was decided by the attending anesthesiologist. The airway was maintained with a facemask or laryngeal mask airway throughout the operation. Anesthesia was maintained with isoflurane and 60% nitrous oxide in oxygen. Regional anesthesia was administered whenever it was appropriate. When surgery was finished, the child was placed in the recovery position and allowed to wake up naturally in the postanesthesia care unit (PACU). Behavior at awakening was evaluated with a four-point wake-up score (Table 1). Time taken for readiness to be discharged from the PACU was recorded.

Outcome Measures

The primary end-points were behavior and sedation status at separation from the parent and at induction of anesthesia. Secondary end-points included systolic BP (SBP) and HR changes, wake-up behavior, and time until ready for discharge from the PACU. Standard discharge criteria were used in the PACU. Patients were discharged from the PACU to the ward when they were awake, with reasonable control of pain and with vital signs within 20% of baseline values. Observations of sedation status and vital signs, including HR and SpO_2 , were made at 5 min and BP at 15 min intervals until the patient was ready to be discharged.

Power Analysis

In a previous study, about 70% of children demonstrated satisfactory sedation within 30 min of 0.5

Table 2. Patients' Demographic Data

	Group M (n = 32)	Group D _{0.5} (n = 32)	Group D ₁ (n = 32)	P
Age (yr)	6.4 ± 3.0 [2–12]	6.8 ± 3.1 [2–12]	6.1 ± 2.7 [2–12]	0.615
Body weight (kg)	24.1 ± 8.6	25.5 ± 11.9	21.6 ± 5.8	0.228
Sex, M:F	30:2	29:3	30:2	0.857
Type of induction, gas: IV	12:20	13:19	9:23	0.553
Type of surgery				
High ligation hydrocele/orchidopexy	2 (6.3%)	2 (6.3%)	5 (15.6%)	0.657
Excision lymph nodes or lumps	6 (18.8%)	4 (12.5%)	3 (9.4%)	
Circumcision/other penile surgery	20 (62.5%)	24 (75%)	21 (65.6%)	
Cystoscopy/colonoscopy/EUA	4 (12.5%)	2 (6.3%)	3 (9.4%)	
Duration of surgery (min)	27.7 ± 10.1 [10–50]	29.5 ± 9.0 [15–50]	33.4 ± 14.1 [15–85]	0.117
Time from premedication to induction (min)	70.5 ± 15.7 [40–105]	61.7 ± 23.3 [20–120]	68.0 ± 18.1 [40–110]	0.180

Values in mean ± sd [range] or no. (%).

EUA = examination under anesthesia.

mg/kg oral midazolam⁶; hence, a sample size of 96 (32 patients per group) provided 80% power at 0.05 level of significance to detect a 35% difference in the proportion of children who attain satisfactory sedation between oral midazolam and intranasal dexmedetomidine.

Statistical Methods

Sedation, behavior, and wake-up behavior scores were analyzed by Kruskal–Wallis test. When a significant result was obtained, the Mann–Whitney *U*-test was applied for *post hoc* pairwise comparisons. Categorical data were analyzed by χ^2 test. The adjusted *P* value was applied to the *post hoc* pairwise comparisons for nonparametric and categorical data. The adjusted *P* value for the 0.05 level of significance was 0.017. Hemodynamic variables including BP and HR were analyzed by ANOVA. When a significant result was obtained, the Tukey test was applied for *post hoc* pairwise comparisons. The changes of BP and HR from baseline among the three groups were tested by Kruskal–Wallis *t*-test. The statistical software used was SPSS 15.0 for Windows (SPSS Inc., USA).

For statistical analysis, sedation scores were categorized as being satisfactory when rated between 1 and 4 and unsatisfactory when rated 5 or 6. Behavior scores and wake-up scores were categorized as satisfactory when they were 1 or 2, and unsatisfactory when they were 3 or 4.

RESULTS

Patients

Demographic characteristics for all patients are summarized in Table 2. Patients in the three groups were comparable with respect to age, weight, gender, type of surgery, duration of surgery, and type of induction.

Five of 96 (5.2%) children resisted intranasal drug administration and 1 of 91 (1%) resisted oral medication. Five children (1 in group D0.5 and 4 in group D1) did not take the oral medication (placebo) because they were too sleepy. No child complained of pain or discomfort with intranasal drug administration. The

children who resisted the medication were also included in the analysis.

Assessment of Sedation and Behavior at Separation and at Induction

The median sedation scores at separation from the parent were 6, 3, and 1.5 for groups M, D0.5, and D1, respectively. The sedation scores of children from group D0.5 and group D1 were significantly different from that of group M at separation from parents (*P* = 0.001 and <0.001). Moreover, 21.9%, 59.4%, and 75% of the children from groups M, D0.5, and D1 achieved satisfactory sedation at separation from parents. There were significantly more children in groups D0.5 and D1 who achieved satisfactory sedation when compared with group M (*P* = 0.002 and <0.001, respectively) (Table 3). The median sedation scores at induction were 6, 5, and 4 for groups M, D0.5, and D1, respectively. Group D1 patients were significantly more sedated than group M at induction of anesthesia (*P* = 0.009). At induction of anesthesia, 18.8%, 40.6%, and 53.1% of the children from groups M, D0.5, and D1, respectively, were satisfactorily sedated. Significantly more children from group D1 achieved satisfactory sedation when compared with group M (*P* = 0.004) (Table 3).

There was no evidence found for a difference in behavior scores at separation from parents and at induction of anesthesia among the three groups. All children except one in group M and two in group D0.5 had satisfactory behavior at separation from parents (*P* = 0.771) (Table 3). Most children had satisfactory behavior at induction of anesthesia with no evidence of a difference among groups (*P* = 0.148) (Table 3). The proportion of children who had satisfactory behavior at separation from parents, but became distressed at induction of anesthesia, were 0%, 3.3%, and 18.8% from groups M, D0.5, and D1, respectively. Although there was a tendency for more children who had received dexmedetomidine to develop unsatisfactory behavior at induction of anesthesia, and the *P*

Table 3. Distribution of Behavior and Sedation Status at Parental Separation and at Induction, Proportion of Children Who Had Change of Behavior and Sedation from Satisfactory to Unsatisfactory at Induction, Time Ready for Discharge from Postanesthetic Care Unit (Minutes)

	Group M	Group D _{0.5}	Group D ₁	P
Successful parental separation				
Yes	31 (96.9%)	30 (93.7%)	32 (100%)	0.771
No	1 (3.1%)	2 (6.3%)	0 (0%)	
Sedation at separation from parent				
Satisfactory	7 (21.9%)	19 (59.4%)	24 (75%)	<.001*†
Unsatisfactory	25 (78.1%)	13 (40.6%)	8 (25%)	
Behavior at induction				
Satisfactory	31 (96.9%)	29 (90.6%)	26 (81.3%)	0.148
Unsatisfactory	1 (3.1%)	3 (9.4%)	6 (18.8%)	
Sedation at induction				
Satisfactory	6 (18.8%)	13 (40.6%)	17 (53.1%)	0.016*
Unsatisfactory	26 (81.3%)	19 (59.4%)	15 (46.9%)	
Change of behavior at induction from satisfactory to unsatisfactory n/total (%)	0/31 (0)	1/30 (3.3)	6/32 (18.8%)	0.012
Change of sedation at induction from Satisfactory to Unsatisfactory n/total (%)	1/7 (14.3)	6/19 (31.6)	7/24 (29.2)	0.828

Values in number (%) or mean ± SD.

* Significantly different between Group M and Group D₁ at 0.05 level.

† Significantly different between Group M and Group D_{0.5} at 0.05 level.

Table 4. Sedation Scores in Different Age Groups

	Group M (n = 15)	Group D _{0.5} (n = 13)	Group D ₁ (n = 15)	P
Age 2–5				
Baseline	6 [6–6]	6 [6–6]	6 [6–6]	0.393
Separation from parent	6 [6–6]	2 [1–5]	1 [1–2]	<.001*†
At induction	6 [6–6]	2 [1–5]	2 [2–6]	<.001*†
	Group M (n = 10)	Group D _{0.5} (n = 12)	Group D ₁ (n = 13)	P
Age 6–9				
Baseline	6 [6–6]	6 [6–6]	6 [6–6]	0.287
Separation from parents	5.5 [4.75–6]	2.5 [1.25–5.75]	2 [1–6]	0.122
At induction	6 [5–6]	6 [4.25–6]	6 [3–6]	0.691
	Group M (n = 7)	Group D _{0.5} (n = 7)	Group D ₁ (n = 4)	P
Age 10–12				
Baseline	6 [6–6]	6 [6–6]	6 [6–6]	1.000
Separation from parent	6 [1–6]	5 [3–6]	2 [1.25–2]	0.112
At induction	6 [1–6]	6 [5–6]	4.5 [2.5–5.75]	0.527

Values in median [IQR].

* Significantly different between Group M and Group D_{0.5} at 0.05 level.

† Significantly different between Group M and Group D₁ at 0.05 level.

value from χ^2 test was 0.012, *post hoc* pairwise comparisons did not reveal any significant difference among the three groups. Of the children from groups M, D0.5, and D1, respectively, 14.3%, 31.6%, and 29.2% were awoken by the transfer from the preoperative holding area to the OR. There was a tendency for more children who had received dexmedetomidine to awaken during this transfer, although these differences were not statistically significant ($P = 0.828$) (Table 3).

The median behavior score and sedation score were further analyzed with the children divided into three

different age groups, age 2–5, age 6–9, and age 10–12 yr. The median behavior scores at baseline, at separation from parent, and at induction were not different among the children from groups M, D0.5, and D1 in all age groups. The median sedation scores of group D0.5 and D1 were significantly different from that of group M at separation from parent and at induction in children of age 2–5 yr (Table 4). In age Group 2–5 yr, the median sedation scores at separation from parent were 6, 5, and 2 from group M, D0.5, and D1, respectively ($P < 0.001$). For the same age group, the median sedation scores at induction of anesthesia

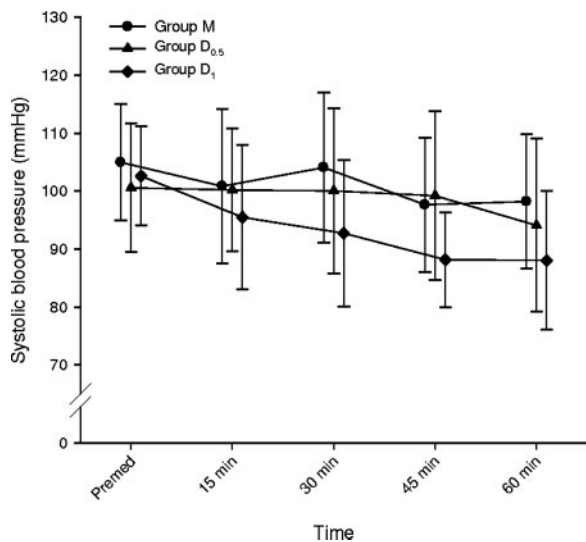


Figure 1. Mean systolic blood pressure \pm SD during the premedication period.

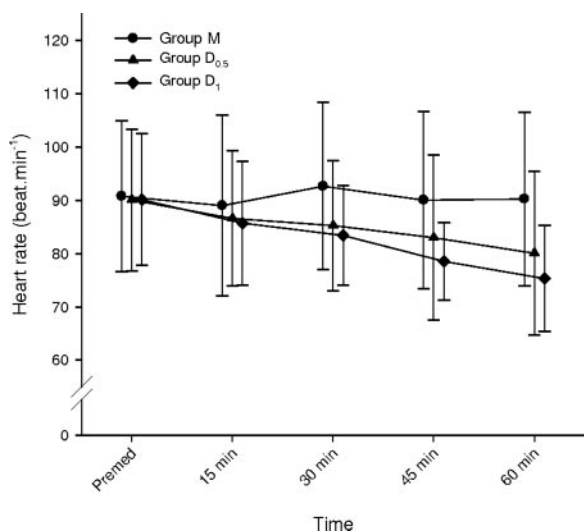


Figure 2. Mean heart rate \pm SD during the premedication period.

were 6, 2, and 2 for group M, D0.5, and D1, respectively ($P < 0.001$). These differences were not observed in older children (Table 4).

Nine children receiving midazolam were noted to become euphoric or restless after premedication, but none after dexmedetomidine. As this paradoxical behavior was not prospectively sought in our observations as *a priori* outcome variable, it was not statistically tested.

Respiratory and Hemodynamic Effects

Overall, we did not observe any clinically significant effects of the study drugs on SpO_2 and no child had a reduction of SpO_2 to below 95% during the observation period after premedication.

The mean SBP and HR during the premedication period are shown in Figures 1 and 2. Only children who stayed for more than 60 min after premedication were included in the analysis of SBP and HR during the premedication period by repeated measures of ANOVA. Consequently 25, 19, and 18

children from groups M, D0.5, and D1, respectively, were included in this analysis.

There were significant group and time effects on SBP ($P = 0.025$ and <0.001 , respectively). There was no significant group \times time interaction ($P = 0.085$). *Post hoc* analysis showed that SBP decreased significantly in group D1 when compared with group M ($P = 0.004$). Moreover, SBP decreased with time and it was significantly different from baseline at 30 min ($P = 0.003$), 45 min ($P < 0.001$), and 60 min ($P < 0.001$) after drug administration in group D1 (Figure 1). The SBP was reduced by 14.1% at 60 min in group D1.

There was also a significant time effect on HR ($P < 0.001$) and group \times time interaction ($P < 0.001$). The group effect on HR was not significant ($P = 0.102$). *Post hoc* analysis showed that HR decreased significantly with time in group D0.5 ($P < 0.001$) and group D1 ($P < 0.001$). The HR became significantly reduced from baseline at 45 and 60 min after drug administration in group D0.5 ($P = 0.006$ and <0.001 , respectively). The HR became significantly reduced from baseline at 45 and 60 min after drug administration in group D1 ($P < 0.001$) (Fig. 2). It was decreased by 11.1% and 16.4% from baseline in group D0.5 and group D1 at 60 min, respectively, after drug administration.

DISCUSSION

Sedative and Anxiolytic Effects

This prospective, double-blind, randomized, controlled trial compared intranasal dexmedetomidine and oral midazolam as premedication in healthy children between 2 and 12-yr-of-age. Children premedicated with 1 $\mu\text{g}/\text{kg}$ of intranasal dexmedetomidine attained more significant and satisfactory sedation at parental separation and at induction of anesthesia than those patients who received oral midazolam. Although patients premedicated with 0.5 $\mu\text{g}/\text{kg}$ dexmedetomidine were initially effectively sedated, these children were aroused more easily with external stimulation. Hence, the 0.5 $\mu\text{g}/\text{kg}$ dose may not be adequate for children. Most children tolerated the intranasal and oral study drugs. Previous studies have shown that intranasal administration is an effective way to administer premedication and sedation to children.²³⁻²⁵ It is a relatively easy and noninvasive route with a high bioavailability. However, cooperation is still required and it may be more difficult in younger children. Oral administration may be even more difficult in uncooperative children. Unlike conventional gabaminergic sedative drugs, such as midazolam, dexmedetomidine's site of action in the central nervous system is primarily in the locus coeruleus where it induces electroencephalogram activity similar to natural sleep.²⁶ It is, therefore, not surprising that external stimulation should facilitate arousal. Patients are also less likely to become disorientated and uncooperative. A recent study has demonstrated that

75% and 92% of adult healthy volunteers attained significant sedation after 1 and 1.5 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine, respectively.²² In this investigation, we have shown that 75% of the children attained a satisfactory level of sedation after 1 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine. Moreover, 70.8% of these sedated patients allowed IV or inhaled induction without showing signs of distress or awakening. The doses of 0.5 and 1 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine were chosen in this preliminary investigation in order to evaluate the lowest effective dose. Although 0.5 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine produced effective sedation at parental separation, it was not effective when the children were transferred to the OR.

Subgroup analysis revealed that children from age group 2–5 yr seemed to be more sedated with intranasal dexmedetomidine. However, the lack of a significant sedative effect of intranasal dexmedetomidine in age groups 6–9 and 10–12 could be real or due to an inadequate sample size. Since this study was not designed to investigate the sedative effect of intranasal dexmedetomidine in different age groups, we cannot draw a conclusion on this. Future studies could address the sedative effect of intranasal dexmedetomidine on children of varying ages. The reported sedative effects of midazolam are quite variable. Effective sedation has been reported to range from 39% to 75%^{27–30} when a parental preparation was used for oral administration. In two different studies, commercially prepared oral midazolam has been shown to produce satisfactory sedation in 97% and 81% of children.^{5,9} Our study has shown that only 21.9% of children receiving 0.5 mg/kg of oral midazolam were sedated. The great variability may be due to a difference in study design, different carrier vehicle for midazolam, and different bioavailabilities of the midazolam preparation.

Although previous studies have documented the effectiveness of oral midazolam as a preoperative anxiolytic,^{3,4,10,30–32} our behavior scoring system did not allow us to evaluate the anxiety level of children. We have shown in this investigation that the behavior of children at separation from parents and at induction of anesthesia were similar in children who received oral midazolam and intranasal dexmedetomidine based on our behavior scale. Although oral midazolam did not produce significant sedation in our subjects, it could have produced significant anxiolytic and/or amnesic effects. It is also uncertain if the sedative effect of intranasal dexmedetomidine is associated with any anxiolytic effect. The use of other validated anxiety scales such as the modified Yale Preoperative Anxiety Scale³³ would allow evaluation of the change in anxiety level of children after premedication and to delineate the sedative effect from anxiolytic effect.

Hemodynamic Effects

α_2 -Agonists produce a modest reduction in BP and HR. When dexmedetomidine is infused as an IV bolus

at doses ranging from 0.25 to 2 $\mu\text{g}/\text{kg}$ over 2 min in healthy volunteers,³⁴ it causes a dose-dependent decrease in BP ranging from 14% to 27%. When clonidine was given as premedication, it was shown to effectively attenuate the cardiovascular responses to tracheal intubation in children undergoing induction of anesthesia.^{18,19} In a recent study comparing midazolam, clonidine, and dexmedetomidine for premedication in children, both clonidine and dexmedetomidine were shown to reduce mean BP and HR before and during surgery.¹⁷ In a pharmacokinetic study of IV dexmedetomidine in children, it was shown that 0.66 and 1 $\mu\text{g}/\text{kg}$ IV dexmedetomidine given over 10 min produced a significant reduction of HR (<15% compared with baseline) and SBP (<25% compared with baseline).³⁵ Munro et al.³⁶ reported that the reduction of blood pressure and HR were <20% of baseline in children who were sedated with an initial dose of 1 $\mu\text{g}/\text{kg}$ IV dexmedetomidine, followed by a maintenance infusion during cardiac catheterization. In this study, we have shown that preoperative 0.5 and 1 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine reduces HR and blood pressure in healthy children during the first hour after drug administration.

Limitations of this Study

We did not evaluate the onset time and peak effect of the two doses of intranasal dexmedetomidine or the blood concentrations. The onset time of 1 and 1.5 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine was about 45 min with a peak effect at 60–105 min after intranasal dexmedetomidine in healthy adults.²² In this study, the premedication period was 60 min for intranasal dexmedetomidine; however, some children were transferred to the OR slightly earlier in order not to interfere with the normal OR schedule. If a longer premedication period had been allowed, possibly more subjects could have attained satisfactory sedation at separation from parents and at induction of anesthesia.

The sedation produced by dexmedetomidine differs from other sedatives as patients may be easily aroused and cooperative. Some children who were premedicated with dexmedetomidine became distressed when they were aroused at the induction of anesthesia, despite being very much sedated at the time of parental separation. Anesthetic technique may need to be adjusted to provide optimal conditions for induction in children sedated with dexmedetomidine.

CONCLUSION

Although midazolam is the most commonly used premedication in children, it may not be the most suitable preoperative sedative and anxiolytic in all children and in all circumstances. Finley et al.³⁷ have shown that children with impulsive traits did not benefit from midazolam premedication. In this study, we have shown that 1 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine is another technique for producing sedation in

children and it causes no discomfort during administration. Intranasal drug administration is relatively quick, simple, and may have benefits over transmucosal routes or rectal administration, which requires more patient cooperation. We have established that this route is feasible for dexmedetomidine administration and future studies could now be directed to further evaluate the effect of this interesting drug on various outcome measures including preoperative anxiety levels, induction time, emergence excitation, postoperative analgesic requirements, and postoperative behavior disturbances.

In summary, 1 $\mu\text{g}/\text{kg}$ intranasal dexmedetomidine produces significant sedation in children between 2 and 12-yr-of-age. Behavior of the children at parental separation and at induction of anesthesia was comparable to children who received oral midazolam. The hemodynamic effects of the two doses of intranasal dexmedetomidine were modest.

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