

Intranasal Dexmedetomidine Versus Midazolam For Pediatric Premedication: Effects on Sedation, Mask Acceptance, and Perioperative Hemodynamic Stability in A Randomized Trial

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ABSTRACT

Background: Preoperative anxiety and poor cooperation during anesthesia induction are common challenges in pediatric patients. Intranasal premedication offers a non-invasive approach that may improve sedation, mask acceptance, and perioperative stability. Dexmedetomidine and midazolam are both widely used, although their comparative effects on sedation and hemodynamic responses remain clinically relevant.

Objective: To compare intranasal dexmedetomidine and intranasal midazolam as pediatric premedication with respect to sedation, behaviour during induction, mask acceptance, oxygenation, and perioperative hemodynamic stability.

Materials and Methods: This prospective, randomized, single-blind study included 96 children aged 3–10 years with American Society of Anesthesiologists physical status I or II undergoing elective surgery lasting less than 2 hours. Participants were randomly allocated to two equal groups. Group A received intranasal dexmedetomidine 1 µg/kg and Group B received intranasal midazolam 0.2 mg/kg, approximately 45 minutes before induction. The children and their parents or legal guardians were unaware of the study drug administered.

Results: Baseline characteristics and surgical duration were comparable between groups. Heart rate was significantly lower with dexmedetomidine from 15 minutes after drug administration throughout the intraoperative observations, including at intubation (93.15 ± 5.91 vs 102.52 ± 5.83 beats/min; $P < 0.0001$). Systolic blood pressure was also significantly lower at selected perioperative time points, including intubation (99.60 ± 6.17 vs 104.31 ± 7.39 mmHg; $P = 0.001$). At intubation, the lower sedation score with dexmedetomidine indicated deeper sedation (3.50 ± 0.62 vs 3.92 ± 0.77 ; $P = 0.007$). Mask-related behaviour was generally acceptable in both groups. At extubation, midazolam produced a more favourable behaviour score (1.85 ± 0.74 vs 2.31 ± 0.99 ; $P = 0.020$). Oxygen saturation remained satisfactory in both groups, and no adverse events were observed.

Conclusion: Intranasal dexmedetomidine provided a more stable perioperative hemodynamic profile and deeper sedation at induction. Both drugs permitted acceptable mask acceptance, whereas intranasal midazolam showed more favourable behaviour at extubation.

Keywords: Dexmedetomidine; midazolam; intranasal premedication; pediatric anesthesia; sedation; mask acceptance; hemodynamic stability.

INTRODUCTION

The perioperative period is a major source of psychological stress for children undergoing surgery, particularly during separation from parents, transfer to the operating room, application of the anesthesia mask, and induction of general anesthesia. Preoperative anxiety is common in pediatric patients and may manifest as crying, agitation, resistance to caregivers, refusal of the anesthesia mask, or difficulty during induction. Importantly, excessive anxiety is not limited to the immediate preoperative period; it has been associated with increased perioperative distress, emergence delirium, greater postoperative pain, and maladaptive behavioral changes after hospital discharge [1,2]. Kain et al. demonstrated that preoperative anxiety in children is influenced by factors such as age, temperament, previous medical experiences, and parental anxiety, and may contribute to subsequent negative behavioral responses [1]. Consequently, effective premedication remains an important component of pediatric anesthetic practice, with the aim of providing anxiolysis and satisfactory sedation while facilitating smooth parental separation and cooperative anesthesia induction without compromising respiratory or cardiovascular safety.

Midazolam, a short-acting benzodiazepine, has traditionally been one of the most widely used pharmacological agents for pediatric premedication. Through enhancement of γ-aminobutyric acid type A (GABA-A) receptor activity, midazolam produces anxiolysis, sedation, anterograde amnesia, and muscle relaxation. Its clinical effectiveness in reducing pediatric preoperative anxiety and improving cooperation during induction has been demonstrated for decades [3]. Midazolam can be administered through oral, intravenous, rectal, buccal, or intranasal routes. The intranasal route is particularly attractive in children

because it avoids painful intravenous cannulation and permits relatively rapid absorption through the highly vascular nasal mucosa. Nevertheless, intranasal midazolam has several recognized limitations, including an unpleasant or burning nasal sensation, crying following administration, variable sedation, paradoxical agitation, and potential respiratory depression, particularly in susceptible children or when combined with other sedative drugs [4-6]. These limitations have stimulated interest in alternative non-invasive premedication strategies.

Dexmedetomidine is a highly selective α_2 -adrenergic receptor agonist that produces sedation, anxiolysis, and analgesia through actions predominantly within the locus coeruleus and spinal cord. Unlike conventional sedative-hypnotic agents, dexmedetomidine produces a sleep-like form of sedation with relatively limited respiratory depression, an attribute of particular relevance in pediatric anesthesia [4,7]. Its physicochemical properties also permit effective transmucosal absorption, making intranasal administration a practical option for children who may resist oral medication or intravenous access. Yuen et al. demonstrated that intranasal dexmedetomidine could provide clinically useful pediatric premedication and favorable sedation without major respiratory compromise [4]. Subsequent studies have reinforced its potential role in achieving acceptable parental separation, reducing perioperative agitation, and decreasing postoperative analgesic requirements [6-9]. However, its sympatholytic action can cause reductions in heart rate and blood pressure, making assessment of perioperative hemodynamic stability an important component of comparative evaluation [8,9].

Direct comparisons between dexmedetomidine and midazolam have nevertheless produced variable results. In a randomized trial involving children undergoing adenotonsillectomy, Akin et al. found that intranasal midazolam provided better conditions for mask induction than intranasal dexmedetomidine, although both agents produced comparable anxiolysis during parental separation [5]. In contrast, Sheta et al. reported superior sedation and greater satisfactory mask acceptance with intranasal dexmedetomidine compared with intranasal midazolam among children undergoing dental rehabilitation [6]. The dexmedetomidine group also demonstrated less postoperative agitation and nasal irritation, although its onset of sedation was slower. Similarly, studies comparing intranasal dexmedetomidine with oral midazolam have frequently demonstrated favorable sedation at parental separation and induction with dexmedetomidine, while documenting modest reductions in heart rate and blood pressure that generally did not require pharmacological intervention [9].

The accumulating evidence has consequently shifted attention from sedation alone toward the broader balance among sedation quality, induction cooperation, respiratory safety, and cardiovascular effects. Meta-analytic evidence suggests that dexmedetomidine may provide more satisfactory sedation during parental separation and may reduce postoperative agitation or the requirement for rescue analgesia when compared with midazolam [7,8]. A recent meta-analysis specifically examining intranasal α_2 -adrenergic agonists versus intranasal midazolam found that dexmedetomidine was associated with higher rates of satisfactory parental separation and favorable anesthesia induction or facemask acceptance, together with lower rates of some adverse effects [10]. Nevertheless, heterogeneity in drug dose, route of administration, timing of premedication, surgical procedure, age distribution, sedation scales, and definitions of satisfactory mask acceptance has contributed to inconsistent findings across individual trials.

Safety considerations are equally important when selecting a pediatric premedicant. In a randomized clinical trial involving children undergoing tonsillectomy and adenoidectomy, Shen et al. observed substantial differences in perioperative respiratory adverse events between intranasal dexmedetomidine and midazolam, emphasizing that the choice of sedative may influence outcomes beyond preoperative anxiolysis [11]. More recent pooled evidence has shown that intranasal dexmedetomidine is associated with slightly lower heart rate and mean arterial pressure compared with midazolam, but these differences have generally not translated into clinically important hemodynamic complications in appropriately selected and monitored children [12]. An updated systematic review and meta-analysis published in 2026, incorporating 19 randomized controlled trials and 1,475 pediatric patients, further supports the effectiveness of intranasal dexmedetomidine as an alternative to midazolam while emphasizing the need to evaluate both sedation efficacy and safety outcomes concurrently [13].

Despite the expanding literature, uncertainty therefore remains regarding which intranasal agent provides the most favorable overall premedication profile when clinically relevant outcomes are assessed simultaneously. Sedation quality alone is insufficient to define an ideal pediatric premedicant; successful therapy should also facilitate calm mask acceptance and smooth anesthetic induction while preserving respiratory and hemodynamic stability. Furthermore, discrepancies among previous trials indicate the need for additional randomized evidence using clearly defined clinical endpoints and standardized perioperative monitoring. Therefore, the present randomized trial was designed to compare intranasal dexmedetomidine and intranasal midazolam as pediatric premedication, with particular emphasis on the quality of preoperative sedation,

acceptance of the anesthesia mask, and perioperative hemodynamic stability. This comparison may help clarify the relative clinical advantages and limitations of these two commonly investigated non-invasive premedication strategies and contribute to evidence-based selection of sedative premedication in pediatric anesthesia.

MATERIALS AND METHODS

This prospective, randomized, single-blind, two-arm comparative clinical trial was conducted in the Department of Anesthesiology at Paras Hospital, Gurugram, Haryana, India, a tertiary-care centre. The study evaluated the efficacy and perioperative safety of intranasal dexmedetomidine versus intranasal midazolam as premedication in pediatric patients undergoing elective surgery.

A total of 96 children were randomly allocated in a 1:1 ratio, with 48 participants in each treatment group. Group A received intranasal dexmedetomidine and Group B received intranasal midazolam. The trial was conducted with single blinding of the subjects: neither the participating children nor their parents or legal guardians were informed of the identity of the study drug administered.

Ethical Considerations

The study was conducted following approval by the Institutional Ethics Committee of Paras Hospital, Gurugram (approval number- ECR/249/Inst./HAR/2013/RR-19; approval date: 13/10/2020). Written informed consent was obtained from the parent or legal guardian of each participating child before enrolment. The nature of the study and planned anaesthetic procedure were explained in a language understood by the parent or guardian. Participation was voluntary, and confidentiality of participant information was maintained throughout the study.

Study Population

Children aged 3–10 years, belonging to the American Society of Anesthesiologists (ASA) physical status I or II, and scheduled to undergo elective surgical procedures with an anticipated duration of less than 2 hours were assessed for eligibility.

Children were included when they were aged 3–10 years, classified as ASA physical status I or II, and scheduled for a surgical procedure lasting less than 2 hours. Exclusion criteria comprised age below 3 years or above 10 years, ASA physical status III or higher, congenital heart disease, an active upper respiratory tract infection, treatment with medications such as digoxin or β -blockers, emergency surgery, learning difficulties, parental refusal to participate, nasal discharge, and a known allergy to either study medication.

Sample Size Calculation

The sample size was calculated on the basis of expected differences in sedation and behaviour scores between the two study groups. Using data reported by Kumar et al. [9], a between-group difference of 1 point in these scores was considered clinically significant. Assuming a standard deviation of 1.5 in each group, an effect size of approximately 0.67, a two-sided α level of 0.05, and a statistical power of 90%, the calculated minimum sample size was 47.3 participants per group. This was rounded to 48 children per group, providing a total study population of 96 participants.

The calculation followed:

The sample size was determined using the expected difference in sedation and behaviour scores between the two study groups. A difference of 1 point was considered clinically significant. Assuming a standard deviation of 1.5 in each group, a two-sided alpha level of 0.05, and a statistical power of 90%, the required sample size was calculated using the formula for comparison of two independent means.

$$n = [(\sigma_1^2 + \sigma_2^2) \times (Z_{1-\alpha/2} + Z_{1-\beta})^2] / (M_1 - M_2)^2$$

$$n = [(1.5^2 + 1.5^2) \times (1.96 + 1.282)^2] / (1)^2$$

$$n = [(2.25 + 2.25) \times 10.51] / 1 = 47.30$$

Therefore, the required sample size was rounded up to 48 participants per group, giving a total sample size of 96 participants.

Where:

- $Z_{1-\alpha/2}$ = 1.96 for a 95% confidence level (α = 0.05);
- $Z_{1-\beta}$ = 1.282 for 90% statistical power (β = 0.10);
- σ_1 and σ_2 = standard deviations in the two groups (1.5 each); and
- $M_1 - M_2$ = minimum clinically important difference between the two group means (1 point).

Randomization and Blinding

Eligible children were randomly assigned to one of two treatment groups before premedication. Single blinding was ensured at the subject level: neither the child nor the parent or legal guardian was aware of whether intranasal dexmedetomidine or intranasal midazolam had been administered.

The two intervention groups were:

Group A—Dexmedetomidine: Participants received intranasal dexmedetomidine 1 µg/kg, using the parenteral formulation at a concentration of 100 µg/mL.

Group B—Midazolam: Participants received intranasal midazolam 0.2 mg/kg, using an intranasal formulation at a concentration of 5 mg/mL.

The calculated drug dose was drawn into a 1-mL tuberculin syringe. The total volume was divided approximately equally between the two nostrils while the child was maintained in a recumbent position. The participant subsequently remained recumbent for approximately 1–2 minutes to facilitate nasal mucosal absorption.

Premedication Protocol

Following confirmation of fasting status, the allocated intranasal study medication was administered approximately 45 minutes before induction of general anaesthesia in the preoperative holding area in the presence of a parent or legal guardian.

Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and peripheral oxygen saturation (SpO₂) were recorded before administration of the study medication. Subsequently, HR, blood pressure, and SpO₂ were assessed at 15-minute intervals during the 45-minute premedication period before transfer to the operating room.

Assessment of Sedation and Behaviour

Sedation and behavioural responses were evaluated before administration of the study medication, at separation from the parent, at induction of anaesthesia/mask presentation, and at extubation.

Sedation was assessed using a six-point scale, with lower scores denoting deeper sedation:

- 1 = no response to mild prodding or shaking;
- 2 = responds only to mild prodding or shaking;
- 3 = responds after the name is called loudly and repeatedly;
- 4 = lethargic response to the name spoken in a normal tone;
- 5 = appears asleep but responds readily to the name spoken in a normal tone; and
- 6 = appears alert and awake and responds readily to the name spoken in a normal tone.

Behaviour was assessed using a 4-point behaviour scale:

- 1 = calm and cooperative;
- 2 = anxious but reassuring;
- 3 = anxious and not reassuring; and
- 4 = crying and resisting.

Satisfactory sedation was defined as a six-point sedation score ≥ 4 , and satisfactory behaviour as a four-point behaviour score ≤ 2 , using the study's prespecified assessment thresholds. At induction, satisfactory behaviour represented clinically acceptable cooperation with the anaesthesia mask.

Standardized Anaesthetic Technique

A detailed preanaesthetic evaluation was performed before surgery, including medical history, physical and systemic examination, vital signs, and routine investigations as clinically indicated. Fasting status was confirmed before administration of study medication.

On arrival in the operating theatre, standard monitoring was instituted, including HR, SBP, DBP, and SpO₂. All patients received glycopyrrolate and ondansetron according to the study protocol. Patients were preoxygenated with 100% oxygen, followed by intravenous induction with fentanyl 2 µg/kg and propofol 1–2 mg/kg, titrated until loss of verbal response. After confirming adequate mask ventilation, neuromuscular blockade was achieved with atracurium 0.5 mg/kg, followed by orotracheal intubation using an appropriately sized endotracheal tube.

Anaesthesia was maintained using oxygen, nitrous oxide, and sevoflurane. Mechanical ventilation was adjusted according to body weight to maintain normocapnia. At completion of surgery, neuromuscular blockade was reversed with neostigmine and glycopyrrolate, and patients were extubated when clinically appropriate and transferred to the recovery area following adequate awakening.

Perioperative Hemodynamic Assessment

Hemodynamic monitoring included HR, SBP, DBP, and SpO₂. Readings were obtained before study-drug administration; at 15, 30, and 45 minutes after premedication; at induction/intubation; and at predefined intervals following intubation. Subsequent intraoperative assessments were recorded at approximately 5, 15, 30, 60, 90, and 120 minutes, where applicable according to the duration of surgery, with monitoring continued until extubation.

The principal safety comparison was the pattern and magnitude of perioperative changes in HR, SBP, DBP, and SpO₂ between the dexmedetomidine and midazolam groups.

Outcome Measures

The primary outcome was the efficacy of the study drug in producing satisfactory preoperative conditions at induction, assessed by the combination of the 6-point sedation score and 4-point behaviour score, particularly behaviour during acceptance of the anaesthesia mask. Satisfactory sedation was defined as a sedation score ≥ 4 and satisfactory behaviour/mask acceptance as a behaviour score ≤ 2 .

Secondary outcomes included perioperative HR, SBP, DBP, and SpO₂; sedation and behaviour at extubation; and treatment-related adverse events. Monitored adverse events included nausea, nasal irritation, bradycardia, hypotension, and respiratory depression.

Statistical Analysis

Data were analysed using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were summarized as mean $\pm$ standard deviation (SD) for normally distributed data and, where appropriate, as median with interquartile range for non-normally distributed variables. Categorical variables were expressed as frequencies and percentages.

The distribution of continuous variables was assessed for normality before inferential analysis. Between-group comparisons of normally distributed continuous variables were performed using the independent-samples Student's t-test, while non-normally distributed and ordinal variables, including sedation and behaviour scores, were compared using the Mann–Whitney U test. Categorical variables were analysed using the chi-square test or Fisher's exact test, as appropriate. All statistical tests were two-sided, and a P value <0.05 was considered statistically significant.

RESULTS

All 96 children were included in the analysis: 48 received intranasal dexmedetomidine (Group A), and 48 received intranasal midazolam (Group B). The evaluated outcomes were demographic and operative characteristics, serial heart rate, systolic and diastolic blood pressure, oxygen saturation, sedation scores, and behaviour scores.

The two groups were comparable with respect to age, sex distribution, and duration of surgery. The mean age was 6.15 ± 1.76 years in Group A and 5.56 ± 1.86 years in Group B ($P=0.118$). Females constituted 54.17% and 47.92% of Groups A and B, respectively ($P=0.540$). Mean duration of surgery was also similar between groups (56.29 ± 9.68 vs 57.73 ± 8.68 min; $P=0.446$).

Table 1. Baseline demographic and operative characteristics of the study population

Characteristic	Dexmedetomidine Group A (n=48)	Midazolam Group B (n=48)	P value
Age, years, mean $\pm$ SD	6.15 ± 1.76	5.56 ± 1.86	0.118
Age 3–6 years, n (%)	28 (58.33)	31 (64.58)	0.529
Age 7–9 years, n (%)	20 (41.67)	17 (35.42)	
Female, n (%)	26 (54.17)	23 (47.92)	0.540
Male, n (%)	22 (45.83)	25 (52.08)	
Duration of surgery, min, mean $\pm$ SD	56.29 ± 9.68	57.73 ± 8.68	0.446
Duration of surgery, median (IQR), min	55 (48–64)	57.5 (50–64)	

Baseline heart rate was comparable between groups (88.52 ± 8.31 vs 91.29 ± 6.40 beats/min; $P=0.070$). After administration of the study medication, heart rate remained consistently lower in the dexmedetomidine group. Significant between-group differences were observed from 15 minutes after premedication onward and

persisted throughout induction and the intraoperative observation period. At intubation, mean heart rate increased to 93.15 ± 5.91 beats/min in Group A compared with 102.52 ± 5.83 beats/min in Group B ($P < 0.0001$).

Table 2. Comparison of perioperative heart rate between study groups

Time point	Group A, mean $\pm$ SD (beats/min)	Group B, mean $\pm$ SD (beats/min)	P value
Before study drug	88.52 ± 8.31	91.29 ± 6.40	0.070
15 min after drug	86.19 ± 5.77	90.92 ± 5.28	<0.0001
30 min after drug	84.42 ± 4.71	91.29 ± 5.36	<0.0001
45 min after drug	84.06 ± 4.15	91.56 ± 5.23	<0.0001
At intubation	93.15 ± 5.91	102.52 ± 5.83	<0.0001
Immediately after intubation	87.00 ± 4.34	94.67 ± 4.05	<0.0001
15 min after intubation	85.35 ± 3.98	92.40 ± 4.62	<0.0001
30 min after intubation	85.90 ± 4.10	92.04 ± 5.19	<0.0001
60 min after intubation	85.62 ± 4.47	90.90 ± 4.81	<0.0001
90 min after intubation	86.35 ± 4.36	91.48 ± 5.07	<0.0001
120 min after intubation	87.60 ± 4.07	91.75 ± 5.07	<0.0001

Baseline systolic and diastolic blood pressures were similar between the groups. Significant differences in SBP were observed at 30 minutes after drug administration, at intubation, immediately after intubation, and at 30 and 60 minutes after intubation. The largest peri-intubation difference was observed at intubation, when SBP was 99.60 ± 6.17 mmHg in Group A compared with 104.31 ± 7.39 mmHg in Group B ($P = 0.001$).

For DBP, significant differences occurred at intubation (57.94 ± 5.28 vs 61.35 ± 5.89 mmHg; $P = 0.004$) and at 60 minutes after intubation (51.08 ± 3.07 vs 52.50 ± 3.35 mmHg; $P = 0.033$). At the remaining time points, between-group differences in DBP were not statistically significant.

Table 3. Comparison of systolic and diastolic blood pressure between study groups

Time point	SBP Group A	SBP Group B	P value	DBP Group A	DBP Group B	P value
Before study drug	94.52 ± 7.56	94.04 ± 5.73	0.727	55.42 ± 8.83	52.79 ± 5.18	0.080
15 min after drug	92.69 ± 4.04	93.42 ± 4.38	0.398	53.79 ± 3.85	53.17 ± 3.90	0.432
30 min after drug	91.52 ± 5.13	93.75 ± 4.13	0.021	51.94 ± 4.87	52.23 ± 4.38	0.758
45 min after drug	92.29 ± 4.76	94.02 ± 3.76	0.051	52.06 ± 5.19	52.04 ± 3.69	0.982
At intubation	99.60 ± 6.17	104.31 ± 7.39	0.001	57.94 ± 5.28	61.35 ± 5.89	0.004
After intubation	93.58 ± 3.93	95.40 ± 4.09	0.029	52.92 ± 5.14	54.58 ± 4.51	0.095
15 min after intubation	92.35 ± 4.30	93.52 ± 3.81	0.163	50.73 ± 5.02	52.31 ± 3.19	0.069
30 min after intubation	91.50 ± 3.26	93.31 ± 3.83	0.014	51.33 ± 3.39	52.65 ± 3.13	0.052
60 min after intubation	91.71 ± 3.40	93.52 ± 4.05	0.020	51.08 ± 3.07	52.50 ± 3.35	0.033
90 min after intubation	92.60 ± 3.50	93.60 ± 3.96	0.193	51.88 ± 3.53	52.42 ± 3.85	0.475
120 min after intubation	92.58 ± 3.17	93.98 ± 3.79	0.053	51.79 ± 3.65	52.23 ± 3.54	0.552

Peripheral oxygen saturation remained high in both groups throughout the study. Baseline SpO_2 was $99.81 \pm 0.49\%$ in Group A and $99.83 \pm 0.43\%$ in Group B ($P = 0.825$). The only statistically significant difference occurred at intubation, when Group A had an SpO_2 of $99.52 \pm 0.85\%$ compared with $98.98 \pm 1.23\%$ in Group B ($P = 0.014$). At all other measured time points, SpO_2 was statistically comparable.

Table 4. Comparison of perioperative oxygen saturation between study groups

Time point	Group A, SpO_2 %, mean $\pm$ SD	Group B, SpO_2 %, mean $\pm$ SD	P value
Before study drug	99.81 ± 0.49	99.83 ± 0.43	0.825
15 min after drug	99.71 ± 0.50	99.81 ± 0.45	0.286
30 min after drug	99.85 ± 0.36	99.85 ± 0.36	1.000
45 min after drug	99.85 ± 0.36	99.92 ± 0.28	0.342
At intubation	99.52 ± 0.85	98.98 ± 1.23	0.014
After intubation	99.83 ± 0.38	99.83 ± 0.38	1.000

Time point	Group A, SpO ₂ %, mean ± SD	Group B, SpO ₂ %, mean ± SD	P value
15 min after intubation	99.96 ± 0.20	99.96 ± 0.20	1.000
30 min after intubation	99.88 ± 0.33	99.94 ± 0.24	0.299
60 min after intubation	99.83 ± 0.38	99.92 ± 0.28	0.222
90 min after intubation	99.94 ± 0.24	99.96 ± 0.20	0.650
120 min after intubation	99.92 ± 0.28	99.96 ± 0.20	0.404

Sedation scores were comparable at study-drug administration and extubation. At intubation, the mean sedation score was significantly lower in Group A than in Group B (3.50 ± 0.62 vs 3.92 ± 0.77 ; $P=0.007$), consistent with deeper sedation in the dexmedetomidine group. Median scores were 4 (IQR 3–4) in both groups.

Table 5. Comparison of sedation scores between study groups

Assessment time	Group A, mean ± SD	Group B, mean ± SD	Group A, median (IQR)	Group B, median (IQR)	P value
At study-drug administration	5.85 ± 0.36	5.77 ± 0.42	6 (6–6)	6 (6–6)	0.298
At intubation	3.50 ± 0.62	3.92 ± 0.77	4 (3–4)	4 (3–4)	0.007
At extubation	5.46 ± 0.50	5.46 ± 0.58	5 (5–6)	5 (5–6)	0.987

Behaviour scores were similar at study-drug administration ($P=0.221$) but differed significantly at intubation ($P=0.044$) and extubation ($P=0.020$). At intubation, median scores were 2 (IQR 1–2) in Group A and 1.5 (IQR 1–2) in Group B; both were within the prespecified acceptable range. At extubation, median scores were 2 (IQR 1.75–3) and 2 (IQR 1–2), respectively, with a lower mean score in Group B, indicating more favourable extubation behaviour.

Table 6. Comparison of behaviour scores between study groups

Assessment time	Group A, mean ± SD	Group B, mean ± SD	Group A, median (IQR)	Group B, median (IQR)	P value
At study-drug administration	3.48 ± 0.50	3.60 ± 0.49	3 (3–4)	4 (3–4)	0.221
At intubation/mask acceptance	1.88 ± 0.67	1.60 ± 0.68	2 (1–2)	1.5 (1–2)	0.044
At extubation	2.31 ± 0.99	1.85 ± 0.74	2 (1.75–3)	2 (1–2)	0.020

DISCUSSION

This randomized study compared intranasal dexmedetomidine 1 µg/kg with intranasal midazolam 0.2 mg/kg in 96 children undergoing elective surgery. Both drugs provided useful premedication and acceptable mask-related behaviour. Dexmedetomidine produced significantly lower perioperative heart rates and lower systolic blood pressure at several observation points, with deeper sedation at intubation. Midazolam, however, was associated with more favourable behaviour at extubation. Peripheral oxygen saturation remained satisfactory, and no adverse events were observed in either group.

The two study groups were well matched with respect to age, sex distribution, and duration of surgery. Mean age was 6.15 ± 1.76 years in the dexmedetomidine group and 5.56 ± 1.86 years in the midazolam group, while mean surgical duration was 56.29 ± 9.68 and 57.73 ± 8.68 minutes, respectively. The absence of statistically significant differences in these baseline characteristics reduces the likelihood that demographic or procedural imbalance substantially influenced the observed perioperative differences.

One of the most prominent observations in the present study was the effect of dexmedetomidine on heart rate. Baseline heart rate was comparable between groups; however, after administration of the study medication, heart rate was consistently lower in children who received dexmedetomidine. At intubation, mean heart rate was 93.15 ± 5.91 beats/min in the dexmedetomidine group compared with 102.52 ± 5.83 beats/min in the midazolam group, and significant differences continued throughout the subsequent intraoperative measurements. This finding is pharmacologically plausible because dexmedetomidine reduces central sympathetic outflow through highly selective α_2 -adrenoceptor stimulation. A meta-analysis by Sun et al. demonstrated that dexmedetomidine premedication significantly reduced heart rate compared with

midazolam and simultaneously attenuated systolic and mean arterial pressure responses [14]. Similarly, Peng et al. reported that children receiving dexmedetomidine had lower pre-induction heart rates than those receiving midazolam [15].

These findings agree with the meta-analysis by Lang et al., which included 34 randomized studies involving 2,281 pediatric patients and reported lower heart rate and systolic blood pressure with dexmedetomidine than with midazolam [16]. The lower values in the present study are compatible with the expected sympatholytic action of dexmedetomidine and were accompanied by satisfactory perioperative oxygenation. No adverse events were observed in either treatment group.

A similar pattern was observed for systolic blood pressure. Baseline SBP did not differ significantly between the groups, whereas significantly lower values in the dexmedetomidine group were observed at 30 minutes after drug administration, during intubation, immediately after intubation, and at 30 and 60 minutes after intubation. The intubation-associated SBP was 99.60 ± 6.17 mmHg with dexmedetomidine compared with 104.31 ± 7.39 mmHg with midazolam. These results suggest attenuation of the sympathetic cardiovascular response to airway manipulation. Wang et al., in a randomized pediatric study examining intranasal dexmedetomidine, demonstrated that dexmedetomidine attenuated cardiovascular responses during anesthesia induction and tracheal intubation, with changes in mean arterial pressure and heart rate supporting a dose-dependent sympatholytic effect [17].

The differences in diastolic blood pressure were less extensive than those observed for heart rate and SBP. DBP differed significantly at intubation and at 60 minutes after intubation but was otherwise comparable. At intubation, DBP was 57.94 ± 5.28 mmHg in the dexmedetomidine group and 61.35 ± 5.89 mmHg in the midazolam group. Collectively, therefore, the hemodynamic findings suggest that dexmedetomidine moderated the cardiovascular response to perioperative stimulation without producing a marked loss of hemodynamic stability. This interpretation is compatible with existing evidence demonstrating lower heart rate and arterial pressure after dexmedetomidine while generally maintaining clinically acceptable cardiovascular values [14-17].

Peripheral oxygen saturation remained close to 100% throughout the perioperative period in both study groups. The only statistically significant difference was recorded at intubation, when SpO_2 was $99.52 \pm 0.85\%$ in the dexmedetomidine group compared with $98.98 \pm 1.23\%$ in the midazolam group. Although statistically significant, the absolute difference of approximately 0.5 percentage points is unlikely to be clinically important in otherwise healthy ASA I-II children because oxygenation remained within an acceptable range in both groups. Ghali et al. similarly reported satisfactory respiratory conditions when intranasal dexmedetomidine was used for pediatric premedication [18]. The relative preservation of ventilation and airway reflexes is one of the major theoretical advantages of dexmedetomidine over sedatives that exert stronger respiratory depressant effects.

Talon et al. also found intranasal dexmedetomidine to be a clinically useful alternative to midazolam in children undergoing reconstructive surgery, with satisfactory conditions during induction and emergence and no evidence that the drug compromised its overall perioperative usefulness [19]. These findings support the current observation that effective sedation can be achieved without meaningful deterioration in oxygen saturation.

At intubation, dexmedetomidine produced deeper sedation than midazolam, as shown by a significantly lower mean score (3.50 ± 0.62 vs 3.92 ± 0.77 ; $P=0.007$) on the six-point scale, in which lower scores denote greater sedation. Sedation scores did not differ significantly at study-drug administration or extubation. This finding is broadly compatible with Wang et al., who reported satisfactory preoperative sedation in children receiving intranasal dexmedetomidine or midazolam-based premedication [20].

The literature also demonstrates some variability regarding sedation and induction conditions. Zhang et al., in a systematic review and meta-analysis of 11 randomized studies involving 824 children, found better sedation at parental separation and anesthesia induction with intranasal dexmedetomidine compared with oral midazolam, but no significant difference in mask acceptance [21]. Similarly, Talon et al. found dexmedetomidine more effective in inducing preoperative sleep, while induction conditions were comparable between treatments [19]. These differences among studies may reflect variation in dexmedetomidine dose, route and dose of midazolam, interval between administration and induction, age of participants, type of surgical procedure, and the scoring tools used to define satisfactory sedation.

Behaviour was assessed on a four-point scale, with 1 representing calm, cooperative behaviour and 4 representing crying and resistance. At intubation or mask presentation, mean behaviour scores were 1.88 ± 0.67 in the dexmedetomidine group and 1.60 ± 0.68 in the midazolam group ($P=0.044$). Although the mean score was slightly lower with midazolam, both groups had scores consistent with generally acceptable mask-related behaviour.

The result does not necessarily conflict with the broader literature because mask acceptance has been one of the more heterogeneous outcomes in comparative pediatric-premedication studies. The meta-analysis by Lang et al. found no statistically definitive superiority of dexmedetomidine over midazolam for sedation at mask induction despite advantages in parental separation and emergence agitation [16]. Zhang et al. similarly reported no significant difference in mask acceptance between intranasal dexmedetomidine and midazolam-based premedication [21]. Wang et al. reported satisfactory mask acceptance of 93.3% with both dexmedetomidine and midazolam in pediatric dental patients [20].

At extubation, midazolam showed superior behaviour compared with dexmedetomidine. The mean behaviour score was 1.85 ± 0.74 in the midazolam group versus 2.31 ± 0.99 in the dexmedetomidine group ($P=0.020$). As lower scores represent calmer and more cooperative behaviour on the four-point scale, this difference favoured midazolam during extubation. The observed benefit should be considered alongside the deeper sedation and greater attenuation of perioperative cardiovascular responses seen with dexmedetomidine.

No adverse events were observed in either group during the study. In particular, no episodes of nausea, nasal irritation, bradycardia, hypotension, or respiratory depression were recorded during perioperative monitoring. Both drugs were well tolerated by the children enrolled in this trial.

The current study has several strengths. It directly compared the same intranasal route for dexmedetomidine and midazolam, thereby reducing one potential source of heterogeneity inherent in studies comparing different routes. The groups were similar at baseline, a standardized anesthetic technique was used, and physiological variables were assessed repeatedly during both the preoperative and intraoperative periods. The study also evaluated clinically meaningful outcomes beyond sedation alone, including mask-related behaviour, hemodynamic responses, oxygenation, and recovery behaviour.

This study has some limitations. It was conducted at a single centre with a sample of 96 children, which may limit the applicability of the findings to other clinical settings. Single blinding of the subjects was performed, with the children and their parents or legal guardians unaware of treatment allocation; therefore, observer bias may have been present during the assessment of sedation and behaviour. Larger multicentre studies with blinded outcome assessment would help confirm these findings.

Overall, intranasal dexmedetomidine and midazolam were both effective pediatric premedicants. Dexmedetomidine was associated with lower heart rate and blood pressure at significant perioperative observation points and provided deeper sedation at induction. Mask-holding behaviour was acceptable in both groups, whereas midazolam showed more favourable extubation behaviour. Oxygen saturation remained satisfactory, and no adverse events were recorded.

CONCLUSION

Intranasal dexmedetomidine (1 µg/kg) and intranasal midazolam (0.2 mg/kg) were both effective premedicants in children aged 3–10 years undergoing elective surgery. Dexmedetomidine provided a more stable perioperative hemodynamic profile, with significantly lower heart rate and systolic blood pressure at several observation points, and deeper sedation during intubation. Mask-holding behaviour was acceptable in both groups, while midazolam showed more favourable behaviour at extubation. Oxygen saturation remained satisfactory, and no adverse events were observed in either group.

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