e-ISSN: 0975-9506, p-ISSN:2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(5); 100-105

Original Research Article

Comparison of Intranasal Dexmedetomidine Vs Midazolam for Premedication in Paediatric Patients Undergoing Elective Surgery

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Received: 11-03-2026 / Revised: 15-04-2026 / Accepted: 22-05-2026

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Conflict of interest: Nil

Abstract

Introduction: Preoperative anxiety is common in paediatric patients undergoing elective surgery and may adversely affect induction of anaesthesia, parental separation, and postoperative behaviour. Intranasal premedication is widely used due to its non-invasive and easy administration. Midazolam is traditionally used, but dexmedetomidine, an α2-adrenergic agonist, has emerged as an effective alternative with better sedation and anxiolysis and minimal respiratory depression.

Aims and Objectives: To compare the efficacy and safety of intranasal dexmedetomidine versus intranasal midazolam as premedication in paediatric patients undergoing elective surgery.

Materials and Methods: This prospective, randomized, comparative interventional study was conducted over 1 year at Dinhata Subdivisional Hospital, Coochbehar on 100 paediatric patients undergoing elective surgery under general anaesthesia. Patients were randomly assigned to receive either intranasal dexmedetomidine or midazolam, and outcomes including sedation, parental separation, mask acceptance, and adverse effects were compared.

Results: Baseline characteristics were comparable (age $p = 0.912$, gender $p = 0.841$). Dexmedetomidine showed significantly higher sedation scores at 30 min (3.80 ± 0.72 vs 3.10 ± 0.69) and 45 min (4.20 ± 0.55 vs 3.60 ± 0.60; $p < 0.001$), better parental separation (76% vs 50%; $p = 0.018$), and improved mask acceptance (72% vs 44%; $p = 0.021$), with fewer adverse effects overall ($p = 0.014$).

Conclusion: Intranasal dexmedetomidine is more effective than intranasal midazolam in providing sedation, anxiolysis, and smoother induction conditions in paediatric patients undergoing elective surgery, with a comparable safety profile. It can be considered a superior alternative for premedication in this population.

Keywords: Dexmedetomidine, Midazolam, Intranasal, Paediatric premedication, Preoperative anxiety, Sedation.

DOI: 10.25258/ijpqa.17.5.15

Introduction

Preoperative anxiety is a frequent and significant problem in paediatric patients undergoing elective surgical procedures. It is estimated that nearly 40–75% of children experience varying degrees of anxiety before surgery, which can adversely affect induction of anaesthesia, increase postoperative pain perception, lead to emergence delirium, and contribute to long-term behavioural disturbances such as sleep disorders and separation anxiety [1,2]. The perioperative experience in children is influenced by multiple factors including age, previous hospital exposure, parental anxiety, and unfamiliar hospital environments [3]. Therefore, effective premedication plays a crucial role in improving both psychological comfort and perioperative outcomes.Premedication in paediatric anaesthesia is primarily aimed at reducing anxiety, facilitating smooth parent-child separation, improving cooperation during induction of anaesthesia, and minimizing postoperative behavioural changes [4]. An ideal paediatric premedicant should have rapid onset, predictable action, minimal side effects, and should not cause respiratory or haemodynamic instability. Various pharmacological agents have been used for this purpose, including benzodiazepines, alpha-2 adrenergic agonists, ketamine, and opioids. Among these, midazolam has long been considered the standard premedicant in paediatric practice [5]. Midazolam is a short-acting benzodiazepine that

acts on the gamma-aminobutyric acid (GABA-A) receptor complex, producing anxiolysis, sedation, and anterograde amnesia. It is widely used due to its rapid onset, ease of administration, and relatively favourable safety profile [6]. Intranasal administration of midazolam offers a non-invasive route that is particularly useful in uncooperative children. However, its limitations include inconsistent sedation quality, variable absorption, burning sensation in the nasal mucosa, and the potential for paradoxical reactions such as agitation, disinhibition, and restlessness in a subset of paediatric patients [7]. These drawbacks have encouraged the exploration of alternative agents with better efficacy and tolerability. Dexmedetomidine is a highly selective alpha-2 adrenergic receptor agonist that produces sedation, anxiolysis, and analgesia without significant respiratory depression. It acts on the locus coeruleus in the brainstem, producing a sedation state that closely resembles natural sleep [8]. Intranasal dexmedetomidine has gained increasing attention as a paediatric premedicant due to its non-invasive administration, smooth sedative profile, and minimal respiratory adverse effects. It also provides better haemodynamic stability compared to many other sedatives, although mild bradycardia and hypotension may occur in some cases [9]. Several studies have compared dexmedetomidine and midazolam in paediatric premedication and have demonstrated that dexmedetomidine provides superior anxiolysis, better parent separation scores, and improved mask acceptance during induction. However, the onset of sedation with dexmedetomidine is relatively slower compared to midazolam, which may limit its use in situations requiring rapid preoperative preparation [10]. Despite this, the overall quality of sedation and smoother perioperative course have led many anaesthesiologists to prefer dexmedetomidine as an emerging alternative to midazolam. Given the ongoing debate regarding the optimal intranasal premedicant in children, it is essential to further evaluate and compare the efficacy and safety profiles of dexmedetomidine and midazolam. This study is therefore designed to compare intranasal dexmedetomidine and intranasal midazolam in paediatric patients undergoing elective surgery, with a focus on sedation quality, ease of parental separation, mask acceptance, haemodynamic stability, and adverse effects.To compare the efficacy and safety of intranasal dexmedetomidine versus intranasal midazolam as premedication in paediatric patients undergoing elective surgery.

Materials and Methods

Study design: Prospective, randomized, comparative interventional study.

Study setting: Dinhata Subdivisional Hospital, Coochbehar.

Period of study: 1Year

Study population: The study population consisted of 100 paediatric patients scheduled for elective surgery under general anaesthesia.

Sample size: 100

Inclusion criteria

- Paediatric patients aged 2–10 years scheduled for elective surgery under general anaesthesia
- ASA physical status I and II
- Patients requiring premedication for anxiety reduction
- Patients with fasting as per standard anaesthesia guidelines
- Patients whose parents/guardians provided written informed consent

Exclusion criteria

- Patients with ASA III and above
- Known allergy or hypersensitivity to dexmedetomidine, midazolam, or related drugs
- Children with upper respiratory tract infection or nasal pathology (e.g., nasal obstruction, epistaxis, deviated septum)
- Patients with cardiac conduction abnormalities or significant cardiovascular disease
- Children with neurological or psychiatric disorders
- Patients receiving sedative, anticonvulsant, or psychoactive medications preoperatively
- Emergency surgeries
- Refusal of parental consent

Statistical Analysis: For statistical analysis data were entered into a Microsoft Excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Z-test (Standard Normal Deviate) was used to test the significant difference of proportions. Once a t value is determined, a p-value can be found using a table of values from Student's t-distribution. If the calculated p-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis. P-value $\leq$ 0.05 was considered for statistically significant.

Result

Table 1: Age distribution of study groups

Age group (years)	Dexmedetomidine (n=50)	Midazolam (n=50)	Total	p-value
2–4	18	17	35	0.912
5–7	20	21	41	
8–10	12	12	24	
Total	50	50	100	

Table 2: Gender distribution

Gender	Dexmedetomidine (n=50)	Midazolam (n=50)	Total	p-value
Male	28 (56%)	27 (54%)	55	0.841
Female	22 (44%)	23 (46%)	45	
Total	50	50	100	

Table 3: Sedation score (mean ± SD)

Time point	Dexmedetomidine	Midazolam	p-value
15 min	2.10 ± 0.61	2.45 ± 0.58	0.032
30 min	3.80 ± 0.72	3.10 ± 0.69	<0.001
45 min	4.20 ± 0.55	3.60 ± 0.60	<0.001

Table 4: Parental separation score

Score category	Dexmedetomidine (n=50)	Midazolam (n=50)	p-value
Easy (1–2)	38 (76%)	25 (50%)	0.018
Moderate (3)	10 (20%)	18 (36%)	
Difficult (4)	2 (4%)	7 (14%)	

Table 5: Mask acceptance during induction

Mask acceptance	Dexmedetomidine (n=50)	Midazolam (n=50)	p-value
Excellent	36 (72%)	22 (44%)	0.021
Good	10 (20%)	18 (36%)	
Poor	4 (8%)	10 (20%)	

Table 6: Adverse effects

Adverse effect	Dexmedetomidine (n=50)	Midazolam (n=50)	p-value
Bradycardia	2 (4%)	0 (0%)	0.014
Hypotension	1 (2%)	0 (0%)	
Nasal irritation	3 (6%)	8 (16%)	
Paradoxical agitation	0 (0%)	5 (10%)	

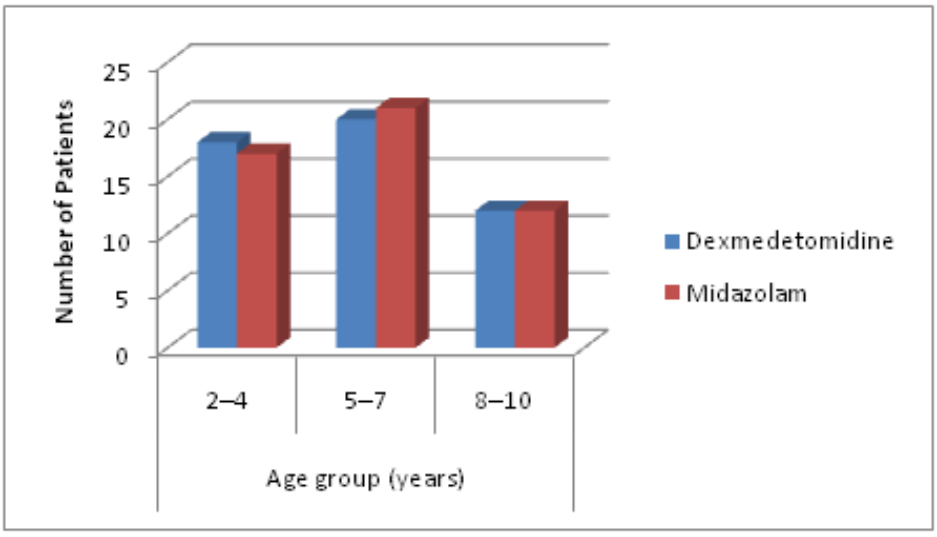

Figure 1: Age distribution of study groups

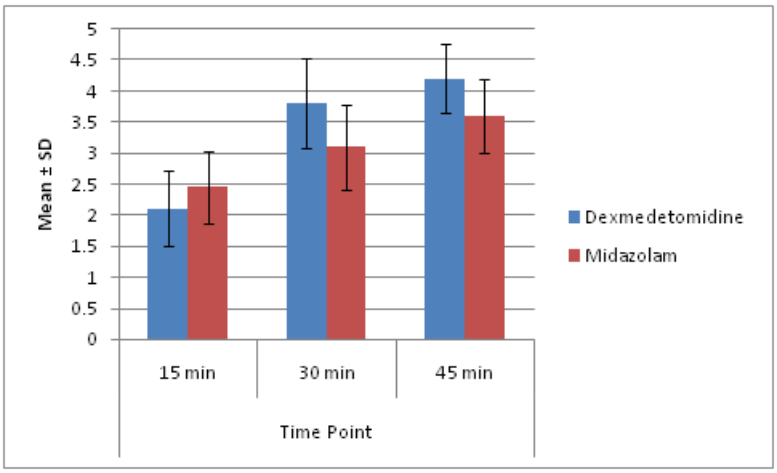

Figure 2: Sedation score (mean ± SD)

Age distribution of study groups

Result: In the dexmedetomidine group, 18 patients (36%) were aged 2–4 years, 20 patients (40%) were 5–7 years, and 12 patients (24%) were 8–10 years. In the midazolam group, 17 patients (34%) were aged 2–4 years, 21 patients (42%) were 5–7 years, and 12 patients (24%) were 8–10 years. The distribution was comparable between groups ($p = 0.912$).

Interpretation: There was no statistically significant difference in age distribution between the two groups, indicating that both groups were well matched for age.

Gender distribution

Result: The dexmedetomidine group included 28 males (56%) and 22 females (44%), while the midazolam group included 27 males (54%) and 23 females (46%). The difference between the groups was not statistically significant ($p = 0.841$).

Interpretation: Both groups were comparable in terms of gender distribution, with no significant difference observed.

Sedation score (mean ± SD)

Result: At 15 minutes, the mean sedation score was 2.10 ± 0.61 in the dexmedetomidine group and 2.45 ± 0.58 in the midazolam group ($p = 0.032$). At 30 minutes, it was 3.80 ± 0.72 vs 3.10 ± 0.69 ($p < 0.001$). At 45 minutes, it was 4.20 ± 0.55 vs 3.60 ± 0.60 ($p < 0.001$).

Interpretation: Dexmedetomidine showed significantly better sedation scores at 30 and 45 minutes compared to midazolam, indicating superior and more sustained sedation.

Parental separation score

Result: Easy separation was observed in 38 patients (76%) in the dexmedetomidine group and 25 patients (50%) in the midazolam group. Moderate separation occurred in 10 (20%) vs 18 (36%), while difficult separation was seen in 2 (4%) vs 7 (14%) respectively. The difference was statistically significant ($p = 0.018$).

Interpretation: Dexmedetomidine provided significantly better parental separation conditions compared to midazolam.

Mask acceptance during induction

Result: Excellent mask acceptance was observed in 36 patients (72%) in the dexmedetomidine group and 22 patients (44%) in the midazolam group. Good acceptance was seen in 10 (20%) vs 18 (36%), and poor acceptance in 4 (8%) vs 10 (20%) respectively. The difference was statistically significant ($p = 0.021$).

Interpretation: Dexmedetomidine resulted in significantly better mask acceptance during induction compared to midazolam.

Adverse effects

Result: Bradycardia occurred in 2 patients (4%) in the dexmedetomidine group and none in the midazolam group.

Hypotension occurred in 1 patient (2%) vs none. Nasal irritation was seen in 3 (6%) vs 8 (16%), and paradoxical agitation occurred only in the midazolam group (5 patients, 10%). The overall difference was statistically significant ($p = 0.014$).

Interpretation: Both drugs were generally safe; however, midazolam was associated with higher incidence of nasal irritation and paradoxical agitation, while dexmedetomidine showed mild bradycardia in a small proportion of patients.

Discussion

In the present study comparing intranasal dexmedetomidine and intranasal midazolam as premedication in paediatric patients undergoing elective surgery, both groups were comparable with respect to age and gender distribution, indicating adequate randomization and baseline homogeneity.

Preoperative anxiety is a well-recognized problem in paediatric anaesthesia, and effective premedication plays a key role in improving induction conditions, reducing psychological stress, and ensuring smoother perioperative management [11,12].Dexmedetomidine demonstrated significantly better sedation scores at 30 and 45 minutes compared to midazolam, indicating a more consistent and sustained sedative effect. This is attributed to its selective α2-adrenergic agonist action on the locus coeruleus, producing a sedation state similar to natural sleep without significant respiratory depression [13,14]. In contrast, midazolam acts via the GABA-A receptor complex and, although it has a rapid onset, it may produce variable sedation depth and occasional paradoxical reactions in children, which can affect overall cooperation. The findings of the present study are in agreement with previous research demonstrating superior sedation quality with dexmedetomidine compared to midazolam in paediatric premedication. Parental separation was significantly smoother in the dexmedetomidine group compared to the midazolam group.

This may be explained by the more profound anxiolytic and sympatholytic effects of dexmedetomidine, leading to reduced agitation and crying at separation. Similar results have been reported in earlier studies where dexmedetomidine significantly improved separation compliance and reduced preoperative distress in children. Improved parental separation is clinically important as it reduces both child and parental anxiety, which are known predictors of poor perioperative behaviour. Mask acceptance during induction was also significantly better in the dexmedetomidine group. Smooth induction is essential to avoid complications such as breath-holding, laryngospasm, and increased anaesthetic requirement. Previous studies have shown that dexmedetomidine provides better cooperative behaviour during induction due to its sedative and anxiolytic properties, whereas midazolam may sometimes be associated with disinhibition or inadequate sedation levels [15]. The results of this study are consistent with these findings and support the use of dexmedetomidine as a superior premedicant. Regarding safety, both drugs were generally well tolerated. However, midazolam was associated with a higher incidence of nasal irritation and paradoxical agitation, while dexmedetomidine showed mild bradycardia in a small number of patients. These findings are consistent with earlier literature where benzodiazepines have been associated with behavioural disturbances, while dexmedetomidine has been linked to dose-dependent bradycardia due to sympatholytic effects [16,17]. Importantly, no clinically significant respiratory depression was observed in either group, confirming the safety of intranasal administration of both agents in paediatric patients. Overall, dexmedetomidine demonstrated superior efficacy in terms of sedation quality, parental separation, and mask acceptance, with a comparable safety profile to midazolam. These findings align with multiple comparative studies and support the growing evidence favouring dexmedetomidine as an effective alternative to midazolam for paediatric premedication [18–20]. However, limitations such as single-centre design, relatively small sample size, and lack of long-term behavioural follow-up should be considered. Further large-scale multicentric studies are recommended to validate these findings and establish standardized dosing protocols for routine clinical practice.

Conclusion

Intranasal dexmedetomidine is more effective than intranasal midazolam as a premedication in paediatric patients undergoing elective surgery. It provides better and more consistent sedation, improved ease of parental separation, and superior mask acceptance during induction of anaesthesia.

Both drugs were found to be safe with minimal adverse effects; however, dexmedetomidine showed a more favourable overall perioperative profile with fewer behavioural disturbances compared to midazolam. Hence, intranasal dexmedetomidine can be considered a better and reliable alternative to midazolam for paediatric premedication in routine anaesthetic practice.

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