Section: Anesthesiology

Original Research Article

COMPARISON OF INTRANASAL AND ORAL MIDAZOLAM AS PREMEDICATION FOR SEDATION IN PEDIATRIC PATIENTS UNDERGOING ELECTIVE SURGERY: A PROSPECTIVE RANDOMIZED SINGLE-BLINDED STUDY

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ABSTRACT

Background: Preoperative anxiety is a common concern among pediatric patients undergoing surgery and is associated with difficult parental separation, poor cooperation during anesthetic induction, increased perioperative stress, and adverse postoperative behavioral changes. Midazolam is one of the most frequently used sedative premedicants because of its rapid onset, anxiolytic, amnestic, and sedative properties. Both oral and intranasal routes are widely used; however, the intranasal route may provide faster drug absorption by bypassing first-pass hepatic metabolism. The aim is to compare the efficacy and safety of intranasal midazolam and oral midazolam as preoperative sedative premedication in pediatric patients undergoing elective surgery under general anesthesia. **Materials and Methods:** This prospective, randomized, single-blinded study included 60 children aged 6 months to 6 years with American Society of Anesthesiologists (ASA) physical status I or II who were scheduled for elective surgery. Participants were randomly allocated into two equal groups. Group A received intranasal midazolam (0.3 mg/kg) administered via a transnasal atomizer, while Group B received oral midazolam syrup (0.5 mg/kg). Sedation was assessed using the Ramsay Sedation Scale, and parental separation and mask acceptance were evaluated using standardized scoring systems at predefined time intervals. Hemodynamic parameters, oxygen saturation, and adverse events were also recorded. Statistical analysis was performed using SPSS version 15.0, with a p-value <0.05 considered statistically significant. **Result:** Baseline demographic characteristics were comparable except for age and weight. Intranasal midazolam produced significantly higher sedation scores at 5, 10, 15, and 20 minutes compared with oral midazolam ($p<0.05$), indicating a faster onset of sedation. Parental separation scores were also significantly better in the intranasal group throughout the observation period. Mask acceptance during anesthetic induction was comparable between the two groups ($p=0.154$). Mild transient adverse effects, including nasal irritation, watering of the eyes, and nasal congestion, were observed only in the intranasal group, while no episodes of respiratory depression, bradycardia, or clinically significant oxygen desaturation occurred in either group. **Conclusion:** Intranasal midazolam provides faster and more effective preoperative sedation and facilitates smoother parental separation than oral midazolam in children undergoing elective surgery. Although associated with minor local nasal discomfort, it demonstrated an excellent safety profile and comparable mask acceptance. Intranasal midazolam may therefore be considered a preferred route for pediatric premedication when rapid and reliable sedation is required.

INTRODUCTION

Preoperative anxiety is a common and significant problem among pediatric patients undergoing surgical procedures under general anesthesia. It has been reported that approximately 50–70% of children experience moderate-to-severe anxiety before surgery, which may manifest as crying, agitation, fear of separation from parents, and resistance to medical procedures. Excessive anxiety activates the sympathetic nervous system and hypothalamic–pituitary–adrenal axis, resulting in tachycardia,

hypertension, increased oxygen consumption, and elevated stress hormone secretion. Furthermore, preoperative anxiety has been associated with difficult anesthetic induction, increased postoperative pain, emergence delirium, prolonged recovery, and long-term maladaptive behavioral changes such as sleep disturbances, separation anxiety, temper tantrums, and fear of healthcare settings.[1,2]

Effective premedication plays a pivotal role in reducing perioperative anxiety and facilitating smooth induction of anesthesia in children. Although non-pharmacological interventions, including parental presence during induction, behavioral preparation, distraction techniques, and audiovisual aids, can reduce anxiety in selected patients, pharmacological premedication remains the most reliable and widely adopted approach, particularly in younger children who are often unable to cooperate during anesthetic induction.[1–4]

Midazolam, a short-acting benzodiazepine, is the most frequently used sedative premedicant in pediatric anesthesia because of its rapid onset of action, anxiolytic, sedative, amnestic, and anticonvulsant properties. By enhancing gamma-aminobutyric acid (GABA)-mediated neurotransmission, midazolam provides effective anxiolysis while preserving cardiovascular stability and maintaining spontaneous ventilation when administered in recommended doses. Its favorable pharmacokinetic profile, including a short elimination half-life and rapid recovery, makes it particularly suitable for ambulatory and elective pediatric surgical procedures.[3,4-13]

Midazolam can be administered through several routes, including oral, intravenous, intramuscular, rectal, sublingual, and intranasal. The oral route is widely accepted because it is non-invasive and generally well tolerated by children. However, its clinical effectiveness may be limited by delayed gastrointestinal absorption, variable bioavailability due to extensive first-pass hepatic metabolism, and occasional refusal because of its bitter taste. In contrast, intranasal administration offers rapid absorption through the highly vascular nasal mucosa, bypasses first-pass metabolism, and results in faster onset of sedation and higher systemic bioavailability. The use of mucosal atomization devices has further improved drug distribution across the nasal mucosa, increasing absorption while minimizing discomfort.[5-9]

Several clinical studies have demonstrated that intranasal midazolam provides earlier sedation, improved parental separation, and satisfactory conditions for inhalational induction compared with placebo and other premedication regimens. Nevertheless, oral midazolam continues to be widely used because of its ease of administration and better patient acceptance. Although both routes are considered safe and effective, differences in onset of action, quality of sedation, parental separation, mask acceptance, and adverse effects remain clinically relevant and continue to be debated.[5-9]

The present prospective randomized single-blinded study was therefore undertaken to compare intranasal midazolam (0.3 mg/kg) administered via a transnasal atomization device with oral midazolam syrup (0.5 mg/kg) as preoperative sedative premedication in pediatric patients undergoing elective surgery under general anesthesia. The primary objective was to compare the onset and degree of sedation, while the secondary objectives included evaluation of parental separation, acceptance of face-mask induction, ease of drug administration, and the incidence of adverse events. The findings of this study may help identify the more effective and practical route of midazolam administration for optimizing perioperative care in pediatric anesthesia.[3–6,10,11]

MATERIALS AND METHODS

Study Design and Setting: This prospective, randomized, single-blinded comparative study was conducted in the Department of Anaesthesiology, Virudhunagar Government Medical College, Virudhunagar, Tamil Nadu, India. The study was conducted from March 2025 to March 2026. The study was approved by the Institutional Ethics Committee before commencement, and written informed consent was obtained from the parents or legal guardians of all participating children. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

Study Population: A total of 60 pediatric patients scheduled for elective surgical procedures under general anesthesia were enrolled. Children aged between 6 months and 6 years belonging to the American Society of Anesthesiologists (ASA) physical status I or II were included. Participants were randomly allocated into two equal groups comprising 30 patients each.

Study Period: The study was conducted over a period of one year, from March 2025 to March 2026.

Inclusion Criteria

1. Children aged between 6 months and 6 years scheduled for elective surgical procedures under general anesthesia.
2. American Society of Anesthesiologists (ASA) physical status I or II, indicating medically fit or mildly symptomatic patients.
3. Patients of either sex (male or female).
4. Children undergoing elective surgery requiring preoperative sedative premedication and inhalational induction of general anesthesia.
5. Written informed consent obtained from parents or legal guardians prior to enrollment in the study.

Exclusion Criteria

1. Children with upper respiratory tract infection, nasal obstruction, or active nasal pathology that could interfere with intranasal drug absorption.

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2. Known hypersensitivity or allergy to midazolam, benzodiazepines, or any component of the study medication.
3. Patients with significant systemic illness, including severe hepatic dysfunction, renal impairment, cardiovascular disease, neurological disorders, or developmental delay that could influence sedation assessment.
4. Children classified as American Society of Anesthesiologists (ASA) physical status III or higher, or those with anticipated difficult airway requiring specialized anesthetic management.
5. Patients receiving sedative, anticonvulsant, or psychoactive medications, or those whose parents/legal guardians declined to provide written informed consent.

Sample Size: A total of 60 pediatric patients scheduled for elective surgical procedures under general anesthesia were enrolled in this prospective randomized single-blinded study. The participants were randomly allocated into two equal groups of 30 patients each. Group A received intranasal midazolam (0.3 mg/kg) via a transnasal atomization device, while Group B received oral midazolam syrup (0.5 mg/kg). The sample size was considered adequate to compare the efficacy of the two routes of administration with respect to sedation, parental separation, mask acceptance, and safety outcomes within the study setting.

Study Groups: The enrolled participants were randomly assigned into two equal groups, with 30 patients in each group, according to the route of midazolam administration.

- Group A (Intranasal Midazolam): n = 30
- Group B (Oral Midazolam): n = 30
- Total Sample Size: N = 60

Group A (Intranasal Midazolam Group): Children allocated to Group A received intranasal midazolam at a dose of 0.3 mg/kg, administered using a transnasal mucosal atomization device approximately 30 minutes before induction of general anesthesia.

Group B (Oral Midazolam Group): Children allocated to Group B received oral midazolam syrup at a dose of 0.5 mg/kg, administered 30 minutes before induction of general anesthesia.

Randomization and Blinding: Participants who fulfilled the eligibility criteria and whose parents or legal guardians provided written informed consent were randomly allocated in a 1:1 ratio into one of two study groups using a computer-generated randomization sequence. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes, which were opened only after patient enrollment. Thirty children were assigned to Group A (intranasal midazolam 0.3 mg/kg) and thirty to Group B (oral midazolam 0.5 mg/kg).

The study was conducted using a single-blinded design. The anesthesiologist responsible for administering the study medication was aware of the assigned intervention, whereas the anesthesiologist who evaluated the study outcomes, including sedation score, parental separation score, mask acceptance score, and perioperative observations, remained blinded to the route of drug administration throughout the study. Data analysis was performed using coded group assignments to minimize observer bias.

Study Procedure: After obtaining written informed consent from the parents or legal guardians, all eligible children underwent a comprehensive pre-anesthetic evaluation one day before surgery. Demographic details, medical history, physical examination findings, American Society of Anesthesiologists (ASA) physical status, and baseline vital parameters were recorded. Standard preoperative fasting guidelines appropriate for the child's age were followed.

On the day of surgery, patients were transferred with one parent to the preoperative holding area. Baseline heart rate, non-invasive blood pressure, peripheral oxygen saturation (SpO_2), Ramsay Sedation Scale score, and parental separation score were documented before administration of the study medication. Patients were then randomly assigned to receive either intranasal midazolam (0.3 mg/kg) via a transnasal mucosal atomization device (Group A) or oral midazolam syrup (0.5 mg/kg) (Group B). All resuscitation equipment and monitoring devices were kept readily available throughout the observation period.

Following administration of the study medication, children were continuously observed in the preoperative holding area. Heart rate, blood pressure, oxygen saturation, sedation score, and parental separation score were assessed at 5, 10, 15, 20, and 30 minutes after premedication. At the end of the 30-minute observation period, patients were transferred to the operating room. Standard monitoring, including electrocardiography, pulse oximetry, non-invasive blood pressure, and capnography, was instituted. General anesthesia was induced using oxygen, nitrous oxide, and sevoflurane via a face mask. The quality of mask acceptance was evaluated before intravenous cannulation using a standardized four-point scoring system. Anesthesia was subsequently maintained according to institutional protocols based on the type and duration of surgery. Following completion of surgery, patients were transferred to the post-anesthesia care unit (PACU), where recovery parameters and any adverse events, including respiratory depression, oxygen desaturation, bradycardia, nausea, vomiting, nasal irritation, watering of the eyes, and nasal congestion, were monitored. All participants were followed for 24 hours postoperatively to assess the safety and tolerability of the study medications.

Outcome Measures

Primary Outcome: The primary outcome of the study was the degree of preoperative sedation, assessed using the Ramsay Sedation Scale (RSS). Sedation scores were recorded at baseline (before premedication) and at 5, 10, 15, 20, and 30 minutes

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following administration of the study drug. The onset and progression of sedation were compared between the intranasal and oral midazolam groups.

Secondary Outcomes: The secondary outcomes included the quality of parental separation, assessed using a standardized four-point parental separation score, and mask acceptance during inhalational induction of anesthesia, evaluated using a four-point mask acceptance scale. In addition, hemodynamic parameters, including heart rate, non-invasive blood pressure, and peripheral oxygen saturation (SpO_2), were monitored throughout the observation period to assess physiological stability. The safety profile of both routes of administration was evaluated by recording adverse events such as nasal irritation, watering of the eyes, nasal congestion, nausea, vomiting, respiratory depression, bradycardia, oxygen desaturation, and any other drug-related complications during the perioperative period.

Sedation Assessment: The degree of sedation was evaluated using the Ramsay Sedation Scale (RSS), a validated six-point clinical scale widely used to assess the level of sedation in pediatric and adult patients. Sedation assessments were performed at baseline (before administration of the study drug) and subsequently at 5, 10, 15, 20, and 30 minutes after premedication by an anesthesiologist who was blinded to the route of drug administration. Higher Ramsay Sedation Scale scores indicated a deeper level of sedation.

The Ramsay Sedation Scale was defined as follows:

- Score 1: Anxious, agitated, or restless.
- Score 2: Cooperative, oriented, and tranquil.
- Score 3: Responds only to verbal commands.
- Score 4: Brisk response to a light glabellar tap or loud auditory stimulus.
- Score 5: Sluggish response to a light glabellar tap or loud auditory stimulus.
- Score 6: No response to external stimuli.

The onset, progression, and degree of sedation achieved with intranasal midazolam and oral midazolam were compared based on the Ramsay Sedation Scale scores recorded at each predefined assessment interval.

Mask Acceptance Score: Acceptance of the anesthesia face mask during inhalational induction was assessed 30 minutes after administration of the study medication using a standardized four-point Mask Acceptance Score. The assessment was performed by the anesthesiologist who was blinded to the route of drug administration. The score reflected the child's level of cooperation during placement of the face mask for induction of general anesthesia, with lower scores indicating better acceptance.

The Mask Acceptance Score was graded as follows:

- Score 1 (Very Good): Immediate acceptance of the face mask without resistance.
- Score 2 (Good): Slight resistance to mask placement but cooperative without significant struggle.
- Score 3 (Moderate): Noticeable struggle or resistance during mask placement.
- Score 4 (Difficult): Marked resistance requiring restraint or forceful application of the face mask.

Mask acceptance scores were compared between the intranasal midazolam and oral midazolam groups to determine the effectiveness of premedication in facilitating smooth inhalational induction of anesthesia.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee before the commencement of the study. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the Indian Council of Medical Research (ICMR) Ethical Guidelines for Biomedical Research Involving Human Participants. Written informed consent was obtained from the parents or legal guardians of all participating children prior to enrollment. Participation was voluntary, and confidentiality of patient information was maintained throughout the study by anonymizing all collected data. Participants were free to withdraw from the study at any time without affecting their standard medical care. Continuous monitoring was ensured during the perioperative period, and any adverse events were managed according to standard clinical protocols.

Statistical Analysis: Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 15.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The independent samples Student's t-test was used to compare continuous variables between the two groups, and the Chi-square test or Fisher's exact test, where appropriate, was used to compare categorical variables. All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant.

RESULTS

A total of 60 pediatric patients scheduled for elective surgery under general anesthesia were enrolled in this prospective randomized single-blinded study. Participants were randomly assigned to either the intranasal midazolam group (Group A, n=30) or the oral midazolam group (Group B, n=30). All enrolled patients completed the study, and no participants were excluded after randomization.

Baseline Characteristics: The baseline demographic characteristics of the study population are presented in [Table 1]. The mean age was significantly lower in Group A than in Group B (19.60 ± 13.17 months vs. 30.03 ± 19.75 months, p=0.019). Similarly, the mean body weight was significantly lower in the intranasal group (9.33 ±

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2.72 kg) compared with the oral group (11.73 ± 4.84 kg, p=0.021). The distribution of sex and ASA physical status was comparable between the two groups, with no statistically significant differences (p>0.05).

Table 1: Baseline Characteristics of the Study Population

Variable	Group A (Intranasal Midazolam) (n=30)	Group B (Oral Midazolam) (n=30)	P value
Age (months), Mean ± SD	19.60 ± 13.17	30.03 ± 19.75	0.019
Weight (kg), Mean ± SD	9.33 ± 2.72	11.73 ± 4.84	0.021
Male, n (%)	20 (66.7)	21 (70.0)	1.000
Female, n (%)	10 (33.3)	9 (30.0)	
ASA I, n (%)	26 (86.7)	26 (86.7)	1.000
ASA II, n (%)	4 (13.3)	4 (13.3)	

Note: Data are presented as mean ± standard deviation (SD) for continuous variables and number (percentage) for categorical variables. The two groups were comparable with respect to sex distribution and ASA physical status, whereas significant differences were observed in age and body weight (p<0.05).

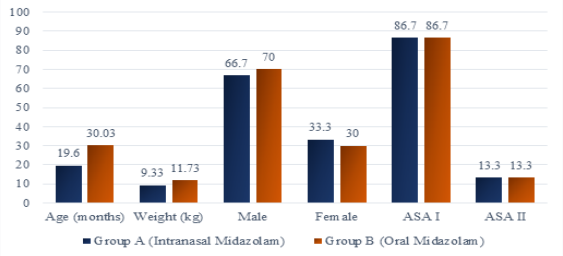

Figure 1: Baseline Characteristics of the Study Population

Figure Note: The figure illustrates the baseline demographic and clinical characteristics of children enrolled in the intranasal and oral midazolam groups. Although significant differences were observed in mean age and body weight between the groups (p<0.05), the distribution of sex and ASA physical status was comparable, indicating similar baseline clinical characteristics except for age and weight.

Comparison of Sedation Scores: Baseline sedation scores were similar between the two groups (p=0.064). Following administration of the study medication, the intranasal midazolam group demonstrated significantly higher sedation scores at 5, 10, 15, and 20 minutes compared with the oral midazolam group (all p<0.05). At 30 minutes, sedation remained marginally higher in the intranasal group (p=0.050), indicating a faster onset and greater depth of sedation.

Table 2: Comparison of Ramsay Sedation Scores Between Groups

Time	Group A Mean ± SD	Group B Mean ± SD	P value
Baseline	1.27 ± 0.52	1.07 ± 0.25	0.064
5 minutes	2.90 ± 1.06	1.17 ± 0.46	<0.001
10 minutes	3.97 ± 1.16	1.50 ± 0.73	<0.001
15 minutes	4.30 ± 0.95	3.63 ± 0.62	0.002
20 minutes	4.80 ± 0.71	4.13 ± 1.13	0.003
30 minutes	5.10 ± 0.55	4.80 ± 0.61	0.050

Note: Sedation scores are presented as mean ± SD. Children receiving intranasal midazolam demonstrated significantly higher sedation scores from 5 to 20 minutes compared with the oral midazolam group, indicating a faster onset and greater depth of sedation.

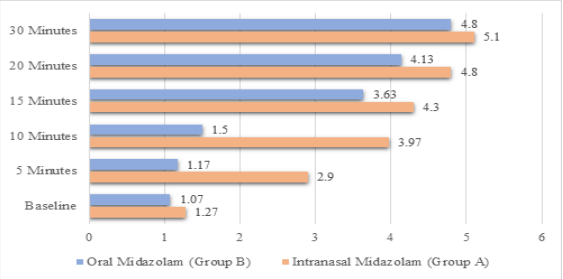

Figure 2: Comparison of Mean Ramsay Sedation Scores Between the Intranasal and Oral Midazolam Groups

Figure Note: The figure illustrates the changes in mean Ramsay Sedation Scale scores at baseline and at 5, 10, 15, 20, and 30 minutes following premedication. Children receiving intranasal midazolam achieved significantly higher sedation scores from 5 to 20 minutes compared with those receiving oral midazolam, indicating a faster onset and greater depth of sedation. Values represent mean ± standard deviation (SD).

Comparison of Parental Separation Scores: There was no significant difference in parental separation scores at baseline (p=0.262). However, children receiving intranasal midazolam achieved significantly better parental separation scores at 5, 10, 15, 20, and 30 minutes than those receiving oral midazolam, indicating earlier anxiolysis and improved cooperation.

Table 3: Comparison of Parental Separation Scores Between Groups

Assessment Time	P value
Baseline	0.262
5 minutes	<0.001
10 minutes	<0.001

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15 minutes	0.041
20 minutes	0.026
30 minutes	0.026

Note: Parental separation was assessed using a standardized four-point separation score. Intranasal midazolam produced significantly better parental separation after premedication, reflecting improved anxiolysis and cooperation before induction of anesthesia.

Comparison of Mask Acceptance: The quality of mask acceptance during inhalational induction was comparable between the two study groups. Although a greater proportion of children in the intranasal group demonstrated very good mask acceptance, the overall distribution of mask acceptance scores did not differ significantly between the groups (p=0.154).

Table 4: Comparison of Mask Acceptance Scores

Mask Acceptance	Group A n (%)	Group B n (%)
Very Good	7 (23.3)	2 (6.7)
Good	18 (60.0)	24 (80.0)
Moderate	5 (16.7)	4 (13.3)
P value	0.154	

Note: Mask acceptance was evaluated using a standardized four-point scoring system during inhalational induction. Although both groups demonstrated satisfactory mask acceptance, no statistically significant difference was observed between the two routes of midazolam administration.

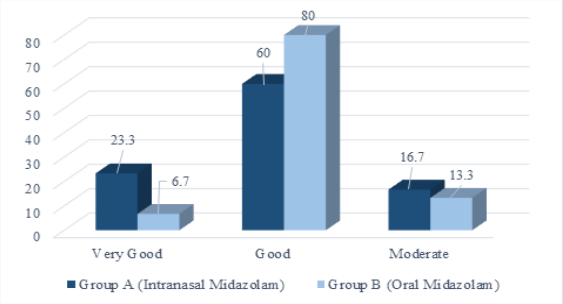

Figure 3: Comparison of Mask Acceptance Scores Between the Intranasal and Oral Midazolam Groups

Figure Note: The figure illustrates the distribution of mask acceptance scores during inhalational induction of anesthesia in the two study groups. Although a higher proportion of children in the intranasal midazolam group demonstrated very good mask acceptance, the overall distribution of mask acceptance scores was comparable between the groups, with no statistically significant difference (p = 0.154). Data are presented as percentages of patients in each group.

Adverse Events: Both routes of administration were well tolerated. Mild adverse events, including transient nasal irritation, watering of the eyes, and nasal congestion, were observed only in children receiving intranasal midazolam. No episodes of clinically significant respiratory depression, oxygen desaturation, bradycardia, or serious adverse drug reactions were observed in either group throughout the perioperative period.

Table 5: Adverse Events Observed During the Study

Adverse Event	Intranasal Midazolam	Oral Midazolam
Nasal irritation	Present	Absent
Watering of eyes	Present	Absent
Nasal congestion	Present	Absent
Nausea/Vomiting	None	None
Bradycardia	None	None
Oxygen desaturation	None	None
Respiratory depression	None	None
Serious adverse events	None	None

Note: Both intranasal and oral midazolam were well tolerated without any serious adverse events. Mild transient nasal irritation, watering of the eyes, and nasal congestion were observed only in the intranasal group, while no episodes of respiratory depression, oxygen desaturation, or bradycardia occurred in either group.

DISCUSSION

The present prospective randomized single-blinded study compared the efficacy and safety of intranasal midazolam (0.3 mg/kg) and oral midazolam (0.5 mg/kg) as preoperative sedative premedication in pediatric patients undergoing elective surgery under general anesthesia. The principal findings of this study demonstrate that intranasal midazolam produced a significantly faster onset of sedation, facilitated smoother parental separation, and provided comparable mask acceptance when compared with oral midazolam, while maintaining an excellent safety profile. These findings support the use of the intranasal route as an effective alternative to oral administration for pediatric premedication.[3,4]

Preoperative anxiety remains one of the most challenging aspects of pediatric anesthesia. Anxiety associated with unfamiliar surroundings, separation from parents, and fear of medical procedures may

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result in poor cooperation, difficult anesthetic induction, increased perioperative stress responses, and adverse postoperative behavioral changes. Effective premedication therefore plays an important role in improving the overall perioperative experience for both children and their caregivers. Midazolam continues to be the most frequently used pediatric premedicant because of its rapid onset, anxiolytic, sedative, and amnestic properties, together with its favorable safety profile.[1–4]

One of the most important observations in the present study was the significantly faster onset of sedation achieved with intranasal midazolam. Children receiving intranasal midazolam demonstrated significantly higher Ramsay Sedation Scale scores from 5 to 20 minutes following drug administration compared with those receiving oral midazolam. These findings can be explained by the pharmacokinetic advantages of the intranasal route. The nasal mucosa is highly vascular, allowing rapid systemic absorption while bypassing first-pass hepatic metabolism, thereby resulting in higher bioavailability and earlier achievement of therapeutic plasma concentrations. In contrast, oral midazolam undergoes extensive first-pass metabolism and exhibits variable gastrointestinal absorption, which delays its clinical onset.[5,6,8]

The present findings are consistent with previous clinical studies that have reported more rapid and reliable sedation following intranasal administration of midazolam. Similar observations have been reported by Wilton et al., Karl et al., and Bhakta et al., who demonstrated earlier onset of sedation and superior anxiolysis with intranasal midazolam in pediatric surgical patients. These studies concluded that intranasal administration is particularly advantageous when rapid preoperative sedation is desired or when oral administration is impractical.[5-9]

An equally important finding of this study was the significantly improved parental separation observed in the intranasal midazolam group. Successful parental separation is an important indicator of adequate anxiolysis before transfer to the operating room. Children who are calm and cooperative during separation generally experience smoother anesthetic induction and reduced emotional distress. The better parental separation scores observed in the present study are likely a direct consequence of the faster onset and greater depth of sedation produced by intranasal administration. These findings corroborate earlier studies demonstrating that rapid anxiolysis facilitates easier transfer of pediatric patients to the operating room and reduces perioperative stress for both children and parents.[1,5–9]

Although intranasal midazolam produced superior sedation and parental separation, mask acceptance during inhalational induction was comparable between the two groups. Both routes of administration provided satisfactory conditions for mask placement, and no statistically significant difference was observed. Similar findings have been reported in previous comparative studies, suggesting that once an adequate level of sedation is achieved, both oral and intranasal midazolam provide acceptable cooperation during induction of anesthesia.[6,8,9] Therefore, while intranasal administration offers a faster onset of sedation, oral midazolam remains an effective option for facilitating inhalational induction when sufficient time is available before surgery.

Safety is an important consideration when selecting a premedication technique for pediatric patients. In the present study, both routes of administration were well tolerated without clinically significant respiratory depression, oxygen desaturation, bradycardia, or major cardiovascular instability. Mild transient adverse effects, including nasal irritation, watering of the eyes, and nasal congestion, were observed only in the intranasal group. These local effects were self-limiting and did not require medical intervention. Similar transient nasal discomfort has been reported in previous studies evaluating intranasal midazolam and is attributed to the acidic pH of the formulation and local mucosal irritation rather than systemic toxicity.[5,6,8,9] Importantly, no serious adverse events occurred, further confirming the favorable safety profile of both routes of administration.[3,4,10,11]

The findings of the present study have important clinical implications. Intranasal administration eliminates the need for intravenous access before adequate sedation is achieved and is particularly useful in uncooperative children or in situations requiring rapid onset of preoperative anxiolysis. The use of a mucosal atomization device further improves drug distribution over the nasal mucosa, enhancing absorption while reducing drug loss.[6,9] Consequently, intranasal midazolam represents a practical and effective alternative to oral premedication in routine pediatric anesthesia practice.[3,4,13]

The present study has certain limitations. The study was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Long-term postoperative behavioral outcomes, parental satisfaction, recovery characteristics, and cost-effectiveness were not evaluated. Furthermore, plasma midazolam concentrations were not measured, preventing direct pharmacokinetic correlation with the observed clinical effects. Future multicenter randomized controlled trials with larger sample sizes and longer follow-up are warranted to validate these findings and evaluate additional patient-centered outcomes.[1,2,12,14,15]

Overall, the present study demonstrates that intranasal midazolam provides faster and more effective preoperative sedation and significantly improves parental separation compared with oral midazolam while maintaining a comparable safety profile and satisfactory mask acceptance. These findings support the routine use of intranasal midazolam as an effective premedication strategy for

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pediatric patients undergoing elective surgical procedures under general anesthesia.[3-6]

Limitations: The present study has several limitations. First, it was conducted at a single center with a relatively small sample size of 60 participants, which may limit the generalizability of the findings. Second, the study included only children with ASA physical status I and II undergoing elective surgical procedures; therefore, the results may not be applicable to children with significant comorbidities or those undergoing emergency surgery. Third, postoperative recovery characteristics, emergence delirium, parental satisfaction, and long-term behavioral outcomes were not assessed. Finally, plasma midazolam concentrations were not measured; hence, the pharmacokinetic differences between the intranasal and oral routes could not be directly correlated with the observed clinical outcomes.

CONCLUSION

The findings of this prospective randomized single-blinded study demonstrate that intranasal midazolam (0.3 mg/kg) is more effective than oral midazolam (0.5 mg/kg) for preoperative sedation in pediatric patients undergoing elective surgery under general anesthesia. Intranasal administration resulted in a significantly faster onset of sedation and facilitated smoother parental separation while providing mask acceptance comparable to that of oral midazolam. Both routes were well tolerated, with no clinically significant cardiorespiratory adverse events; however, mild transient nasal irritation was observed only in the intranasal group. Overall, intranasal midazolam offers a safe, effective, and practical alternative to oral midazolam and may be considered the preferred route for pediatric premedication when rapid and reliable preoperative sedation is desired.

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