Original Article

pISSN 2383-9309 ▮ eISSN 2383-9317
J Dent Anesth Pain Med 2025;25(2):109-122 ▮ https://doi.org/10.17245/jdapm.2025.25.2.109

Comparative evaluation of the effectiveness and acceptance of intranasal dexmedetomidine and intranasal midazolam for sedation in children aged 5–8 years using a mucosal atomizer device: a randomized controlled clinical study

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Background: Patient age, preoperative anxiety, dental requirement, risks associated with pharmaceutical management, safety, parental expectations, and cost influence the choice of pharmacological behavior management. Thus, this randomized controlled clinical study aimed to compare the effectiveness and acceptance of intranasal dexmedetomidine and midazolam for sedation in children aged 5–8 years using a mucosal atomizer device (MAD).
Methods: A total of 48 participants with Frankl's II behavior were randomly divided into two groups: Group I received intranasal midazolam (0.25 mg/kg), and Group II received intranasal dexmedetomidine (1.5 μg/kg). The primary outcomes assessed were drug acceptance, onset and effectiveness of sedation, and pre-and post-treatment anxiety levels. Secondary measures were also evaluated pre- and post-treatment.
Results: Intranasal dexmedetomidine demonstrated significantly better drug acceptance ($P < 0.001$). Midazolam had a faster onset but was less effective than dexmedetomidine ($P < 0.001$). Additionally, dexmedetomidine exhibited better anxiolytic properties than midazolam ($P < 0.001$).
Conclusion: Dexmedetomidine was better accepted by children aged 5–8 years, was more effective, and had superior anxiolytic properties compared with midazolam.

Keywords: Administration, Intranasal; Anxiety; Dexmedetomidine; Drug Delivery Systems; Midazolam.

INTRODUCTION

Pediatric dentistry plays a crucial role in addressing children's oral health needs by providing preventive, diagnostic, and therapeutic care tailored to their developmental and psychological requirements [1]. Despite advancements in dental techniques, managing fear and anxiety in pediatric patients remains a challenge. Negative past experiences, parental anxiety, and an intimidating clinical environment often contribute to dental fear, leading to uncooperative behavior, delayed treatment, and poor oral health outcomes [2]. Effective behavioral management and sedation techniques are essential in overcoming these challenges and ensuring successful dental care.

Behavioral management strategies in pediatric dentistry range from non-pharmacological approaches, such as positive reinforcement and distraction, to pharmaco-

Received: December 19, 2024 • Revised: March 2, 2025 • Accepted: March 4, 2025
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logical interventions using sedative agents [3]. Pharmacological sedation is particularly beneficial for children with severe anxiety, special healthcare needs, or those undergoing extensive dental procedures. Among available sedatives, midazolam and dexmedetomidine are commonly used to ensure effective treatment while maintaining patient safety and comfort [4,5].

Midazolam, a benzodiazepine derivative, is widely used in pediatric dentistry because of its rapid onset, anxiolytic, and amnesic properties. This enhances the inhibitory effects of gamma-aminobutyric acid (GABA) on the central nervous system, leading to sedation and reduced anxiety [6]. Its multiple administration routes—oral, intranasal, and intravenous—offer flexibility for clinicians. The short half-life and predictable recovery of the drug minimize prolonged sedation effects, making it a preferred choice for brief dental procedures [7]. However, potential drawbacks include paradoxical reactions such as agitation and the risk of respiratory depression, necessitating careful monitoring and dose adjustments [8].

Dexmedetomidine, a selective alpha-2 adrenergic agonist, has emerged as a promising alternative for pediatric dental sedation. Its unique pharmacological profile provides sedation without causing significant respiratory depression, allowing patients to maintain spontaneous ventilation [9]. In addition, dexmedetomidine possesses analgesic and anxiolytic properties that enhance patient comfort during dental procedures. Although it offers advantages such as rapid onset and titratable effects, it may cause hemodynamic instability, including bradycardia and hypotension, which requires vigilant monitoring. Its suitability for pediatric patients with complex medical conditions highlights its growing relevance in dentistry [10].

The intranasal route, facilitated by a mucosal atomizer device (MAD), is a noninvasive and efficient method for pediatric sedation. Bypassing first-pass metabolism ensures higher systemic absorption and rapid onset of action. MAD provides a well-tolerated approach, particularly for uncooperative children, delivering consistent and predictable sedation outcomes. Intranasal midazolam and dexmedetomidine have demonstrated promising results in achieving effective sedation with minimal distress. This highlights the need for comparative studies to evaluate their relative efficacy and acceptance [11].

Although midazolam remains widely used in pediatric dentistry, its side effects, including respiratory depression and paradoxical reactions, necessitate the exploration of alternative agents, such as dexmedetomidine. The intranasal route via the MAD offers a compelling option for sedative administration in young children because of its ease of use and rapid effectiveness. However, comparative studies evaluating the use of intranasal midazolam and dexmedetomidine for pediatric sedation during dental procedures are lacking. This study aimed to bridge this gap by assessing the effectiveness and acceptance of these sedatives in children aged 5–8 years undergoing dental treatments.

METHODS

Study design: This was an in vivo, double-blinded, randomized clinical study conducted in the Department of Pediatric and Preventive Dentistry, KMSDCH, SumandeepVidyapeeth, Piparia, Vadodara. This study was approved by the Institutional Ethics Committee (IEC) of (SVIEC/ON/DENT/BNPG21/D22067) and registered with the Clinical Trial Registry (CTRI) (CTRI/2022/07/044010).

Sample size estimation: Using the formula for one-proportion sample size estimation,

$$n = \left(\frac{Z_{\alpha/2} \cdot \sqrt{p(1-p)}}{d} \right)^2$$

where p is the expected proportion (90.5%), d is the clinically significant difference (13%), and α is 0.05, the required sample size per group was calculated to be 20. However, considering a potential dropout rate of 20%, the adjusted sample size was adjusted to 24 participants per group. Thus, the total sample size required for the

Table 1. Selection criteria

Selection criteria	
Inclusion criteria	Exclusion criteria
1. Children aged between 5-8 years of age. 2. Frankle's behavior rating scale II children were included. 3. Children with ASA I or II health status were included. 4. Children with Pre-anesthetic checkup done were included 5. Preoperative heart rate of 55 to 100 beats per minute and Respiratory rate of 14-16 beats per minute. 6. Maximum blood pressure reading of 140/100 mmHg. 7. Patients who require LA administration for dental procedure.	1. Patient without any systemic illness. 2. A history of allergy or intolerance to benzodiazepines. 3. An upper respiratory tract infection with nasal discharge or respiratory distress. 4. Parents not giving consent for the study.

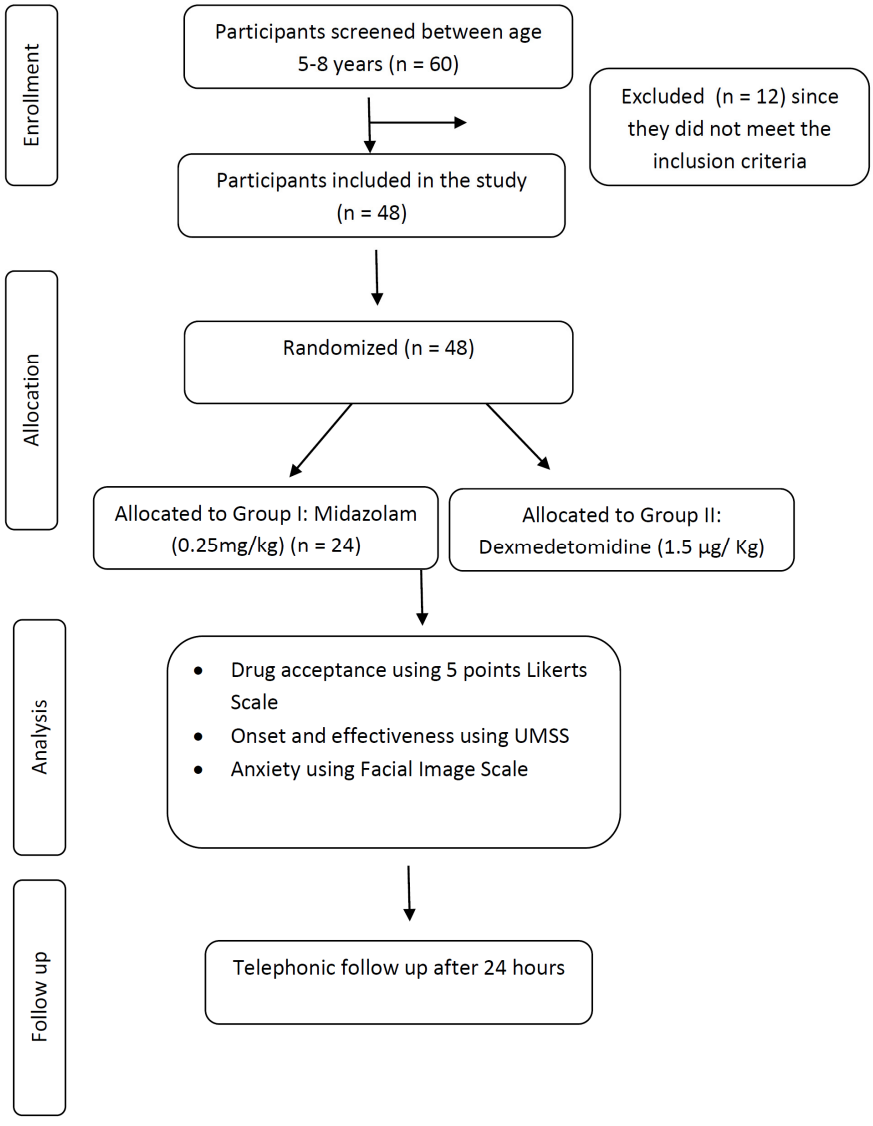

Fig. 1. Consolidated standards of reporting trials (CONSORT) flow diagram. n, number; UMSS, University of Michigan sedation scale.

study was 48 (24 per group) to ensure adequate statistical power.

Selection and randomization: A stratified randomization method was used to select participants from children visiting the Department of Pediatric and Preventive Dentistry, KMSDCH. A total of 48 participants (boys and girls) aged 5–8 years were screened based on the inclusion and exclusion criteria (Table 1).

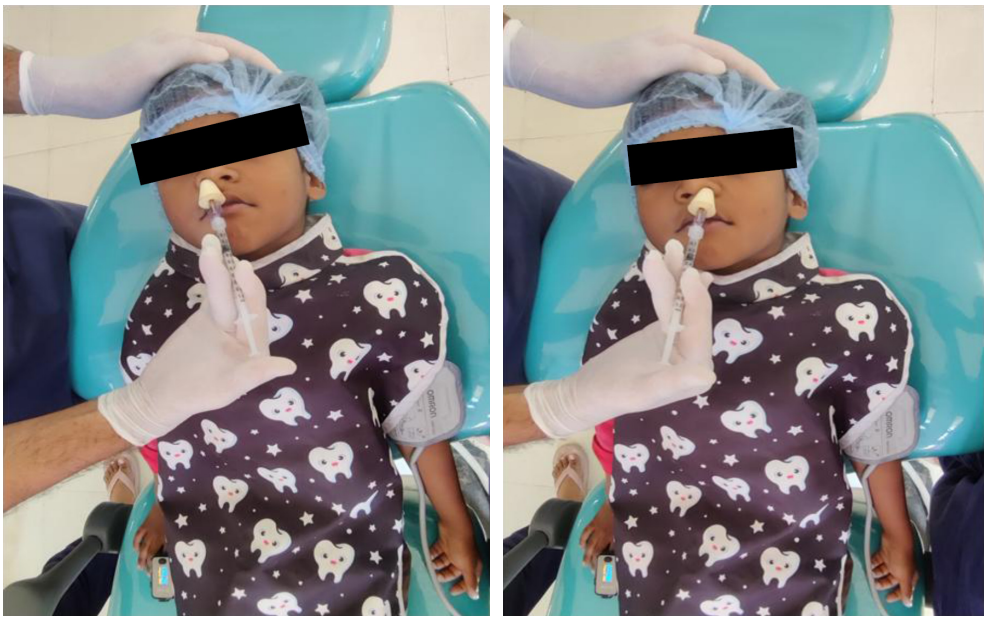

Fig. 2. Administration of dexmedetomidine/midazolam using a mucosal atomizer device (MAD).

Randomization was performed using the lottery method, where each child picked one chit from a bowl containing 48 chits—24 for Group I and 24 for Group II. The selected chit was handed to the staff nurse of the department based on the group allotted to the prepared tray armamentarium for the administration of either of the drugs (Fig. 1).

Clinical procedure: Participants and parents were informed about the study, and written consent and assent were obtained. After randomization and allocation to either group, general extra-oral and intra-oral examinations were performed using a mouth mirror and straight explorer under proper illumination of the teeth. Intraoral periapical radiography (IOPAR) were performed, if required. The diagnosis, treatment plan, and inclusion in the study were explained to the parents and children. Since participants with Frankl's II behavior were included, uncooperative behavior was expected because of the dental fear and anxiety observed during the first dental visit. Therefore, pharmacological behavioral management was planned. The department staff nurse based on the group allotted arranged the armamentarium and dose preparation of the drug allotted (Group I: midazolam [0.25 mg/kg], Group II: dexmedetomidine [1.5 μg/kg]). The co-investigator recorded the demographic details and each participant's weight, pre-treatment heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and oxygen saturation (SpO_2) (using an automated blood pressure and pulse oximetry unit). Dental fear and anxiety levels were measured before treatment using a Facial Image Scale (FIS).

Investigator calibration for drug administration and anxiety assessment: To ensure standardized and reliable drug administration and anxiety assessment, the primary investigator underwent calibration and training by an expert in pediatric sedation. The training included:

- **Intranasal drug administration using a MAD:** Hands-on sessions were conducted to ensure proper technique, dosage accuracy, and patient positioning to maximize drug efficacy and minimize discomfort.
- **Anxiety assessment using the FIS:** calibration involved practice sessions with pediatric patients to ensure consistent interpretation and scoring.
- **Sedation depth evaluation using the University of Michigan sedation scale (UMSS):** The investigator was trained to accurately observe and classify sedation levels, thus reducing interobserver variability.

After calibration, inter-examiner reliability was tested, and an intra-class correlation coefficient (ICC) of > 0.90

Table 2. Age, Gender and Weight Distribution (* = Independent t test)

Age-wise distribution				
		Group		
		Group I : Midazolam	Group II : Dexmedetomidine	Total
Age	5	8	9	17
	6	5	7	12
	7	3	3	6
	8	8	5	13
Total		24	24	48
Gender distribution				
		Group I : Midazolam	Group II : Dexmedetomidine	Total
Male		8	8	16
Female		16	16	32
Total		24	24	48
Mean weight				
		Group I : Midazolam	Group II : Dexmedetomidine	P value *
Weight (kgs)		17.79±4.21	17.63±2.52	0.869

Table 3. Intergroup comparison of hemodynamic vital parameters (* = Independent t test)

		Group		
		Group I : Midazolam	Group II : Dexmedetomidine	P value*
Pre-treatment vital values of both the groups	Pre treatment SBP (mm/Hg)	116.25 ± 1.89	116.42 ± 2.04	0.771
	Pre treatment DBP (mm/Hg)	74.08 ± 3.31	75.83 ± 2.43	0.043*
	Pre treatment heart rate (betas/min)	92.5 ± 2.72	93.42 ± 2.54	0.233
	Pre treatment SpO_2 (%)	97.08 ± 1.02	97.08 ± 1.02	1
		Group		
		Group I : Midazolam	Group II : Dexmedetomidine	P value*
Post-treatment vital values of both the groups	Post treatment SBP (mm/Hg)	117.67 ± 2.81	118.33 ± 1.4	0.304
	Post treatment DBP (mm/Hg)	76.25 ± 3.4	78.42 ± 1.56	0.00
	Post treatment heart rate (betas/min)	93.08 ± 2.28	95.08 ± 1.86	0.002
	Post treatment SpO_2 (%)	97.08 ± 1.02	98 ± 0	< 0.001

was achieved, indicating excellent agreement.

Drug administration and treatment procedure: After completing the pre-treatment assessments, participants were informed about the procedure using the Tell-Show-Do technique. The primary investigator administered the assigned sedatives intranasally using the MAD (Fig. 2). The co-investigator, then

1. Recorded drug acceptance using Likert's 5-Point Rating Scale.
2. The onset and effectiveness of sedation were monitored using the UMSS.

Once satisfactory sedation was achieved, local anesthesia (LA) was administered according to the required procedure and the primary investigator proceeded with the planned dental treatment. All procedures were conducted according to strict sterilization guidelines and the American Academy of Pediatric Dentistry (AAPD) protocol.

At the end of the procedure, the co-investigator recorded post-treatment vital signs and anxiety levels to assess sedation effects and recovery.

Evaluation instrument: Drug acceptance was evaluated using Likert's 5 point rating scale [12] (1: Strongly Disagree, 2: Disagree. 3: Neutral, 4: Agree, 5: Strongly Agree), onset of sedation and effectiveness using the UMSS, is a five-point observational scale used to assess the depth of sedation in pediatric patients. It ranged from 0 (awake and alert) to 4 (unarousable). The original validation and reliability of this scale were published in the British Journal of Anaesthesia [13]. Anxiety using FIS, initially introduced by Buchanan and Niven in 2002 [14]. It is a widely recognized tool designed to assess

Table 4. Intragroup comparison of hemodynamic vital parameters (*= paired t test)

Parameter	Group I		Group II	
	Pre-treatment (mean ± SD)	Post treatment (mean ± SD)	Pre-treatment (mean ± SD)	Post treatment (mean ± SD)
SBP	116.25 ± 1.89	117.67 ± 2.81	116.42 ± 2.04	118.33 ± 1.4
	P = 0.029*		P < 0.001*	
DBP	74.08 ± 3.31	76.25 ± 3.4	75.83 ± 2.43	78.42 ± 1.56
	P = 0.008*		P < 0.001*	
Heart rate	92.5 ± 2.72	93.08 ± 2.28	93.42 ± 2.54	95.08 ± 1.86
	P = 0.11*		P = 0.003*	
SpO_2 (%)	97.08 ± 1.02	97.08 ± 1.02	97.08 ± 1.02	98 ± 0
	-		P < 0.001*	

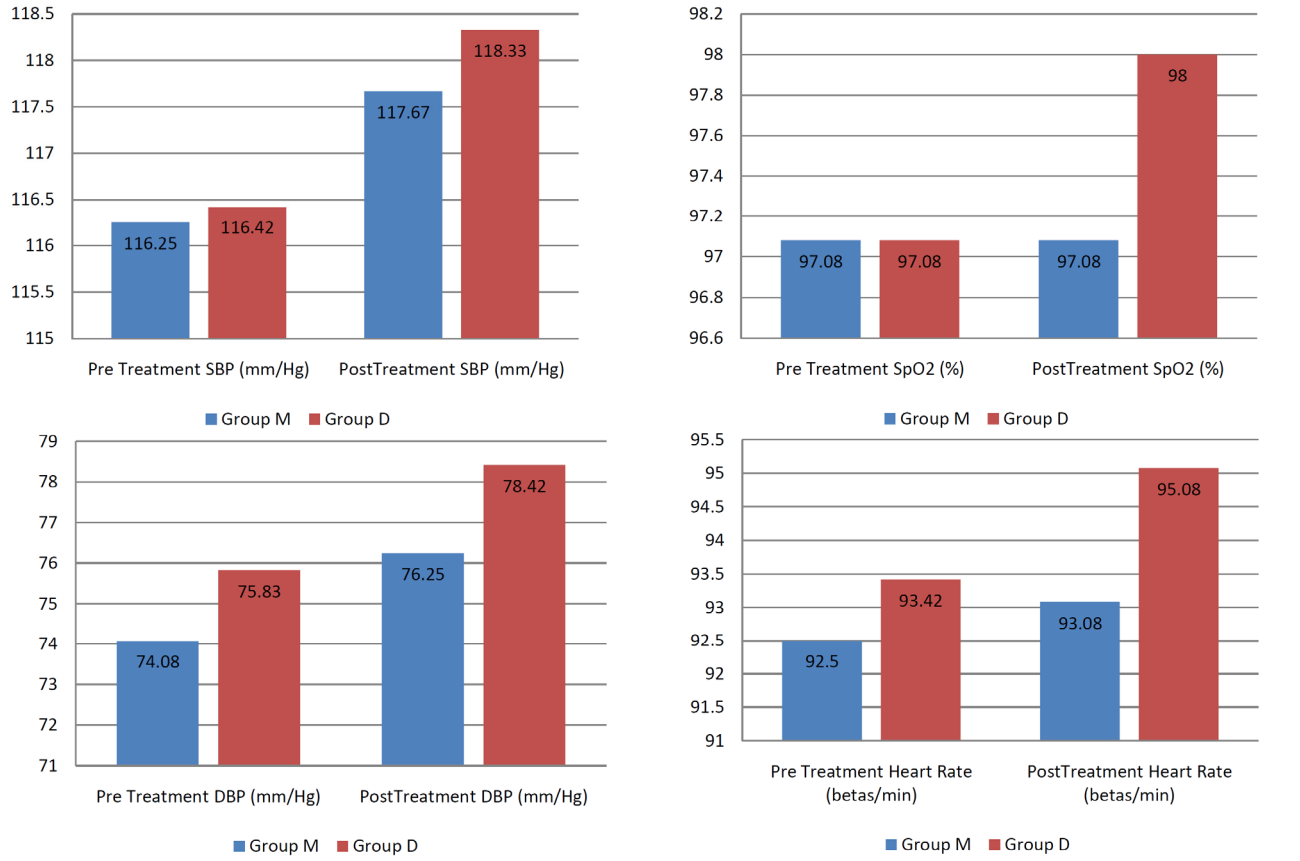

Fig. 3. Bar graphs showing pre- and post-treatment comparison of hemodynamic vital parameters. Group M, midazolam group; Group D, dexmedetomidine group.

anxiety levels in children, particularly in dental settings. It uses a series of five facial expressions, ranging from very happy to very unhappy, allowing children to indicate their feelings before undergoing treatment. This tool is particularly valuable because it accommodates children with limited verbal abilities, making it practical and easy to use in clinical settings.

Statistical analysis: All collected data were entered into a computer and analyzed using SPSS software. Descriptive and inferential statistical analyses were conducted, including:

- Chi-square analysis to assess categorical variables.
- Student's t-test (two-tailed, independent) was used for inter-group comparisons of continuous variables.
- Mann-Whitney U test was performed for anxiety assessment because anxiety scores obtained from the FIS were ordinal in nature and did not follow a normal distribution.

Table 5. Inter group comparison of drug acceptance, effectiveness, onset and anxiety (* = Independent t test)

	Group		
	Group I : Midazolam	Group II : Dexmedetomidine	P value*
Drug acceptance	2.42 ± 0.97	3.83 ± 0.57	< 0.001
Effectiveness and onset of sedation	30.79 ± 3.04	41.42 ± 3.15	< 0.001
Anxiety pre-operative	4.08 ± 0.83	3.58 ± 0.78	0.036
Anxiety post-operative	2.08 ± 0.78	1.38 ± 0.5	< 0.001

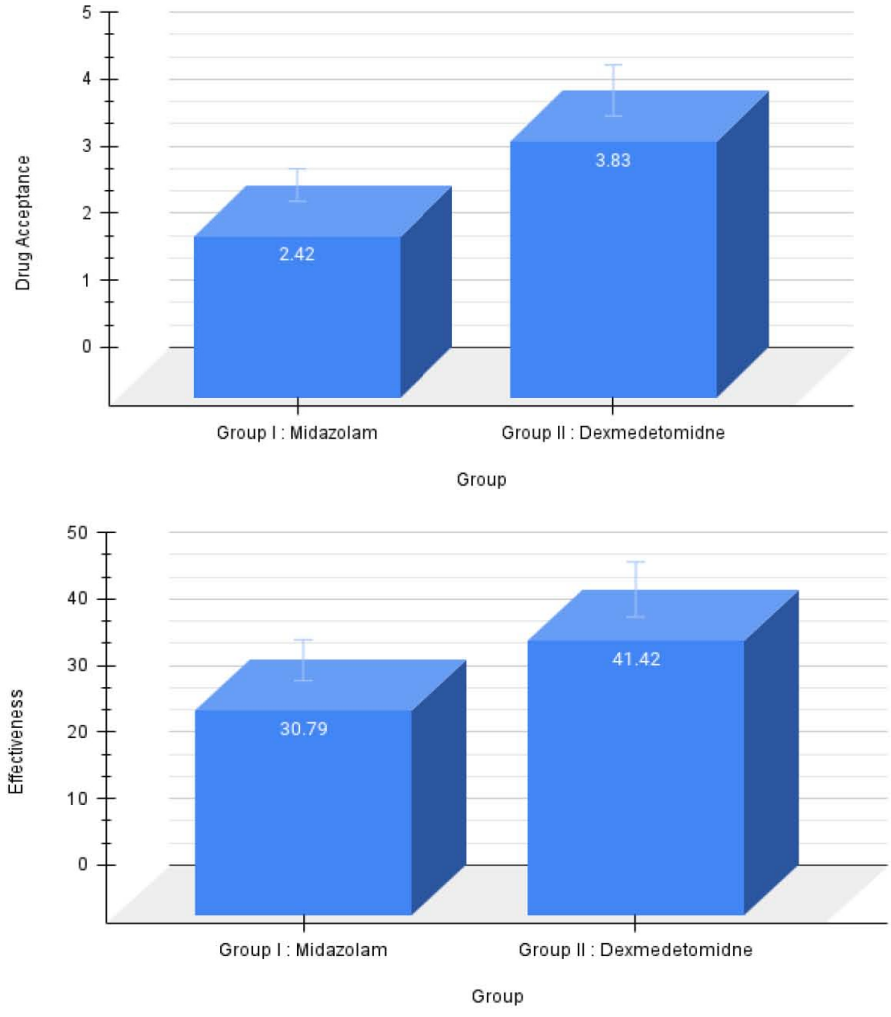

Fig. 4. Inter group comparison of drug acceptance and effectiveness.

RESULTS

Descriptive: As per the selection criteria and randomization process, 60 participants were enrolled, of which 48 who met the selection criteria were included in the study. Group I: midazolam, included 24 participants, and Group II: dexmedetomidine, included 24 participants; thus, a total of 48 participants were included. No participants dropped out of the study. This corresponds to a 100% turnout ratio. Of the 48 participants involved in the study, the age group of 5–8 years, sex, and age distribution are shown in Table 2.

Vital parameters: Significant differences were observed in the vital parameters between and within the groups. Pre-treatment DBP was significantly higher in Group II

Table 6. Intra group comparison of anxiety. (*= paired t test)

Parameter	Group I		Group II	
	Pre-treatment (mean ± SD)	Post treatment (mean ± SD)	Pre-treatment (mean ± SD)	Post treatment (mean ± SD)
Anxiety	4.08 ± 0.83	2.08 ± 0.78	3.58 ± 0.78	1.38 ± 0.5
	P = < 0.001*		P = < 0.001*	

Table 7. Non – parametric Mann-Whitney U test comparing anxiety (pre-operative, post-operative and difference)

Variable	Mann-Whitney U	Z-score	P-value
Anxiety pre-operative	193.000	-2.098	0.036
Anxiety post-operative	144.000	-3.221	0.001
Anxiety difference	274.500	-0.358	0.721

than in Group I (P = 0.043). Post-treatment, Group II exhibited significantly higher DBP (P = 0.008), heart rate (P = 0.002), and oxygen saturation (SpO_2) (P < 0.001) than Group I. Intra-group analysis revealed that in Group I, both SBP (P = 0.029) and DBP (P = 0.008) significantly increased post- treatment. Similarly, in Group II, all measured parameters (SBP, DBP, heart rate, and SpO_2— were significantly elevated post-treatment, with p <0.001 for SBP, DBP, and SpO_2, and P = 0.003 for heart rate. These findings highlight the more pronounced effect of dexmedetomidine on vital parameter changes than midazolam (Table 3 & 4) (Fig. 3).

Drug acceptance: Comparison of the drug acceptance between the two groups showed that drug acceptance was significantly higher in Group II (P < 0.001) (Table 5) (Fig. 4).

Effectiveness and onset of sedation: Assessment of the effectiveness of the two groups showed that effectiveness was higher in Group II and was statistically significant, with a P-value < 0.001 (Table 5) (Fig. 4).

Anxiety: Significant reductions in anxiety levels were observed within and between the two groups. In Group I, pre-operative anxiety levels were significantly higher than post-operative levels (P < 0.001). Similarly, in Group II, pre-operative anxiety levels exceeded post-operative levels, with a difference of 2.208 (P < 0.001). Inter-group analysis revealed that pre-operative anxiety was significantly higher in Group I than in Group II (P = 0.036). Postoperatively, anxiety levels remained significantly higher in Group I (P < 0.001). However,

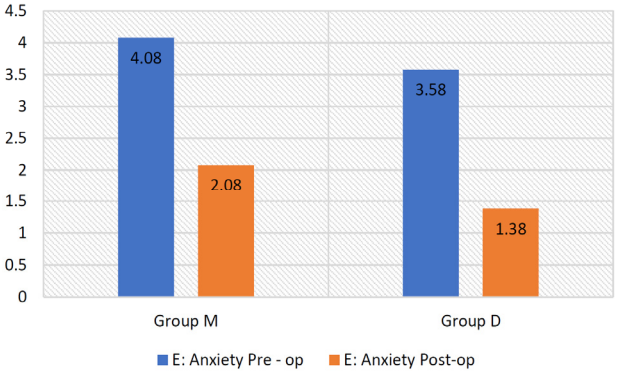

Fig. 5. Inter group comparison of pre and post treatment anxiety levels. Group M, midazolam group; Group D, dexmedetomidine group.

the difference in anxiety reduction between the two groups was not statistically significant (P = 0.783). This study compared anxiety levels between Groups I and II across three time points: pre-operative and post-operative and the difference between pre-operative and post-operative anxiety scores. Descriptive statistics and non-parametric Mann-Whitney U tests were used to analyze the data. Group I had significantly higher anxiety levels before and after the procedure than Group II. Despite the differences in absolute anxiety levels, both groups showed similar reductions in anxiety (no significant differences in anxiety). The lower postoperative anxiety in Group II suggests that the intervention was more effective in managing postoperative anxiety. These results suggest that both sedatives effectively reduce anxiety, with dexmedetomidine demonstrating slightly better outcomes (Table 5, 6 & 7) (Fig. 5, 6).

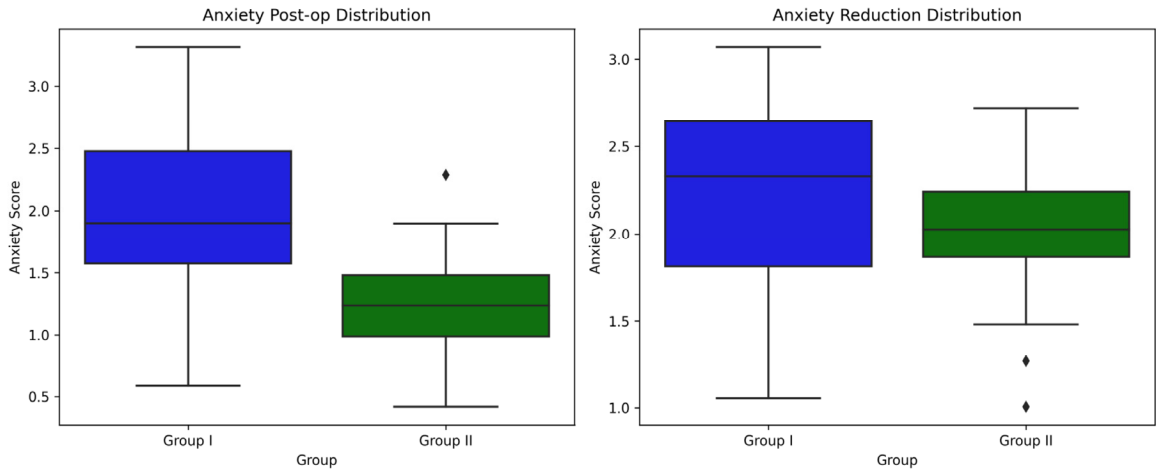

Fig. 6. Box-plot comparing inter group anxiety (pre-operative, post-operative and difference). Group 1, midazolam group; Group 2, dexmedetomidine group.

DISCUSSION

Dental fear and anxiety (DFA) are significant challenges in pediatric dentistry and are often exacerbated by factors such as parental anxiety, unfamiliar environments, and anticipation of pain [3]. While local anesthetics effectively manage pain, dealing with uncooperative children may require physical restraint, leading to additional emotional trauma and reinforcing dental fear. Although alternative methods, such as hypnosis, exist, their effectiveness varies. Therefore, sedation is crucial to alleviate DFA during pediatric dental procedures [4].

Sedation facilitates dental treatment in uncooperative children without resorting to general anesthesia in operating rooms. Although intravenous (IV) therapy is the conventional method, its use in children is limited. Hence, alternative approaches such as intranasal sedation are promising. Intranasal sedation is a needleless and painless technique that eliminates the need for intravenous catheterization. The rich blood flow in the nasal mucosa ensures rapid drug absorption into the bloodstream and cerebrospinal fluid, bypassing liver metabolism and ensuring quick drug action [15].

Intranasal sedation serves dual purposes in clinical practice: acting as both sedation and premedication before general anesthesia, as well as improving patient compliance and reducing anxiety. Although it does not relieve pain, it effectively reduces anxiety, particularly during preoperative preparation and dental procedures. Intranasal sedatives can be administered via drops using a syringe, dropper, or atomized medication via spray systems to ensure optimal drug dispersion in the nasal cavity [16,17].

Our randomized clinical study compared the efficiency and safety of intranasal midazolam (0.25 mg/kg) and dexmedetomidine (1.5 μg/kg) in pediatric dental patients aged 5–8 years. This study followed ethical guidelines, including approval from the IEC and registration with the Clinical Trial Registry, India, ensuring research integrity and validity.

Midazolam, a benzodiazepine, is widely used in pediatric dentistry because of its sedative and anxiolytic effects. This enhances GABA activity, reduces anxiety, and improves patient cooperation. Its rapid onset and effective intranasal absorption make it ideal for short procedures. However, careful monitoring is required because of the risk of respiratory depression [18].

Dexmedetomidine, an alpha-2 adrenergic agonist, is a new alternative for pediatric sedation, with sedative, anxiolytic, and analgesic effects. It also reduces sympathetic activity and promotes calmness and relaxation. Intranasal administration is favored because of its rapid absorption, predictable pharmacokinetics, and non-invasive delivery [9,19]. Dexmedetomidine's short

elimination half-life of dexmedetomidine supports quick recovery, making it a safe and effective choice for pediatric dental procedures [20].

With a sample size of 48 evenly distributed participants across two groups, the study had sufficient statistical power to detect meaningful differences between the drugs Importantly, the absence of dropouts resulted in a 100% turnout ratio, indicating a high participant compliance and minimal attrition bias. This study used a robust methodology with a triple-blind randomized design, ensuring impartiality in both drug administration and assessment. The careful selection criteria maintained homogeneity among participants, thereby enhancing the internal validity of the study. The implementation of examination methods, randomization procedures, and blinding techniques was meticulous to minimize bias, and the triple-blinding approach ensured that both investigators and participants remained unaware of the drug administered, reducing observer bias.

The observed hemodynamic changes, particularly the significant increases in SBP, DBP, and heart rate after post-treatment, have important clinical implications. Although dexmedetomidine resulted in greater changes in vital parameters than midazolam did, these effects remained within safe physiological limits. This suggests that dexmedetomidine can be used effectively for pediatric dental sedation without causing clinically significant cardiovascular instability. However, its more pronounced effect on heart rate and blood pressure necessitates the careful monitoring of children with preexisting cardiovascular conditions.

The primary outcome measures, including drug acceptance (measure using Likert's 5 point scale), onset and effectiveness (using the UMSS), and pre- and post-treatment anxiety levels (using the facial image scale), were evaluated using validated scales to enhance the reliability of the findings.

The intranasal route of drug administration has gained significant attention in pediatric dentistry because of its unique advantages, particularly in managing DFA in children. This route eliminates the need for invasive techniques such as injections, which are difficult for pediatric patients. The rich vascular supply of the nasal mucosa enables rapid drug absorption, providing onset times comparable to those of intravenous administration while avoiding first-pass metabolism, as highlighted by Wolfe et al. (2010) [21]. Thus, intranasal administration is a reliable, efficient, and minimally traumatic option for sedative delivery in pediatric settings.

Intranasal midazolam (IN-MDZ), with doses ranging from 0.2 to 0.6 mg/kg, has been extensively studied for its effectiveness in conscious sedation [22-24]. Studies, including Shanmugaavel et al. (2016) [25], demonstrated that IN-MDZ effectively reduces anxiety levels, although nasal irritation and a bitter taste negatively impact patient acceptance. Karl et al. (1993) [11] and Griffith et al. (2013) [26] observed that up to 74% of children experienced crying or discomfort during administration, which limited their overall acceptance. Despite these drawbacks, IN-MDZ remains effective, with a bioavailability of 55%, which is significantly higher than that of oral administration (15%) [27,28].

Whereas, intranasal dexmedetomidine (IN-DEX), has emerged as a promising alternative due to its superior pharmacological profile. Studies by Sheta et al. (2014) [29] and Cimen et al. (2013) [30] demonstrated that IN-DEX at 1 μg/kg provides excellent sedation with fewer adverse effects. Compared to midazolam, dexmedetomidine demonstrated higher patient acceptance and tolerability, which was attributed to the lack of nasal irritability and its dual sedative and anxiolytic effects. The findings of this study align with those of previous research, showing that IN-DEX offers superior patient compliance and efficacy, making it a more suitable option for pediatric sedation.

These results reinforce the use of the intranasal route as an effective drug delivery method in pediatric dentistry, particularly for anxious or uncooperative children. While both IN-MDZ and IN-DEX are effective, the better acceptance and safety profile of dexmedetomidine make it the preferred agent for managing DFA during dental procedures.

The onset of sedation plays a critical role in pediatric dental procedures because rapid and effective sedation facilitates patient cooperation, minimizes anxiety, and ensures procedural efficiency. Intranasal administration has emerged as the preferred route owing to its non-invasive nature and fast-acting properties. Extensive studies have evaluated the efficacy and safety of intranasal sedatives, providing valuable insights into their use in pediatric dentistry.

Al-Rakaf et al. (2001) [16] demonstrated the effectiveness of intranasal midazolam (IN-MDZ) across doses of 0.3–0.5 mg/kg, showing sedation onset within 8–15 minutes and improved behavior in uncooperative children, irrespective of fasting status. Jahromi et al. (2012) [31] compared intranasal midazolam and ketamine, and concluded that midazolam provided deeper and more effective sedation. Similarly, Cimen et al. (2013) [30] observed superior sedation and procedural acceptance scores with intranasal dexmedetomidine (IN-DEX) compared with buccal administration, reinforcing the advantages of the intranasal route.

Surendar et al. (2014) [32] compared intranasal midazolam, dexmedetomidine, and ketamine, and noted that midazolam exhibited the fastest onset of sedation. However, dexmedetomidine emerged as the most efficacious drug, achieving higher treatment success rates. Shanmugaavel et al. (2016) [25] found comparable efficacies of intranasal and sublingual midazolam, highlighting patient satisfaction with both methods. Patel et al. (2018) [33] further demonstrated the utility of IN-DEX, noting its rapid onset and procedural acceptance despite the higher acceptance of oral dexmedetomidine. In this context, our study also found that midazolam exhibited a faster onset of sedation than dexmedetomidine, with a mean difference of 10 min. However, dexmedetomidine was more effective in achieving satisfactory sedation levels. These findings align with those of previous studies, confirming the rapid action of midazolam and superior sedation depth and procedural success of dexmedetomidine. Collectively, this evidence underscores the potential of intranasal administration as a valuable sedative approach for pediatric dentists.

Managing DFA in pediatric patients is fundamental for promoting positive dental experiences and ensuring optimal oral health outcomes. Behavioral strategies, such as communication, desensitization, distraction, and positive reinforcement, are widely employed to alleviate fear and build trust. However, for children with severe DFA or uncooperative behavior, pharmacological sedation is an effective adjunct to behavioral management.

Intranasal sedation has gained attention because of its ease of administration, rapid onset, and effectiveness in pediatric dental settings. Several studies have highlighted the efficacy of intranasal sedative agents. Janiani et al. (2023) [34] compared IN-MDZ, IN-DEX, and nitrous oxide (N_2O) in managing pain during dental treatment and found all three to be effective, with midazolam showing slightly lower intraoperative pain levels. Nie et al. (2023) [35] reported enhanced sedation success rates with a combination of IN-DEX and oral midazolam compared to oral midazolam alone in managing children with DFA.

Salem et al. (2022) [36] observed comparable sedation effectiveness between IN-MDZ and IN-DEX, although midazolam was associated with more favorable behavioral outcomes in highly anxious children. Similarly, Srinivasan et al. (2021) [37] found intranasal midazolam comparable to N_2O sedation, noting better patient acceptance and fewer adverse effects with midazolam. Sado-Filho et al. (2021) [38] reported quicker recovery and satisfactory sedation with IN-DEX than with ketamine. Meanwhile, Xin et al. (2021) [39] demonstrated superior sedation adequacy and treatment completion with dexmedetomidine compared to esketamine.

Mahdavi et al. (2018) [40] found that IN-DEX and IN-MDZ were equally effective premedications for uncooperative pediatric dental patients, underscoring the versatility of these agents. Collectively, these studies confirmed the potential of intranasal sedation to effectively manage pediatric dental anxiety, with

dexmedetomidine demonstrating particular advantages in drug acceptance, sedation adequacy, and safety.

This study has some limitations. As this was a single-center study, the findings may not be generalizable to broader populations, highlighting the need for multicenter trials to validate our results. Additionally, fixed doses of midazolam (0.25 mg/kg) and dexmedetomidine (1.5 mcg/kg) were used, limiting the exploration of individualized sedation protocols tailored to patient-specific needs. This study also focused solely on short-term outcomes, leaving the long-term effects of intranasal sedation unexamined. Furthermore, while intranasal midazolam and dexmedetomidine were compared, other commonly used sedatives such as nitrous oxide and ketamine were not included, restricting the comprehensive evaluation of sedation options. Future multicenter comparative studies with various sedative agents and personalized dosing strategies are necessary to address these limitations.

In conclusion, intranasal dexmedetomidine appears to outperform midazolam in several parameters, including post-treatment vital stability and anxiety reduction, making it a promising option for pediatric dental sedation. However, the choice of agent should be tailored to the individual patient's needs and the clinical context to optimize outcomes.

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ACKNOWLEDGMENTS: We acknowledge the Department of Pediatric and Preventive Dentistry, K.M. Shah Dental College and Hospital, for providing the necessary basic requirements for conducting this research.

DECLARATION OF INTERESTS: The authors declare no conflict of interest related to this study. This study was conducted without external funding.

FUNDING: Statement of informed consent and Institutional Review Board approval.

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