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Comparing Acceptance of Nasal Spray in Children Receiving Intranasal Sedation During Dental Treatment: Parent-administered versus Dentist-administered - A Randomised Clinical Trial

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Introduction: In pediatric dentistry, behavior management is crucial. When non-pharmacological methods are inadequate, pharmacological therapies, like intranasal conscious sedation, are routinely used. The nasal spray is used for the delivery of sedative medications through the nose. To improve behavior control tactics in pediatric dentistry, this study evaluates the acceptance of nasal spray in pediatric patients. Aim: The primary outcome of the study is to compare the acceptance of nasal spray in children receiving sedation by the parent or the dentist during dental treatment. The secondary outcome is to assess the anxiety level of children in each group. Materials and methods: 40 children aged 4-10 years were included in each group. Group A received intranasal drug delivery via a nasal spray administered by parents, whereas Group B received the same treatment administered by dentists. The anxiety levels of the children were recorded before treatment and after delivering the intranasal sedation using the Facial Image Scale. Additionally, the acceptance of the nasal spray was evaluated using the Mask Acceptance Scale. Results: Mann Whitney U test was performed to assess intergroup comparison and Wilcoxon signed rank test was used for intragroup comparison. The statistical level of significance was set at $p<0.05$. The number of children being calm in Group A (13.9%) is lesser than in Group B(22.2%). More children remained calmer in group A (95%) when compared to group B. Conclusion: Children sedated with intranasal drugs delivered by parents and dentists exhibited no significant difference in acceptance rates. Thus, intranasal drug delivery by both parents and dentists is a viable option, given that the correct dosages and titration are established by an anesthetist and administered under their supervision.

Parental presence during administration of intranasal sedation may reduce anxiety in children. Children tend to have an increased level of acceptance of nasal spray in the presence of parents.

Keywords: Pediatric dentistry, intranasal sedation, mucosal atomisation device, anxiety.

1. Introduction

One of the most important parts of an individual's overall health is oral health(Baiju et al. 2017). Pediatric dentistry is a branch of dental science that exists because oral health problems in children exist (Kilibarda et al. 2023). In the journey of treating children, one of the nightmares faced by dentists is managing the behavior of the child. Uncooperative or anxious behavior exhibited by children is due to fear caused by exogenous factors like parental, familial or peer discussion on previous dental experience and endogenous factors such as genetically attained anxiety disorder, and developmental and medical conditions(Wu and Gao 2018).

Anxiety and fear towards dental treatment could lead to missing appointments, and avoidance of meeting the dentist resulting in worsening of existing oral issues(Appukuttan 2016; Alenezi and Aldokhayel 2022). This fear of dentists, fear of injection or fear of the unknown can result in a negative attitude towards dental treatment affecting the quality of life of children. This attitude of the child might continue into adulthood(Carter et al. 2014). Hence the operator needs to provide preventive, comprehensive and therapeutic dental care by instilling a sense of trust in the child by reducing dental anxiety and fear(Noble et al. 2020). Different approaches have been followed through the years for the same including non-pharmacological and pharmacological behavior management techniques(Gizani et al. 2022; Al Zoubi et al. 2019; M and Anthonet Sruthi 2024). Most accepted non-pharmacological techniques by parents include Tell-Show-Do with its modifications, distraction, modeling, desensitization and positive reinforcement. More invasive techniques like voice control, HOME and HOMAR, and physical restraints have controversial acceptance among parents but are still used(Al Zoubi et al. 2019; Qureshi et al. 2023). The vast majority of children can be effectively treated using solely non-pharmacological approaches but in cases where these methods prove ineffective, a highly efficacious alternative is pharmacological behavior management, encompassing options such as conscious sedation and general anesthesia (Aminabadi et al. 2016; Gao and Wu 2023; Janiani, Gurunathan, and Nuvvula 2023).

The choice of a suitable pharmacological method is of multifactorial dependance such as patient's age, systemic safety and risk, degree of pre-operative anxiety and cooperation, extent of dental treatment requirement and socioeconomic affordability(Hampl et al. 2023). For each individual-child or adult, there are certain drug-induced levels of sedation attainable according to the American Society of Anesthesiologists(Das and Ghosh 2015; Kotian, Subramanian, and Jeevanandan 2022). In conscious sedation there will be a depression in consciousness and the levels of sedation are named as minimal, moderate or deep based on the response of patients to commands and stimulation(Das and Ghosh 2015). Sedative drugs are administered through various routes such as oral, intranasal, inhalational, intravenous, intramuscular, sublingual, subcutaneous and rectal(Matharu and Ashley 2006; Kienitz et al. 2022; Fallahinejad Ghajari et al. 2015). Each route exhibits different advantages and disadvantages. One of the most popular routes of drug administration among pediatric patients is the oral route as it does not

induce needle phobia in children as the intravenous or intramuscular route which though has a rapid onset of action is not much accepted by children due to the fear of injections(Ferrazzano et al. 2021; Sebastiani, Dym, and Wolf 2016). In some cases, anatomical factors of children like small veins and excess fat interfere with the visualization of vesicular access for intravenous administration. Though administration through the oral route is easy, convenient and inexpensive it needs vigilant monitoring with pulse oximetry as it might cause hypoxemia because of the decreased oxygen reserve in children (Sheikh et al. 2023; Janiani, Gurunathan, and Manohar 2024). In case of any mishap, the dental office should always have appropriate child-sized resuscitation equipment (Sheikh et al. 2023). The bitterness of the drug might cause a wavering in the acceptance of the drug in some children (Mennella et al. 2013). The bioavailability of the drug after oral administration is very less due to reduced absorption and extensive first-pass metabolism. The rectal administration route is acknowledged for its safety and lack of pain, yet it may potentially lead to uncomfortable situations for children, adolescents, and dental staff(Hua 2019; Srinivasan et al. 2021). The intranasal administration of drugs either as drops or as mist using a mucosal atomisation device (MAD) or nasal spray surpasses all the above-mentioned disadvantages of other routes. It has a faster onset of action as it skips the first-pass metabolism and enters the central circulation directly by bypassing the entero-hepatic circulation(Bhat et al. 2016). Diseases related to nasal mucosal alterations will affect its physiology(Bhat et al. 2016). It has an ease of administration, and limited requirement of skilled staff compared to those needed for venous insertion. Intranasal drug delivery through a mucosal atomisation device is considered to be superior over drops as the cushion-like conical plug of the device prevents backlink of the material from the nostrils, thereby increasing absorption.

The mucosal atomization device (MAD) comprises a soft, conical plug and stylet connected to a pressure syringe for drug loading and delivery (Wei et al. 2022; Ann Preethy and Somasundaram 2022). A nasal spray for drug delivery consists of a container holding the medication, a pump mechanism with a nozzle, and an actuator that, when pressed, disperses the liquid as a fine mist for quick absorption(Chokshi et al. 2013). This design allows for rapid and efficient administration of medications like sedatives in pediatric dentistry. Similar to needle phobia, children commonly experience syringe aversion, rendering this device less accepted and challenging to persuade children to undergo its administration (Orenius et al. 2018). Thus the objective of this study is to compare the acceptance of nasal spray among the pediatric population when administered by either a parent or a dentist during dental treatment under the supervision of an anesthetist. Additionally, each group's children's levels of anxiety will be evaluated as part of the study.

2. Materials and methods :

The comparative study was carried out in the Department of Pediatric and Preventive Dentistry following the approval from the Institutional Review Board [IHEC/SDC/PEDO-2102/22/TH-083] from January 2023 to April 2023. The sample size was calculated from a previous study with 95% power using G power analysis and arrived at a total sample of 80; 40 in each group.

Before enrollment, written informed consent was obtained from the parents or guardians of the children deemed eligible for the study. Detailed explanations regarding the study's nature,

treatments administered, follow-up procedures, as well as the potential benefits and risks involved, were provided to the parents or guardians. They were informed of their right to withdraw from the study at any point without impacting the required treatment course.

The inclusion criteria considered are :

- Children in the age group of 5-10 years.
- Children with a physical status of ASA I (American Society of Anesthesiologists)
- Children with a positive behavior rating according to the Frankl behavior

classification scale.

- Children who require a pulpectomy in any primary tooth in the maxillary or mandibular arch.
- The patients for whom non-pharmacological behavior guidance techniques have not been successful.
- Parents/Guardians who gave their signed consent after explaining the full

details of the treatment procedure and its possible outcomes, discomfort,

risks, and benefits.

The exclusion criteria are

- Children who have recently used medications like erythromycin or anticonvulsants that may interfere with the pharmacokinetics of midazolam.
- Children with known hypersensitivity to benzodiazepines.
- Children with any systemic disease and special needs.
- Children exhibiting uncooperative behavior according to the Frankl behavior rating who need to be treated under general anesthesia.
- Children with any condition that predisposes them to airway obstruction or difficulties (eg adenoid hyperplasia, nasal septum problems, enlarged

turbinates or nasal polyp).

- Children with upper or lower respiratory tract infections.
- Children who were not cleared by the anesthetist for the sedation procedure.

Patient's behavior was assessed using Frankl's behavior rating scale (Hosey and Blinkhorn et al., 1995) before including them in the study, with initial attempts at non-pharmacological behavior modification made before enrollment. Only patients for whom the former was ineffective were included. A comprehensive health assessment was conducted by the anesthetists, at Saveetha Dental College, Chennai (India) for all patients before enrollment, covering tonsil and adenoid evaluation, mouth-breathing, speech, hypo-nasality, snoring, airway, and chest examination. The fasting protocol adhered to the guidelines of the American Academy of Pediatric Dentistry(Coté et al. 2019), with instructions provided verbally and in writing to parents. Parents were advised not to provide solid or non-clear liquids for four hours

before the sedation procedure. On the day of sedation, each patient underwent a physical fitness reassessment by the anesthetist, including weight measurement and baseline evaluations of oxygen saturation and pulse rate using a pulse oximeter. Continuous monitoring by the anesthetist was maintained throughout the procedure for all patients.

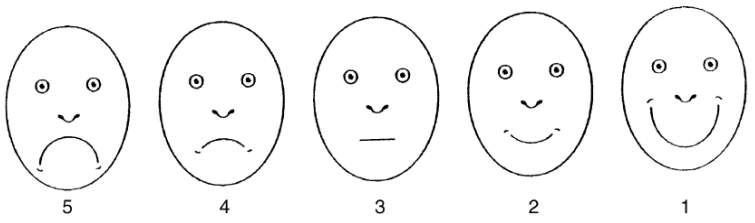
An initial preview video of the intranasal sedation procedure was shown to the parents before obtaining consent. Children under group A received intranasal sedation using nasal spray by their parents while children under group B received it from dentists. Allocation of children to each group was done by computer randomization. Although parents placed the mucosal atomization device in the nostrils of the children, this placement only involved positioning the device. The titration of sedatives was carried out prior by an anesthetist, and the plunger of the syringe was pressed by a dentist for both groups in a way such that the drug was delivered to the nose. In this study, intranasal Midazolam was administered at a dose of 0.5 mg/kg using a nasal spray, with 0.25 mg/kg delivered into each nostril, in a semirecumbent position 15 minutes before the procedure.

Parameters measured in this study were acceptance of nasal spray and the anxiety level of the child. Acceptance of the nasal spray (Table 1)is the primary outcome and it was measured using the mask acceptance scale. The secondary outcome measured was the anxiety level of the child before and after delivery of the drug(Table 2).

Table 1: Mask Acceptance Scale

MAS Score	Characteristics
1	The child is calm, cooperative or asleep
2	Moderate fear of the device, manageable with reassurance
3	Cries, combative and needs restraining

Table 2: Facial Image Scale



The scoring pattern for the facial image scale was according to five different faces: 1 = no distress to 5 = severe distress

1: Represents a calm or neutral expression, indicating minimal or no anxiety.

2: Represents a slightly worried or mildly anxious expression

3: Represents a moderately anxious or concerned expression.

4: Represents a noticeably anxious or distressed expression.

5: Represents a highly anxious or extremely distressed expression.

All the observations were made by a single, skilled observer who was not involved in the clinical procedures. Patients' information, including age, sex, medical history, interventions done, group to which he/she is assigned, anxiety level before and after delivery of the sedative, and acceptance towards nasal spray, was recorded on a form for every patient. All statistical analyses were done with the SPSS (Statistical Package for the Social Sciences)Version 23. The level of significance was set to be $p<0.05$.

3. Results :

Table 3 shows the descriptive statistics of age and gender. Tables 4a and 4b reveal the nasal spray acceptance and anxiety scores of the population using the Mann Whitney U test between the groups(Figure 1a,1b,1c). The number of calmer children was more in group A (82.5%) when compared to group B(60%). The number of children who had a fear of nasal spray was more in the dentist-given group (35%) when compared to the parent-given group (12.5%). A majority of the patients of the parent-given group exhibited reduced anxiety after drug delivery (95%) . P values of nasal spray acceptance level ($p = 0.000$) and anxiety level ($p = 0.000$) are <0.05 indicating that there is statistical significance between group A and group B. Wilcoxon signed-rank test was performed to evaluate the intergroup anxiety levels before and after drug delivery (Table 5).

Table 3: Age and gender distribution

	Age (Mean + SD)	Gender	
		Male	Female
Group A	6.282±1.651	18(45%)	22(55%)
Group B	6.423±1.712	10(25%)	30(75%)
P Value	0.721	0.824	

*$p<0.05$ indicates significant difference

Table 4a: Comparison of the level of acceptance using Mann Whitney U test between the groups

Variable	Frequency (%)		
	Points	Group A	Group B
Acceptance of nasal spray	1	33(82.5%)	24(60%)
	2	5(12.5%)	14(35%)
	3	2(5%)	2(5%)
P value		0.000*	

* $p<0.05$ indicates a significant difference; Group A- Parent given, Group B - Dentist given

Table 4b: Comparison of the level of anxiety using Mann Whitney U test between the groups

Variable		Frequency (%)			
		Group A		Group B	
Anxiety	Points	Baseline	After delivery of the sedative	Baseline	After delivery of the sedative
	1	19(47.5%)	38(95%)	0	0
	2	15(35%)	1(2.5%)	10(20%)	9(18%)
	3	0	0	16(32%)	13(26%)
	4	1(2.5%)	0	8(16%)	9(14%)
	5	6(15%)	1(2.5%)	6(12%)	9(18%)
p Value		0.023*		0.048*	

* $p<0.05$ indicates a significant difference; Group A- Parent given, Group B - Dentist given

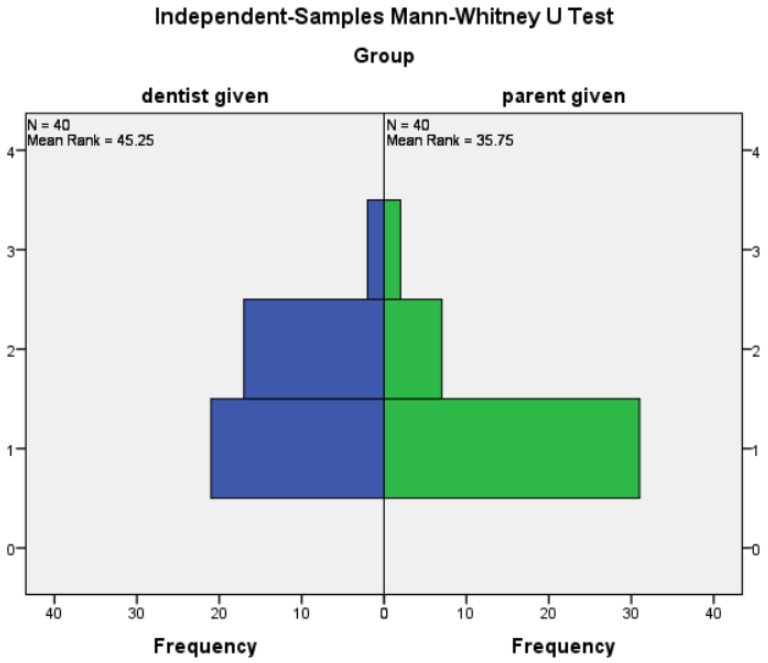


Figure 1a : Comparison of the level of acceptance using Mann Whitney U test between the groups

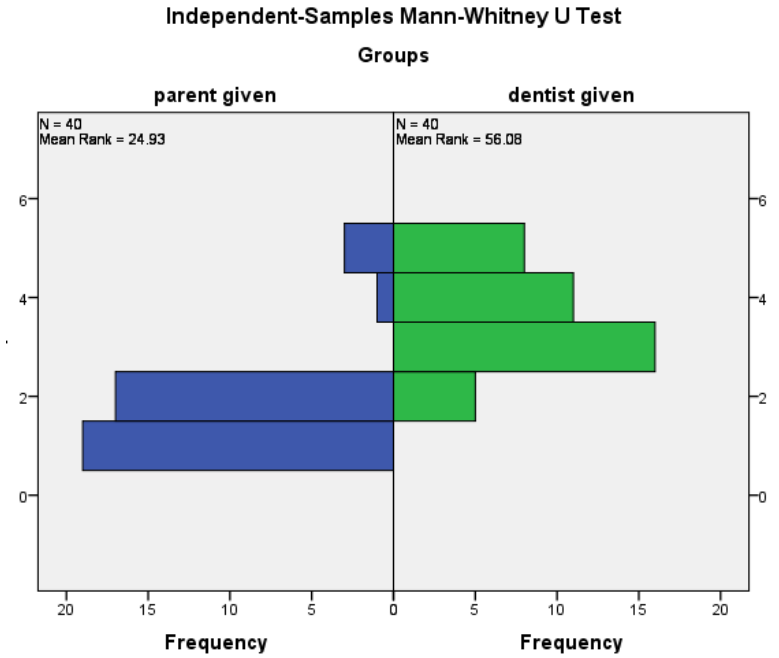


Figure 1b : Comparison of the level of anxiety before treatment using Mann Whitney U test between the groups

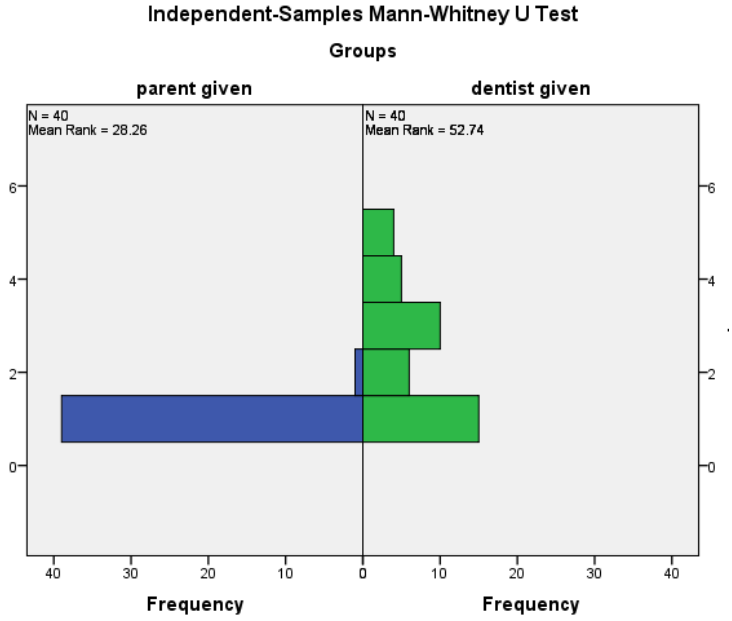


Figure 1c: Comparison of the level of anxiety after drug delivery using Mann Whitney U test between the groups

Table 5: Intergroup comparison of level of anxiety using Wilcoxon Signed Rank test

Groups	Anxiety	P Value
A	Baseline	.000*
	After drug delivery	
B	Baseline	.000*
	After drug delivery	

* $p<0.05$ indicates a significant difference; Group A- Parent given, Group B - Dentist given

4. Discussion:

The management of a child in the dental chair and office is the challenge that pediatric dentists encounter the most(Nelson and Xu 2015). This is a result of the child frequently displaying worry and terror. One of the most painful emotional and sensory experiences a patient can have is pain. The dental environment is one such stressful circumstance where there may be varied degrees of unpleasant sensations that cause anxiety and suffering(Appukuttan 2016). It can be difficult to reduce children's fear because it starts not just from being separated from their parents but also from the nearby dental equipment. Fear tends to alter how much pain is felt, making its reduction a challenge. To deal with these issues and provide effective treatment, pedodontists have employed a variety of behavior management approaches. A long-lasting restorative or endodontic procedure is simply one component of a good treatment; another is a happy patient who has had favorable psychological experiences. These pleasant experiences are essential to a child's general development because they provide them a chance to internalize traits that will stick with them for a very long time. Consequently, over time, both pharmacological and non-pharmacological behavior management approaches have been employed(Baakdah et al. 2021). Pharmacological treatments are used to treat patients who do not cooperate with non-pharmacological approaches effectively and with little to no discomfort(Ketenci and Zure 2021). General anesthesia and conscious sedation are examples of pharmacological techniques. Intranasal sedation has been gaining popularity in recent times due to its ease of administration. Numerous devices, including droppers, syringes, pressurized metered-dose inhalers, breath-powered bi-directional nasal devices, and pressurized olfactory delivery devices, have been approved for medical use and categorized as tools for dispensing intranasal medications(Parida and Senthilnathan 2023). The choice of dispensing method depends on the medication's formulation - solid, liquid or semi-solid(Parida and Senthilnathan 2023). Liquid administration remains the oldest, most cost-effective, and least painful method. Nasal sprays distribute more effectively, coating the olfactory area and facilitating mucociliary clearance(Parida and Senthilnathan 2023). Particle size affects the surface area available for drug absorption. When drug particles are smaller, they have a larger total surface area than larger particles of the same mass(Labiris and Dolovich 2003). This increased surface area provides more contact points between the drug and the absorbing surface, such as mucosal membranes in the nasal cavity. This increased contact area allows for more efficient absorption of the drug(Hua 2019). More drug molecules can be absorbed per unit of time, leading to a faster onset of action and potentially higher bioavailability (Rangaraj et al. 2022). Therefore,

reducing the particle size can enhance drug absorption by maximizing the available surface area for interaction with the absorbing surface, ultimately improving therapeutic outcomes(Alqahtani et al. 2021). In addition, the semi-permeable soft nozzle in the nasal sprayer cushions the naris and prevents the back leak of the drug thus enhancing the rapid absorption of the drug into systemic circulation (Li et al. 2016). Hence nasal spray was used in the present study for drug delivery.

Parental presence or absence during dental procedures is one of the methods described in the guidelines of the American Academy of Pediatric Dentistry for behaviour modification(Riba et al. 2018). The guideline recommends judicial decision-making on the part of the practitioner to benefit from either parental presence or absence to achieve cooperation of the child. The dentist should evaluate the pros and cons of the presence of the parent, and this decision should be based on the individual child and the parental involvement of that particular child(Riba et al. 2018). This decision to allow the parent to participate during treatment should be based on the behavior of the child, the past experiences of the child and the operator, feedback from the parent, and the comfort level of the operator. There are different views among dentists on the benefit of parental presence during dental treatment of their children. Parental presence can be helpful in the case of very young and or extremely anxious patients(Riba et al. 2018; Palomares González et al. 2023). Parental presence in the dental operatory is advocated to gain emotional support and avoid the effect of the traumatic separation, especially in younger ages and in patients with special health care needs(Palomares González et al. 2023). The present study suggests that parental presence can improve the acceptance of MAD by the pediatric population and cause an anxiety reduction.

Future studies are warranted to define the optimal dose in the clinical setting. Enrollment of patients was done with restrictive inclusion. This sampling method increased the feasibility of the study completion but it may have potentially limited its generalizability.

Further extensive multicenter trials with larger sample sizes over a broader range of patient age groups are warranted to evaluate the optimal approach and clinical benefits of these regimens.

5. Conclusion:

According to the study, nasal spray provided by parents or a dentist are both acceptable choices. Children may feel less anxious when their parents are present during intranasal drug administration through nasal spray and generally have a higher level of acceptance when their parents are around. However, to prevent insufficient sedation and improper delivery, it is crucial to guarantee proper administration which can be done only by trained professional dentists or anesthetists.

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