ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 3, Issue – 6, December - 2020, Page No. : 129 - 136

Comparison of Oral and Intranasal Midazolam Sedation in 3-6-Year-Old Uncooperative Dental Patients

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Citation of this Article: Dr. Kritika Bajaj, Dr. Rohini Dua, Dr. Ripin Garewal, Dr. Annupriya Sikri, "Comparison of Oral and Intranasal Midazolam Sedation in 3-6-Year-Old Uncooperative Dental Patients"**,** IJDSIR- December - 2020, Vol. – 3, Issue - 6, P. No. 129 – 136.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Preoperative anxiety in children leading to behavioral problems incurred during dental treatment needs better pre-anesthetic sedation. Among the drugs used for alleviating anxiety in children, Midazolam is one of the most commonly used.

Aim: The aim of this study was to compare the effect of intranasal and oral midazolam in children with appreciable levels of dental anxiety.

Materials And Methods: A total of 15 children between the age group 3 and 6 years were selected for the study that required at least two dental treatment visits. Cases were randomly given midazolam through oral and intranasal routes in each visit.

Results: Results were analysed using HOUPT'S scale. Intranasal administration of midazolam is more likely to improve patient cooperation compared to oral sedation.

Conclusion: Intranasal Midazolam gave a more satisfactory outcome than the oral Midazolam when sedating uncooperative children.

Keywords: Anxiety, Sedation, Children, Midazolam, Intranasal, Oral sedation.

Introduction

One of the biggest challenges faced by pediatric dentists in daily practice is child behavior management. Any impression from a dental experience is going to be reflected through an individual's future dental attendance by the creation of positive or negative memories[1]. The prevalence of preoperative anxiety is high and is reported to range from 40% to 60% among young children. 20% of these children will continue to demonstrate negative behaviour even 6 months after surgery[2, 3]. Various approaches have been identified to enable the operator to overcome behavioral problems in children. One of the commonly used approaches is the use of pre-anaesthetic medication which will allay apprehension regarding anaesthesia and any kind of surgery and lessen the trauma of separation[1]. Although many studies examined the effects of different premedication drugs including Midazolam, until now, there is no widely accepted drug of choice. The ideal premedication drug should have an easy

and effective route of administration with no or little adverse reactions. Moreover, it should have a rapid onset of action with a little effect on cardiovascular stability[4].

Midazolam is a γ-aminobutyric acid (GABA) receptor inhibitor i.e. benzodiazepine medication. It is used frequently as premedication in pediatrics due to its sedative, anxiolytic, and amnesic effect. It is the most frequently used premedication in pediatrics[5, 6]. It has been used through various routes, viz. oral, rectal, intramuscular, intranasal and intravenous routes, each route with their own merits and demerits[7]. It is important to note that each route has its advantages and disadvantages and could not be considered for every case at every clinical situation.[8]

Although various combinations of drugs and routes of administration have been used in children for pre-anaesthetic sedation, the oral route remains the least threatening method of drug administration but has its own demerits such as initiation of sedation effect, long (delayed) onset time, unreliable absorption level. Another major issue in oral sedation is lack of titration capacity and its long-lasting effect delaying the patient's discharge[7]. On the other hand, intranasal sedation is a more recent approach which is considered as one of the alternate ways for prescribing certain medications to the existing oral technique. Intranasal sedation is known as a non-invasive way of drug administration, which is safe and is tolerated by children, with direct absorption potential of the sedative agent into the bloodstream without entering the liver and stomach. It also saves the fearful child from receiving more injections. The level of drug's absorption is almost similar to that of the IV sedation with peak plasma levels being reached in approximately 10 minutes [9-10].

The aim of this study was to compare the efficacy of intranasal midazolam with oral methods in sedating children for dental procedures.

Materials and Methods

A double-blind, prospective, randomized study, involving 30 children aged three to six years, was performed at National Dental college and Hospital, Dera Bassi, Punjab. The study was conducted after obtaining written informed consent from the parent/guardian and after obtaining institutional ethical clearance. Uncooperative 3–6- year-old children with negative and definitely negative Frankel scale in ASA I or II were included in this dental treatment process. ASA grade III and IV children with full stomach, with respiratory and cardiac diseases or having upper respiratory tract infection, with seizures, mentally retarded children, patients on drugs that interfere with midazolam, those with history of prematurity and chronic illness were excluded from the study.

All the children were requested to be kept at NPO status for 6 hours (solid foods) and 4 hours (water and liquids) preoperatively. The children were randomly assigned to two groups for the starting technique of A: intranasal sedation and B: oral sedation.

The selection of the patients was done randomly by allocating 30 Patients into 2 groups by computer generated randomized table

1. Group O (n = 15) received oral midazolam 0.5 mg/kg proprietary midazolam Oral formulation
2. Group N (n=15) received intranasal midazolam 0.2 mg/kg dispensed through nasal spray in upright position during inspiration.

Oxygen saturation was monitored at various steps of the study starting with premedication time at baseline using Pulse Oximeter (Trueview, India).

All the measurements were made at the time of local anaesthetic injection followed by initiation of dental

treatment. Houpt Scale was used to record every change in child's behavior with the following criteria: the amount of crying (C), sleeping (S) and movement (M) and overall behavior (O) (Table 1). In case of poor cooperation, further sedative drugs were administered if needed in order to complete the treatment process while the least score was recorded for the case and sedation technique. Attempts were made to limit each treatment session to a maximum of 35 minutes.

The children were discharged when full consciousness was achieved and all vital signs returned to normal ranges. Data were analysed using Wilcoxon test and paired t-test.

Table 1: HOUPT Sedation rating scale

Rating Scale	Definition	Score
Sleep	• Fully awake, alert • Drowsy, Disoriented • Asleep	1 2 3
Movement	• Violent movement that interrupts treatment • Continuous movement that makes treatment difficult • Controllable movement that does not interfere with treatment • No movement	1 2 3 4
Crying	• Hysterical crying that interrupts treatment • Continuous, persistent crying that makes treatment difficult • Intermittent, mild crying that does not interfere with treatment • No crying	1 2 3 4
Overall Behaviour	• Aborted • Poor • Fair • Good • Very Good • Excellent	1 2 3 4 5 6

Results

Socio-Demographic Data: The two groups were comparable in an age, sex and weight distribution. In Group O there were 10(66.6%) male and 5(33.4%) female children with age ranging from 3-6years (mean 4.4±1.1) and mean weight of 13.9±2.3kgs. In Group N there were 11(73.3%) male and 4(26.7%) female children with age ranging from 3-6 years (mean 4.1±0.9) and mean weight of 13.7± 2.9kgs. (Table2)

Table 2: Socio-demographic data of children in the study

Socio Demographic Factors	Group O	Group N
Age(years)	4.4±1.1	4.1±0.9
Sex(male/female)	10/5	11/4
Weight(kg)	13.9±2.3	13.7±2.9

Data from all the 30 children aged 3–6, were recorded. An initial behavior rating scale (Frankel scale) evaluation revealed that 27 cases (90%) were negative while 3 (10%) cases were judged to be completely negative.

Comparison of sleep (S), movement (M), crying (C) and overall behavior (O) parameters showed significant differences between oral and nasal groups during the treatment (P<0.05) in favor of intranasal sedation.

As detailed in the "Materials and Methods" section, all the participants were selected from those classified as negative /definitely negative with the drug administration being carried out by force in both sessions. Since each patient served as control, comparison of the outcomes showed little or no difference in drug acceptance rates. The success rates of oral and nasal administrations at different measured steps showed that the difference was statistically significant after 15 and 30 minutes (P<0.05).

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Sleep:

The summary of ratings for sleep parameter of Houpt scale for all subjects is presented in Fig 1. Thirteen children (86.6%) who were premedicated with intranasal midazolam were drowsy during the treatment as compared to 2 children (13.3%) who received oral midazolam and the difference was found to be statistically significant (p<0.05)

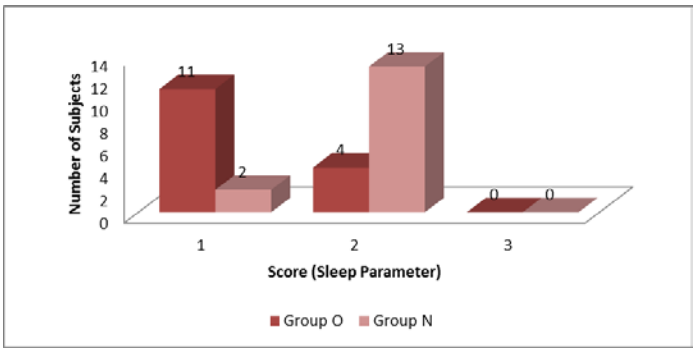

Fig.1 Comparison of Oral and Intranasal Midazolam using Sleep Parameter of Houpt sedation rating Scale

Movement

Fig, 2 illustrates the summary of ratings for movement parameter of Houpt scale for all subjects. Nine (60%) out of 15 children who received intranasal midazolam did not show any movement during the dental procedure. On the contrary, 10 (66.6%) out of 15 children who were premedicated with oral midazolam were continuously moving throughout the treatment. This difference was statistically significant (p < 0.05).

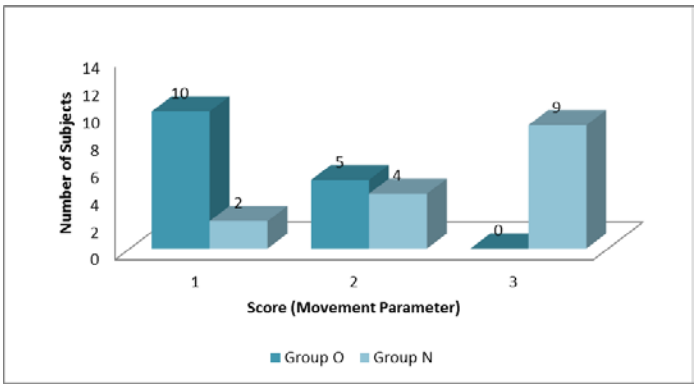

Fig.2 Comparison of Oral and Intranasal Midazolam using Movement Parameter of Houpt sedation Scale

Crying

The summary of ratings for sleep parameter of Houpt scale for all subjects is presented in Fig 3. Thirteen (86.6%) children who received intranasal midazolam did not did not cry, not interfering with operative procedures. Hysterical cry (score 1) was observed in only one patient. Majority of the children (66.6%) premedicated with oral midazolam were continuously crying during the treatment. This difference was statistically significant ($p<0.05$).

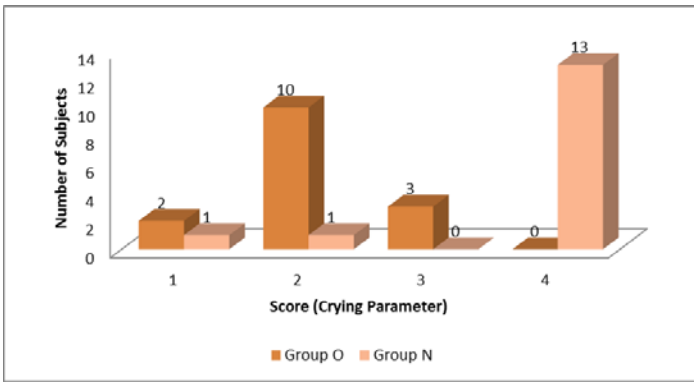

Fig. 3: Comparison of Oral and Intranasal Midazolam using Crying Parameter of Houpt sedation rating Scale

Overall Behavior

The summary of overall evaluation for all subjects is illustrated in Fig 4 Nine (60%) out of 15 children who received intranasal midazolam showed excellent overall behaviour during the whole treatment. On the contrary, 8 (66.6%) out of 15 children who were premedicated with oral midazolam showed poor behaviour ($p < 0.05$).

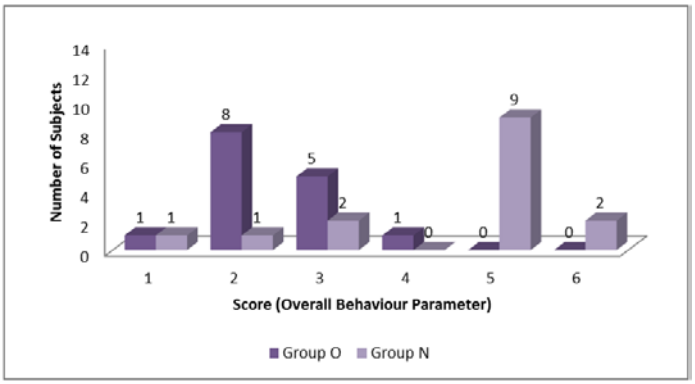

Fig.4 Comparison of Oral and Intranasal Midazolam using Overall Behavior Parameter of Houpt sedation rating Scale

No adverse effects (such as vomiting or allergic manifestations) were observed, and the vital signs -- pulse and oxygen saturation -- remained unchanged. Pulse rate increased during insertion of the mouth prop or placement of rubber dam, but quickly returned to normal when these stimuli ended. Oxygen saturation did not decrease below 95%.

Discussion

Separation from the fogeys to a completely unknown operating room environment with unknown faces makes the operative experience traumatic for young children and can evoke stress and anxiety. Preanesthetic medication might decrease the adverse psychological and physiological sequelae of induction of anesthesia in a distressed child[11]. Numerous drugs and routes of administration have been tried with the purpose of finding an ideal premedication drug in children. Selecting an appropriate premedication depends on its safety, rapid onset, effectiveness in reducing anxiety, and facilitating a smoother induction of anesthesia[12]. Among different medications available, the midazolam (a benzodiazepine), has become the most frequently used preanesthesia medication given to children scheduled for treatment[13].It exhibits many positive effects, including hypnotic sedation, amnesia, muscle relaxation and alleviation of anxiety. Its ability to create anterograde amnesia is much higher when compared to other benzodiazepines[14, 15].

Although oral midazolam has been found to be effective for day-to-day anesthetic requirements in children[16] yet there are instances where oral Midazolam is not acceptable to some children owing to sensory acceptability concerns. Despite efforts to disguise the bitter taste by mixing the parenteral formulation with the sweetening agents or juices, children often spit or regurgitate the medication resulting in variation of bioavailability of the drug, when administered orally[17].

Intranasal and oral transmucosal (buccal and sublingual) delivery of sedative medications provide alternatives that give some advantage over the conventional methods in properly elect minor procedure: they're faster than oral or rectal forms and conjointly less painful than i.m injection forms[18].

In the present study, we made an attempt to compare oral and nasal routes in terms of sedation score in pediatric patients.

The two groups were comparable in age, sex and weight distribution. In Group O there were 66.6% male and 33.4% female children with age ranging from 3-6 years (mean 4.4±1.1) and mean weight of ranging from 11-17kgs. In Group N there were 73.3% male and 26.7% female children with age ranging from 3-6 years (mean 4.1±0.19) and weight ranging from 10-16kgs. Patients of either sex were randomly allotted to both the groups. These demographic data were in correlation with the data of Balda N[19] reports.

Children in nasal group did not show any adverse effects with intranasal midazolam spray at any point of observation that indicates safety of spray. Similar effects were observed in studies by Baldwa NM, et al (2012)[19], Lane RD (2008)[20], and Klein EJ et al (2011)[21].

Children in oral group also did not show any adverse effects of the drug at any point of observation indicating safety of oral midazolam. Weldon C et al (1992)[22], Rosenberg M. et al (2000)[23] and Koppal R.et al [24](2011) also reported no adverse effects of the drug. So from the present study it can be concluded that the use of intranasal midazolam spray and the oral midazolam suspension are safe to be used for premedication in pediatric patients.

In the present study, the sedation scores for all the parameters [Figure1, 2, 3, 4] were found to be significantly higher in nasal Midazolam Group as compared to oral group. Compared to the current study, Yildirim et al.[25] did not find a significant difference in sedation scores of oral and nasal routes. Similar to the present study, Verma et al.[26] and Raval and Gunga[27] also found better sedation scores in nasal group as compared to oral group. Abhishek et al.[28] in their study while using a different scoring system for sedation, also found the performance of nasal group to be better than oral group (86% vs. 83%) but did not find a significant difference between two groups.

Among the two techniques of sedation, the intranasal method provided a higher and more satisfactory sedation rate, and the difference was found to be statistically significant.

On reviewing the literature, we did not find a single study citing the better outcome of oral as compared to nasal route. Intranasal administration involves a path in which the drug is administered, aiming to have an immediate absorption into the bloodstream, because of high vascularity of nasal mucosa and increased drug bioavailability without first pass metabolism effect. The technique is simple and effective and requires minimal cooperation[28, 29].

The administration of intranasal midazolam has two pragmatic drawbacks: this drug/route combination causes transient burning discomfort, and intranasal midazolam cannot be adequately employed when the child has an upper respiratory tract infection with copious nasal secretions. More prospective studies are needed to determine the predictive value of the various parameters affecting pediatric sedation behavior during dental treatment, thereby optimizing the success rates of different sedation drugs as well as their routes.

Conclusion

The present study was carried out to compare the efficacy of Midazolam administered by oral and intranasal routes as premedicants in terms of sedation score in pediatric

patients. In conclusion, on the basis of our study, we found that use of intranasal midazolam spray over oral midazolam should be preferred as it has better sedation than oral midazolam.

References

1. Hosey MT. Anxious Children: Coping in dental practice. Dental Update 1995;22:210-5.
2. Bhakta P, Ghosh BR, Roy M, Mukherjee G. Evaluation of intranasal premedication for preanasthetic sedation in paediatric patients. Indian J Anaesth 2007;51(2):111-16.
3. Kain ZN, Mayes LC, O'Connor TZ, Cicchetti DV. Preoperative Anxiety in Children; Predictors and Outcomes. Arch Pediatr Adolesc Med. 1996;150:1238- 45.
4. Kain ZN, Hofstadter MB, Mayes LC, Krivutza DM, Alexander G, Wang SM, et al. Midazolam: Effects on amnesia and anxiety in children. *Anesthesiology*. 2000;**93**(3):676-84.
5. Almenrader N, Passariello M, Coccetti B, Haiberger R, Pietropaoli P. Premedication in children: A comparison of oral midazolam and oral clonidine. Paediatr Anaesth. 2007;17(12):1143-9.
6. Feng JF, Wang XX, Lu YY, Pang DG, Peng W, Mo JL. Effects of dexmedetomidine versus midazolam for premedication in paediatric anaesthesia with sevoflurane: A meta-analysis. J Int Med Res. 2017;45(3):912-23.
7. Malamed SF. Sedation: A Guide to Patient Management; The Spectrum of Pain and Anxiety Control, 5th ed. China: Elsevier; 2010. p. 14-22.
8. Safranek DJ, Eisenberg MS, Larsen MP. The epidemiology of cardiac arrest in young adult. Ann Emerg Med 1992;21:1102-6.
9. Malamed SF. Sedation: A Guide to Patient Management. Oral Sedation, 5th ed. China: Elsevier; 2010.p. 95-118.
10. Primosch RE, Guelmann M. Comparison of drops versus spray administration of intranasal midazolam in two-and three-year-old children for dental sedation. Pediatric Dent 2005;27:401-8.
11. Baldwa NM, Padvi AV, Dave NM, Garasia MB. Atomised intranasal midazolam spray as premedication in pediatric patients: comparison between two doses of 0.2 and 0.3 mg/kg. J Anesth 2012;26:346–50
12. Qiao H, Xie Z, Jia J. Pediatric premedication: A double-blind randomized trial of dexmedetomidine or ketamine alone versus a combination of dexmedetomidine and ketamine. *BMC Anesthesiol*. 2017;**17**(1):158.
13. Egan KJ, Ready LB, Nessly M, Greer BE. Self-administration of midazolam for postoperative anxiety: A double blinded study. Pain. 1992;49:3–8.
14. Bhatangar S, Mishra S, Gupta M, Srikanti M, Mondol A, Diwedi A. Efficacy and safety of a mixture of ketamine, midazolam and atropine for procedural sedation in pediatric oncology: a randomized study of oral versus intramuscularroute. J Pediatr Child Health 2008;44:201-4.
15. Damle SG, Gondhi M, Laheri V. Comparison of oral ketamine and oral midazolam as sedative agents in pediatric dentistry. J Indian Soc Pedo Prev Dent 2008;26:97-101.
16. Parnis SJ, Foate JA, van der Walt JH, Short T, Crowe CE. Oral midazolam is an effective premedication for children having day-stay anaesthesia. Anaesth Intensive Care. 1992;20:9–14.
17. Brosius KK, Bannister CF. Midazolam Premedication in Children: A Comparison of Two Oral Dosage

Formulations on Sedation Score and Plasma Midazolam Levels. Anesth Analg 2003;96:392–95.

18. Mehdi I, Parveen S, Choubey S, Rasheed A, Singh P, Ghayas M. Comparative Study of Oral Midazolam Syrup and Intranasal Midazolam Spray for Sedative Premedication in Pediatric Surgeries. Anesth Essays Res. 2019 Apr-Jun;13(2):370-375.
19. Baldwa NM, Padvi AV, Dave NM, Garasia MB. Atomised intranasal midazolam spray as premedication in pediatric patients: comparison between two doses of 0.2 and 0.3 mg/kg. J Anesth 2012;26:346–50.
20. Lane RD, Schunk JE. Atomized intranasal Midazolam Use for Minor Procedures in the Pediatric Emergency Department. Pediatric Emergency Care 2008;24(5):300-3.
21. Klein EJ, Brown JC, Kobayashi A, Osincup D, Seidel K. A Randomized Clinical Trial Comparing Oral, Aerosolized Intranasal, and Aerosolized buccal Midazolam. Ann Emerg Med. 2011 Jun 18.
22. Weldon BC, Watcha MF, White PF. Oral Midazolam in Children: Effect of Time and Adjunctive Therapy. Anesth Analg 1992;75: 51-55
23. Rosenberg M, Norris L H. Oral Midazolam Syrup as a Safe Sedative for Pediatric Dentistry. Dental News 2000; Vol VII(III).
24. Koppal R, Adarsh ES, Ambi U, AnilKumar G. Comparison of the midazolam transnasal Atomizer and oral midazolam for sedative premedication in paediatric cases. JCDR 2011;5(5):932-34.
25. Yildirim SV, Guc BU, Bozdogan N, Tokel K. Oral versus intranasal midazolam premedication for infants during echocardiographic study. Adv Ther. 2006;23:719–24.
26. Raval DL, Gunga TS. Comparative study of oral and trans nasal midazolam as a sedative premedication in paediatric patients. J Clin Exp Res. 2014;2:158–62.
27. Abhishek R, Sharma AN, Ganapathi P, Shankaranarayana P, Aiyappa DS, Nazim M. A comparative study of intranasal midazolam spray and oral midazolam syrup as premedication in pediatric patients. Karnataka Anaesthe J. 2015;1:186–90.
28. Safranek DJ, Eisenberg MS, Larsen MP. The epidemiology of cardiac arrest in young adult. Ann Emerg Med 1992;21:1102-6.
29. Hossain AA. Mechanism of nasal absorption of drugs. Prog Clin Biol Res 1989;292:261-72.