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Review Article

The Effect of Rectal Midazolam on Clinical Conditions in Pediatric Dentistry: A Systematic Review Study

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ABSTRACT

Background: Before dental procedures, children often require mild to moderate sedation. This study was conducted to determine the effect of rectal midazolam on pediatric dental pain using a systematic review method.

Methods: In this systematic review study, articles published from 2000 up to the beginning of 2025 that focused on the effect of rectal midazolam on the clinical condition of pediatric patients undergoing dental services were included. The search was conducted by both authors of the article: one holding a specialization degree in pediatric dentistry and the other being a pharmacist. The search keywords included "pediatrics," "tooth," "dentistry," "dental services," "midazolam," "rectal midazolam," "children," and "clinical indicators." The search was performed across all international databases, including PubMed, Scopus, Web of Science, Embase, EBSCO, and the Google Scholar search engine. After searching for the articles, the relevant data were extracted using a checklist designed by the researchers, and the findings were reported in table format using a descriptive method.

Results: The result showed the initial search yielded 189 articles. After reviewing and evaluating the articles based on research objectives, methodology, the type of drug prescribed to patients, the method of drug administration, the manner of reporting findings, the language of publication, and the availability of the full article files, 5 articles proceeded to the systematic review stage. Also, in all extracted studies, the administration of rectal midazolam resulted in a positive effect on the clinical conditions of the patients, and the administration of this drug caused no side effects in the patients.

Conclusion: The administration of midazolam rectally has proven effective in achieving the study objectives, including maintaining stable clinical conditions for the patients and resulting in no significant clinical side effects. Therefore, the rectal administration of this drug is recommended.

Introduction

Prior to dental procedures, children often require mild to moderate sedation. These sedatives help manage and prevent stress and anxiety resulting from being in an unfamiliar environment or due to the fear of pain [1]. Modern anesthesia strives to create the best conditions with minimal deficits to perform surgery. This involves establishing a state of deep sleep, adequate analgesia, and appropriate muscle relaxation so that surgical procedures or various medical and dental services can be completed with the fewest complications [2]. To select the most suitable drug, many factors, such

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as potential drug interactions, pharmacokinetics, and pharmacodynamics of each drug, must be considered [3].

Various medications, including acetaminophen, ibuprofen, and midazolam, are administered for reducing anxiety and pain and providing sedation for individuals undergoing dental treatments [4]. Midazolam is one of the preferred benzodiazepines for sedation. Desirable characteristics of midazolam include rapid onset of action and short duration of effect, a wide margin of safety, and a high therapeutic index [5-6]. Midazolam is often used as a sedative agent for conscious sedation. Furthermore, using midazolam in the anesthetic drug regimen reduces recovery complications such as headache, myalgia, and nausea. The most significant side effect of midazolam is respiratory depression, which can be reversed with flumazenil [7].

Midazolam has muscle relaxant, sedative, and anxiolytic effects, it also acts as a tranquilizer and has minimal effects on the cardiovascular system, including a slight increase in heart rate. Therefore, factors such as rapid onset, limited duration of action (approximately 45 to 50 minutes), and the absence of major side effects make midazolam a favorable choice for specialists in this field [8-10].

It is used as a sedation agent in short-term diagnostic procedures such as bronchoscopy, gastroscopy, cystoscopy, and angiography. It is also used in minor surgeries, dental surgeries, seizure management, and treatment of intractable hiccups [11-12]. Midazolam is administered to patients through various routes, including intravenous, inhalation, oral, and rectal. In dental treatments, one of the methods for administering midazolam is the rectal route [13].

Given the above points, this study was conducted to determine the effect of rectal midazolam on pediatric dental pain using a systematic review method.

Methods

This systematic review study included articles published from 2000 to the beginning of 2025 that focused on the effect of rectal midazolam on the clinical condition of pediatric patients undergoing dental services. The search was conducted by both authors of the article: one holding a specialization degree in pediatric dentistry and the other being a pharmacist.

The search keywords included "pediatrics," "tooth," "dentistry," "dental services," "midazolam," "rectal midazolam," "children," and "clinical indicators." The search was performed across all international databases, including PubMed, Scopus, Web of Science, Embase, EBSCO, and the Google Scholar search engine.

After searching for the articles, the relevant data were extracted using a checklist designed by the researchers, and the findings were reported in table format using a descriptive method.

Results

According to the findings, the initial search yielded 189 articles. After reviewing and evaluating the articles based on research objectives, methodology, the type of drug prescribed to patients, the method of drug administration, the manner of reporting findings, the language of publication, and the availability of the full article files, five articles proceeded to the systematic review stage (Table 1). According to the findings, in all extracted studies, the administration of rectal midazolam resulted in a positive effect on the clinical conditions of the patients, and the administration of this drug caused no side effects in the patients (Table 1).

Table 1- Specifications of published articles

-	Author	Years	Age	N		Result
1	Soltani et al. [14]	2008	1-10		ketamine	The scores for Separation from Parent were 1.91 (0.2), Mask Acceptance was 3.47 (0.7), Anxiolysis was 3.75 (0.5), and Sedation was 1.91 (0.6). Additionally, the success rates for separation from parent were 90.6%, mask acceptance was 90.6%, anxiolysis was 96.9%, and sedation was 71.9%.
2	Alzoubi et al. [15]	2024	3.8(0.8)		-	In addition to midazolam, ketamine was also administered to the patients. According to the findings, the patients' SPO_2 index M(SD) was 98.3 (1.04) before treatment, 97.4 (1.25) during treatment, and 98.1 (1.07) after treatment. Regarding the patients' PR (Pulse Rate) index, it was 96 (2.55) before treatment, 94.67 (3.89) during treatment, and 95.47 (2.14) after treatment. Pertaining to the SBP (systolic blood pressure) index, values of 10.52 (0.23) were reported before treatment, 11.10 (0.27) during treatment, and 10.83 (0.28) after treatment. Moreover, the DBP (diastolic blood pressure) index was reported as 6.4

						(0.26) before treatment, 6.5 (0.25) during treatment, and 6.53 (0.22) after treatment. In fact, the administration of rectal ketamine along with midazolam is effective in managing patients who do not cooperate with dental treatments.
3	Okcu et al. [16]	2004	4.56(1.51)		Oral Midazolam	The acceptance rate of LOCAL ANESTHESIA with Oral Midazolam was 11 (44%) in the good condition, 9 (36%) in the moderate condition, and 5 (20%) in the poor condition. Regarding rectal midazolam, the rates were 5 (20%) in the good condition, 15 (60%) in the moderate condition, and 5 (20%) in the poor condition. Furthermore, concerning operating conditions in the Oral Midazolam group, 5 (20%) of the subjects were in the excellent condition, 7 (28%) in the good condition, 10 (40%) in the medium condition, and 3 (12%) in the poor condition. On the other hand, for rectal midazolam, 1 (4%) was in excellent condition, 11 (44%) in good condition, and 2 (8%) in poor condition.
4	Yoshino et al. [17]	2019	2.5	10	-	A total of 10 patients were studied, 2 of whom were male and 8 of whom were female. In 8 of the patients, the surgical site was the tongue, and in the other two patients, tooth breakage and luxation. The level of sedation of the patients was drowsy in 3 patients, calm in 5 patients, and alert in 2 patients 15-30 minutes after drug administration. Regarding the acceptance of treatment by dentists, 10 patients were in the difficult to Treat category, 6 patients were in good to treat category, and 2 patients were in the Excellent to treat.
5	Jensen et al. [18]	2002	4.11	25	-	Regarding the level of drowsiness (somnolence), 16 subjects in the oral group and 22 subjects in the rectal group were drowsy. Concerning mask acceptance, 21 subjects in the oral group and 23 subjects in the rectal group had a positive acceptance of the oxygen mask. Seventeen individuals in the oral group retained the color of the balloon, in contrast to only fourteen individuals in the rectal group. The sedative effect of rectal administration was greater than that of oral administration, but this difference was not statistically significant.
6	Lindh-Strömberg [19]	2001	4.5	120	-	Ten minutes before the procedure, midazolam at a dose of 0.3 mg/kg was administered to the patients rectally. In the performed treatments, 39.6% of cases were evaluated as having required parental assistance or experienced minor difficulties, while 60% of them were assessed as having proceeded without any difficulty. Furthermore, no side effects were observed during the patients' treatment, and in accordance with the findings, midazolam is recognized as an effective drug for pediatric dental treatments.

Discussion

Children are susceptible to various diseases due to their young age, and if they contract an illness, they may face numerous consequences. Consequences of pediatric hospitalization can include infection, readmission, stress, reduced self-confidence, anxiety, and academic decline [20-21]. Stress and anxiety have significant impacts on patient health and lead to related complications [22-23].

Dental anxiety is a condition that occurs in all age groups, especially in the pediatric population. In this state, contemplating dental treatments leads to unpleasant feelings in patients, resulting in distress and fear. Dental anxiety exists in approximately 5 to 20 percent of the child and adolescent population, and the use of anxiolysis and analgesic medication is recommended for its relief [24-25].

According to the findings of studies included in systematic reviews, the rectal administration of

midazolam has been reported as an effective drug in the provision of dental services. In fact, in all five reviewed articles, midazolam was reported as an effective agent. The results of other studies published before the year 2000 and between 1990 and 2000 regarding the rectal administration of midazolam are also consistent with this study [26-28]. Rabassa-Blanco et al. conducted a systematic review study across 11 countries in children aged 2 to 14 years with a sample size of 4,374 subjects. Twenty-eight studies were reviewed, most of which assessed behavioral scales. Midazolam was administered through various routes, including oral, enteral, and intranasal, and generally, midazolam administration was effective in reducing anxiety in children, improving their cooperation, and encouraging subsequent dental visits. Regarding reported side effects, mild adverse events such as nausea and vomiting were reported [25]. In fact, midazolam, through moderate sedation, leads to a reduction in consciousness and the patient's adherence to verbal commands (with or without the help of an attendant) [29]. Yeo et al. conducted a study between 2016 and 2021 involving 109 children, where the use of fentanyl and midazolam resulted in better operating conditions [30]. Zhang et al., in a meta-analysis study involving 420 pediatric patients, found that both midazolam and dexmedetomidine were effective in dental surgical sedation. However, dexmedetomidine was more effective in maintaining stable diastolic blood pressure. Furthermore, both drugs had similar effects on systolic blood pressure, heart rate, and SPO_2 [31].

Conclusion

The administration of midazolam rectally has proven effective in achieving the study objectives, including maintaining stable clinical conditions for the patients and resulting in no significant clinical side effects. Therefore, the rectal administration of this drug is recommended.

References

[1] Gharavi M, Salem K, Ahmadi SAY, Baradaran HR. A Comparative Evaluation of Midazolam, Ketamine and Their Combination as Sedative Agents in Pediatric Dentistry: A Systematic Review and Meta-analysis. Front Dent. 2025; 22:34.

[2] Alizadeh A, Kayalha H, Heyrat B, Rastak S, Sofiabadi M. Comparison Hemodynamic Effects of Midazolam and Dexmedetomidine as a Premedication in Patients Undergoing Upper Limb Surgeries: A Double-blind Intervention. J North Khorasan Univ Med Sci. 2020; 11(4):45-51.

[3] Shetabi H, Haidari SM, Moradi FD, Bechari Z. A comparison of sedation quality with midazolam-ketamine versus propofol-ketamine during Phacoemulsification surgery. Tehran Univ Med J. 2021; 79(1):18-25.

[4] Rienhoff J, Splieth CH, Veerkamp JSJ, Krikken JB, Rienhoff S, Halsband U, et al. The Role of Ibuprofen and Midazolam in Pediatric Dentistry: A Retrospective Study and Neurophysiological Considerations. Brain Sci. 2024; 14(11):1073.

[5] Nashibi M, Mottaghi K, Faraji M, Delavari A, Taghipour H, Amiri M. Comparison of analgesic and sedative effects of ketamine-propofol (ketofol) and fentanyl-midazolam (fentazolam) combinations in outpatient orthopedic procedures. Trauma Mon. 2017; 22(5).

[6] Masoudifar M, Nazemroaya B, Rahimi Z, Khademi M. Effects of midazolam and dexmedetomidine on sedation levels, hemodynamics and, complications under brain stereotaxic surgery. Jundishapur Sci Med J. 2019; 18(3):311-7.

[7] Nazemroaya B, Masoudifar M, Rajabi Moghadam M. Comparison of dexmedetomidine versus midazolam on hemodynamic parameters, bleeding, satisfaction of surgeons and patients who Underwent laminectomy surgery by spinal anesthesia. Tehran Univ Med J. 2021; 79(5):343-50.

[8] Kamalfar S, Mousavi R, Alinaghimaddah SM. Effect of Midazolam on the Incidence of Agitation in Patients Undergoing Electroconvulsive Therapy: A Randomized Clinical Trial. Iran J Psychiatry Clin Psychol. 2023; 29(2):188-201.

[9] Gencer M, Sezen O. A study comparing the effect of premedication with intravenous midazolam or dexmedetomidine on ketamine-fentanyl sedoanalgesia in burn patients: A randomized clinical trial. Burns. 2021; 47(1):101-9.

[10] Tadler SC, Mickey BJ. Emerging evidence for antidepressant actions of anesthetic agents. Curr Opin Anaesthesiol. 2018; 31(4):439-45.

[11] Cravero JP, Beach M, Thyr B, Whalen K. The effect of small dose fentanyl on the emergence characteristics of pediatric patients after sevoflurane anesthesia without surgery. Anesth Analg. 2003; 97(2):364-7.

[12] Sanatkar M, Goudarzi M, Espahbodi E. Comparison of the efficacy of two pre-treatment medication of dexmedetomedine-fentanyl and midazolam-fentanyl in cataract surgery. Tehran Univ Med J. 2020; 78(3):155-64.

[13] Inoue T, Yamamoto T, Kishimoto N, Seo K. Comparison of Anesthetic Features in Diazepam and Midazolam for Sedation Dentistry: A Scoping Review. Cureus. 2025; 17(2):e79079.

[14] Ebrahim Soltani A, Arbabi SH, Nahvi H, Moshirian N. Rectal premedication in pediatric anesthesia: midazolam versus ketamine. Tehran Univ Med J. 2008; 66(2):113-7.

[15] Alzoubi H, Kabbani S, Taleb A, Bshara N, Altinawi MK, Almonakel MB, et al. Rectal Sedation With Ketamine and Midazolam in the Management of Uncooperative Children During Dental Treatment: A Case Series and Method Description. Cureus. 2024;

16(2):e54825.

[16] Aydintug YS, Okcu KM, Guner Y, Gunaydin Y, Sencimen M. Evaluation of oral or rectal midazolam as conscious sedation for pediatric patients in oral surgery. Mil Med. 2004; 169(4):270-3.

[17] Yoshino A, Seto M, Mano R, Kita R, Ishida S, Aoyagi N, et al. Rectal administration of midazolam plus ketamine as conscious sedation for injured paediatric patients requiring Oral surgery. J Oral Maxillofac Surg Med Pathol. 2019; 31(4):241-4.

[18] Jensen B, Matsson L. Oral versus rectal midazolam as a pre-anaesthetic sedative in children receiving dental treatment under general anaesthesia. Acta Paediatr. 2002; 91(8):920-5.

[19] Lindh-Strömberg U. Rectal administration of midazolam for conscious sedation of uncooperative children in need of dental treatment. Swed Dent J. 2001; 25(3):105-11.

[20] Sarafi M, Azimi B, Karimian M, Ebrahimisaraj G. Assessment of Clinical Characteristics of Patients with Penetrating Abdominal Trauma. Arch Anesth Crit Care. 2025; 11(4):509-12.

[21] Sarafi M, Azimi B, Vasigh A, Ebrahimisaraj G. Assessment of Chronic Postoperative Inguinal Hernia Pain (CPIP) in Children. Arch Anesth Crit Care. 2025.

[22] Borji M, Nourmohammadi H, Otaghi M, Salimi AH, Tarjoman A. Positive Effects of Cognitive Behavioral Therapy on Depression, Anxiety and Stress of Family Caregivers of Patients with Prostate Cancer: A Randomized Clinical Trial. Asian Pac J Cancer Prev. 2017; 18(12):3207-12.

[23] Shokri M, Tarjoman A, Borji M, Solaimanizadeh L. Investigating psychological problems in caregiver of pediatrics with cancer: A systematic review. J Child Adolesc Psychiatr Nurs. 2020; 33(4):229-38.

[24] Baier K, Milgrom P, Russell S, Mancl L, Yoshida T. Children's fear and behavior in private pediatric dentistry practices. Pediatr Dent. 2004; 26(4):316-21.

[25] Rabassa-Blanco J, Cahuana-Bartra P, González-Chópite Y, Rocha-Eiroa MD, Ramírez-Rámiz A, Mashala EI, et al. Efficacy of Midazolam in Outpatient Pediatric Dentistry: A Systematic Review. Spec Care Dentist. 2025; 45(5):e70107.

[26] van der Bijl P, Roelofse JA, Stander IA. Rectal ketamine and midazolam for premedication in pediatric dentistry. J Oral Maxillofac Surg. 1991; 49(10):1050-4.

[27] Roelofse JA, van der Bijl P, Stegmann DH, Hartshorne JE. Preanesthetic medication with rectal midazolam in children undergoing dental extractions. J Oral Maxillofac Surg. 1990; 48(8):791-7.

[28] Lökken P, Bakstad OJ, Fonnelöp E, Skogedal N, Hellsten K, Bjerkelund CE, et al. Conscious sedation by rectal administration of midazolam or midazolam plus ketamine as alternatives to general anesthesia for dental treatment of uncooperative children. Scand J Dent Res. 1994; 102(5):274-80.

[29] Ashley P, Anand P, Andersson K. Best clinical practice guidance for conscious sedation of children undergoing dental treatment: an EAPD policy document. Eur Arch Paediatr Dent. 2021; 22(6):989-1002.

[30] Yeo XH, Shehabi Z. Effectiveness and safety of dentist-led conscious sedation using fentanyl with midazolam in dentistry: a five-year retrospective service evaluation. Br Dent J. 2023:1-6.

[31] Zhang Y, Li C, Shi J, Gong Y, Zeng T, Lin M, et al. Comparison of dexmedetomidine with midazolam for dental surgery: A systematic review and meta-analysis. Medicine (Baltimore). 2020; 99(43):e22288.