

# 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 <sub>2</sub> 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 |

|   |                      |      |            |     |                |  |
|---|----------------------|------|------------|-----|----------------|--|
| 3 | Okcu et al. [16]     | 2004 | 4.56(1.51) |     | Oral Midazolam | <p>(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.</p> <p>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.</p> <p>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.</p> |
| 4 | Yoshino et al. [17]  | 2019 | 2.5        | 10  | -              | <p>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.</p>  |
| 5 | Jensen et al. [18]   | 2002 | 4.11       | 25  | -              | <p>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.</p>   |
| 6 | Lindh-Strömberg [19] | 2001 | 4.5        | 120 | -              | <p>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.</p>  |

## 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<sub>2</sub> [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.

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