# Double-Blind Comparison of Rectally Administered Diazepam to Placebo for Pediatric Sedation: The Cardiovascular Response

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## Summary

The sedative and cardiovascular effects of rectally administered diazepam (0.6 mg/kg) were compared to placebo in uncooperative children who required sedation during dental treatment. Twelve healthy preschool children, who required amalgam restorations, were treated during two standardized restorative appointments in a double-blind, crossover study. Blood pressure and pulse were obtained during four specified intervals during the appointment. The behavior of the children during the treatment visits was videotaped and later statistically analyzed using a kinesics/vocalization instrument. Behavioral ratings of cooperation were significantly improved during the treatment visit following diazepam. All interfering bodily movements, patient vocalizations and operator commands for the diazepam group were reduced significantly ($p \leq 0.0001$). No significant differences were observed for noninterfering behavioral response. Rectally administered diazepam did not alter blood pressure or pulse significantly in these sedated children when compared to the placebo. These findings indicate that rectal diazepam is an effective sedative agent with minimal effect on the cardiovascular system for the management of the young pediatric dental patient.

Pharmacologic management of apprehensive patients is a necessary therapeutic modality for treating some uncooperative children during restorative appointments. A wide variety of drugs are used, such as chloral hydrate, nitrous oxide, alphaprodine, barbiturates, and diazepam. With the exception of nitrous oxide, drugs are usually administered orally which can result in delayed absorption, unpredictable maximal effect, and prolonged offset. Rectally administered diazepam is an alternative to the limitations of oral premedication and has been used in the dental office with favorable results.[1] These limited data from one study, however, have not been replicated in controlled clinical trials in pediatric dental patients.

Rectal diazepam in solution appears to have several pharmacologic properties which make it useful for treatment of the young child. Diazepam, dispensed rectally, adapts well to clinical practice because it is rapidly absorbed, producing peak blood levels in 5-10 min in children.[2-4] The rapid rate of absorption of rectal diazepam is due in part to a lipophilic component of the vehicle, propylene glycol.[5] In addition, the duration of action of this drug is advantageous for the clinical setting because the majority of the sedative effect is dissipated within the first hour.[1,5] This sedative effect is accomplished using a safe route of administration, which requires minimal patient cooperation and does not involve an intravenous injection.

The present study evaluates the sedative efficacy and cardiovascular responses of rectally administered diazepam during routine dental treatment as an alternative approach for the pharmacologic management of the young, uncooperative, pediatric dental patient.

## Methods

Subjects for the study were 12 children between the ages of 2 and 6 with a mean age of 3.8 years. Selection of difficult-to-manage pediatric patients was made during an initial examination visit by pediatric dentistry faculty. All children were identified

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as being negative or definitely negative toward dental treatment as defined by the Frankl scale, ratings 1 and 2.[6] Minimum treatment requirements for the children were two Class I amalgam restorations on primary molars.

The investigation was conducted using a double-blind design in which the dental operator, child and parent were unaware of the agent dispersed. Following the initial visit, each patient was required to return to the dental clinic for two treatment visits. The subjects were randomly assigned to two groups. Group A, consisting of 7 children, received the placebo at the first treatment visit and diazepam at the second visit; while Group B, consisting of 5 children, received diazepam at the first visit and the placebo at the second visit. The parents were instructed to make certain that the children should not take anything by mouth 4 hours prior to the treatment visit as a precautionary measure against vomiting and aspiration.

A sedative dose of 0.6 mg/kg of diazepam in solution (Injectable Valium®) was administered through a soft rubber catheter with the assistance of the parent. This dose was based on the satisfactory sedative effects reported by Lundgren and coworkers[1] for a commercially available rectal solution of diazepam administered to young pediatric dental patients. In a similar manner, bacteriostatic sodium chloride was administered as the placebo.

The drug treatments and dental therapy were administered to the child by a pediatric dentist in a standardized operatory, equipped with an overhead camera. The treatment and management of the young patients were performed by the same dentist and dental assistant throughout the entire study. Trained personnel videotaped the restorative treatment appointments.

The restorative procedure was initiated 10 to 15 min after administering the medication. The videotaped appointments were divided into 6 one-minute segments for future evaluation. The first 3 min of the film included the local anesthetic injection and the period prior to and following the injection. The fourth minute coincided with rubber dam application. The fifth minute started with cavity preparation, and the final minute included the condensation and carving of the amalgam restoration. The average length of the operative procedure was 35 minutes.

The blood pressure and arterial pulse rate of the patients were recorded four times during the treatment appointment by the operator. These cardiovascular readings were obtained prior to the administration of the rectal solution (preoperative measurement); 5 min following the dispensation of the rectal agent (postsedation measurement); and 5 min following the injection of the local anesthetic with 2% lidocaine with 1:100,000 epinephrine (postanesthetic measurement). The final readings were taken prior to the dismissal of the patient which was approximately 1 hr after the rectal drug administration (postoperative measurement). Readings for blood pressure were obtained from the left brachial artery and arterial pulse values were taken from the left radial artery.

The videotapes were reviewed by two pediatric dentists and a certified dental assistant utilizing the kinesics/vocalization instrument.[7] The six categories evaluating the child's responses included: (1) Head and oral movements; (2) upper extremity movements; (3) torso movements; (4) lower extremity movements; (5) vocalizations by the patients; (6) requests and commands by the dentist. The patients' movements were divided into interfering and noninterfering behavior. Interfering behavior was defined as those acts which produced a disruption in the clinical procedure, while noninterfering behavior was judged as not impeding the progress of treatment.

Each evaluator viewed the filmed treatment appointment and independently recorded the behavioral responses of the child and the voice commands of the dentist during the specified 6-min period. An audible tone was incorporated into the soundtrack of the film which divided each of the minutes into 10-sec intervals, in order to quantify the duration of the behavioral responses. The minimum number of responses for each behavioral category during the 6 min of filmed tape was 0 and the maximum number of recorded responses was 36. After the final review of the filmed treatment appointment, the evaluators assigned a Frankl rating to the entire procedure.

One-way analysis of variance (ANOVA) was used to evaluate the sedative effect of diazepam and placebo on the behavior of the children during the treatment visits. Statistical comparison was made between the treatments for six categories of behavior, defined by the kinesics/vocalization instrument. The means and standard deviations were determined for each of the four readings for blood pressure and arterial pulse rate. A paired *t*-test was used to evaluate the differences in cardiovascular readings across treatments and over time. A significance level of $p \leq 0.05$ was considered sufficient to reject the null hypothesis for both statistical tests.

## Results

A pronounced sedative effect was demonstrated in the diazepam treatment group. A significant reduction in the number of disruptive behaviors made by the child was seen for diazepam in comparison to placebo pretreatment ($p < 0.0001$). All categories of interfering bodily movements and vocalizations by the child and operator were significantly reduced when the child had been sedated with rectally administered diazepam (Tables 1 and 2). However, no significant difference was noted between the diazepam and placebo groups when noninterfering behaviors were analyzed (Table 1). Furthermore, when the effect of sequential treatment appointments was examined, no clinically significant difference in the average Frankl ratings was observed for the

**TABLE 1.** Total Interfering and Noninterfering Movements During a Dental Procedure in the Placebo and Diazepam Premedicated Groups [a]

| | Head/oral ($\bar{X}\pm SD$) | Upper Extremities ($\bar{X}\pm SD$) | Lower Extremities ($\bar{X}\pm SD$) | Torso' ($\bar{X}\pm SD$) |
|---|---|---|---|---|
| Interfering Responses | | | | |
| Placebo (n=12) | 9.5±13.0 | 9.1±12.4 | 5.7±11.9 | 7.3±13.0 |
| Diazepam (n=12) | 1.7± 1.7 [b] | 2.7± 5.0 [b] | 0.3± 1.0 [b] | 0.8± 2.4 [b] |
| Noninterfering responses | | | | |
| Placebo (n=12) | 7.6± 5.2 | 11.0± 7.6 | 11.8± 8.9 | 2.9± 5.1 |
| Diazepam (n=12) | 8.5± 6.0 | 11.1± 7.0 | 11.9± 8.3 | 2.6± 3.1 |

[b]Significant difference between diazepam and placebo treatment at $p \leq 0.0001$ ANOVA.
[a]Possible score: minimum=0; maximum=36 for each behavioral category.

**TABLE 2.** Total Patient Vocalizations and Operator Commands During a Dental Procedure in the Placebo and Diazepam Premedication Groups [a]

| | Patient vocalizations ($\bar{X}\pm SD$) | Operator commands ($\bar{X}\pm SD$) |
|---|---|---|
| Placebo (n=12) | 17.1±13.5 [b] | 12.6±10.5 [b] |
| Diazepam (n=12) | 7.4±6.6 | 5.8±6.1 |

[a]Possible score: minimum=0; maximum=36 for each vocalization category.
[b]Significant difference between diazepam and placebo treatment of $p \leq 0.0001$ ANOVA.

treatment groups. However, a trend was noted in the diazepam-treated group for a more favorable response when diazepam was administered at the second operative appointment.

Blood pressure readings measured during the restorative appointments did not demonstrate any clinically significant difference between the diazepam and placebo-treated groups (Table 3). In addition, these values did not differ among the four specified times that the blood pressure readings were obtained. Preoperative readings in these young children were similar to those values following administration of the sedative agent, the injection of local anesthetic, and prior to patient dismissal from the restorative appointment.

**TABLE 3.** Blood Pressure and Pulse of Children Before, During, and After Dental Procedures in Placebo and Diazepam Premedicated Groups

| | Preoperative ($\bar{X}\pm SD$) | Postsedation ($\bar{X}\pm SD$) | Postanesthetic ($\bar{X}\pm SD$) | Postoperative ($\bar{X}\pm SD$) |
|---|---|---|---|---|
| Blood pressure [a] | | | | |
| Placebo (n=12) | 83±4 / 52±4 | 83±4 / 52±4 | 84±3 / 53±4 | 83±4 / 53±4 |
| Diazepam (n=12) | 83±3 / 51±5 | 85±4 / 51±5 | 85±3 / 52±6 | 84±3 / 51±5 |
| Arterial pulse (rate/min) | | | | |
| Placebo (n=12) | 101±9 | 99±9 | 101±9 | 102±7 |
| Diazepam (n=12) | 101±10 | 98±12 | 100±12 | 99±9 |

[a]Systolic/diastolic in mmHg.

Arterial pulse rates were recorded immediately following the blood pressure measurement. There was no significant difference between the diazepam and placebo-treated groups for pulse rates (Table 3). In addition, no significant difference was detected over time when compared to preoperative pulse rates.

## Discussion

Rectally administered diazepam resulted in a measurable sedative effect on the pediatric dental patient without a clinically detectable effect on the cardiovascular system. Most of the young children were able to tolerate the single operative procedure with an increased level of cooperation as measured by the kinesics/vocalization instrument.[7] Interfering behavioral responses by the children which impede the progress and safety of dental treatment were decreased when diazepam had been administered. In contrast, no differences in noninterfering movements by the children were observed during the treatment appointments. These findings aided in evaluating the level of sedation attained during the restorative procedure, since the young patients were able to engage in an acceptable range of bodily movements. All dental treatment could be successfully completed without physical restraints for the 12 children during the diazepam appointment. In contrast, restraint was utilized at various times during the restorative procedure on 10 of the children during the placebo appointments. Following the local anesthetic injection, further treatment was aborted for 2 of the children because their behavior could not be safely controlled under the conditions of this investigation.

The rectal administration of 0.6 mg/kg of diazepam in solution provided adequate sedation in these healthy children for single dental procedures without lowering the patients' responsiveness or alertness to an unsafe degree. This sedative effect was observed without causing clinically significant changes in blood pressure and pulse rate when compared to a placebo. In addition, concurrent administration of a local anesthetic with epinephrine did not significantly influence the cardiovascular measurements in these healthy young children. In contrast, other investigators[8-10] have reported that the greatest amount of uncooperative behavior occurred during the injection of the local anesthetic with a subsequent rise in blood pressure and pulse. In this study, approximately 7 min lapsed following the local anesthetic administration, which would have allowed the pulse to return to its normal baseline level. In addition, these young children demonstrated the most uncooperative behavior during the initial placement of the rubber dam and at the beginning of the cavity preparation and not during the injection period.

The side effects observed in this study, during the diazepam treatment appointment, were similar to those described by other investigators when sedative dosages had been administered to the pediatric population.[1-4] The majority of the children experienced hypotonicity, mild ataxia, and drowsiness. During the restorative appointment, muscle relaxation and drowsiness contributed to a more favorable working environment. Although no adverse effects were observed during the diazepam appointment, the possibility of a child developing respiratory depression does exist due to the rapid absorption rate of this drug rectally.[1-3] However, to date, no cases of respiratory depression due to rectally dispensed diazepam have been reported when sedatives doses have been administered.

These findings are in general agreement with studies of diazepam in a rectal solution as a sedative in pediatric patients prior to surgical procedures performed under general anesthesia[11-13] and for routine dental treatment.[1] Rectal diazepam is advantageous due to its pharmacologic similarity to an intravenous injection but without the introduction of an aversive stimulus (i.e., venipuncture). Lundgren and co-workers[1] obtained sufficient sedation to successfully complete treatment for all but one of 33 pediatric dental patients. Sedative results were less predictable, however, when rectal diazepam was administered as a preanesthetic medication.[13] Although high serum drug levels were obtained, Ahn recommended that diazepam be given in combination with analgesics for a more comfortable postoperative surgical recovery.[13] When rectal diazepam was administered as a sedative premedication to children in these studies in dosages ranging from 0.4 mg/kg to 0.75 mg/kg, no adverse effects were observed.[1,11-13] Thus, the present study and the findings of Lundgren and co-workers[1] indicate that rectally administered diazepam in a dose of 0.6 mg/kg results in a measurable improvement in the behavior of the uncooperative pediatric dental patient. These data and the work of other investigators [11-15] indicate that rectally administered diazepam is relatively free of adverse effects. This relationship of improved efficacy, without a measurable increase in adverse effects, suggests that rectally administered diazepam represents a rational alternative to pharmacologic management with drugs, such as narcotics, which depress the respiration of a young child while producing therapeutic effects.

## References


1. Lundgren S, Ekman A, Blomback U: Rectal administration of diazepam in solution. A clinical study on sedation in paediatric dentistry. Swed Dent J 2:161-166, 1978.
2. Dulac O, Aicardi J, Rey E, Olive G: Blood levels of diazepam after single rectal administration in infants and children. J Pediatr 93:1039-1041, 1978.
3. Agurell S, Berlin A, Ferngren H, Hellstrom B: Plasma levels of diazepam after parenteral and rectal administration in children. Epilepsia 16:277-283, 1975.
4. Knudsen FO: Plasma diazepam in infants after rectal administration in solution and by suppository. Acta Paediatr Scand 66:563-567, 1977.

5. Lundgren S and Rosenquist JB: Comparison of sedation, amnesia, and patient comfort produced by intravenous and rectal diazepam. J Oral Maxillofac Surg 42:646-650, 1984.
6. Frankl S, Shiere FR, Fogels HR: Should the parent remain with the child in the dental operatory? J Dent Child 29:150-163, 1962.
7. Nowak AJ, Smith RC, Kerber PE: Development and testing of an instrument to measure patient kinesics. J Dent Res 58(A): 323, 1979.
8. Venham L and Quatrocelli S: The young child's response to repeated dental procedures. J Dent Res 56:734-738, 1977.
9. Howitt JW and Stricker G: Sequential changes in response to dental procedures. J Dent Res 49:1074-1077, 1970.
10. Meyers DR. Kramer WS, Sullivan RE: A study of the heart action of the child dental patient. J Dent Child 39:99-106, 1972.
11. Blom H, Schmidt JF, Rytlander M: Rectal diazepam compared to intramuscular pethidine/promethazine/chlorpromazine with regard to gastric contents in paediatric anaesthesia. Acta Anaesthesiol Scand 28:652-653, 1984.
12. Mattila MA, Ruoppi MK, Ahlstrom-Bengs E, Larni HM, Pekkola PO: Diazepam in rectal solution as premedication in children, with special reference to serum concentrations. Br J Anaesth 53:1269-1272, 1981.
13. Ahn NC, Andersen GW, Thomsen A, Valentin N: Preanaesthetic medication with rectal diazepam in children. Acta Anaesth Scand 25:158-160, 1981.
14. Meberg A, Langslet A, Bredesen JE, Lunde PK:Plasma concentration of diazepam and N-desmethyldiazepam in children after a single rectal or intramuscular dose of diazepam. Eur J Clin Pharmacol 14:273-276, 1978.
15. Langslet A, Meberg J, Bredesen JE, Lunde PK: Plasma concentration of diazepam and N/desmethyldiazepam in newborn infants after intravenous, intramuscular, rectal and oral administration. Acta Paediatr Scand 67:699-704, 1978.