Assessment of a low dose of IV midazolam used orally for conscious sedation in pediatric dentistry

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ABSTRACT

Background and the purpose of the study: Midazolam is preferably used in pediatric dentistry for quick onset of action and recovery. The aim of this prospective, observer-blind and placebo-controlled study was to assess the efficacy of a low dose of oral midazolam in modification of the behavior of young pediatric dental patients.

Methods: Forty children aged 3 to 5 years who displayed ratings 1 or 2 on the Frankl Scale and were healthy by the American Society of Anesthesiologists-I status were randomly divided into two experimental and control groups of 20 each. All children required pulpotomy and restoration of D and E teeth and received either 0.25mg/kg of a 15mg/3ml IV midazolam mixed in black cherry syrup or the syrup alone. Subjects were continuously observed and monitored with pulse oximetry. Houpt's Behavioral Ratings was used to determine the overall behavior, the degree of crying and movement during treatment. Mann-Whitney U test was used for statistical analysis.

Results and major conclusion: Patients who received 0.25mg/kg of the prepared oral midazolam significantly behaved better during treatment than the placebo controls ($P<0.05$). In comparison with the placebo group, reduced movement and crying were observed in the midazolam group ($P<0.05$). No adverse effects were observed and treatments were completed successfully. A low dose of 0.25mg/kg of a 15mg/3ml IV midazolam mixed in black cherry syrup was found to be effective in conscious sedation of young pediatric dental patients.

Keywords: Conscious sedation, Oral midazolam, Clinical efficacy.

INTRODUCTION

While sedation can be used to relieve anxiety about dental treatment; unfortunately it is difficult to determine from published research which agents, dosages and techniques are helpful (1). Pediatric dentists are continuously looking for better ways to sedate patients safely and effectively (2). Conscious sedation, an anxiety control technique for pediatric patient in dental office, has been advocated by the American Academy of Pediatric Dentistry (AAPD) (3-5). This technique is usually employed for the management of extremely anxious pre-school dental patients (6,7). Midazolam has a wide toxic/therapeutic ratio and margin of safety and is routinely used in pediatric dentistry for short procedures because of its fast onset of action, quick recovery time, and reported amnesic effects (8,9). The most serious adverse events associated with the use of midazolam in the pediatric population include hypoventilation, decreased oxygen saturation, a dose-related risk of apnea, laryngospasm and hypotension (10-12).

Administered doses for oral midazolam, vary among the world's dentists. A range of 0.2-1.0mg/kg of the body weight has been repeatedly reported for pediatric dental treatment (13-17).

Previous studies have used syrups to disguise bitter taste of IV midazolam, but its bioavailability is not known (18). In the present study, the clinical efficacy of a tasty formulation containing 0.25 mg/kg midazolam was investigated.

MATERIAL AND METHODS

The research protocol was reviewed and approved by the Ethics Committee of the School of Dental Medicine at Shiraz University of Medical Sciences, Shiraz Iran. The study involved children, aged 3-5 years, who attended the post-

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graduate pediatric clinic. Forty children who could not cooperate sufficiently to permit the required and identical treatment for their D and E teeth, pulpotomy and restoration were included in this study. All children were rated 1 or 2 on the Frankl Behavioral Rating Scale as negative or definitely negative (19). Fifteen (75%) of children were in Frankl rating 2 (negative) and five (25%) were in Frankl rating 1 (definitely negative) for both groups. Mean age was 3.99±0.38.

Children had no respiratory distress or remarkable (>50%) adenoid hypertrophy. They did not have neurological impairment or contra-indication to midazolam. The risks and possible discomforts as well as the benefits of the procedure were explained to parents. Parental informed consent was also obtained before the study commenced.

Study medication

To prepare a 0.25 mg/kg oral midazolam solution, vials containing 15mg/3ml of midazolam were diluted with 12ml of distilled water. Total dosage for each patient was mixed with 100ml of black cherry beverage for better taste and ease of drinking (20). To use this preparation later, it was kept in the refrigerator in a dark and closed bottle. Placebo was just the same amount of black cherry beverage.

Study design

Parents received comprehensive verbal as well as a written instruction regarding the subsequent appointment, which was scheduled for sedation. The parents were meticulously told not to give their child solid food or milk at least 4-6 hrs before the sedation but they could give the child a glass of clear liquid at least 2 hrs before the commencement of treatment (21). Pre-operative assessment was carried out by the attending anesthetist. Children were weighed in terms of kg and were randomly given medication or placebo in a plastic cup by a dental nurse. All patients willingly drank the beverage (placebo or medication). Medication was already administered by the operator, blind to the drug used. Patients were not restrained in a papoose board. Then, a pulse oximeter sensor was freely attached to a digit on a hand. A pericordial stethoscope was also used to listen for breath sounds. Vital signs were monitored before, and after sedation every 10 minutes as required (22).

Evaluation

The general behavior of the child during treatment was evaluated by a senior investigator who applied separate rating scale for either the overall behavior or the degree of crying and/or movement described by Houpt et al (23,24). Post-operative patient discharge was based on the child's ability to sit unaided, talk and have intact protection reflexes. Parents were also requested to report any adverse effect noted within hrs post-operatively. Houpt Behavioral Rating data were entered in a computer using SPSS version 14. Mann-Whitney U test was used for statistical analysis. Statistical significance was accepted at the level of 0.05.

RESULTS AND DISCUSSION

Ratings of overall behavior are described in Table 1. The mean rank scores which were 1.6±0.75 for placebo and 5.1±0.72 for midazolam verify significant differences ($P<0.05$) between the two groups. Midazolam contribution was lacking in rating 1 to 3 (aborted, poor, and fair) for general behavior (Table 1) which conveys improved behavior could be expected when a low dose of oral midazolam is used as a premedication for young children.

Ratings for the degree of movement are described in Table 2. The mean rank scores, which were 1.5±0.69 for placebo and 3.3±0.47 for midazolam, verify significant differences ($P<0.05$) between the two groups. Midazolam contribution was lacking in rating 1 to 2 (violent and continuous) for movement (Table 2) which accounts for the effectiveness of midazolam with regard to reducing movement during treatment.

Ratings for the degree of crying are described in Table 3. The mean rank scores, which were 1.5± 0.69 for placebo and 3.1±0.72 for midazolam, verify significant differences ($P<0.05$) between the two groups. midazolam contribution is lacking in rating 1 (hysterical crying) in Table 3 which indicates that the premedication could reduce hysterical crying during treatment.

In the midazolam group, none of the patients slept during treatment but remained relaxed or sleepy, which could, meaningly attributed to the low dose of midazolam which was used. This matter would be welcome by pediatric dentists who preferred a sedated but awake patient (15).

Oral midazolam did not induce nausea and vomiting. Onset of action was approximately 25 minutes. Serious adverse effects were not observed during and after treatment. Vital signs were stable and within normal limits. Oxygen saturation remained close to, 100% during procedures. It has been reported that oral midazolam, when used as a premedication, improves the ease of separation from parents and increases the patient's acceptance of events surrounding the procedure (18,25).

It may finally be concluded that orally prepared midazolam as small as 0.25 mg/kg could be an effective and safe premedication for conscious sedation of pediatric dental patients.

Table 1. Rating scale for overall behavior

Overall behavior	Placebo (n)	Midazolam (n)	Score
Aborted-No treatment rendered	11	0	1
Poor-Treatment interrupted, only partially completed	6	0	2
Fair-Treatment interrupted, eventually all completed	3	0	3
Good-Difficult but all treatment performed	0	4	4
Very good-Some limited crying or movement	0	10	5
Excellent-No crying or movement	0	6	6

Distribution of the children in the study according to Houpt rating scale. Mean rank for placebo = 1.6±0.75 and for midazolam = 5.1± 0.72. n = 20 children per each group, P< 0.05, Mann-Whitney U test.

Table 2. Rating scale for movement

Movement	Placebo (n)	Midazolam (n)	Score
Violent, treatment interrupted	12	0	1
Continuous, making treatment difficult	6	0	2
Controllable, not interference with treatment	2	14	3
No crying	0	6	4

Distribution of the children in the study according to Houpt rating scale. Mean rank for placebo = 1.5±0.69 and for midazolam = 3.3± 0.47. n = 20 children per each group, P< 0.05, Mann-Whitney U test.

Table 3. Rating scale for crying

Crying	Placebo (n)	Midazolam (n)	Score
Hysterical crying	12	0	1
Continuous or strong crying	6	4	2
Intermittent or mild crying	2	10	3
No crying	0	6	4

Distribution of the children in the study according to Houpt rating scale. Mean rank for placebo = 1.5±0.69 and for midazolam = 3.1± 0.72. n = 20 children per each group, P< 0.05, Mann-Whitney U test.

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