Effect of Sedation with Midazolam and Time to Discharge among Pediatric Dental Patients

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Objective: *The aim of this study was to examine the recovery time of children who underwent conscious sedation with oral or rectal midazolam.* ***Study design:*** *The medical files in the Department of Pediatric Dentistry of all the children who underwent conscious sedation with midazolam between 3/2013-4/2016 were examined. The total duration of sedation and time to discharge were calculated. Descriptions of the children's behavior before and during sedation were compared.* ***Results:*** *The files of 120 children were retrieved. They included 64 girls, mean (± standard deviation) age 5.7 ±_2.67 years and 56 boys, mean age 4.9 ±1.06 years. The mean weight for the entire cohort was 18.7 ± 5.2 kg. Eighty-one children (67.5%) received oral sedation and 39 (32.5%) received rectal sedation. The mean total duration of sedation was 105 ± 26 min, and the mean time to discharge after treatment was 55:17 ± 22:30 min. A hundred and seven children exhibited positive behavior before undergoing sedation, but the behavior deteriorated during sedation in 36 cases.* ***Conclusion:*** *The time to discharge post-midazolam sedation correlated to the child's age and weight and total amount of administered midazolam. Sedation negatively affected behavior in 43.6% of the cases.*

Key words: *sedation, midazolam, time to recovery, behavior*

INTRODUCTION

The practitioner may need to use pharmacological means to obtain quiescent and cooperative pediatric patients in order to provide them with highest quality dental care [1]. Sedation can be used safely and effectively for patients who are unable to cooperate due to lack of psychological or emotional maturity and/or mental, physical, or medical disability [2] Conscious sedation is defined as a minimally depressed level of consciousness that retains the patient's ability to independently and continuously maintain an airway and respond appropriately to physical stimulation and verbal commands, and that is produced by a pharmacologic or non-pharmacologic method or a combination thereof [3].

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Midazolam is the most lipid-soluble member of the benzodiazepine family. The lipophilic nature of midazolam accounts for its rapid absorption and metabolism in the gastrointestinal tract as well as its efficient entry into brain tissues. This property produces rapid onset of effect and recovery [4]. Midazolam is potentially an ideal sedative agent for pediatric dentistry because it can be administered orally and because it has anxiolytic and anterograde amnesic effects [5]. Rectal administration was found to have a faster onset of sedative action than oral administration due to its more rapid absorption [6].

When conscious sedation is administered to a dental outpatient, it is very important to facilitate his/her safe discharge home. Therefore, after the dental treatment is completed, the patient must be allowed to take the time necessary to recover to normal fitness, thereby delaying the time to discharge. Recovery must be complete, with absolutely no doubt in the mind of the doctor that the patient is able to function normally. This is the disadvantage of sedation for outpatient dental surgery [7]. According to the American Academy of Pediatric Dentistry, the criteria for discharging a child after a sedation should include: satisfactory and stable cardiovascular function and airway patency, being easily arousable, intact protective reflexes, ability to talk (if age appropriate), ability to sit up unaided (if age appropriate), and an adequate state of hydration. For a very young or handicapped child incapable of the usually expected responses, the pre-sedation level of responsiveness or a level as close as possible to the normal level for that child should be achieved [8].

The effectiveness of oral sedation in the pediatric patient is dependent upon age, body weight, level of anxiety, temperament, and the time of the day the sedation is administered [3]. The time to discharge following sedation with midazolam was found to vary

from 85-103 min, and to be related to its dosage [9], but there is a paucity of conclusive information about appropriate discharge time in the pediatric dental literature. The purpose of this study was to examine the recovery time of children who went under conscious oral/rectal sedation by means of midazolam as it relates to type of administration, age, and weight.

MATERIALS AND METHOD

This study was performed in the Department of Pediatric Dentistry of Tel Aviv University and approved by the ethical committee of the university. Data were retrieved from the medical files of children who had undergone conscious sedation for dental treatment by post-graduates residents from 3/2013-4/2016. Inclusion criteria were healthy children (ASA I/II), aged 2.5-12.5 years, and sedated by midazolam (with or without nitrous oxide) administered orally or rectally. Cases for which data were incomplete were excluded from the study.

All the children were admitted in the morning. They received 0.5 mg/kg midazolam, and the exact hour of the drug administration, the beginning and end of treatment, and the time of discharge home were recorded. The total duration of sedation, the duration of treatment, the time interval between drug administration and the initiation of treatment, and the interval between the end of treatment until the time to discharge home were calculated and recorded.

Behavior was estimated by the physician at the time of the drug administration and during sedation. It was rated as "excellent" = calm, relaxed and cooperative, good = mild resistance and slight agitation, and "bad" = agitated, very restless, and crying.

Alertness was recorded before and at the end of the treatment. It was graded on a scale from 1 to 4: 1 = asleep with eyes shut, does not wake up to physical stimulation; 2 = asleep with eyes shut, responds to verbal instructions; 3 = crying and/or incoherent; 4 = wide awake.

Sedation effectiveness was recorded at the end of the treatment on a scale from 1 to 4: (1 = ineffective: the child was uncooperative, moved in the chair and/or kept crying; 2 = effective: the child was cooperative but moved around in the chair and/or some crying; 3 = very effective: the child was fully cooperative; 4 = sedated too deeply). The side effects of sedation were noted at the end of the sedation as follows: 1 = severe nausea and/or vomiting; 2 = headache; 3 = dizziness; 4 = dyspnea; 5 = other.

Treatment types were divided into 5 categories and ranked by complexity: 1 = restorations; 2 = stainless steel crowns; 3 = pulp treatments (pulpotomy and pulpectomy); 4 = extractions; 5 = failed treatment defined as incomplete treatment due to the patient's lack of cooperation. When several treatments were performed, the most complex was considered.

Statistical analyses

Data analyses were performed using SPSS 15.0 software (SPSS Inc., Chicago. IL., USA). Two-tailed independent t-tests, Pearson correlation coefficient and Spearman's rank correlation coefficient were used to look for associations between predictor variables (demographic information, sedation regimen, root of drug administration, behavior characteristics, level of alertness) and outcome variables (duration of sedation, time of discharge). The significance level was set at $P<.05$ for all tests.

RESULTS

The study included 120 children that were treated with conscious sedation with midazolam and met the inclusion criteria. There were 64 girls (53%) with a mean age of 5.7 ± 2.67 years and 56 boys (47%) with a mean age of 4.9 ±1.06 years. The mean weight of the entire cohort was 18.7 ±5.2 kg. The majority of the children were ASA I (94.5%), and the rest were ASA II.

Table 1 summarizes the treatments and type of sedations. Most of the 120 cases (n = 107, 89.2%) were treated with midazolam and nitrous oxide and only 13 were treated with midazolam alone. Since there was no statistical significant difference between the results of these two groups in the sedation time frames, they were combined into one group. Most of the children (81, 67.5%) received oral sedation and the rest (39, 32.5%) received rectal sedation.

Table 1. Treatments and type of midazolam sedation

		Number (%)
Sedation Type	With nitrous oxide	107 (89.2)
	Without nitrous oxide	13 (10.8)
Administration	Oral	81 (67.5)
	Rectal	39 (32.5)
Treatment Type	Restoration	43 (35.8)
	Stainless steel crowns	16 (13.3)
	Pulp treatment	29 (24.2)
	Extraction	23 (19.2)
	Failed	9 (7.5)

The most frequent treatment consisted of restorations (n = 43, 35.8%), followed by 29 (24.2%) pulp treatments, 23 (19.2%) extractions, and 16 (13.3%) stainless steel crowns. Only 9 patients (7.5%) were considered as "failed cases" in whom the treatment could not be completed.

Thirteen children (10.8%) exhibited side effects: 7 suffered from severe nausea and/or vomiting, 5 suffered from headaches and one child suffered from an unspecified side effect.

Most of the children were awake and calm before the drug administration (86.4%), while the rest were categorized as "crying and/or incoherent". During the sedation, 60% were categorized as "crying and/or incoherent" and the rest as "awake and calm". Almost one-half of the sedations were graded as "effective", 29% as "very effective" and 21% as "ineffective".

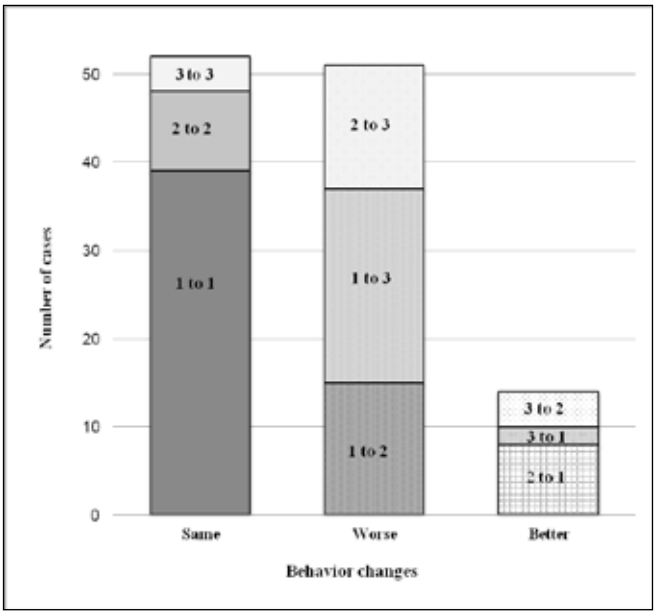
Table 2 summarizes the time frames of the sedations. All children were admitted during the morning. The mean time of midazolam administration was 09:50 ± 46, the mean time until the dental treatment commenced was 14 ± 5 min, the mean total duration of treatment was 35 ± 18.5 min, and the mean time to discharge home was 55:17 ± 22:30 min. The mean total duration of sedation was 105 ± 26 min.

Table 2. Time frames of sedation by oral/rectal midazolam

Time of administration	09:50 ± 46
Time from drug administration until onset of treatment (min)	14 ± 5.5
Treatment duration (min)	35 ± 18.5
Time to discharge after treatment (min)	55:17 ± 22:30
Total duration of sedation (min)	105 ± 26

Evaluation of the child's behavior and cooperation before and during treatment revealed that most of the children were categorized as "excellent" (65%) before drug administration, 26.5% as "good", and the rest as "bad". During sedation, the behavior and cooperation of 41.6% of the children were scored as "excellent", 34.2% as "bad" and only 24.2% as "good". Figure 1 describes the changes in the children's behavior and cooperation before and during treatment: 52 stayed on the same level, 51 exhibited deterioration, and only 14 improved. About one-half of the patients who exhibited "excellent" behavior before treatment exhibited deterioration and the other half remained at the same level. Among the patients who exhibited "good" behavior, 43% deteriorated and only 25% improved. Six of the patients who exhibited "bad" behavior improved and 4 remained the same.

Figure 1: The changes in the patient's behavior from the time of the drug administration throughout sedation (1. Excellent behavior; 2. Good behavior; 3. Bad behavior).



There was a significant difference in the duration of sedation between the children that were given the sedation orally to those who were sedated rectally. The total sedation time was shorter with rectal midazolam compared to the oral route (94 ± 26 vs. 111 ± 25 min respectively, P = 0.0006, t-test). The time to discharge was also sorter when the child was given the sedation rectally (49 ± 22 vs. 59 ± 22 min, respectively, P = 0.037, t-test). The total duration of sedation correlated significantly with the child's age, weight, and the total amount of midazolam given (r=0.368, P=0) (r=0.333, P=0) (r=0.275, P=0.02) (Pearson correlation).

The total duration of sedation correlated significantly with the level of alertness during the treatment (r=-0.313, P=0). Specifically, the patients who were at a higher alertness level during treatment had a shorter duration of sedation and were discharged home earlier (Spearman's rho correlation). There was also a significant correlation between the time to discharge home and the total amount of midazolam that was administered (r=0.204, P=0.025) (Pearson correlation).

No correlation was found between the duration of sedation or time to discharge home and the child's gender, the time of day of drug administration (i.e. early or late in the morning), the type of dental treatment, the total amount of local anesthesia or the child's behavior before and during the sedation. There was a significant correlation between sedation effectiveness and the child's behavior during the sedation (r=-0.772, P=0): when the dentist categorized the child as being well behaved, the sedation was also noted as having been effective. There was also a significant correlation between the child's behavior at the time of the drug administration and his/her behavior during the sedation (r=0.230, P=0.012), which indicates similar behavior before and during treatment (Spearman's rho correlation)

In order to examine the influence of the child's age on the measured variables, the children were divided into one group ≤4 years of age and another group >4 years of age. The younger group included 41 children (mean age 3.5 ± 0.5 years), and the older group included 79 children (mean age 6.2 ± 2.02 years). There was a significant correlation between the older patients and the total duration of sedation (r=0.375, P=0.001), while a negative correlation (non-significant) correlation was found between the younger group and the total duration of sedation (r=-0.157, P=0.328) (Pearson correlation). The correlation between the child's behavior at the time of the drug administration and sedation effectiveness was significant only for the older patients (r=-0.250, P=0.028) (Spearman's rho correlation).

DISCUSSION

Both orally and rectally administered midazolam have a fast absorption rate and are rapidly excreted, with a half-life of only about 2 hours [10]. The purpose of the current study was to examine the effect of selected variables on the duration of sedation and the time to discharge home among children who underwent conscious oral sedation with midazolam. The mean duration of total sedation was 105 ± 26 min, and the mean time from the end of treatment until discharge home was 55:17 ± 22:30 min. Somri *et al* found that the discharge time varied from 85 min to 103 min, depending upon the doses of midazolam (0.5-1 mg/kg), and that the dosage significantly influenced the discharge time [9]. In the current study, there was a significant correlation between the total duration of sedation and the time to discharge to the total amount of midazolam that had been administered. The total duration of sedation also correlated significantly with the child's age and weight. In addition, the total duration of sedation was longer for children older than 4 years. As such, it should be expected that sedation with midazolam given at the same doses to children younger and older than 4 years of age would result in a longer recovery time for the older children.

A comparison of the total duration of sedation and the time to discharge according to the route of drug administration revealed that midazolam given rectally led to a shorter period of sedation than midazolam given orally. This finding is in agreement with that of Tolksdorf and Eick who concluded that rectally administered midazolam had the fastest onset of sedative action due to a more rapid absorption of the drug [6].

No correlation was found between the duration of the sedation or the time to discharge and the child's gender, the time of day of drug administration, the type of dental treatment, the amount of anesthesia or to the child's behavior before and during the sedation.

Before the treatment started, over 91% of the children exhibited "excellent" or "good" behavior, which deteriorated in 43.6% of the cases, stayed the same in 44.4% and improved in only 12%. Similar findings were reported by Primosch and Bender, who found that a significant percentage of the children who received midazolam for conscious sedation displayed positive behaviors preoperatively had shown deterioration in their intraoperative behavior [11].

CONCLUSIONS

The results of this study were that time to discharge home was correlated to the age and weight of the child as well as to the total amount of midazolam that was administered. Although most of the children exhibited good behavior before receiving sedation with midazolam, the behavior deteriorated in 43.6% of the cases.

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