Oxygen Saturation and Pulse Rate Change in Children during Sedation with Oral Midazolam and Nitrous Oxide

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Objective: *We aimed to examine if changes in oxygen saturation and pulse rate of pediatric patients during conscious sedation with midazolam and nitrous oxide are associated with child's behavior, midazolam dose, the type and duration of the treatment and demographic parameters.* ***Study Design:*** *This study was a retrospective chart review of consecutive pediatric patients, aged 2.5-12.5 years, who had undergone conscious sedation for dental treatment with oral midazolam (with or without nitrous oxide) between January 2011 and September 2015 at the Department of Pediatric Dentistry of Tel Aviv University. Oral midazolam was administered according to the patients' weight, either at 0.4 mg/kg, 0.5 mg/kg or at a maximum dose of 10 mg. In all cases pulse rate and oxygen saturation were monitored every 15 minutes during treatment,* ***Results:*** *147 sedation sessions (82 of females and 65 of males) were included in the study. Sedation was successful in 80% of cases. Children with poor behavior scores had statistically significant different mean saturation levels, albeit within normal range, during the treatment ($p<0.012$) as well as a clinically significant higher mean pulse rate ($p=0.0001$), compared to children with good or excellent behavior scores. Treatment duration, the type of dental procedure or the patients' weight were not correlated with the change in oxygen saturation or pulse rate during the treatment.* ***Conclusions:*** *Poor behavior of pediatric patients does not affect oxygen saturation, but it increases the pulse rate of children under sedation with midazolam and nitrous oxide.*

Key words: Sedation, Midazolam, Nitrous Oxide

INTRODUCTION

Sedation may be used safely and effectively in pediatric patients who are unable to cooperate due to lack of psychological or emotional maturity and/or mental, physical, or medical disability.[1, 2] In pediatric patients the aims of sedation are to decrease fear and pain perception during treatment, to facilitate pain management, and to prevent development of fear and anxiety in future dental treatments. Additionally, the complexity of the treatment (i.e. the number of planned treatments) should also be taken into account when considering sedation.[3]

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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.[4] Oral sedation is considered the oldest, easiest and most cost-effective method of administering sedative drugs to pediatric patients. One of the most common pharmacologic agents used for sedation in dentistry is midazolam.[1] Midazolam is a benzodiazepine sedative capable of inducing sleep while acting as an effective anxiolytic, muscle relaxant, and amnesic agent. Its lipophilic nature in physiologic pH accounts for its rapid absorption and metabolism in the gastrointestinal tract as well as its efficient entry into brain tissue producing rapid onset of action.[5] The rapid redistribution of midazolam, as well as high liver clearance, accounts for its relatively short hypnotic and hemodynamic effects.[6]

Midazolam has minimal effects on the cardiovascular system and on respiratory system dynamics in patients with American society of Anesthesiology (ASA) classification I or II.[7] The greatest threat to the safety of a sedated patient is airway compromise and/or respiratory arrest, with hypoxia generally manifesting as the first symptom in sedation-related morbidity and mortality [8]; therefore, appropriate monitoring of the patient's respiratory and physiologic functions is mandatory to rapidly identify respiratory compromise. Normal oxygen saturation in children ranges from 97 to 100%.The heart rate

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of infants and children is higher than that of adults, decreasing with age and ranging from 120 ± 20 beats/minute (bpm) in 6 month-old babies to 70 ± 17 bpm in 12 year-olds.[8] Pulse oximetry remains the most widely used monitor during procedural sedation.

We aimed to examine if changes in oxygen saturation and pulse rate of pediatric patients during conscious sedation with midazolam and nitrous oxide are associated with demographic parameters, child's behavior, midazolam dose, and the type and duration of the treatment.

MATERIALS AND METHODS

This study was a retrospective chart review of consecutive pediatric patients, aged 2.5-12.5 years, who had undergone conscious sedation for dental treatment with oral midazolam (with or without nitrous oxide) between January 2011 and September 2015 at the Department of Pediatric Dentistry of Tel Aviv University. The study was approved by Tel Aviv University's Ethics Committee.

Records of patients were included in the analysis if the patient was classified as healthy (ASA I or II), and if the following parameters were recorded on the chart: behavior and alertness before and during the treatment, oxygen saturation and pulse rate every 15 minutes from the time of midazolam administration until the end of treatment. Patients who had ASA III and above, had received rectal midazolam or another drug, or received general anesthesia during the treatment were excluded from the analysis. All children were admitted in the morning. All dental treatments were carried out by post-graduate residents assisted by a trained dental sedation assistant. If a patient underwent a series of sedation sessions for operative procedures, only the first session was included in the study. Oral midazolam (Midolam, Rafa Laboratories Ltd., Jerusalem, Israel) was administered 15 minutes before the dental procedure according to the patients' weight (0.4 mg/kg, 0.5 mg/kg) or at a maximum dose of 10 mg. Sedation also included nitrous oxide and oxygen (30-40% N_2O). Post-graduate residents administrated the medication, recorded the patients' weight before the first appointment and monitored pulse rate and oxygen saturation by a pulse oximeter (Smiths Medical ASD Inc., St. Paul, MN, USA) that was put on one of the patient's fingers every 15 minutes during the treatment.

Behavior was estimated by the operating dentist at the time of drug administration and during sedation. It was rated on a scale of 1 to 3, where 1 = excellent: calm, relaxed and cooperative, 2 = good: mild resistance and slight agitation, and 3 = poor: agitated, very restless, and crying. At the end of sedation, each dentist graded the effectiveness of sedation on a scale from 1 to 3 (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). Sleepiness was recorded before and at the end of the treatment. It was graded on a scale of 1 to 4, where 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. The side effects of sedation were noted at the end of the sedation as follows: 1 = 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.

Data analyses were performed using SPSS 15.0 software (SPSS Inc., Chicago IL, USA). All data were analyzed using descriptive statistics. Analysis of variance (ANOVA) with repeated measures and logistic regression were used to look for an association between predictor variables (demographic information, behavior characteristics, level of alertness) and outcome variables (pulse rate and oxygen saturation). The significance level was set at $P<0.05$ for all tests.

RESULTS

One-hundred and forty-seven sedation sessions of children (82 females and 65 males) who underwent conscious sedation with oral midazolam were included in the study. Patient demographics are summarized in Table 1. The majority of children (138/147, 93.9%) were healthy (ASA I); 9 children (6.1%) were classified ASA II. Before the treatment, 59% of children (87 of 147) exhibited good to excellent behavior and most (89.1%) were completely awake (Table 2). During treatment, 33.3% of children remained completely awake and 57.8% were drowsy or crying. The mean duration of treatment was 37 ± 21 minutes (range: 10 minutes to 75 minutes). The majority of patients (95.2%) were administered lidocaine as the local anesthetic agent. None of the patients had hypoxia. Nine patients (6.1%) had adverse effects that included dizziness (5 patients, 3.4%), nausea/vomiting (3 patients, 2%), and headache (1 patient, 0.7%). Sedation was considered effective in 80% of sessions.

Effect on oxygen saturation levels

Mean oxygen saturation levels remained stable, at approximately 98%, for the duration of the treatment and no difference in mean saturation levels was observed between males and females or between children under 6 years of age and children above 6 years of age.

The mean oxygen saturation levels of children with a poor behavior score prior to treatment, increased from a baseline level of 97.78 ± 0.97% to 98.33 ± 0.87% during the treatment then decreased to below baseline levels (97.33 ± 1.32%, Figure 1). Compared to children with good or excellent behavior scores, children with poor behavior scores had statistically significant different mean saturation levels during the treatment ($p<0.012$).

Logistic regression analysis adjusted for demographic variables (age, age percentile, gender) behavior and baseline oxygen saturation levels showed that both baseline oxygen saturation levels and poor behavior were significantly associated with oxygen saturation levels during treatment ($p=0.037$ and $p=0.001$, respectively).

Effect on pulse rate

In children over 6 years of age, the mean pulse rate remained similar to baseline rates (90-91bpm) for the duration of the treatment, while in children under 6 years of age the mean pulse rate increased during the treatment from baseline levels of 95.06 ± 15.01 bpm to 105.76 ± 16.94 bpm after 75 minutes (Figure 2). The mean pulse rate during the treatment was statistically significantly higher in the younger age group compared to the older age group ($p<0.001$).

Children with a poor behavior score had statistically and clinically significant higher mean pulse rate of approximately 10 units both at baseline and during the treatment compared to children with good or excellent behavior scores. (Figure 3, $p=0.0001$).

Table 1: Demographic and baseline parameters

Parameter	Patients N=147
Gender	
Males	82 (55.8%)
Females	65 (44.2%)
Age (years)	6.1 ± 2.6
Weight (kg)	20.2 ± 6.9
Health assessment	
ASA I	138 (93.9%)
ASA II	9 (6.1%)
Type of sedation	
Midazolam	135 (91.8%)
Midazolam and Nitrous oxide	12 (8.2%)
Midazolam dose	
0.4 mg/kg	84 (57.1%)
0.5 mg/kg	21 (14.3%)
10 mg	42 (28.6%)
Mean midazolam dose (mg)	7.83 ± 1.95
Type of treatment	
Restoration	50 (34.0%)
Stainless steel crown	23 (15.6%)
Pulpotomy/pulpectomy	31 (21.1%)
Root extraction	34 (23.1%)
Aborted	9 (6.1%)
Treatment duration (minutes)	37 ± 21

Continuous variables are displayed as mean ± standard deviation. Categorical values are displayed as N (%).

Table 2: Assessment of patient sleepiness prior to and during dental treatment

	Number of patients (%)		
Parameter	Before treatment	During treatment	At discharge
Sleepiness			
1	0	3 (2.0%)	0
2	0	10 (6.8%)	0
3	15 (10.2%)	85 (57.8%)	5 (3.4%)
4	131 (89.1%)	49 (33.3%)	108 (73.5%)

Sleepiness scale: 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.

Logistic regression analysis adjusted for demographic variables (age, age percentile, gender), behavior and baseline pulse rate showed that poor behavior during the treatment, the patient's age and pulse rate before the treatment were all significantly associated with the change in pulse rate during the treatment ($p<0.001$).

Treatment duration, the type of dental procedure or the patients' weight were not correlated with the change in oxygen saturation or pulse rate during the treatment.

Figure 1: Oxygen saturation during treatment by behavior of patients before treatment

The patients' oxygen saturation levels before treatment and 15 and 75 minutes during sedation with oral midazolam was evaluated according to their behavior on a scale of 1 to 3 where 1 = excellent: calm, relaxed and cooperative, 2 = good: mild resistance and slight agitation, and 3 = poor: agitated, very restless, and crying. A significant difference was observed between mean oxygen saturation levels in the poor behavior group and mean oxygen saturation levels in the excellent and good behavior groups (p=0.012).

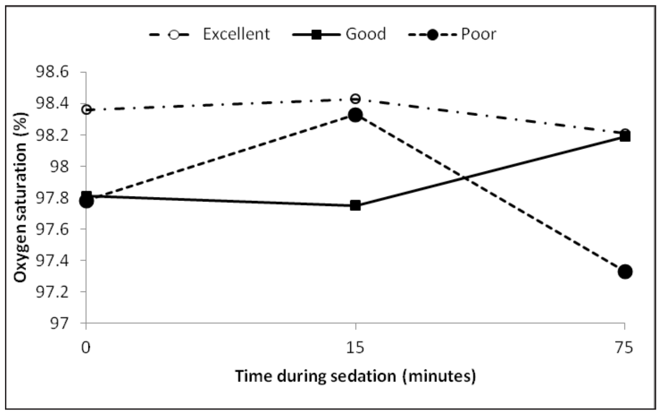


Figure 2: Analysis of pulse rate during sedation by age

The patients' pulse rate before treatment and 15 and 75 minutes during sedation with oral midazolam was evaluated according to the patients' age: below 6 years of age and above 6 years of age. Mean pulse rates in the younger age group were significantly higher than those in the older age group (p<0.0001).

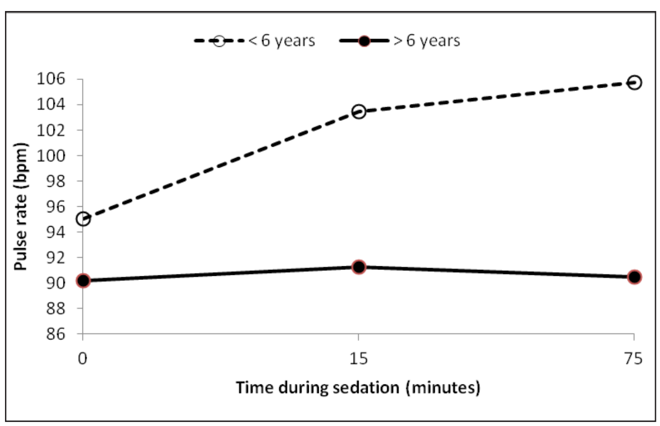
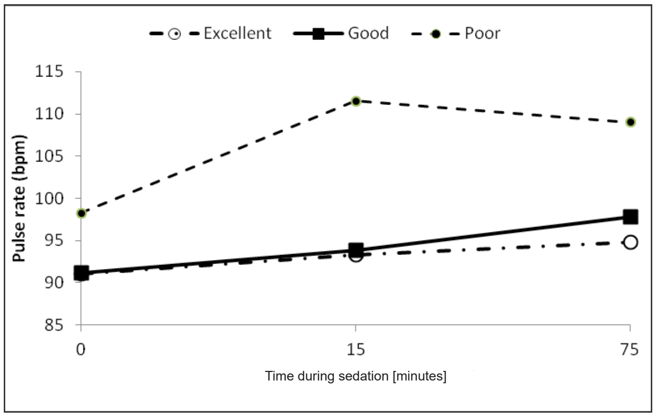


Figure 3: Pulse rate during treatment related to behavior

The patients' pulse rate before treatment and 15 and 75 minutes after sedation with oral midazolam was evaluated according to their behavior on a scale of 1 to 3 where 1 = excellent: calm, relaxed and cooperative, 2 = good: mild resistance and slight agitation, and 3 = poor: agitated, very restless, and crying. A significant difference was observed between mean pulse rates in the poor behavior group and mean pulse rates in the excellent and good behavior groups (p=0.0001).



DISCUSSION

The major finding of the present study was that poor behavior during conscious sedation with oral midazolam and nitrous oxide decreases the pediatric patient's oxygen saturation levels and increases his/her pulse rate compared to children with excellent or good behavior. Nonetheless, oxygen saturation levels remained within the normal range (97-100%), while pulse rate was clinically significantly higher. Chowdhury *et al* evaluated the success of sedation with 0.65 mg/kg oral midazolam plus nitrous oxide 50% in a younger pediatric population aged 2-5years. Similar to our study, the physiological variables were within the normal range and no prolonged periods of oxygen saturation were observed, but higher heart rates, which were consistent with the children's' age were recorded. However, the increased heart rate was consistent with the children's age.[9] The success of sedation in that study was not associated with age, preoperative behavior, or type of dental procedure performed; however the effect of behavior on physiologic parameters was not assessed.

Isik *et al* [10] assessed sedation with oral midazolam at a higher dose than the one used in our study, 0.75 mg/kg, and nitrous oxide in children aged 4 to 8 years. They found that psychosomatic behavior problems and inflexible temperament were associated with failure of oral sedation for dental treatment, but, contrary to our findings, they did not find an association between various behaviors according to the Houpt scale and saturation or pulse rate.[10] Fraone *et al* assessed sedation with oral midazolam 0.5 mg/kg in younger children aged 2 years to 4 years and 10 months but did not find any statistically significant difference in behavior (evaluated by the Ohio State Behavior Rating Scale) across all age groups, nor were there any statistically significant differences in physiological parameters including heart rate, oxygen saturation, systolic and diastolic blood pressure.[11] Similarly, no effect on oxygen saturation and heart rate were observed in children aged 3-9 years who were administered oral midazolam 0.5 mg/kg.[12]

Our finding regarding adverse effects and desaturation were in accordance with the findings reported by Somri *et al* [13] who reported one case of desaturation (defined as SaO2<95%) when using a midazolam dose of 0.5 mg/kg with nitrous oxide. Notably, Somri *et al* reported a case as desaturation only if it lasted for more than 30 seconds, while we recorded desaturation if SaO2<94%t occurred at any time point.

CONCLUSIONS

Poor behavior of pediatric patients does not affect oxygen saturation, but it increases the pulse rate of children under sedation with midazolam and nitrous-oxide.

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