

Nitrous Oxide Sedation and Bispectral Index

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ABSTRACT

Objectives: To determine whether bispectral analysis (BIS) changes during nitrous oxide (N₂O) sedation in anxious children undergoing extraction of primary teeth.

Methods: In this prospective study 45, ASA physical status I children, aged between 7 to 12 years and scheduled for primary teeth extraction under N₂O/O₂ sedation are included. At baseline (T0) and during the sedation procedure (T1-6); BIS levels, Ramsay Sedation Scores (RSS), oxygen saturation (SpO₂), and heart rate (HR) were recorded at one-minute intervals. Forty percent N₂O in O₂ was given by a nasal hood, and N₂O concentration was enhanced to 60% in a two-minute period. Paired measurements of BIS levels with Observer's Assessment of Alertness and Sedation (OAA/S) scores were obtained during sedation procedure.

Results: Since 5 patients refused application of the nasal hood, a total 40 of the original 45 subjects completed the study. Mean age and weight of the children were 9.5 ± 1.4 years and 23.7 ± 9.7 kg, respectively. Nitrous oxide inhalation produced no changes in BIS levels despite a sedation level in OAA/S scores were observed at 40-60% N₂O concentrations.

Conclusions: BIS values do not change during N₂O/O₂ sedation and the BIS monitor is not appropriate to evaluate the depth of sedation provided by N₂O/O₂ during primary teeth extraction in children. (Eur J Dent 2007;1:240-245)

Key Words: Nitrous oxide sedation; Bispectral index; Anxiety; Ramsay sedation scale.

INTRODUCTION

Some children need sedation because of fear or anxiety in pediatric dentistry.¹⁻³ In pediatric dental

practice, for which analgesia is accomplished by local or regional anesthesia, sedation application is considerably different from medical practice.¹⁻⁵ To assess the depth of the sedation, physiological signs such as heart rate, blood pressure, and respiratory rate are important. But physiological signs exhibit large inter-patient variability and are quite dependent on the medications used. Also, they are only indirect expressions of the drugs' effects on the brain and other major systems. The use of sedation scales is the most frequent method of quantifying the sedative effect. Most commonly, subjective clinical scoring methods are used.⁵⁻⁷ The most popular is the Observer's Assessment of Alertness and Sedation (OAA/S) scale (Table 1).⁸⁻¹⁰ It measures the level of alertness in sedated

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subjects based on the assessment of 4 categories: responsiveness, speech, facial expression and ocular appearance. Also, the Ramsay Sedation Scale (RSS)¹¹ (Table 2) is well established for the evaluation of sedation. It is easy and inexpensive to perform. But sedation scales are not objective methods. The bispectral index (BIS) offers a potential alternative to subjective scales when they do not work well or may not be sufficiently sensitive to evaluate sedation level. Bispectral index is a processed electroencephalographic (EEG) parameter, expressed as a numeric value ranging from 0 (isoelectric) to 100 (awake with eyes open) that is used clinically as a measure of hypnosis. It is currently used most commonly intraoperatively to monitor the effects of anesthetic and sedative

agents as a means of judging the depth of sedation or anesthesia.^{12,13} Bispectral index monitoring is suggested to non anesthesiologist in order to avoid too deep sedation.¹⁴ Some studies have shown a significant correlation between BIS and OAA/S scores by using different sedative drugs with N₂O/O₂, but others have shown that N₂O has no effect on BIS in human volunteers when used solely.^{10,13,15,16} The other researchers showed that paradoxical changes might occur at BIS values during induction of anesthesia.^{13,17-19} Although N₂O has been widely used as an anesthetic adjuvant, its effect on EEG activity is poorly understood because it is usually studied in the presence of additional anesthetics, including inhaled anesthetics. Leduc et al²⁰ showed that N₂O/O₂ at peri-MAC partial

Table 1. Observer's Assessment of Alertness/Sedation (OAA/S) Scale.

Responsiveness	Speech	Facial expression	Eyes	Score
Responds readily to name spoken in normal tone	Normal	Normal	Clear, no ptosis	5
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	4
Responds only after name is called loudly or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed and marked ptosis (more than half the eye)	3
Responds only after mild prodding or shaking	Few recognizable words	-	-	2
Does not respond to mild prodding or shaking	-	-	-	1

Table 2. Ramsey Sedation Scale.

Descriptions	Scores
Patient is anxious and agitated or restless, or both	1
Patient is co-operative, oriented, and tranquil	2
Patient responds to commands only	3
Patient exhibits brisk response to light glabellar tap or loud auditory stimulus	4
Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus	5
Patient exhibits no response	6

pressures prevents EEG activation resulting from noxious electrical stimulation in rats. However, Hall et al²¹ found correlation with increasing doses of N₂O from approximately 35 to 70%. But Puri²² reported two cases with paradoxical changes in BIS during N₂O administration.

Previous data regarding the use of BIS during N₂O sedation remain insufficient. The aim of the current study was to assess any BIS changes during N₂O/O₂ sedation in pediatric dentistry.

MATERIALS AND METHODS

This prospective research was performed in Gazi University Faculty of Dentistry. After obtaining Gazi University Faculty of Dentistry Ethic Committee approval and informed parental consent, 45 children having ASA physical status I, aged 7 to 12 years, weighing 21 to 33 kg (Table 1), and scheduled for primary teeth extraction were enrolled into the study. The participant were seen for their initial exam and it was determined that they definitely exhibited “definitely negative” behavior according to the Frankl Scale²³ (Table 3). Exclusion criteria were refusal to have application of nasal hood or insufficient sedation (body movements, complaints, moaning, and crying). Sedation levels were evaluated and graded according to the OAA/S⁴ (Table 1) and RSS⁷ (Table 2) scales.

Sedation procedure

Patients fasted two hours before sedation. No other premedication was given. Before sedation procedure, patients were assessed with RSS and then monitored with pulse oximetry (Datex-Ohmeda TuffSat®) and BIS (Aspect Medical Systems, A-2000 BIS®). A disposable BIS sensor was applied to the patient’s forehead. Sedation was induced in standardized manner for all patients by nasal hood inhalation of 40% N₂O in O₂, and continued with 40-60% N₂O in O₂

(inspired N₂O fraction) with high fresh flow of 5 L min⁻¹. The patient’s heart rate (HR), peripheral oxygen saturation (SpO₂), and BIS measurements were recorded before (T0=initial base values) and during the sedation (T1=third minute after initiation of N₂O inhalation through a nasal hood and, respectively, T2=4th min, T3=5th min, T4=6th min), and recovery period (T5=7th min, T6=8th min) at one minute intervals. Paired measurements of BIS, RSS and OAA/S scores were obtained during the sedation period and recorded at one minute intervals. The investigator who performed the RSS and OAA/S assessments was blinded to the BIS values and N₂O/O₂ concentration. At the end of the extraction, N₂O inhalation was discontinued and 100% O₂ inhalation was performed for two minutes. Nasal hood and monitors were removed when the patient was alert and HR and SpO₂ values were within the normal range. If any complication was observed, it was noted down.

Dental treatment

Topical anesthesia in the form of benzocaine gel 20% was applied to the dried mucosa adjacent to the tooth. Lidocaine 2% with 1:80000 adrenaline was then given in a standardized manner to each quadrant just before acquiring the BIS values (T2=4th min after initiation of N₂O inhalation through a nasal hood). Once analgesia had been achieved, the primary teeth were extracted (T4=6th min after initiation of N₂O/O₂ inhalation through a nasal hood).

Statistical analysis

SPSS version 15.0 for Windows was used for statistical analysis. The time course of the parameters during the T1-6 periods of the BIS, SpO₂ and HR and control sessions (T0) were evaluated using one-way analysis of variance (ANOVA) with repeated measurements and then the post hoc Tamhane test was performed if difference was significant. Using cross tabulation, a chi-square analysis was done between BIS levels and OAA/S scores in all time periods and correlation was calculated with Pearson Correlation Coefficient (r) value (r=0-0.25 weak correlation, 0.251<r<0.500 moderate correlation, 0.501<r<0.750 strong correlation, 0.751<r<1.00 most strong correlation). P<.05 was considered as significant difference.

Table 3. Frankl behavioral scale.

Descriptions	Score
Refusal/Distress	1
Uncooperative/Reluctant	2
Co-operative/Reserved	3
Interested/Enjoyed	4

RESULTS

Five patients who refused to have application of nasal hood were excluded from the study, and finally 40 patients were studied. Demographic properties are presented in Table 4. At baseline (T0) and during the sedation procedure (T1-T6) vital signs, including SpO₂ and HR were recorded. The comparison of time dependent mean values of SpO₂ and HR (T1, T2, T3, T4, T5 and T6 time points between T0 sessions) were similar (P>.05) and statistically not different in normal clinical range.

The comparison of time dependent mean BIS values at T1, T2, T3, T4, T5 and T6 time points between T0 sessions were similar and statistically not different (P>.05). The mean value of BIS was 97.4. Before N₂O/O₂ sedation, patients' RSS were determined as 1 but after the administration of N₂O/O₂, at the T1-6 time points patients' RSS were 2 and OAA/S scores of patients' were 4 or 5. During T1-6 time points all patients (n=40) were relax and not reject the extractions. Although administration of 40–60% N₂O concentration is enough to provide sedation according to the OAA/S scores in 40 children during the study period, no changes were obtained in BIS values. No correlation was found between BIS and the OAA/S scores levels at the T1-6 periods (P=.126,

Table 4. Demographic variables and duration of teeth extraction period.

Variables	
Age (year)	9.5 ± 1.4
Weight (kg)	23.7 ± 2.7
Sex (M/F)	21/19
Extraction period (min)	4.7±1.3

Table 5. Significant HR values during study period.

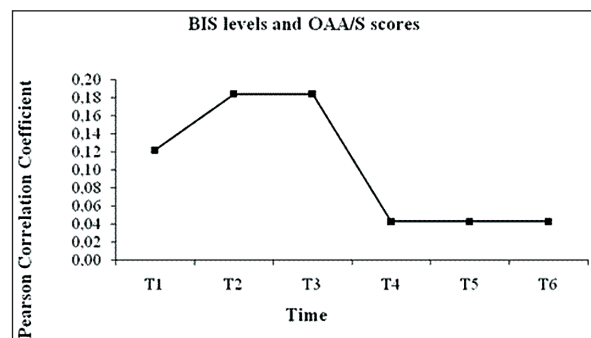
Time	T ₀	T ₁	T ₂	T ₃	T ₄	T ₅	T ₆
T ₀		*	*	*	*		
T ₁	*			*	*	*	*
T ₂	*				*	*	*
T ₃	*	*			*	*	*
T ₄	*	*	*	*			*
T ₅		*	*	*			*
T ₆		*	*	*	*	*	

* : P<.05, indicates significant differences among HR values during study period

r=0.1). Ramsay Sedation Scores and OAA/S correlations cannot be computed because at least one of the variables is constant. Figure 1 shows all the Pearson correlation coefficients between BIS levels and OAA/S scores during the study period. Pearson coefficient values indicate that weak correlation was obtained between BIS levels and OAA/S scores at all time periods (r<0.25). There was no complication except nausea and vomiting at two patients during the recovery period.

DISCUSSION

In this research, children were clinically sedated with 40–60% N₂O/O₂ according to the RSS and OAA/S, but BIS values did not alter or paradoxical changes occur during the sedation procedure. Pediatric patients who are referred to the dental clinics are especially anxious with dental extractions. Administration of N₂O in O₂ is widely used to induce both analgesia and sedation and to improve patient cooperation during dental



Pearson Correlation Coefficient (r) value: r =0-0.25 weak correlation

Figure 1. Correlation legend between Bispectral Index (BIS) levels and Observer's Assessment of Alertness/Sedation (OAA/S) scores.

treatments.^{1,2,24,25} Investigations were recognized that BIS scores were decreased by different sedation or hypnosis techniques.^{6,9,12,26} Sadhasivam et al⁹ researched the validation of BIS for sedation with oral chloral hydrate, in meperidine+promethazine, IV midazolam+fentanyl, and IV pentobarbital+midazolam+fentanyl, and it demonstrates that the BIS scores were significantly correlated with their paired OAA/S scores. Religa et al²⁷ conducted a study on pediatric patients, requiring dental restorations, between 3 to 6 years of age who received oral sedation with chloral hydrate or meperidine or hydroxyzine intraoperatively and N₂O/O₂ was also administered. A significant association was detected between observed patient behaviors during sedation and levels of sedation as measured by BIS. In an earlier study including 2 of 13 volunteers, BIS did not change with inspired N₂O concentrations up to 50%. The authors emphasized the stimulatory changes at lower and higher frequency ranges of EEG, which decreased at low N₂O concentration.¹⁵ Ramesh et al²⁸ suggested that N₂O affects BIS values in patients under isoflurane anesthesia. Park et al¹⁰ reported that N₂O when used for sedation during epidural anesthesia does not have the expected effect on BIS signals. Two research showed that no change in BIS or Cerebral State Index value while the participants breathed 70% N₂O in O₂ although all of them lost consciousness clinically.^{29,30} In their research on 22 healthy volunteers who were sedated by low N₂O, Hall et al²¹ reported that no correlation was found with OAA/S and BIS. But a correlation was found when N₂O concentration was increased from 35% up to 70%. However Puri has reported paradoxical changes in BIS during N₂O administration.²² Previous data regarding the use of BIS during N₂O sedation remain insufficient. Probably, the conflicting results of various studies may be explained by the differential effects of N₂O on EEG when administered at high/low concentrations or alone/in combination with sedative or anesthetics. In this research, the administration of N₂O alone was adequate to perform teeth extraction but no alteration or paradoxical changes were observed at BIS values.

Nitrous oxide sedation is a reliable and practical method for pediatric dentistry. Nitrous oxide is effective and the anesthetic effect wears

off quickly so there is no extended recovery time.¹⁻³ In our study none of the patients were observed to exceed the level of 3 with respect to OAA/S which is described as patient who responds only after loud or repeated calling. However adequate sedation (OAA/S=4.5) was obtained at study group. Morse et al³¹ assessed the use of BIS monitoring in 22 patients undergoing conscious sedation with midazolam or midazolam plus ketamine for dental surgery and found that the BIS values remained close to baseline. In this research mean BIS value was 97.4 and it was similar to results of Morse et al.

In children, especially at the little age group, it is difficult to perform BIS and its devices.²⁷ In our study group, children were aged between 7-12 years old. BIS and its devices were applied easily. Although the results of our study showed that N₂O/O₂ is enough to sedate children according to the RSS and OAA/S scores, we did not observe any significant changes BIS values. This means that using N₂O/O₂ to sedate children undergoing dental extractions without any sedative agents does not require measuring the depth of sedation with BIS monitor.

CONCLUSIONS

Further investigations are needed for the validity and clinical applicability of BIS assessment with N₂O/O₂ sedation at different concentrations or combined with other sedative drugs of in a larger pediatric population under dental treatments.

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