Bispectral Analysis During Deep Sedation of Pediatric Oral Surgery Patients

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Purpose: Bispectral (BIS) analysis uses electroencephalogram information from a forehead electrode to calculate an index score (0 to 100; 0 = coma; 90 to 100 = awake). This index score correlates with the level of alertness in anesthetized patients. Classically, sedation has been monitored with clinical sedation scales such as the Observer's Assessment of Alertness Sedation Scale (OAA/S), Modified Ramsey Scale, or a Visual Analog Scale (VAS). Our objective was to determine the correlation between clinical sedation scales and BIS index in pediatric patients undergoing sedation in an outpatient oral surgery setting.

Materials and Methods: Prospective cohort study of patients aged 2 to 17 years undergoing sedation in an outpatient oral surgery office. Sedation was performed in the customary manner with the addition of BIS monitoring. Three clinical sedation scores (OAA/S: 5 to 1; 5 = awake, 1 = unresponsive; Modified Ramsey: 1 to 6; 1-2 = awake, 6 = unresponsive; VAS: 0 to 10; 0 = awake, 10 = unresponsive) were assigned every 5 minutes by an investigator blinded to the BIS index. Data were analyzed using a repeated measures linear regression model.

Results: Sixteen subjects undergoing oral surgery, ages 4.5 years to 17 years, were enrolled, mean age 12.6 years ± 4.3 years (standard deviation). Patients received methohexital in addition to 1 or more of the following: nitrous oxide, fentanyl, or midazolam. The results of the longitudinal regression analysis showed a highly significant association between the sedation scales and the BIS index.

Conclusion: The BIS monitor may be a useful adjunct in monitoring pediatric patients receiving sedation in the outpatient setting.

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The performance of oral surgery in children frequently requires sedation to minimize the trauma associated with the procedure and to ensure proper performance. The American Academy of Pediatric Dentistry and American Academy of Pediatrics have stressed the importance of monitoring vital signs and level of consciousness during sedation to ensure patient safety.[1-3] At present, there is no objective, universally accepted measure for level of sedation. Consequently, observers frequently use clinical scoring systems like the Observer's Assessment and Alertness/Sedation Scale (OAA/S), Modified Ramsey Sedation Scale, or a Visual Analog Scale (VAS),[4] that have been created as tools for measuring the level of sedation. However, observational instruments such as these may be subject to inter-rater variability because different practitioners may have different standards for intensity of sedation. In addition, observational instru-

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The BIS monitor (A-2000) was supplied by Aspect Medical Systems, Newton, MA.

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ments may not be sensitive to differences between moderate and deep sedation assessment, and as such, may not provide reliable and reproducible results.

Bispectral analysis (BIS) monitoring is a relatively new, noninvasive technology used clinically to evaluate level of sedation. This technology is based on the principle that electroencephalogram wave forms change with the level of alertness. In general, when an individual is awake, electroencephalogram waveforms are high frequency and low amplitude. When the individual is deeply sedated, the frequency decreases and amplitude increases, and there are changes in relationships among different frequencies.

Using these principles, an algorithm for digital signal processing was developed that produces a numeric value known as the BIS index, ranging from 0 to 100.[5] The manufacturer's guidelines are as follows: a BIS index of 70 to 90 represents light to moderate sedation, 60 to 70 deep sedation, 40 to 60 general anesthesia, and less than 40 a deep hypnotic state. A BIS score of 0 represents no brain activity and is seen in coma and death.

The BIS monitor was approved in 1996 by the US Food and Drug Administration for use in the setting of general anesthesia to aid in assessing the depth of anesthesia with adults. From a previous study, it is known that BIS monitoring correlates with the concentration of sevoflourane administered to children undergoing general anesthesia.[6] It has also been shown to be an objective measure of the level of alertness in adults undergoing procedural sedation with certain sedatives, excluding ketamine.[7-10] One study found an association between observed patient behaviors and BIS levels when using oral sedatives in pediatric patients.[11] There have been no published studies showing that BIS monitoring correlates with the level of sedation in children undergoing deep sedation with intravenous medications for oral surgery. Because the pediatric patient is different from the adult patient, both neurologically and physiologically, BIS monitoring requires validation with this patient population. Such an objective measure would permit better assessment of the patient, less chance of under- or overmedicating, and possibly a shorter recovery time following the procedure.

Our objective was to determine whether bispectral analysis correlates with clinical sedation scales in pediatric patients undergoing procedural sedation for oral surgery in the outpatient setting.

Materials and Methods

This study was approved by The Institutional Review Board of Rhode Island Hospital. A sample of patients from 2 to 17 years of age undergoing deep sedation for oral surgery was evaluated for inclusion. We excluded children under 2 years of age to avoid compliance issues with wearing the forehead electrode and to eliminate confounding between infants and children. A previous study noted differences in bispectral index between infants and children during emergence from anesthesia.[12]

Patients were recruited when they presented for oral surgery that required sedation and an investigator was available. Children were excluded from the study if they were unable or unwilling to wear the forehead electrode during the procedure. We obtained informed consent from parents and assent from patients older than 7 years of age. Demographic information and relevant history, including age, gender, procedure being performed, and past medical history were recorded before the procedure.

Before beginning the sedation procedure, monitoring equipment including blood pressure cuff, pulse oximeter, and cardiac monitor were placed on the patient in standard fashion. In addition, a BIS monitor electrode was placed on the patient's forehead. Each patient was given sedation medications at the discretion of the surgeon performing the sedation. The surgeon performing sedations was blinded to the BIS monitor output and to the sedation scales. The investigators were also blinded to the BIS monitor output. The surgeon selected and administered medications for sedation as per the usual routine. Medications were titrated by the surgeon according to the patient's appearance of alertness and discomfort, and medication, dosage, and time of administration were recorded by the investigator. The investigator recorded vital signs including blood pressure, heart rate, and oxygen saturation every 5 minutes. The investigator also assigned a level of sedation at 5-minute intervals using the OAA/S, the Modified Ramsey Sedation Scale, and the VAS. The OAA/S scale is a validated sedation scale that takes note of 4 patient responses: overall responsiveness, speech, facial expression, and eye opening to produce an ordinal score from 5 to 1; 5 representing wide awake and 1 representing completely unresponsive. The Modified Ramsey scale takes note of patient's response to stimuli to produce an ordinal score from 1 to 6, with 1 to 2 representing awake and 6 representing unresponsive to noxious stimuli. The VAS takes note of the patient's overall appearance and produces a continuous score ranging from 0 to 10, with 0 representing awake and 10 representing unresponsive.

During the study period, the BIS monitor was programmed to download the BIS index every 5 seconds to a laptop computer. All individuals involved with the sedation, including the investigator, were blinded to the BIS monitor and laptop computer for the duration of the sedation. The number of investigators who assessed level of alertness and recorded sedation

Table 1. DEMOGRAPHICS AMONG SUBJECTS

Total subjects	16
Total observations	111
Mean age (range)	12.6 ± 4.3 yrs (SD) (range, 4.5-17)
% Male	50%
Procedures	
Dental extraction	94%
Frenulectomy	6%
Sedatives	
Methohexital, fentanyl, midazolam	73%
Methohexital, fentanyl, midazolam, nitrous oxide	34%
Methohexital, nitrous oxide	4%

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Table 2. BIVARIATE ASSOCIATIONS IN PREDICTING BIS INDEX

	Beta	*P* Value	95% CI
*OAA/S	8.2	<.0001	7.2 to 9.2
†Ramsey	−8.2	<.0001	−9.3 to −7.1
‡VAS	−3.8	<.0001	−4.3 to −3.3

All betas are unadjusted.

*A 1-unit increase in the OAA/S score was associated with an average 8.2-unit increase in BIS index. OAA/S scores range from 1 to 5.

†A 1-unit increase in the Ramsey was associated with an average 8.2-unit decrease in BIS index. Ramsey scores range from 1 to 6.

‡A 1-unit increase in the VAS score was associated with an average 3.8-unit decrease in BIS index. VAS scores range from 1 to 10.

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scores was restricted to 1 individual to eliminate interobserver variability.

Because our data consisted of repeated measures of both BIS score and sedation score, it was decided *a priori* to use a repeated measures regression analysis to analyze the data. To determine all factors that would predict BIS output, we performed a multivariate analysis using BIS score as the dependent variable and OAA/S score, Ramsey score, VAS score, gender, age, and sedation drug as independent variables. We therefore used the generalized estimating equation to adjust for the intrasubject correlation of the repeated measures over time. The advantage of a repeated measures analysis is that it uses *all* the study data and maximizes our power to detect an association between sedation scale and BIS index.

The statistical program STATA Version 7.0 (STATA Corp, College Station, TX) was used for all calculations.

Results

We enrolled 16 subjects, producing a total of 111 observations of BIS indexes. All enrolled patients completed the study. The mean age was 12.6 ± 4.3 years (SD) (range, 4.5 to 17). Fifty percent of subjects were male. Fifteen patients underwent a dental extraction, and the remaining patient had a frenulectomy. Seventy-three percent were sedated with midazolam, fentanyl, and methohexital; 34% with midazolam, fentanyl, methohexital, and nitrous oxide; and 4% with methohexital and nitrous oxide. Table 1 summarizes the patient demographics.

We then performed an unadjusted analysis of BIS score with OAA/S, Ramsey, VAS, age, gender, drug, and procedure as the predictor variables for all 16 subjects (Table 2). The regression analysis showed that OAA/S score, Ramsey score, and VAS score were strong predictors of BIS index, and independent from age, gender, drug, and procedure. As shown in Table 2, a 1-unit increase in the OAA/S score predicted, on average, an 8-unit increase in the BIS index. A 1-unit increase in the Ramsey scale predicted, on average, an 8-unit decrease in the BIS index. A 1-unit increase in the VAS scale predicted a 3.8-unit decrease in the BIS index.

We then generated 3 multivariate models using BIS index as the dependent variable and OAA/S, Ramsey, VAS, gender, age, procedure, and drug as covariates (Table 3). As can be seen in Table 3, the beta coefficients for and OAA/S, Ramsey, and VAS were similar in the multivariate model to the unadjusted beta coefficients in Table 2. There were not associations with age, gender, drug, or procedure, suggesting that these are not confounders.

To illustrate the association between BIS index and VAS score, we constructed a running smoothed plot with a 95% CI (Fig 1). The smoothed function allows for nonlinearities in the association to be observed. We used a span of 0.8 in our plot with the span defined to be (N*span-1)/2, where N is the number of observations. As seen in Figure 1, the relationship appears to be linear. We did not construct smoothed plots for OAA/S and Ramsey scores as unlike VAS, these measures are ordinal, rather than continuous.

Discussion

Studies in adults showed an association between the BIS index and depth of sedation with multiple sedatives

Table 3. MULTIVARIATE MODELS FOR PREDICTING BIS INDEXES

	Beta	*P* Value	95% CI
OAA/S	8.2	<.0001	7.2 to 9.2
Ramsey	−8.2	<.0001	−9.4 to −7.1
VAS	−3.8	<.0001	−4.3 to −3.3

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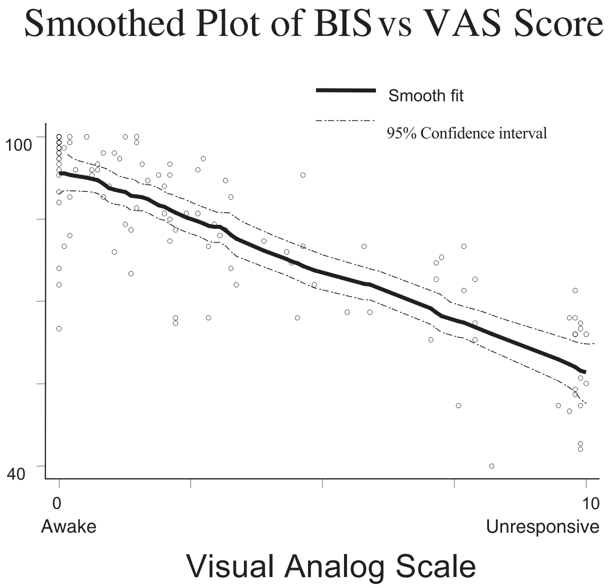

FIGURE 1. Smoothed plot of VAS score versus BIS level with a 95% CI. Each small circle represents 1 or more observations.

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and anesthetics.[13-18] It is of note that the data used to create Bispectral analysis were derived from a population of healthy adults and the majority of studies performed on BIS monitoring have included only adults.[6,18-20] These results cannot be extrapolated to the pediatric population for several reasons. The neurophysiology of children is consistently changing and maturing, and is known to be different from that of the adult population.[21] The largest pediatric study performed to date showed that the addition of BIS monitoring to an anesthesiologist's standard routine shortened the time to extubation and recovery.[13] This suggests there is utility to BIS monitoring in the pediatric population. Religa et al[11] studied the relationship between level of consciousness and BIS index in pediatric dental patients who were sedated with oral agents. They found a significant association, but reported technical difficulties with data collection, patient cooperation, electrode function, and frequent EMG interference during the light stages of sedation. No previous study had been performed to evaluate the relationship between BIS index and level of sedation for pediatric patients undergoing deep sedation with intravenous medications for oral surgery.

Our results indicate that the BIS index correlates with the OAA/S, Modified Ramsey, and VAS. These results are similar to those found in studies of adults using drugs such as methohexital, midazolam, dilaudid, morphine, fentanyl, and propofol.[7,10] Barbiturates (ie, methohexital) and narcotics (ie, morphine, fentanyl) exert an effect on GABA receptors and opioid receptors, respectively. These classes of drugs are known to produce electroencephalographic changes resulting in decreased frequency and increased amplitude.[22] Such neurophysiologic changes result in a lower BIS index, as demonstrated by our results.

This study has the limitation of a relatively small sample size. We enrolled 16 patients, but collected 111 observations on those patients. The mean age of 12.6 years, with the range of 4.5 to 17 years, does not offer much information about infants and toddlers. Further studies examining a larger number of individuals at various ages (ie, infant, toddler, adolescent) might offer additional information about the relationship between BIS index and depth of sedation in different groups. However, given the strength of our association between BIS and the sedation scales and the linearity of the relationship, it seems unlikely that the relationship would be significantly different with a larger number of subjects in the same age range. We believe our study provides evidence that BIS monitoring may be an efficacious adjunct to sedation monitoring in children.

When a more specific correlation is defined between the BIS level and depth of sedation in pediatric patients, it will be essential to design studies to evaluate the utility of bispectral analysis in optimizing deep sedation. Questions that remain to be answered include: Can an oral surgeon better titrate medications with the addition of BIS monitoring and as a result, decrease time until discharge? Is BIS monitoring able to predict or prevent bad outcomes? Does the addition of BIS monitoring improve patient experience? Does BIS monitoring change during certain phases of surgical procedures (eg, induction, local anesthesia administration, initiation of surgery, completion of surgery, eye opening)? The answers to these questions will help determine whether bispectral analysis has a definitive role for pediatric patients undergoing sedation for oral surgery.

In conclusion, this study showed a significant association of BIS index with 3 sedation scales, the OAA/S scale, the Modified Ramsey scale, and the VAS. It appears that the BIS monitor may be useful in pediatric patients undergoing deep sedation and may eventually be a useful adjunct in monitoring depth of sedation during outpatient oral surgery.

References

1. American Academy of Pediatric Dentistry (AAPD): Guidelines for the elective use of conscious sedation, deep sedation and general anesthesia in pediatric dental patients. Pediatr Dent 20:47, 1998
2. American Academy of Pediatrics, Committee on Drugs: Guidelines for monitoring and management of pediatrics during and after sedation for diagnostic and therapeutic procedures. Pediatrics 86:1110, 1992
3. Sa Rego MM, White P: Monitored anesthesia care, *in* Miller RF (ed): Anesthesia. Philadelphia, PA, Churchill Livingstone, 2000, pp 1460-1461

4. Chernik DA, Gillings D, Laine H, et al: Validity and reliability of the observer's assessment of alertness/sedation scale: Study with intravenous midazolam. J Clin Psychopharmacol 10:244, 1990
5. Sigl JC, Chamoun N: An introduction to bispectral analysis for encephalogram. J Clin Monit 10:392, 1994
6. Denman WT, Swanson E, Rosow D, et al: Pediatric evaluation of the Bispectral Index (BIS) monitor and correlation of BIS with end-tidal sevoflourane concentrations in infants and children. Anesth Analg 90:872, 2000
7. Bower AL, Ripepi A, Dilger J, et al: Bispectral index monitoring of sedation during endoscopy. Gastrointest Endosc 52:192, 2000
8. Gill M, Green S, Krauss B: A study of the bispectral index monitor during procedural sedation and analgesia in the emergency department. Ann Emerg Med 41:234, 2002
9. Sandler NA, Hodges J, Sabino, M: Assessment of recovery in patients undergoing intravenous conscious sedation using bispectal analysis. J Oral Maxillofac Surg 59:603, 2001
10. Sandler NA, Sparks B: The use of bispectral analysis in patients undergoing intravenous sedation for third molar extraction. J Oral Maxillofac Surg 58:364, 2000
11. Religa ZC, Ganzberg S, Wilson S, et al: Association between bispectral analysis and level of conscious sedation of pediatric dental patients. Pediatr Dent 24:221, 2002
12. Davidson AJ, McCann M, Devavaram P, et al: The difference in the Bispectral Index between infants and children during emergence from anesthesia after circumcision surgery. Anesthes Analg 93:326, 2001
13. Bannister C, Brosius K, Meyer B: The effects of BIS monitoring on emergence and PACU discharge in children receiving sevoflourane anesthesia. Anesthesiology News 26:10, 2000
14. Doi M, Gajraj R, Mantzaridis H, et al: Relationship between calculated blood concentration of propofol and electrophysiologic variables during emergence from anesthesia: comparison of bispectral index, spectral edge frequency and auditory evoked potential index. Br J Anaesth 78:180, 1997
15. Liu J, Singh H, White PF: Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. Anesth Analg 84:185, 1997
16. Song D, Van Vlymen J, White PF: Is the bispectral index useful in predicting fast-track eligibility after ambulatory anesthesia with propofol and desflurane? Anesth Analg 87:1245, 1998
17. Strachan AN, Edwards N: Randomized placebo-controlled trial to assess the effect of remifentanil and propofol on bispectral index and sedation. Br J Anaesth 84:489, 2000
18. Yli-Hankala A, Vakkuri A, Annila P, et al: EEG bispectral index monitoring in sevoflurane or propofol anesthesia: Analysis of direct costs and immediate recovery. Acta Anaesthesiol Scand 43:545, 1999
19. Glass PS, Bloom M, Kearse L, et al: Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. Anesthesiology 86: 847, 1997
20. Laussen PC, Bascik J, Sullivan LJ, et al: The Bispectral Index predicts patient response to verbal command during intraoperative wake-up test and scoliosis surgery. Anesth Analg 90:s221, 2000
21. Scher M: Pediatric neurophysiologic evaluation, *in* Swainman KF, Ashwal S (ed): Pediatric Neurology. St Louis, MO, Mosby, 1999, pp 142-181
22. Black S, Mahla M, Cucchiara RF: Neurologic monitoring, *in* Miller RF (ed): Anesthesia. Philadelphia, PA, Churchill Livingstone, 2000, p 1329