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The SNAP Index Does Not Correlate with the State Behavioral Scale in Intubated and Sedated Children

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Abstract

Background—Ensuring appropriate levels of sedation for critically ill children is integral to pediatric critical care. Traditionally, clinicians have used subjective scoring tools to assess sedation levels. The SNAP II uses dual frequency processed electroencephalography to evaluate brain activity and may provide an objective assessment of sedation levels.

Objective—This study attempts to find an objective method to monitor sedation in critically ill pediatric patients. We compared the SNAP II, a processed electroencephalography device, with the State Behavioral Scale (SBS), a subjective sedation scoring tool. We hypothesize that the SNAP II correlates with the SBS and has less observer bias.

Methods—This was an IRB approved prospective, observational study. Patients receiving intravenous sedation while being mechanically ventilated were enrolled after informed consent. After the SNAP II monitoring electrodes were attached, blinded bedside nurses assessed sedation levels using the SBS. SNAP indices were collected and compared with SBS scores to determine correlation.

Results—We compared 417 paired data points from 15 patients using Pearson's correlation and Least Squares Means to determine correlation between the SBS and SNAP indices. No correlation was observed. Using covariance model patterning for repeated measures to adjust for covariates again showed no correlation.

Conclusion—The SNAP index does not correlate with SBS scores in our PICU. Its use cannot be recommended to measure levels of sedation in our population. Future research should continue to explore objective ways of measuring sedation in critically ill children.

Keywords

electroencephalography; intensive care; benzodiazepines; mechanical ventilation; intensive care units pediatric; pediatrics

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Conflict of Interest

No conflict of interests to declare.

Background

Ensuring the comfort of critically ill infants and children is fundamental to the practice of pediatric critical care. The developmental immaturity of many pediatric patients makes sedation, not only integral for comfort, but also lifesaving. It allows for ventilator synchronization, prevention of the inadvertent removal of endotracheal tubes, and reduction of metabolic demand.(1) To this end, over 90% of infants and children supported on mechanical ventilation receive some form of sedative therapy.(2) Consequently, routine assessment of the level of sedation has become an important part of the management of intubated patients in the pediatric intensive care unit (PICU).

There is no “gold standard” to assess the level of sedation in mechanically ventilated pediatric patients. In 2009, Hartman et al. published a review describing 21 different sedation scoring systems used in medical and cardiac PICUs.(3) Traditionally, an assessment of clinical signs has been used to assess sedation depth.(4) These assessments can be subjective and are often confounded by professional training and the experience level of those making the observations.

Currently there are no widely accepted or completely validated devices for monitoring sedation depth in the PICU. Several instruments have been developed that use processed electroencephalography (EEG) as an objective way to monitor sedation depth. The SNAP II (Stryker, Kalamazoo, MI) is one such device that analyzes both high-frequency (80–420 Hertz) and low-frequency (0.1–18 Hertz) EEG activity.(5) The addition of high-frequency EEG monitoring, theoretically, improves device responsiveness during increased brain activity making it a superior instrument for monitoring sedation and impending wakefulness.(6) This study aims to determine the effectiveness of the SNAP II as an objective measure of sedation depth for mechanically ventilated pediatric patients in the PICU. We hypothesize that the SNAP indices correlate with the State Behavioral Scale (SBS), the clinical scoring scale currently used in our PICU.(2)

Methods

The following study was a prospective observational study approved by the Human Investigation Committee at Yale University School of Medicine. Patients were considered eligible if they received intravenous sedation, with or without analgesia, while mechanically ventilated for a period of at least 8 hours. Intravenous sedatives included midazolam, lorazepam, pentobarbital and ketamine. Patients were excluded if they received continuous neuromuscular blockade, had no spontaneous movement, or did not require intravenous sedation. Patients aged greater than 18 years and those whose forehead surface area was too small for proper placement of the SNAP II disposable electrodes were also excluded. Finally, patients with diagnoses which could potentially affect brain activity were initially excluded. Examples included patients with seizures, traumatic brain injury and encephalitis. However, after poor patient enrollment during the first 3 months, this exclusion was removed.

After informed consent was obtained from parents or legal guardians, the SNAP II electrodes were attached to the patient's forehead following the manufacturer's instructions. Briefly, the self-adhesive disposable electrodes were placed on one half of the patient's forehead above the eyebrow after the skin was cleaned. The SNAP II monitor was physically covered by opaque material in order to blind bedside nurses to the SNAP indices displayed on the monitor screen. Patients were sedated according to our PICU sedation algorithm. SBS scores were assigned to each patient by the bedside nurse every 1 to 2 hours as clinically indicated and per unit policy. The SBS has been validated in the pediatric

population and is a noninvasive clinical assessment tool with scores that correlate with sedation levels: deep sedation = SBS -2 and -3, moderate sedation = SBS -1, light sedation = SBS 0 and +1, and agitation = SBS +2 (Table 1).(2) SBS scores were documented in the electronic medical record by the bedside nurse at the time of score assignment. Patients were observed for at least 8 hours to a maximum of 5 days. Demographic data and clinical characteristics were obtained from each patient's electronic medical record including the highest oxygenation index (OI), Pediatric Logistic Organ Dysfunction score (PELOD) and associated predicted death rate (PDR) on the day of intubation,(7, 8) as well as sedative drug class and dosages used throughout the observation period. OI was calculated by multiplying the mean airway pressure (MAP) with the fraction of inspired oxygen (FiO2) divided by the partial pressure of oxygen in arterial blood (PaO2): $(OI=MAP*FiO2/PaO2)$.

After the observation period was complete or the patient was extubated, the SNAP II was removed from the patient and the device's memory was interrogated. The mean SNAP index was calculated for the 5 minute period prior to a documented SBS score. The 5-minute mean SNAP index was then compared with the paired SBS score to determine correlation. An interim analysis was scheduled *a priori* in order to establish a SNAP index threshold after the first 15 patients were enrolled. The SNAP index threshold was expected to be a single number or range of SNAP indices that correlated with the SBS score of -1. SNAP indices below the threshold would indicate adequate sedation while indices above the threshold would indicate increased wakefulness and under sedation.

Statistical Analysis

The data analysis for this paper was generated using [SAS/STAT] software, Version [9.3] of the SAS System for PC. Copyright © 2011 SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. Paired SBS scores and 5 minute mean SNAP indices were compared using Pearson's correlation and then adjusted for multiple measurements within subjects using a covariance pattern modeling for repeated observations, which is a form of analysis of variance that does not assume sphericity within the outcome. Other covariates included: age, gender, and primary diagnosis. For the age covariate, patients were divided into 2 groups: <6 months and ≥ 6 months. Primary diagnosis was divided into 4 categories: lower respiratory infection, sepsis, upper respiratory infection, and other. Degree of correlation from the Pearson's correlation was reported as *r*. Mean estimates were reported as Least Squares Means. Lower and upper limits were calculated with a 95% confidence interval. Statistical significance was defined as $p<0.05$.

Results

From November 2010 to February 2012, 298 patients were mechanically ventilated in the PICU. Of these, 273 patients (80%) received intravenous sedation. The majority of mechanically ventilated patients were excluded due to intubation time less than 8 hours or small forehead surface area ($n=137$ and 51 , respectively). The remaining patients ($n=49$) were excluded due to other criteria including continuous neuromuscular blockade infusion use, age >18 years, wards of the State, previous enrollment in the study, and those with diagnoses that could affect brain activity prior to the removal of this exclusion from the study protocol. Of the remaining eligible patients, 36 were asked to participate but only 15 consented. The primary reason for parental refusal was over concern or fear of new technology. The secondary reason was fear of exposing their child to unnecessary equipment.

Of the 15 patients enrolled, two-thirds were males. The median age and weight were 21.9 months (IQR 11.0-53.1 months) and 10.7 kg (IQR 7.5-20.0 kg), respectively (Table 2). The

most common reason for intubation was lower respiratory infection (n=6), followed by sepsis (n=5). The two patients requiring intubation for *other*, both had gastrointestinal diagnoses. Despite removing the initial exclusion criteria of a neurologic co-morbidity that could affect EEG activity, only one patient enrolled in the study had a known seizure disorder. All patients received conventional ventilatory support only. Median OI and PELOD scores on the day of intubation were 17.4 (IQR 9.7-22.8) and 11.0 (IQR 2.5-11.0), respectively. This resulted in a predicted death rate of 1.3% (IQR 0.15-1.3%). All patients were sedated with at least a benzodiazepine; one-third received only intermittent benzodiazepine dosing, while two-thirds received a continuous infusion. Most patients (n=14, 93%) also received opiate analgesia. A small number of patients (n=3) required additional intravenous sedation with either pentobarbital (n=2) and/or ketamine (n=2), and/or an oral agent (chloral hydrate (n=2) or clonidine (n=1)) (Table 2).

After the first 15 patients were enrolled, a planned interim analysis was performed to determine a SNAP index threshold. A total of 417 unadjusted paired data points were compared to determine correlation between the 5 minute mean SNAP indices and SBS scores using Pearson's correlation. No correlation or trend for correlation was observed and a SNAP index threshold could not be determined. ($r=0.18$, $p=NS$). After removing the one patient with a co-morbid seizure disorder, the Pearson's correlation remained not significant ($r=0.19$). Using covariance pattern modeling to adjust for repeated measures within subjects additionally showed no correlation between the SNAP indices and SBS scores (Figure 1). The lack of correlation persisted after adjusting for the covariates: age, gender, and primary diagnosis. Due to the lack of statistical significance or trend toward correlation between the SBS and SNAP II after the interim analysis, the study was ended early due to futility.

Discussion

This is the first pediatric study assessing sedation depth monitoring and wakefulness using the SNAP II in endotracheally intubated and mechanically ventilated children. The SNAP II is a small bedside monitor that is very portable making it ideal for the pediatric patient population. The SNAP index is derived from a unique algorithm created specifically for the SNAP II and is displayed on the monitor graphically and numerically from 0-100, with 100 corresponding to complete alertness in adult patients.⁽⁵⁾ It is unclear what level of consciousness the SNAP index corresponds with in the pediatric population. Unfortunately, we were unable to correlate the SNAP index with the SBS, which prevented us from establishing a SNAP index awakening threshold or a SNAP index reference range for sedation levels in pediatric patients. The use of the SNAP II monitoring device for predicting pediatric sedation cannot be recommended in our population at this time.

The SBS has been validated in the pediatric population and is a noninvasive clinical assessment tool with scores that correlate with sedation levels: deep sedation = SBS -2 and -3, moderate sedation = SBS -1, light sedation = SBS 0 and +1, and agitation = SBS +2.⁽²⁾ It has been used in our PICU for approximately 6 years. In a concurrent study in 2010 the inter-rater reliability of our nursing staff was found to have a Kappa = 0.8 to 1.0 when assigning SBS scores for mechanically ventilated children (unpublished data). With high inter-rater reliability in our PICU, it is possible that the lack of correlation in our study was the result of the patient population we studied.

Due to low enrollment numbers, patients with suspected abnormal EEG activity were not excluded as initially planned. However, despite removing this exclusion criterion, we only enrolled one subject with a known seizure disorder. A *post hoc* analysis was performed after removing the single patient with suspected abnormal EEG activity and continued to show no correlation. Additionally, since every patient received sedation with a benzodiazepine and

all but one also received analgesia with an opioid, specific sedation class and opiate use analyses were not possible.

Previous studies investigating the use of processed EEG for sedation monitoring in pediatric patients have focused on the Bispectral index (BIS).(9-14) Shortcomings of the BIS in the pediatric population have been previously described and include variability based on sensor placement,(10) poor sensitivity predicting over-sedation,(9, 15) and unreliability in patients aged less than 6 months or with opiate sedation.(11) No pediatric data exists comparing the BIS with the SNAP II. Data from adult studies have found that the two indices are not interchangeable but that both devices can reliably monitor the level of sedation in adult patients undergoing general anesthesia.(6, 16, 17) In fact, because the SNAP II assesses both high and low frequency EEG compared with the BIS which only assess low frequency EEG, the SNAP index has been suggested to be a better predictor of impending wakefulness.(6) However, we did not observe this potential benefit when comparing the SNAP II to the SBS.

In this study, we accounted for the minor variability that is seen in the SNAP indices during continuous monitoring in order to improve potential correlations with the SBS. The SNAP index is updated at 1 second intervals while it takes approximately 3-5 minutes to determine an SBS score.(2, 5) To account for this time discrepancy we averaged the SNAP indices for 5 minutes prior to SBS determination. SBS scores are assigned and recorded in the electronic medical record every 1 to 2 hours in our unit. Bedside nurses were blinded to the SNAP II monitor screen to prevent bias while assigning SBS scores. Observing enrolled patients for at least 8 hours allowed us to obtain more paired data points per patient for analysis but still did not result in statistically significant correlations.

Additional limitations should also be entertained when considering why no correlation was found. We depended upon the specific time SBS scores were assigned by the bedside nurses. These times were obtained from the electronic medical record and used to determine which SNAP indices to average. We assumed nurses documented precisely but this could be open to recall bias. Secondly, benzodiazepines have been shown to affect EEG activity.(18-20) It is unclear whether they affect the SNAP index. As mentioned earlier, all of our study patients received benzodiazepines as part of their sedation regimen, as is common practice in our PICU. Future research involving the SNAP II should consider enrolling patients into different sedative class groups in order to study the effects different drugs may have on the SNAP index.

Finally, although the SNAP II minimizes EEG frequency bands most heavily influenced by electromyography, it is unclear how muscle movements in our population affect the SNAP index. We excluded patients who received neuromuscular blockade and patients who did not have spontaneous movement since the SBS cannot be determined in these clinical states. We recognize that this vulnerable patient population would benefit the most from an objective sedation monitoring device like the SNAP II. However, because we were unable to correlate the SNAP Index with the SBS, it remains unclear what levels of consciousness correlate with the SNAP Index in pediatric patients. Once the SNAP Index can be validated against a clinical scoring tool, or a different processed EEG device, future studies can safely focus on monitoring sedation levels in pediatric patients receiving neuromuscular blockade. Additionally, although it is unclear whether muscle movement affects the SNAP index in the pediatric population, it is tempting to speculate that our requirement of observable muscle movement may have uniformly increased the SNAP index in our patient population. Despite these potential limitations and the small patient sample size, we were able to obtain a large amount of paired data points for comparison and found no correlation between the SNAP index and SBS in the patient population we studied. We cannot recommend its use to determine pediatric sedation levels at this time, particularly in patients receiving

benzodiazepine sedation. Future research should continue to explore objective ways to measure sedation in critically ill children.

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Figure 1. Observed SNAP Index vs. SBS. Mean SNAP index was compared with paired SBS scores using Repeated Measures ANOVA. *LSmean* = Least Squares Means predicted by ANOVA.

Table 1

State Behavioral Scale Score

Score	Description
-3	Unresponsive
-2	Responsive to noxious stimuli
-1	Responsive to gentle touch or voice
0	Awake and able to calm
+1	Restless and difficult to calm
+2	Agitated

State Behavioral Scale score assigned as patient's response to voice, then gentle touch, then noxious stimuli. Noxious stimuli defined as planned endotracheal suctioning or <5 seconds of nail-bed pressure. Adapted from reference 2.

Table 2

Patient Characteristics (N=15)

Characteristics	
Males, N (%)	10 (66.7)
Race, N (%)	
Hispanic	6 (40.0)
White	5 (33.3)
Black	3 (20.0)
Other	1 (6.7)
Age, mo	
Median (IQR)	21.9 (11-53.1)
Weight, kg	
Median (IQR)	10.7 (7.5-20)
OI	
Median (IQR)	17.4 (9.7-22.8)
PELOD PDR, %	
Median (IQR)	1.3 (0.15-1.3)
Primary diagnosis, N (%)	
Lower respiratory infection	6 (40.0)
Sepsis	5 (33.3)
Upper respiratory infection	2 (13.3)
Other	2 (13.3)
Neurologic co-morbidity, N (%)	
Seizure disorder	1 (0.07)
Sedation administered, N (%)	
Benzodiazepine only + opiate analgesia	12 (80)
Benzodiazepine + additional sedation + opiate analgesia	3 (20)

Benzodiazepine includes midazolam and lorazepam. Opiate includes morphine and fentanyl. Additional sedation includes pentobarbital, ketamine, chloral hydrate and/or clonidine. Other= pancreatitis (N=1), small bowel obstruction (N=1). *Mo*=month; *kg*=kilograms; *OI*=oxygenation index; *PELOD*=pediatric logistic organ dysfunction score; *PDR*=predicted death rate; *IQR*=interquartile range.