

Comparison of bispectral index and patient state index during sevoflurane anesthesia in children: a prospective observational study

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Research article

Keywords: anesthesia; bispectral index; children; depth of anesthesia, prediction probability; patient state index

Posted Date: August 19th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-53378/v1>

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Abstract

Background: Cortical electroencephalography (EEG)-based devices are used to monitor the depth of anesthesia. In this study, we compared the values of bispectral index (BIS) and patient state index (PSI) during sevoflurane anesthesia in children. The ability/accuracy of BIS and PSI to predict the steady and recovery state of anesthesia was evaluated based on prediction probability (Pk) values and the secondary outcomes were agreement and correlation of two monitors.

Methods: Fifty children (3-12 years old) were enrolled and the patients received sevoflurane anesthesia with remifentanyl. Before the induction of anesthesia, BIS and PSI sensors were simultaneously placed on the forehead, and data were collected until the end of anesthesia. Steady state was defined as the period following intubation until the cessation of sevoflurane, while recovery state was defined as the period following the cessation of sevoflurane until awake. The prediction probability (Pk), agreement or correlation of BIS and PSI in different anesthesia state were calculated.

Results: Anesthesia reduced mean BIS and PSI values. Pk of BIS (95% confidential interval (CI) [0.78-0.91]) and PSI (95% CI [0.82-0.91]) for anesthesia were 0.85 and 0.87, respectively. Agreement was 0.79 for recovery state and 0.73 for steady state.

Conclusions: Pk values were comparable for BIS and PSI. Agreement between BIS and PSI measurements in the same state was relatively good. Therefore, these monitors are appropriate for monitoring for different state of anesthesia in pediatric population.

Trial Registry Number: Clinical Trials.gov NCT03792334.

Background

Cortical electroencephalography (EEG) is commonly used to monitor the cerebral effects of general anesthetics.[1] The popular commercial device for monitoring anesthesia depth/sedation might be the bispectral index (BIS) and was developed using EEG data collected from adult volunteers.[2] Although BIS was developed with adult EEG data, many studies have utilized the BIS to monitor anesthesia depth in children.[3] Now, we have several EEG-based monitors and indicators (e.g., Entropy,[4] Narcotrend,[5] cerebral state index (CSI),[6] index of consciousness (IoC),[7] qCON,[8] A-line autoregression index (AAI),[9] brain anesthesia response (BAR)[10] and patient state index (PSI)[11]) in clinical practice, exhibiting comparable results in many studies.

Among the aforementioned indicators, the PSI is derived from 4-channel EEG data (e.g., Masimo monitor, SedLine monitor).[12] This monitor is advantageous in that it is associated with no pain upon attachment to the forehead and has more channels to give more information than BIS monitors. Although several studies have compared the effects of different monitor types in human patients such as BIS with PSI, Entropy or A-Line ARX,[13–15] no such studies have compared the use of different monitors for performance in children.

In this prospective observational study, we compared the values of BIS and PSI during sevoflurane anesthesia with regard to classification of different anesthetic state in the same patient.

Materials And Methods

Patient recruitment and anesthetic methods

The present study was approved by the Institutional Review Board of Seoul National University Hospital (IRB no. 1811-172-991) and registered at <http://register.clinicaltrials.gov> (NCT03792334). Each participant was given a verbal explanation and had the time to ask questions about the study protocol, and written informed consent was obtained from one parent or guardian. Verbal consent was obtained from patients under 7 years of age, while written informed consent was obtained from patients over 7 years of age. All procedures followed the principles outlined in the Declaration of Helsinki and its revisions.

A total of 54 patients (age range: 3–12 years) undergoing surgery under sevoflurane anesthesia were enrolled. Exclusion criteria were as follows: known cerebral dysfunction, plans to receive intravenous anesthesia, use of antiepileptic drugs, or admission to the postoperative intensive care unit.

All patients fasted in accordance with practice guidelines outlined by the American Society of

Anesthesiologists. Recruited patients did not receive premedication. After arrival in the operating room, electrocardiogram (ECG), heart rate (HR), non-invasive blood pressure (NIBP) data were collected at 1-min intervals. Peripheral oxygen saturation (SpO₂), and E_TCO₂ were also monitored. BIS (version XP; Aspect Medical Systems, Natick, Mass Covidien, BIS-SX, USA) and PSI pediatric sensors (Root, Masimo, USA) were simultaneously attached to the forehead. Preoxygenation was performed, following which anesthesia was induced with 2.5 mg/kg of propofol. Patients were manually ventilated with a mixture of 8 vol% sevoflurane and 100% oxygen after loss of consciousness. Administration of 0.6 mg/kg of rocuronium was followed by endotracheal intubation, which was performed after confirming full neuromuscular blockade.

Anesthesia was liberally maintained using 2–3 vol% of inspiratory sevoflurane concentration and continuous infusion of remifentanyl according to the conventional technique of the attending pediatric anesthesiologist with BIS monitor and hemodynamic changes. We discontinued sevoflurane administration after surgery, following which patients were extubated and transferred to the postanesthetic care unit (PACU).

Steady state was defined as the period from intubation until just prior to sevoflurane cessation, while recovery state was defined as the period from the cessation of sevoflurane administration until extubation,

Study protocol

To obtain EEG data of optimal quality, the skin of the forehead was swabbed with alcohol, following which the two pediatric sensors were gently attached. The BIS sensor was applied closer to the eyebrows, whereas the PSI sensor was applied above the BIS sensor. Although the electrodes were applied in close proximity, the interference between the two monitoring systems is expected to be minimal because they use sophisticated artifact rejection algorithms and amplifiers with medical-grade isolation transformers. The bar readings on the monitors indicating signal quality and electromyogram activity were monitored, as were the raw EEG tracings. BIS and PSI values corresponding to poor signal quality combined with increased electromyogram activity and EEG artifacts were excluded from data analysis. Measurements were obtained once sensor impedance had been checked and accepted by both the BIS and PSI monitors. Two sensors were attached from the beginning of anesthesia to the end of anesthesia. During the study period, all vital signs and parameters were monitored and recorded using a computer for subsequent analysis.

Outcome measures

The ability/accuracy of BIS and PSI to predict the two states (steady state and recovery state) was the primary outcome and evaluated based on prediction probability (Pk) values. Pk values reflect the ability of an indicator to correctly identify different periods of anesthesia without overlap.[16] A Pk value of 1.0 indicates that the parameter predicts the states correctly 100% of the time without overlap. A Pk value of 0.5 indicates that prediction accuracy is no better than chance alone. A Pk value < 0.5 indicates an inverse relationship. Individual PK values were calculated using a specific PK program.

Agreement and correlation of the two devices were regarded as secondary outcomes. Agreement between the BIS and PSI was defined as the percentage of BIS or PSI values for a given state of anesthesia. We also analyzed the correlation between BIS/PSI values and sevoflurane concentration.

Statistical analysis

Statistical analyses were performed using SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Data are expressed as the mean \pm standard deviation for normally distributed continuous variables, as the median [IQR: 25–75%] for non-normally distributed continuous variables, and as counts and percentages for categorical variables. A $P \leq 0.05$ was considered statistically significant.

Results

As data were lost for 4 patients, we analyzed data for a total of 50 patients. The demographic and surgical characteristics of the included patients are shown in Table 1. In 22 patients, BIS and PSI sensors were applied before anesthesia induction to obtain values for the awake state which was usually over 97 of BIS, while the remaining participants refused sensor application. Due to excessive artifacts, awake-state BIS and PSI values were obtained in 5 and 7 patients, respectively.

Table 1
Demographic and surgical characteristics

| Patients (n = 50) | |
|--------------------------|--------------|
| M/F | 40/10 |
| Age | 9.7 ± 2.1 |
| Body weight | 44.2 ± 13.8 |
| Operation type | |
| Orthopedic | 27 |
| Urologic | 22 |
| Plastic | 1 |
| Surgery time (min) | 104.3 ± 52.1 |
| Anesthetic time (min) | 143.7 ± 56.1 |

Figure 1 shows the raw BIS and PSI values plotted against the expired sevoflurane concentration. An inverse relationship was observed between BIS/PSI values and expired sevoflurane concentration. The median BIS and PSI values [IQR 25–75%] during steady state and recovery state were shown in Table 2. Notably, we observed significance differences in BIS/PSI values between steady state and recovery state of anesthesia. We also compared individual Pk values for distinguishing steady state and recovery state in a sample of 50 patients (Table 3). The Pk value for BIS was 0.85 (95% CI 0.78–0.91), while that for PSI was 0.87 (95% CI 0.82–0.91), suggestive of comparable prediction ability.

Table 2
The values of each state of anesthesia

| Anesthetic period | BIS | PSI |
|---------------------------------------|------------|------------|
| Recovery state | 61[57–67]* | 52[45–64]* |
| Steady state | 48[40–56] | 38[28–45] |
| * P < 0.001 compared to steady state. | | |

Table 3
Prediction probability of steady state and recovery state

| | Pk | Standard error | 95% Confidential interval | sensitivity | specificity |
|---------------------|-----------|-----------------------|----------------------------------|--------------------|--------------------|
| Bispectral index | 0.85 | 0.034 | 0.78–0.91 | 0.84 | 0.79 |
| Patient state index | 0.87 | 0.024 | 0.82–0.91 | 0.81 | 0.80 |

Agreement values for BIS or PSI were 0.79 and 0.73 during steady state and recovery state, respectively (Table 4).

Table 4
Agreements of bispectral index and patient state index

| Anesthetic state | Agreements of bispectral index and patient state index |
|-------------------------|---|
| Recovery state | 0.79 |
| Steady state | 0.73 |

We also analyzed the correlation between BIS or PSI values and inspiratory/expiratory sevoflurane concentration during the steady state and recovery state. Pearson’s correlation analysis revealed a negative correlation, as the sevoflurane concentration reflects the depth of anesthesia (Table 5).

Table 5
Correlation between indicators of steady state and volatile anesthetic concentration

| | Bispectral index | Patient state index |
|-------------------------|-------------------------|----------------------------|
| Inspiratory sevoflurane | -0.521 | -0.342 |
| Expiratory sevoflurane | -0.520 | -0.327 |

Discussion

Our results demonstrated that BIS and PSI could both distinguish the steady state and recovery state of anesthesia in children with high prediction probability, although their correlations with sevoflurane concentration were relatively weak.

There is an inverse correlation between BIS values and end-tidal sevoflurane concentration in children, suggesting that EEG-based monitors can be applicable for monitoring anesthesia depth in this population.[17] Our study also demonstrated an inverse correlation between sevoflurane concentration

and BIS/PSI values. Relative to that for BIS values, the correlation between sevoflurane concentration and PSI values was poor in the present study. Although the reasons for this difference could not be determined with certainty, we also observed that fluctuations in PSI values tended to be greater than those in BIS values even at the steady state of inspiratory and expiratory sevoflurane concentration. This may explain why the correlation was weaker for PSI values than for BIS values.

A previous study reported that BIS-based methods are not reliable for assessing the depth of sevoflurane anesthesia in children under 2 years of age.[18] Additional research has revealed that the performance of BIS or entropy improves as age increases.[19] In the present study, all patients were over 3 years of age (mean age: 9.7 years), allowing us to avoid this limitation. Moreover, it is difficult to apply two different sensors to the small foreheads of children under 3 years of age.

Another study reported that elevated BIS values may indicate epileptoid patterns or EEG fast oscillations rather than an insufficient depth of hypnosis under high sevoflurane anesthesia. In this previous study, deep anesthesia was defined as a sevoflurane concentration over 4 vol%.[20] In our study, the mean inspiratory/expiratory sevoflurane concentration during steady state was only 2.2/2.8 vol%, which is not considered high. In addition, our normal EEG findings indicated that the mean inspiratory or expiratory sevoflurane concentrations observed in the present study were within the safe range. Moreover, we did not include the induction period for analysis, which is common when using high concentrations of sevoflurane or bolus administration of propofol to avoid bias.

Several studies have compared the performance of different EEG-derived monitors and other monitors in the patients.[6, 14, 21, 22] Most of these studies reported comparable prediction probabilities for the different monitor types. In the present study, BIS and PSI yielded similar prediction probabilities for distinguishing the steady state from recovery state in children. This result is compatible with those of previous studies. In addition, basically, the present study was planned to compare the values of the two different devices, not to measure the absolute depth of anesthesia in children. Recent research has indicated that EEG parameters such as beta and delta band power are altered based on the depth of anesthesia in children and it would be helpful to develop the monitor with this finding.[23] However, the algorithm of calculation of value of BIS was not unknown and basically developed with EEG of adults. Nevertheless, BIS might be the appropriate monitor for monitoring of depth of anesthesia for children with large number of researches to support this idea. In addition, the result of the present study demonstrated that the agreement and correlation of BIS and PSI was acceptable and it could lead the conclusion of usefulness of PSI in children.

In the present study, propofol administration was followed by inhalation of sevoflurane for the induction of anesthesia in pediatric population. Because BIS or PSI values may represent the mixed effects of these two drugs during the induction period, we did not analyze the correlation between BIS/PSI values and sevoflurane concentration. If sevoflurane had been inhaled from the beginning, BIS or PSI values may have been correlated with sevoflurane concentration.

At the same stable concentration of propofol, BIS values vary in children, relative to those observed in adults,[24] and larger individual variations are observed during halothane or sevoflurane anesthesia in children.[25] Despite these issues, several studies have utilized EEG-based methods to monitor the depth of anesthesia or hypnosis in children, as there is no gold standard for the pediatric population. The PSI is a different EEG-derived index that has been associated with a lack of pain upon attachment in patients. Although BIS and PSI are EEG-based indices, the algorithms used to manage the EEG data differ between the two monitors. Despite these differences, most previous studies have reported very good correlations between the two measures. Our results support the notion that BIS and PSI are comparable with regarding to agreement, correlation and prediction probability in children.

The present study possesses several limitations of note, including the arbitrary definition for the steady state and recovery state in clinical practice. However, this practice is common at our institution and reflects procedures applied in the pediatric population. In addition, we used propofol and sevoflurane for the induction of anesthesia. Therefore, we could not assess BIS and PSI values during the induction period. In addition, it was not easy to apply the BIS and PSI sensors in the alert state because due to fear among the included children.

Conclusion

In conclusion, our findings demonstrate that BIS and PSI can both be used to monitor the steady state and recovery state in pediatric population over 3 years old, although the reference values for the two are different.

Abbreviations

ASA: American Society of Anaesthesiologists, BH: Benzylamine hydrochloride, ENT: Ear-Nose-Throat, E_TCO_2 : End-tidal carbon dioxide, ETT: Endotracheal tube, FIO_2 : Fraction of inspired oxygen, NIBP: Non-invasive blood pressure, NSAID: Nonsteroidal anti-inflammatory drug, PACU: Postanesthetic care unit, PAED: Postanaesthetic emergence delirium, PCA: Patient-controlled analgesia, POST: Postoperative sore throat, RCT: Randomised controlled trial, SpO₂: Peripheral pulse oximetry, VAS: Visual Analog Scale.

Declarations

Ethics approval and consent to participate

The present study was approved by the Institutional Review Board of Seoul National University Hospital (IRB no. 1811-172-991) and registered at <http://register.clinicaltrials.gov> (NCT03792334, Dec 28, 2018, <https://register.clinicaltrials.gov/prs/app/action/SelectProtocol?sid=S0008KCO&selectaction=Edit&uid=U0000Y58&ts=6&cx=-22o4ut>). Each participant was given a verbal explanation and had the time to ask questions about the study protocol, and written informed consent was obtained from one parent or guardian. Verbal consent was obtained from patients under 7

years of age, while written informed consent was obtained from patients over 7 years of age. All procedures followed the principles outlined in the Declaration of Helsinki and its revisions.

Consent to publish

Non applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

Competing interests

No conflicts to report from any of the authors.

Funding

Departmental funding only.

Author's contribution

Sang-Hwan Ji, MD: This author helped in the design of the study, data acquisition, data analysis and interpretation, drafting of the manuscript, and approval of the submitted version of the manuscript.

Young-Eun Jang, MD: This author helped in the design of the study, data acquisition, data analysis and interpretation, statistical analysis and approval of the submitted version of the manuscript.

Eun-Hee Kim, MD: This author helped in the design of the study, data acquisition, data analysis and interpretation, and approval of the submitted version of the manuscript.

Ji-Hyun Lee, MD,PhD: This author helped in the design of the study, data acquisition, and approval of the submitted version of the manuscript.

Jin-Tae Kim, MD,PhD: This author helped in the design of the study, data acquisition, and approval of the submitted version of the manuscript.

Hee-Soo Kim, MD, PhD: This author helped in the design of the study, data acquisition, data analysis and interpretation, statistical analysis, drafting of the manuscript, and approval of the submitted version of the manuscript.

Acknowledgements

None.

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Figures

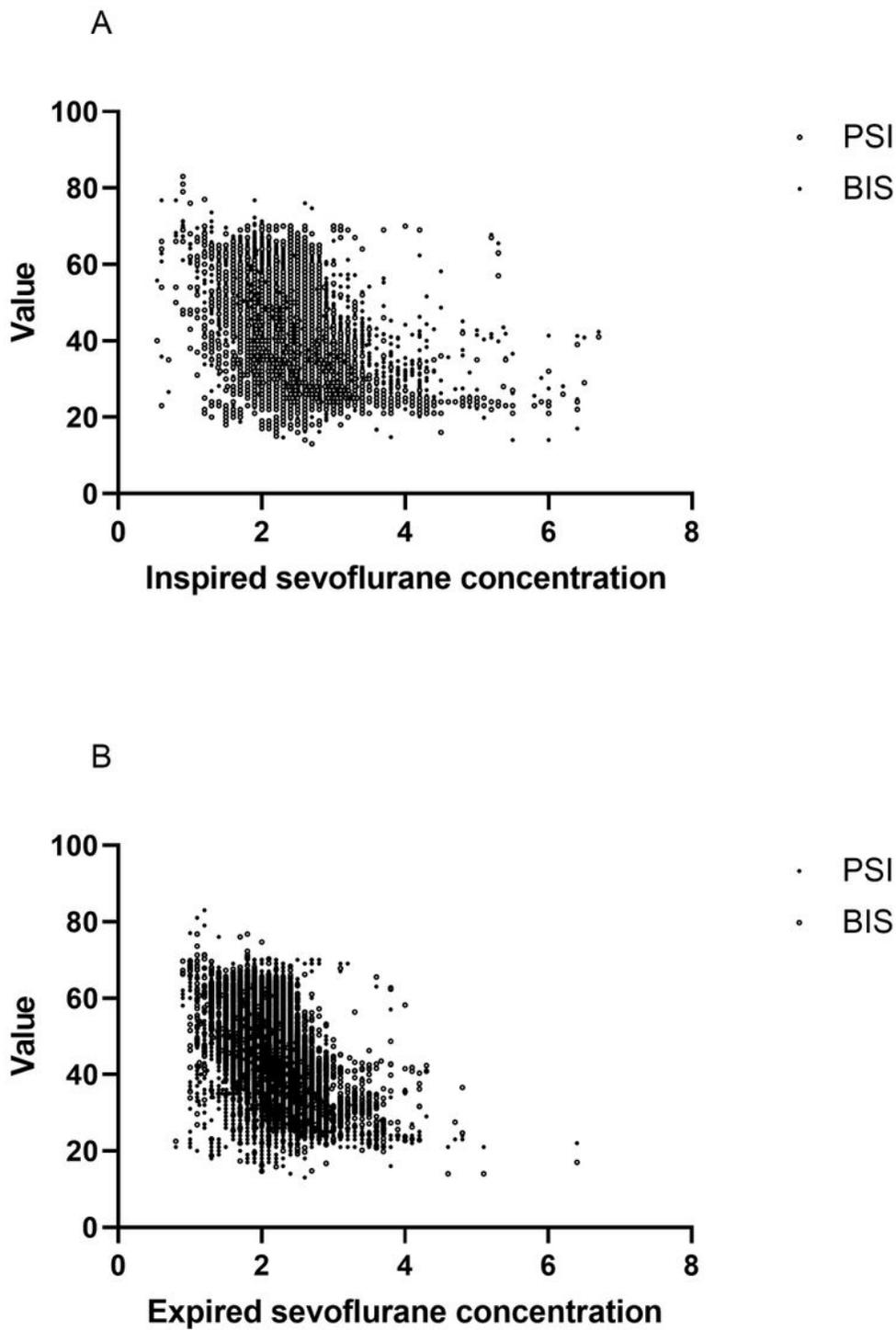


Figure 1

Plots of bispectral index (BIS) and patient state index (PSI) against inspiratory sevoflurane concentration (A) or expiratory sevoflurane concentration (B) during the study period. Comparing to the inspiratory sevoflurane concentration, same values of BIS or PSI had a narrow expiratory sevoflurane concentration.