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Intraoperative awareness and the depth of anesthesia in children: a perspective from pediatric anesthesia

Shoichi Uezono*, Aya Kamata, Osamu Nagata, Makoto Ozaki

Department of Anesthesiology, Tokyo Women's Medical University, 8-1 Kawadacho, Shinjuku-ku, Tokyo 162-8666, Japan

Abstract

The bispectral index (BIS) monitoring, using electroencephalographically-derived method, has shown some promise to measure 'depth of anesthesia' for various anesthetics. A large fraction of the literature that has investigated BIS monitoring demonstrates that BIS correlates well with clinically important endpoints and many clinical utility trials have been undertaken in adults to prove its effectiveness to improve perioperative patient care. As the use of the technology grows, other potential applications have been investigated; BIS as a monitor in pediatric anesthesia and BIS as a monitor to measure the depth of sleep may serve as examples. If the two are proved useful, these successes may bring clinicians another application of this technology: BIS to monitor unconsciousness state of babies to prevent sudden infant death syndrome or apparent life threatening event.

Keywords: Pediatric anesthesia; Monitoring; Bispectral index; Sudden infant death syndrome

1. Introduction

Monitoring pediatric patients during anesthesia was limited to inspection of chest movement and occasional palpation of the pulse until the late 1940s. In the past three decades, we have seen an explosion of new technological advancement in perioperative monitoring, particularly cardio-respiratory monitoring such as pulse oximetry and capnogram [1]. These technologies have been attributed to a substantial decrease in morbidity and mortality related to anesthesia [2]. However, monitoring the central nervous system (CNS) effects of anesthesia in an objective and reliable manner remains challenging, this forced anesthesiologists to provide most anesthetics without measuring drug effect on CNS despite the fact that the primary target organ of general anesthetics is the brain. In fact, most common guide to overall anesthetic effect is usually cardiovascular toxicity. Such a practice of anesthesia may cause overdosage or underdosage of anesthetic agents, thereby potentially leading to prolonged recovery from anesthesia and awareness during general anesthesia, respectively.

Intraoperative awareness is a tremendously frightening experience, and may result in serious emotional injury including recurring nightmares and posttraumatic stress disorder [3]. In addition, with recent increased public knowledge of awareness during general anesthesia, this problem may have medico-legal implications. Therefore, a reliable monitor that could confirm that the level of anesthesia is adequate to ensure lack of awareness is obviously desirable. Although there is no evidence that monitoring the depth of unconsciousness prevents awareness, we may presume that by maintaining a sufficient depth of unconsciousness, this will be achieved. The question then remains whether or not depth of unconsciousness is amenable to measurement and if so what constitutes a sufficient depth to prevent awareness.

In 1996, the US Food and Drug Administration approved a new technology called the bispectral index (BIS), an electroencephalographically derived parameter that was developed specifically to measure the hypnotic component of anesthetic state. With a relative success of BIS monitoring as the first technology that provides continuous and direct CNS assessment of anesthetics, BIS monitoring in the operating room is gaining widespread popularity. The purpose of this review is to provide a quick overview of clinical development and validation of BIS, to discuss its usefulness in pediatric anesthesia, and to explore the possibility of BIS as a monitor of wakefulness for new patient populations such as the patients with sleep disorder or at risk for sudden infant death syndrome (SIDS).

* Corresponding author. Tel./fax: +81-3-5269-7336.
E-mail address: uezono@anes.twmu.ac.jp (S. Uezono).

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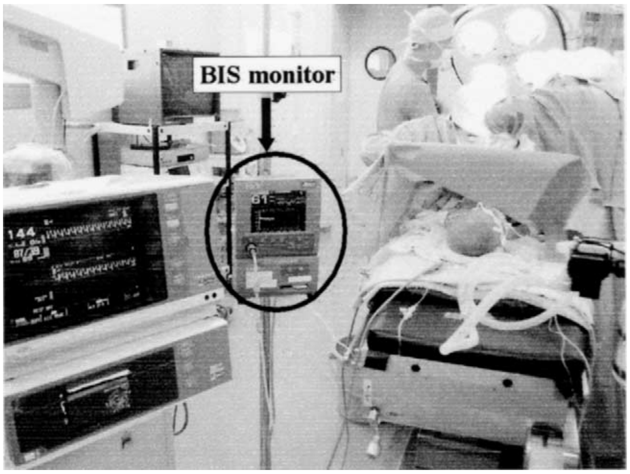

Fig. 1. The BIS monitor (model A-200 monitor; Aspect Medical Systems, Newton, MA) in the operating room. Note how compact the device is compared to a common multiparameter monitoring system.

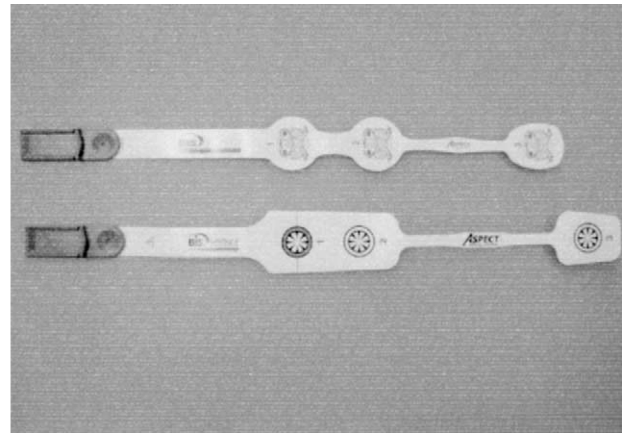

Fig. 3. EEG electrodes used in Aspect Medical Systems for pediatric patients (above) and adult patients (below). These self-prepping, easy-to-use electrodes fairly guarantee adequate impedances for recording of EEGs in the operating room environment.

2. Bispectral index (BIS): theoretical basis and clinical validation

The electroencephalogram (EEG) has long been proposed as a method of measuring anesthetic effect. Significant correlation between anesthetic doses and various specific EEG patterns have been described and established to assess neurological function in certain high-risk procedures [4]. However, practical issues surrounding the EEG preclude its routine use as a monitor of anesthetic effects [5]; it is expensive and bulky; it requires expert interpretation; its effects are not uniform among various anesthetics; the raw EEG creates overwhelming amount of data; application of EEG electrodes requires excessive time; an easily understood display is not feasible and so forth. Because all general anesthetics suppress consciousness by depressing the CNS and we can measure cerebral electrical activity by the EEG, it is reasonable then to believe that some component of the EEG should relate to the effects of anesthesia on the central nervous system. Accordingly, various computer-processed EEG derivatives such as power spectral edge and median frequency were described as potential measures of anesthetic effect on the CNS [6,7]. However, these measures had clear shortcomings: inappropriate dose-response curves, unpredictable performance during light or deep levels of anesthesia, and poor correlation to clinical status.

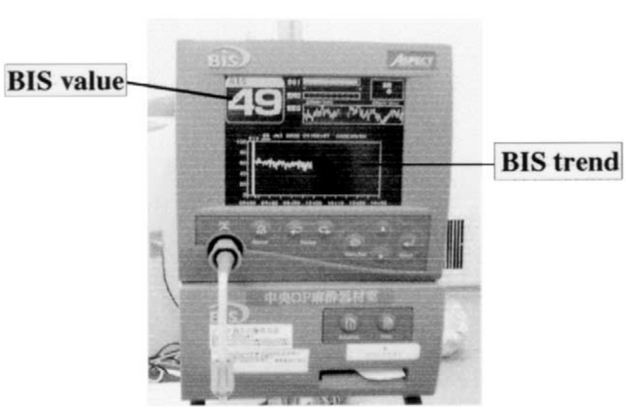

Fig. 2. BIS is displayed as a single value and a trend on the monitor.

To circumvent the difficulties faced by the aforementioned processed-EEG analysis, BIS was developed to capture and quantify the essence of the brain response to anesthesia. Briefly, the analysis is based on bispectral processing that determines the harmonic and phase relations among the various EEG frequencies calculated with Fourier's analysis [8]. BIS represents a different descriptor of the EEG in that inter-frequency phase relationships are measured, whereas the prior generation of EEG measures used a fast Fourier transformation to produce information about power and frequency. Details of the computation of bispectrum were reviewed extensively elsewhere [9]. Data contained in both bispectral analysis and in conventional frequency/power analysis of the EEG are used to create a proprietary parameter called the BIS, which measures the hypnotic component of the anesthetic state. BIS is expressed as a dimensionless number from 0 to 100 with 100 representing an awake EEG and 0 complete electrical silence.

The BIS is an empiric, statistically derived measurement from a large database of EEG activity in healthy adult volunteers at various clinically important endpoints and hypnotic drug concentrations. The relationship between BIS, clinical endpoints and memory function were evaluated in a volunteer study using various anesthetics [10]. With increasing dose of an anesthetic, transition from wakefulness to unresponsiveness to noxious stimuli was observed, which was paralleled by a decrease in BIS. The BIS values correlated better than the measured drug concentration with the validated sedation scale (the Observer's Assessment of Awareness/Sedation). For instance, at the calculated plasma propofol concentration of 2 mcg/ml, some are conscious and others are unconscious. This is in

Fig. 4. A recently introduced pediatric sensor attached to a 5-month-old infant undergoing general anesthesia.

contrast when none are conscious at the BIS of 60. These results indicate that BIS has a high prediction probability for correctly identifying loss of consciousness: probability of unconsciousness is low if BIS is greater than 60 and high if BIS is less than 60. In this regard, BIS is not an absolute measure of state, but a measure of probability of state.

The current BIS monitor (model A-2000; Aspect Medical Systems, Newton, MA) has successfully overcome several fundamental technical issues so that it can be used as a routine monitor of anesthetic effect in the operation room environment: it is a comparatively small, freestanding device (Fig. 1); its display is in a user-friendly format (Fig. 2); it does not require calibration and provides accurate physiologic information in seconds; it uses self-prepping EEG electrodes, and eliminates extensive skin preparation that traditional EEG recording would require (Figs. 3 and 4).

3. BIS and pediatric patients

Although BIS was developed using adult EEGs, with the introduction of a smaller-sized sensor specifically designed for children, this new technology has recently been investigated in infants and children in various settings: during general surgical procedures [11,12], during cardiac surgery [13], and in the pediatric intensive care unit [14]. Denman and colleagues found that there was an approximately linear relationship between BIS and end-tidal sevoflurane in pediatric patients, indicating clinical usefulness of BIS in this population [11]. In a prospective, randomized, clinical utility study in children undergoing inguinal hernia repairs or tonsillectomies, Bannister et al demonstrated that BIS monitoring was associated with a significant (25%) reduction in sevoflurane administration and a 25–40% reduction in recovery time [12]. In pediatric patients who are mechanically ventilated in the pediatric intensive care units, the BIS value was found to correlate well with increasing depth of sedation irrespective of the drugs used for sedation [14]. They also claimed that a BIS value <70 had a high sensitivity (0.87–0.89) and a high positive predictive value (0.68–0.84) to differentiate adequate from inadequate sedation.

Caution is warranted, however, about interpreting these results [15]. First, we should bear in mind that the BIS value is based on adult EEG data and may not apply to the pediatrics population, particularly to children younger than 5 months of age and perhaps up to 5 years. During that period, the brain continues to mature with accompanying EEG changes. Lack of data on EEG changes produced by anesthetic drugs in this patient population makes it difficult to interpret BIS values in children when the database from which BIS values are derived is completely different. Second, the validation of the BIS monitor in pediatric patients poses some problems: the absence of a 'gold standard' for sedation or sleep, difficulties in distinguishing purposeful movement from non-specific startle response, and ethical challenges in recruiting children as volunteers.

4. BIS and naturally occurring sleep

Sleigh et al. examined how physiological sleep affects the BIS in five healthy adult subjects and compared the changes in BIS with the conventional EEG stages of sleep [16]. They found that the BIS decreased during increased depth of sleep in a fashion very similar to the decrease in BIS that would occur during general anesthesia; light sleep, slow-wave sleep and rapid eye movement occurred at the BIS values of 75–92, 20–70, and 75–92, respectively. These striking similarities in BIS measurement may indicate that the transition from consciousness to the natural sleeping state is similar to the unconsciousness induced by anesthesia. Consequently, they speculate that BIS monitoring may be a simple indicator of depth of sleep, suggesting of a usefulness component in postoperative somnographic studies. Their ideas were further supported by the recent study by Tung et al. [17].

They demonstrated that the BIS monitor accurately detected the onset of naturally occurring sleep in non-medicated adult volunteers, and that the changes in BIS values consistently preceded subjective or objective loss of consciousness. Based on these results, they propose BIS monitoring as a potential candidate for an effective monitor of inadvertent sleep onset in sleep-deprived individuals. It needs to be emphasized, however, that these data do not constitute complete validation as a monitor. Further study is warranted before new application of this monitoring is tested in pediatric patients. If it proves promising, such a device would have tremendous potential use in situations where malfunctioning of wakefulness during sleep may have catastrophic consequences as seen in SIDS.

5. Conclusions

As the BIS technology evolves, its application is expanding from strictly intraoperative monitoring to other venues in various clinical settings. With developments in sensor technology designed for infants and children, signal processing methodology and algorithm changes based on a database derived from pediatric patients, this new technology may potentially provide some insights into the prevention of SIDS.

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