REVIEWS

Monitoring for depth of anesthesia: a review

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Abstract

Monitoring depth of anesthesia is a newer advance in the monitoring of anesthesia. Accurate assessment of the depth of anesthesia contributes to tailoring drug administration to the individual patient. Its increasing use may help to prevent awareness or excessive anesthetic depth and to improve the patients' outcomes. Awareness experiences frighten the patients and can leave a lifetime of residual emotional and psychological problems. To date, no monitoring system has been found to measure the depth of anesthesia reliably for all patients and all anesthetic agents. In this review, the author critically analyzes the use of a number of the depth of anesthesia monitors including the traditional techniques and the modern techniques.

Key words

Monitoring, Depth of anesthesia, Sedation

1 Introduction

Many surgical procedures would not be possible without anesthesia or sedation. The goals of anesthesia or sedation are a reversible loss of consciousness with a lack of movement, a lack of awareness or recall, and unresponsiveness to painful stimuli. Inadequate anesthesia or sedation may lead to intraoperative awareness with recall or to prolonged recovery and increased risk of postoperative complications for the patients. Important signs of inadequate anesthesia, signs which develop in response to stress or painful stimuli, are patient movement, increased breathing or blood pressure and increased heart rate [1]. Failure to adjust the anesthetic requirements to individual variations in patient drug requirements and to the intensity of pain stimulation during surgical procedures will also lead to over dosage or under dosage with anesthesia or sedation.

2 Depth of sedation/anesthesia

Minimal sedation (anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes and ventilatory and cardiovascular functions are unaffected.

Moderate sedation (conscious sedation) is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

Deep sedation is a drug-induced depression of consciousness during which patients can not be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

General anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

3 Monitoring for depth of anesthesia

The transition from a state of wakefulness to a state of general anesthesia is accompanied by profound changes in the brain's spontaneous electrical activity recorded from electrodes placed on the scalp (electroencephalogram or EEG). The clinical monitoring is simple and is commonly used by the variety of physicians. Only the advances in computer hardware and signal processing algorithms have enabled the processing of EEG signals.

4 Clinical monitoring

Continuous monitoring of patient undergoing anesthesia or sedation is very important for ensuring the safety of the procedure, and is of paramount importance in order to obtain a correct level of sedation in surgical patients. The physicians need to monitor and evaluate the patients' status and the depth of anesthesia or sedation throughout the procedure. Clinical scoring systems are simple and inexpensive. In addition, clinical observation of the sedated patients can provide an early warning for potentially dangerous problems. The clinical monitoring used to assess intraoperative consciousness are checking for movement, response to verbal command, eyelash reflex, pupillary responses, tearing and pattern of respiration.

4.1 Clinical signs

The most commonly used scoring system is Evans's score [2]. This score assesses autonomic activity related to systolic blood pressure, heart rate, sweating and tears. This system is simple and not requiring specialized equipment. However, these parameters are not specific and the scores can vary widely among individuals. ASA task force members on practice advisory for intraoperative awareness and brain function monitoring have been recommended physicians should be used these clinical signs to assess intraoperative consciousness [3]. Additionally, conventional monitoring systems including electrocardiogram, noninvasive blood pressure, capnography and end tidal anesthetic analyzer are valuable and should be used to help assessment of these clinical signs.

4.2 Skin conductance

Measuring skin resistance level and changes in the resistance of the skin is a simple and noninvasive method for evaluating the sympathetic nerve activity. The measurement of skin conductance is a quantification of the clinical sign of sweat production. Skin conductance is initially low and increases as anesthetic depth is increased. There has a correlation between electrical skin impedance, predicted plasma concentrations of propofol and the MOAAS scale [4]. The individual variability of the measurement values constitutes a problem in the interpretation of skin resistance measurements. In addition, several factors affecting sweating can reduce the accuracy of this monitoring.

4.3 Isolated forearm technique

Isolated forearm technique is a method detecting awareness during clinical practice. The tourniquet is applied to the patient's upper arm before administration of the muscle relaxant, and is inflated above systolic blood pressure to exclude its effect. Movement of the arm indicated wakefulness or light anesthesia, although not necessarily explicit awareness. However, the incidence of movement with this technique can vary with the choice of anesthetic drugs [5]. Other limitations of this technique are the limited time available before the patients are unable to move their arms, level of sedation/anesthesia needed to prevent the movement of patient's arm, and the nonspecific response may be misinterpreted.

4.4 Heart rate variability

Clinically, the beat to beat variability of heart rate may provide information which would be useful for monitoring depth of anesthesia. Three components of the heart rate variability are low, medium and high frequency fluctuations. Heart rate increases during inspiration and decreases during expiration through the parasympathetic reflex. This is called as the respiratory sinus arrhythmia (RSA). The reduction of the RSA is observed during anesthesia together with increase during recovery. Some monitors use the heart rate variability at respiratory frequency or RSA as a method assessing anesthetic depth [6]. However, the vagal tone depends on an intact of autonomic nervous system and healthy myocardial conducting system. Additionally, several factors influencing the heart rate variability in the perioperative setting are conduction abnormalities, autonomic neuropathy and sepsis as well as some medications such as beta-blockers and atropine.

4.5 Ramsay scale

The Ramsay scale was developed in 1970 in order to promote adequate sedation in intensive care units. It is internationally one of the most frequently cited sedation assessment tools. The Ramsay scale mainly involves a positive approach to the patient, designed to cause minimal disturbance to sleep. The level of sedation in mechanically ventilated patients is most often assessed with the Ramsay scale. This sedation scale divides into six score responses [7].

　　1　Anxious, agitated, restless

　　2　Cooperative, tranquil, oriented

　　3　Drowsy, response to verbal command

　　4　Asleep, brisk response to light glabellar tap and loud auditory stimulus

　　5　Asleep, sluggish response to light glabellar tap and loud auditory stimulus

　　6　No response to stimulus

To date, the reliability of the Ramsay scale remains controversial. Many studies show that there are insufficient evidences to support the reliability of the Ramsay sedation scale as a measure of sedation assessment [8, 9]. In contrast, several studies demonstrate that the inter-observer reliability of the level of sedation measurements, performed in daily clinical practice within a large team of physicians, proved to be almost perfect [10, 11]. However, the Ramsay scale is largely outdated and has been superseded by more appropriate, practical scoring tools.

4.6 Modified observer assessment of alertness/sedation scale MOAA/S)

The Modified Observer Assessment of Alertness/Sedation scale (MOAA/S) is a six-point scale ranging from 5 to 0. It entails a positive action that involves eliciting a response to increasingly intense stimuli[12]. Patients are considered to have loss of consciousness at the transition between level 3 and level 2.

　　5　Responds readily to name spoken in normal tone

　　4　Lethargic response to name spoken in normal tone

3   Response only after name is called loudly and/or repeatedly

2   Response only after mild prodding or shaking

1   Response only after painful trapezius squeeze

0   No response after painful trapezius squeeze

To date, the author also uses the MOAA/S for sedation for various gastrointestinal endoscopic procedures [13-15]. Generally, the MOAA/S and the Ramsay scale are not interchangeable with the definitions of the levels of sedation. There is evidence of a correlation between the MOAA/S score and the Bispectral (BIS) measurement in several studies [16]. The monitoring of stress response during surgery is important, because prolonged surgical stress can lead to increased morbidity and delayed postoperative recovery [17]. An appropriate depth of sedation is routinely adjusted by titration of sedative concentration. Generally, the changes in heart rate and arterial blood pressure were used as signs of increased nociception during sedation but their specificity and sensitivity is not very high [18].

5 Anesthetic depth monitoring tools

Because of clinical scoring systems are often inadequate in evaluating the patient's level of consciousness, many instrumental tools of anesthetic depth monitoring have been proposed, and particularly the direct evaluation of the central nervous system actions of anesthetic drugs. The monitor that would enable objective, reproducible and continuous measurement of anesthetic depth has lead to the development of EEG or AEP (auditory evoked potentials) based monitors[1, 19].

6 Factors that interfere EEG measurements

The quality of EEG records is mainly influenced by internal or external sources of electromagnetic waves. Numerous sources of interference can mislead EEG measurements. The common sources of interference are the electrical activity of head muscles [20], cardiac pacemaker [21], hot air blanket systems [22] and the electrocoagulation needles [23]. The EEG activity is also influenced by anesthetic agents. However, ketamine does not change the BIS index even when patients are unconscious[24]. Ketamine has no effects on AEP [25]. The effects of nitrous oxide on EEG or BIS value are varied and therefore unpredictable [24, 26, 27]. So, the current EEG or AEP-based anesthetic monitoring devices are not able to reliably assess the patient's depth of anesthesia when ketamine or nitrous oxide is used.

Physiological conditions, such as age [28], race [29], gender [30], low body temperature [31], acid-base imbalances [32], low blood glucose [33] or cerebral ischemia [26] also have a significant effect on patient can influence the EEG. The changes in the patient's age or general health may require adjustment of anesthetic agents. This variability in drug concentration is caused by variability of physiological effects of drugs on the differences in pharmacodynamics and pharmacokinetics. Neuromuscular blocking agents have the effects on muscle electrical activity and indirectly on the signal quality of EEG measurement [34]. AEP are the responses of the auditory pathway to sound stimuli. An AEP is calculated by repeatedly applying an auditory stimulus to the patient and averaging EEG periods that immediately follow each stimulus[6]. Compared to the raw EEG, AEP is less sensitive to artifacts. However, there still have no direct measure of consciousness available in clinical practice and thus no gold standard against which to test EEG or AEP derived indices of anesthetic depth [35].

7 Commercial monitoring tools

The anesthetic depth monitoring technology is promising and used widely, nevertheless to date no health authority has so far recommended that such monitors should be compulsory during general anesthesia or sedation, but should be considered only on an individual basis. To date, there have many commercial monitoring tools.

7.1 Bispectral Index Monitor

The Bispectral index (BIS) was first introduced in 1992 by Aspect Medical Systems. The main component of the BIS monitor is the bispectral analysis, which evaluates the phase relations from a single channel EEG signal measured from the patient's forehead. Recently, the BIS is developed to ease EEG interpretation. It gives the level of sedation as a constant read-out from the device after analysis of single channel EEG findings. The BIS has been reported to be more precise in measurement of the depth of anesthesia. Among instrumental tools for anesthetic depth monitoring, BIS monitor is now widely used due to its reliability and applicability. In addition, the BIS monitoring is a noninvasive method of assessing patient's level of consciousness. The BIS scale ranges from 0 to 100 (0, no cortical activity or coma; 40-60, unconscious, general anesthesia; 60-70, deep sedation with low probability of explicit recall; 70-95, light to moderate sedation; 95-100, awake). BIS monitor has been employed to monitor the depth of anesthesia [36] and sedation in intensive care unit patients [37]. Additionally, BIS monitor is also the anesthetic depth monitoring that has been routinely used in pediatric anesthesia [38, 39].

Generally, the BIS or alternative EEG-based monitoring of anesthetic depth might be useful in preventing oversedation and in reducing propofol dosages during the maintenance phase of the procedure [40]. However, the previous observational study of BIS during nurse-administered propofol sedation (NAPS) found that the BIS scores lagged substantially behind actual sedation scores during both induction of sedation and recovery[41]. Additionally, several studies also demonstrated that BIS did not lead to reduction in mean propofol dose or recovery time when used as an adjunct to NAPS for colonoscopy, or when used as the primary target for sedation. No clinically important role for BIS monitoring as an adjunct to NAPS has yet been established [42, 43].

7.2 Narcotrend monitor

The Narcotrend monitor is produced by Monitor Technik, Hannover Medical School and was introduced in the year 2000. It performs a computerized analysis of the raw EEG. Narcotrend monitor has two recording modes; the one channel mode as the standard for the assessment of the depth of hypnosis during anesthesia or sedation, and the two channel mode for comparison of signals from the two hemispheres of the brain. After accounting for the artifacts, a multivariate statistical algorithm is used for analysis which results in a six-stage classification from A (awake) to F (general anesthesia/coma) and 14 substages [44]. Additionally, the Narcotrend would have less problems with EMG interference than the BIS monitor[45]. This is most likely due to the fact that the Narcotrend modulates the index value with artifact surrogate analysis. The Narcotrend-guided sedation demonstrated lower hemodynamic changes and fewer complications compared with the clinical assessment-guided sedation for endoscopic retrograde cholangiopancreatography procedure. However, the Narcotrend and clinical assessment-guided deep sedation showed comparable propofol dosage and recovery time [46].

7.3 AEP Monitor/ 2

The first commercial monitor based on AEP was introduced by Danmeter in 2001. After further research, the same company introduced the new version of the monitor. The AEP Monitor/2 (Danmeter A/S, Odense, Denmark) features an auditory evoked potential (AEP) and EEG-derived hybrid index of the patient's hypnotic state. This monitor uses autoregressive models with exogenous input (ARX) to detect the AEP. The ARX was used because the method enables fast responses of the monitor [47]. Like other successful monitors the new version of the index also calculates the AEP-ARX-Index (AAI index), which is a dimensionless number. The AAI index can be displayed on two scales; either from 0 to 100, or from 0 to 60.

Because the EMG is propagated in the same frequency band, the AAI can be influenced by the EMG artifacts. The decision how the AAI is constructed from AEP and EEG analyses is made by the weighting function, which is based on the signal to noise ratio. All of the above parameters must be monitored simultaneously in order to ensure optimal sedation/anesthesia of the patient during general anesthesia[48, 49]. Several studies have compared AAI with BIS and revealed that the AAI was more sensitive in monitoring depth of anesthesia and in predicting recovery to consciousness [50, 51].

7.4 PSA 4000 Monitor

The Patient State Analyzer 4000 (PSA) was developed by the Physiometrix, North Billerica, MA and launched in 2001 in the USA. The PSA monitor calculates the value of the index from four EEG channels. The acquired signals are pre-processed and an artifact removal algorithm is applied. The Patient State Index (PSI) uses a set of features that best describe the variances, which are related to the EEG. The development of the PSI algorithm was based on three databases of EEG records, which were used for development of artifact detection and removal algorithms, classification algorithms and finally a third database was used for calibrating the index [52]. The PSI is a dimensionless number from 100 (awake) to 0 (isoelectricity).

7.5 Cerebral State Monitor

The Cerebral State Monitor (CSM) was introduced by the Danmeter Company in 2004.The ability of CSM for separation of consciousness and unconsciousness was comparable to other commercially available EEG-based devices[53]. Although, CSM has a simpler algorithm in comparison to Narcotrend and PSI, it is the slowest to respond to a change in sedation. The study of Hoymork et al. showed that the CSM was a satisfactory alternative to BIS for monitoring hypnotic effect in 87% of non-paralyzed patients. In 13% of the patients, CSI displayed values indicating an awaked state despite clinical sleep, all correctly identified with the BIS. However, their study was done with the very first version of the CSM, while the BIS monitor has undergone several revisions [54].

7.6 Entropy Module

Another way of using EEG data is for the calculation of entropy, which is a measure of the irregularity, complexity or predictability characteristics of the data [55]. The Entropy Module was introduced in 2003 by the Datex-Ohmeda Company. The increasing depth of anesthesia causes increase in regularity of the EEG, which can then be inferred by the entropy and used to estimate the depth of anesthesia.

Two features of this monitor are state entropy (SE) and response entropy (RE). Both are dimensionless numbers between 91-0 and 100-0, respectively. The SE includes information only from EEG, and the RE includes the EMG activity and can be therefore used as a surrogate parameter. The Entropy monitor is also the anesthetic depth monitor that has been routinely used in pediatric anesthesia [38, 39].

8 The response time of DGA monitors

One of the most important parameters of the anesthetic depth monitor is its response time to a rapid change in the level of sedation/anesthesia. The response time is between 30-100 seconds for the transition between EEG suppression and the awaked state for BIS, Narcotrend and CSM [56]. However, the response time is not constant and is dependent upon the depth of anesthesia. The time delays of the tested indices may limit their value in prevention of recall of intraoperative events. Furthermore, different latencies for decreasing and increasing values may indicate a limitation of these monitors for the pharmacodynamic studies [57].

9 Conclusions

One of the objectives of anesthesia is to ensure adequate depth of anesthesia to prevent the patients' awareness. All available monitors are no predictors whether the depth of anesthesia is sufficient for the painful surgical stimulus. The anesthetic personnel must consider any technique for monitoring of the depth of anesthesia as an individual help in improving care for their patients. Recent advances in the introduction of EEG-based monitors have made important contributions towards understanding of the fundamental changes in brain activity brought about by anesthetic agents. The development of these monitors, which directly measures the state of consciousness, would also enable a safe and cost-effective anesthetic procedure.

Table. Comparison of anesthetic depth monitors

	BIS	Narcotrend	AEP Monitor/2	PSA 4000	CSM	Entropy
First introduced	1992	2000	2001	2001	2004	2003
Produced by	Aspect Medical System	Monitor Technik	Danmeter	Physiometrix	Danmeter	Datex-Oh meda
Time delay Awake to deep anesthesia	61 sec	26 sec	No data	No data	55 sec	No data
Deep anesthesia to awake	63 sec	90 sec	No data	No data	106 sec	No data
Electromagnetic interference	Moderate	Moderate	No data	No data	Moderate	High
Correlation with clinical signs	Yes	Yes	Yes	Needed more studies	Yes	Yes

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