Correlation of bispectral index (BIS) monitoring and end-tidal sevoflurane concentration in a patient with lobar holoprosencephaly

Dario Galante⁵, Donatella Fortarezza⁵, Maria Caggiano⁵, Giovanni de Francisci⁶, Dino Pedrotti⁷, Marco Caruselli⁸

⁵ University Department of Anesthesia and Intensive Care, University Hospital Ospedali Riuniti of Foggia, Italy
⁶ Department of Anesthesia and Intensive Care, Agostino Gemelli Hospital, Catholic University of the Scared Heart, Rome, Italy
⁷ Department of Anesthesia and Intensive Care, S. Chiara Hospital, Trento, Italy
⁸ Department of Anesthesia and Intensive Care, La Timone Children's Hospital, Marseille, France

Received 27 March 2014; accepted 3 July 2014
Available online 25 October 2014

Keywords
Holoprosencephaly; Bispectral index; Sevoflurane; Seizures

Abstract
Objective: The bispectral index (BIS) is a parameter derived by electroencephalography (EEG) which provides a direct measurement of the effects of sedatives and anesthetics on the brain and offers guidance on the adequacy of anesthesia. The literature lacks studies on BIS monitoring in pediatric patients with congenital brain disease undergoing general anesthesia.

Clinical features: A 13-year-old child weighing 32 kg, suffering from lobar holoprosencephaly, underwent surgery in which the bispectral index (BIS) monitoring the depth of anesthesia showed an abnormal response. Detailed analysis of the trends of BIS values in the different observation times demonstrated sudden falls and repetitive values of BIS likely related to repetitive epileptiform electrical activity caused by sevoflurane.

Conclusion: The BIS is a very useful monitoring tool for assessing the degree of depth of anesthesia and to analyze the electroencephalographic variations of anesthetics. Particular attention should be given to patients with congenital disorders of the central nervous system in which the BIS may give abnormal responses that do not reflect an accurate assessment of the depth of anesthesia.

© 2014 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. All rights reserved.
Introduction

Holoprosencephaly

Holoprosencephaly (HPE) is a complex brain malformation in which there is an incomplete separation of the forebrain between the 18th and 28th day of intrauterine life, affecting both the forebrain and the face, causing neurological and facial defects of varying severity. It has a prevalence of 1 in 250 during early embryo development, and 1 in 10,000 to 1 in 20,000 at term.

Three classic forms of progressive severity have been described, classified according to their anatomical features: HPE lobar, semi-lobar, and alobar. A milder subtype, known as middle interhemispheric variant (MIH), was also identified. The HPE phenotype also includes aprosencephalia/atelencephalia (the most severe sign), schizencephaly and septo-preoptic HPE. The less severe forms are defined microforms, characterized by defects in the midline, in the absence of brain malformation typical of HPE. However, the disease is characterized by a continuous spectrum of abnormal separation of the cerebral hemispheres rather than a distinct subdivision of these forms which present, however, significant in clinical inter- and intra-familial variability. In many cases, there is a correlation between the severity of facial abnormalities and brain anomaly (with the exception of mutation cases in the ZIC2 gene). In descending order of severity the main facial features are cyclopia, a proboscis, premaxillary agenesis, a cleft lip, coloboma, retinal dysplasia, choanal stenosis, stenosis of the pyriform sinus, hypotelorism, a single median maxillary incisor, and even a normal face. Severe forms (especially in the presence of a chromosomal abnormality) are often fatal and mortality is associated with the severity of the brain malformation and associated defects. In children who survive, a broad spectrum of related signs has been described: developmental delay, hydrocephalus, motor deficits, eating problems, motor dysfunction, epilepsy, and hypothalamic dysfunction. Endocrine disorders from pituitary abnormalities, such as central diabetes, are common.

Lobar holoprosencephaly is the milder classic form of holoprosencephaly. It is characterized by the separation between the left and right cerebral hemispheres and lateral ventricles with a junction along the frontal neocortex, particularly rostrally and ventrally. Approximately 19% of patients with lobar HPE have the shape.

The bispectral index

Bispectral index (BIS) monitoring allows for an early assessment, in real time, of the effects of anesthetic agents during monitored patient care. The clinical impact of BIS monitoring has been demonstrated in several randomized controlled studies that reveal how this tool also allows for greater patient safety. In particular, this equipment can reduce the risk of a potential awareness and/or intraoperative awareness measured on a continuous, non-invasive level of sedation of the patient by means of special adhesive sensors. The bispectral index is a parameter derived by electroencephalography (EEG) which provides a direct measurement of the effects of sedatives and anesthetics on the brain and offers guidance on the adequacy of anesthesia.

Research shows that under general anesthesia approximately 2 out of 1000 patients experience an intraoperative awareness. The BIS is currently the only technology for monitoring the state of consciousness that can reduce the incidence of intraoperative risk in adults by about 80%. The BIS is represented by a numerical value between 0 and 100, two numbers which indicate the absence of brain activity and wakefulness. The anesthesiologist, thanks to this index, is able to administer...
the optimal quantity of drugs for each patient so as to maintain the BIS value within a range that guarantees a nonverbal response to stimuli and the low probability of explicit memory. Prospective studies have shown that a BIS maintained between 40 and 60 ensures an adequate hypnotic state during anesthesia.

The reliability and accuracy of BIS monitoring for pediatric patients is still being studied, especially in very young children, neonates, and infants. In addition, there are no studies on the use of the BIS in pediatric subjects suffering from rare congenital diseases of the central nervous system. A wide variability in the BIS values has been observed in many children with respect to the dosages of anesthetics used.

Case report

One 13-year-old child weighing 32 kg, suffering from lobar holoprosencephaly, was brought to our attention for orchiopexy surgery. The child was in drug treatment with sodium valproate, clorazepam, levothyroxine sodium, somatropin, and desmopressin. The induction was made via inhalation, without premedication, through a mixture of air, oxygen, and sevoflurane at a concentration of 6% and FiO2 of 0.4, immediately after a peripheral vein was cannulated, followed by the administration of 2 µg/kg of fentanyl and cisatracurium 0.15 mg/kg. Then a ProSeal laryngeal mask airway (PLMA) size 2.5 was inserted. The child was then connected to mechanical ventilation with a mixture of air, oxygen and end-tidal concentration of sevoflurane 3% with FiO2 of 0.4 and subsequently reduced to 2%, as a result of the evaluation with bispectral index, allowing perfect adaptation to artificial ventilation. All routine hemodynamic and respiratory monitoring systems were applied: blood pressure, ECG, ETCO2 and SpO2. From the moment of induction adhesive front sensors were applied for the detection of the bispectral index (BIS Vista Monitoring SystemTM, Aspect Medical System, USA), recording the trends for the duration of the surgery until the awakening of the child. The BIS values were recorded at the following times: T1 (induction), Tsis (surgical incision of the skin), T5 (5 min after incision of the skin), Tsevo2 (after reduction of the concentration of end-tidal sevoflurane 2%), and Trecovery (the cessation of the administration of sevoflurane and upon waking).

During the induction phase with sevoflurane at 6% (T1) the BIS recorded a median value of 27.5 ± 3.5 DS (Fig. 1). At the time of the surgical incision of the skin, with a concentration of end-tidal sevoflurane at 3% (Tsis) a median of 41.5 ± 4.3 DS (Fig. 1), and 5 min after the skin incision (T5) a median of 26.0 ± 4.2 DS (Fig. 2). Having considered the above BIS values too low compared to the 40–60 standard relative to an appropriate anesthesia plan, it was decided to reduce the end-tidal concentration of sevoflurane to 2% (Tsevo2).

During this time we recorded BIS values of 26.5 ± 5.3 SD (Fig. 3). At the end of the surgery, about 75 min after induction, we stopped the administration of sevoflurane (Trecovery) until the child woke up. The median BIS values recorded were 29.5 ± 8.1 DS with a maximum of 47 and a minimum of 17 (Fig. 4). The total BIS values recorded related to the whole duration of the operation showed an excessive depth of anesthesia with median values of 27 ± 6.3 SD (Fig. 5).

The awakening took place without complications and in the absence of agitation or seizures. Throughout the duration of the surgery respiratory and hemodynamic parameters were all within the normal range: heart rate 81.3 ± 3.3 SD, systolic blood pressure 101.3 ± 2.0 SD, diastolic blood pressure 52.0 ± 2.3 SD, mean arterial pressure 68.5 ± 1.8 SD (Fig. 6). During the time (Tsevo2), an electroencephalography was recorded (EEG) that demonstrated an epileptiform EEG activity with spikes (Fig. 7).

Figure 1 BIS values at the time of induction (T1, 27.5 ± 3.5 DS) and surgical incision of the skin (Tsis, 41.5 ± 4.3 DS).

Figure 2 BIS values 5 min after the incision of the skin (T5, 26.0 ± 4.2 DS).
Discussion

The literature lacks studies on BIS monitoring in pediatric patients with congenital brain disease undergoing general anesthesia for surgery. Consequently it is very difficult to interpret the mechanisms by which such monitoring may be subject to change or alteration under anesthesia. The BIS expresses the depth of anesthesia with a numeric value ranging from 0 (deep anesthesia) to 100 (awake patient), while values between 40 and 60 are considered ideal for an adequate surgical anesthesia. In principle, the BIS values recorded in the pediatric age are inversely proportional to the concentration of end-tidal sevoflurane and correlate with BIS values during all the time of surgical procedure (27 ± 6.3 SD).

Figure 3 BIS values with 2% end-tidal sevoflurane (T_{sevo2}, 26.5 ± 5.3 SD).

Figure 4 BIS values during the recovery of the patient (T_{recovery}, 29.5 ± 8.1 DS).

Figure 5 BIS values during all the time of surgical procedure (27 ± 6.3 SD).

Figure 6 Hemodynamic parameters recorded during all the time of surgical procedure (HR, heart rate; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, middle arterial pressure). HR 81.3 ± 3.3 SD, SBP 101.3 ± 2.0 SD, DBP 52.0 ± 2.3 SD, MAP 68.5 ± 1.8 SD.

Figure 7 Epileptiform discharges observed during the time T_{sevo2}.
Correlation between epileptiform activity and holoprosencephaly

The BIS is a very useful monitoring tool for assessing the degree of depth of anesthesia and to analyze the electroencephalographic variations of anesthetics. Particular attention should be given to patients with congenital disorders of the central nervous system in which the BIS may give abnormal responses that do not reflect an accurate assessment of the depth of anesthesia. This is particularly important in the case of high concentrations of sevoflurane that may result in epileptogenic action. In these cases, the choice of a different anesthetic technique should be taken into serious consideration.

## Conflicts of interest

The author declares no conflicts of interest.

## References