

EEG bispectral index and hypnotic component of anaesthesia induced by sevoflurane: comparison between children and adults

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This prospective study was designed to evaluate the correlation between the electroencephalographic bispectral index (BIS) and the hypnotic component of anaesthesia (CA) induced by sevoflurane in 27 children and 27 adult patients. BIS and CA were compared at loss of consciousness (LOC) and on recovery of consciousness (ROC). Mean (SD) BIS decreased significantly at LOC in children and adults from 94 (2.7) to 87.4 (4) and from 96.2 (2) to 86.7 (4.4), respectively, without any difference between groups. Correlation coefficients (ρ) between BIS and CA at LOC were -0.761 in children and -0.911 in adults. BIS increased significantly at ROC in children and adults from 74.1 (4.2) to 86.7 (2) and from 80.2 (5) to 90.7 (3), respectively, without any difference between groups. Correlation coefficients between BIS and CA in ROC were -0.876 in children and -0.837 in adults. BIS values at ROC were not different from those at LOC in either group. These data demonstrate that BIS correlates with the hypnotic component of anaesthesia induced by sevoflurane in children as well as in adults.

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The electroencephalographic (EEG) bispectral index (BIS) has been shown to be a quantifiable measure of the hypnotic effect of anaesthetic drugs on the central nervous system.^{1,2} The potential usefulness of BIS monitoring as an indicator of the depth of hypnosis during inhalation anaesthesia,^{3,4,5} particularly during sevoflurane sedation, has been described.^{6,7} Previous studies that evaluated BIS were performed in adults not children. Sevoflurane is well tolerated⁸ in terms of airway complications (causing minimal breath-holding, coughing, excitement or laryngospasm), with minimal changes in haemodynamics; it is used in adults and children for rapid induction of anaesthesia.^{9,10}

This prospective study was designed to evaluate the correlation between BIS and the clinically assessed hypnotic component of anaesthesia (CA score) in children and adults patients when sevoflurane is used as the sole anaesthetic.

Methods

After obtaining institutional review board approval and written, informed consent from the patients or their parents,

54 ASA I patients scheduled for tympanoplasty were assigned to one of two groups designated as child ($n=27$) or adult ($n=27$).

All patients were admitted on the day before surgery and fasted for at ≥ 12 h before their operation. All patients received oral premedication (hydroxyzine 1 mg kg^{-1} , alprazolam 0.015 mg kg^{-1}) 2 h before surgery. On arrival in the operating room, in addition to routine monitoring (heart rate (HR), non-invasive mean arterial pressure (MAP), pulse oximetry), the EEG signal was acquired using four Zipprep electrodes (Aspect Medical Systems, Natick, MA) applied to the forehead, with one on the outer aspect of each malar bone and one at the centre of the forehead, and the ground electrode above the central electrode. The BIS value was displayed using an Aspect EEG monitor (Model A-1000; Aspect Medical Systems). A 24- (for children) or 18-gauge catheter (for adults) was inserted into a forearm vein and used for administration of fluid and drug. A 5% glucose solution (for children) or Ringer's solution (for adults) was administered at $5 \text{ ml kg}^{-1} \text{ h}^{-1}$. Baseline values for BIS and haemodynamic variables were obtained, and then all patients breathed through a face mask connected to a

Table 1 Hypnotic component of anaesthesia (CA) score

Responsiveness	Score
Responds readily to name spoken in normal tone	0
Lethargic response to name spoken in normal tone	1
Responds only after name is called loudly	2
Responds only after mild prodding or shaking	3
Responds only after painful trapezius squeeze	4
Does not respond to painful trapezius squeeze	5

Table 2 Patient characteristics and duration of anaesthesia (mean (SD) or (for gender) distribution)

	Children (n=27)	Adults (n=27)
Age (yr)	8.6 (3.5–13)	39.5 (22–72)
Gender (female/male)	11/16	13/14
Weight (kg)	29.5 (11.3)	72.6 (9.8)
Duration of anaesthesia (min)	62 (30)	125 (47)

semiclosed anaesthetic circuit. Fresh gas flow into the anaesthetic circuit was 6 litres min⁻¹.⁷ The concentrations of carbon dioxide, sevoflurane and oxygen were measured continuously using an infrared anaesthetic gas analyser (Capnomac, Helsinki, Finland), which was calibrated before anaesthesia for each patient using a standard gas mixture. Anaesthesia was induced with 4% sevoflurane in oxygen; ventilation was assisted as necessary. The inspired concentration of sevoflurane was adjusted to obtain loss of consciousness (LOC) and loss of movement. The end-tidal carbon dioxide concentration was kept between 4.67 and 5.34 kPa during the study period. Just after loss of movement and before tracheal intubation, children and adults received a bolus of alfentanil 25 µg kg⁻¹ i.v. followed by a constant infusion of 0.5 µg kg⁻¹ min⁻¹. Tracheal intubation was performed after 5% lidocaine local anaesthetic had been applied to the glottis. The BIS and hypnotic component of anaesthesia (CA score) were evaluated during the onset of sevoflurane-induced anaesthesia, i.e. at LOC, every 15 s until loss of movement occurred, and on recovery of consciousness (ROC). During the onset and offset periods, the CA score was assessed clinically by using the responsiveness component of the observer’s assessment of alertness/sedation (OAA/S) rating scale (Table 1). From LOC until ROC, BIS was recorded continuously. The end of the recovery period was defined as the time when a patient opened their eyes on verbal command (CA=2). During surgery, sevoflurane concentrations were adjusted according to standard clinical practice to maintain haemodynamic stability and avoid patient movement, with the aim of achieving rapid recovery after surgery.

One-way analysis of variance (ANOVA) was performed for comparison of all continuous variables between groups; when indicated, a Bonferroni’s correction was performed for *post hoc* comparisons within and between groups. The

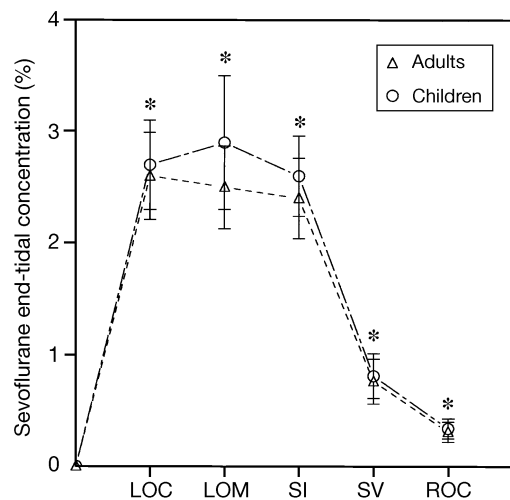


Fig 1 End-tidal concentrations of sevoflurane in child and in adult patients (27 in each group). LOC, loss of consciousness; LOM, loss of movement; SI, skin incision; SV, spontaneous ventilation; ROC, recovery of consciousness. Data are post-stimulus (see Table 1) values. Results are mean ± SD. *Significantly different from baseline values in each group ($P < 0.05$); one-way analysis of variance with Bonferroni’s correction.

relationship between BIS and CA score was evaluated at LOC and ROC using non-parametric Spearman’s correlation analysis. Data are expressed as mean (SD). P values of < 0.05 were considered statistically significant.

Results

Patient characteristics and duration of anaesthesia are shown in Table 2. End-tidal concentrations of sevoflurane during onset of LOC and on recovery were not significantly different between the two groups (Figure 1). With increasing depth of anaesthesia from a CA score of 0 to 5, the BIS decreased significantly from 94 (2.7) in children and from 96.2 (2) in adults to 87.4 (4) ($P < 0.05$) and 86.7 (4.4) ($P < 0.05$), respectively, in the onset period (Table 3). BIS increased significantly from 74.1 (4.2) in children and from 80.2 (5) in adults to 86.7 (2) ($P < 0.05$) and 90.7 (3) ($P < 0.05$), respectively, as the CA score decreased from 5 to 2 in the recovery period (Table 4). BIS values were comparable in the two groups at each time point (Figure 2). Within the two groups, there was no difference between BIS values at LOC and those at ROC. BIS values were inversely correlated with CA scores at LOC in children (Spearman’s $\rho -0.761$) and adults (Spearman’s $\rho -0.911$), and at ROC in children ($\rho -0.876$) and adults ($\rho -0.837$).

Discussion

The main finding of this study was that the EEG BIS correlated with the hypnotic component of anaesthesia induced by sevoflurane in children and in adults. A significant correlation was demonstrated between BIS and CA score during onset of and recovery from sevoflurane-

Table 3 Changes in BIS during the onset of sevoflurane-induced anaesthesia (ANOVA= analysis of variance; *significantly different from a CA score of 0 ($P<0.05$))

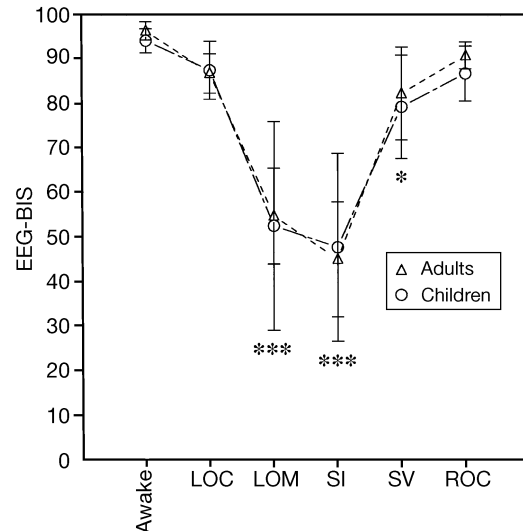
CA score	BIS index		ANOVA (Bonferroni)
	Children (n=27)	Adults (n=27)	
0	94 (2.7)	96.2 (2)	NS
1	93.4 (3)	93 (3.1)	NS
2	93.1 (3.2)	91 (2)	NS
3	91 (5)	90 (2)	NS
4	89 (3)	89.3 (4.2)	NS
5	87.4 (4)*	86.7 (4.4)*	NS

Table 4 Changes in BIS during recovery from sevoflurane-induced anaesthesia (ANOVA=analysis of variance; *significantly different from a CA score of 5)

CA score	BIS index		ANOVA (Bonferroni)
	Children (n=27)	Adults (n=27)	
5	74.1 (4.2)	80.2 (5)	NS
4	80.7 (3)	83.3 (3)	NS
3	82.3 (2)	85.6 (3)	NS
2	86.7 (2)*	90.7 (3)*	NS

induced anaesthesia. An increasing CA score was associated with a decrease in BIS, whereas a decreasing CA score was associated with an increasing BIS.

In this work, adults served as a control group for children as no studies have been done in children to our knowledge. Many studies in adults have demonstrated the ability of the BIS to define depth of sedation induced by sevoflurane⁷ or its ability to predict patient movement in response to skin incision during isoflurane¹¹ or propofol–nitrous oxide anaesthesia.^{12,13} In our study, the CA score did not include the motor response to noxious stimuli. At present, it is not acceptable to include movement in the assessment of depth of anaesthesia and to correlate it with BIS; EEG BIS is a form of cortical function monitoring which cannot predict a response to noxious stimuli mediated by subcortical structures.⁷ Cortical activity does not accurately predict motor response to noxious stimuli.^{3,14} Cortical and subcortical (motor, haemodynamic and endocrine stability) components of anaesthetic ‘adequacy’ are independent of each other. For educational purposes, when it is compared with BIS, depth of anaesthesia should be referred to as the ‘hypnotic component of anaesthesia’. For this reason, in this study, BIS values were not compared with CA scores during surgery, and were only recorded to compare the two groups. Even though the BIS cannot predict directly motor response to noxious stimuli, it can serve in clinical practice as an indicator of depth of anaesthesia as defined by its hypnotic component, for lack of a more specific one. The hypnotic component of anaesthesia can be defined by a threshold of amnesia, beyond which intraoperative recall disappears.

**Fig 2** EEG BIS in child and adult patients (27 in each group). Abbreviations as in Figure 1. Awake=baseline values. Data are post-stimulus (see Table 1) values. Results are mean ± SD. ***Significantly different from baseline values within group ($P<0.001$); one-way analysis of variance with Bonferroni's correction where indicated.

During propofol-induced sedation², none of the patients were able to recall pictures shown during the operation at an OAA/S score of 2, with a corresponding BIS of 80.8 (8.3) (mean (SD)). In the present study, the threshold of amnesia would correspond to a CA score of 3. Further studies are necessary in order to assess the relationship between intraoperative recall and BIS during sevoflurane-induced sedation and anaesthesia. In this study, when using sevoflurane during a monitored anaesthetic technique, the anaesthetist attempted to titrate the drugs to optimize patient comfort, while maintaining cardiorespiratory stability. Further studies are needed to determine whether it will be possible to improve the administration of sevoflurane by using BIS monitoring as an adjunct to routine clinical assessment. Meanwhile, these results inform anaesthetists of the BIS value at which LOC and loss of movement occur in anaesthetized children or adults, allowing adjustment of the sevoflurane concentration to avoid undesirable recall² or movements, and to predict recovery of consciousness if BIS is used.¹⁵ Stable anaesthetic concentrations of sevoflurane could not be obtained in this study during onset of sevoflurane-induced anaesthesia in children because of the excitation period that prohibits noxious stimulation.

The dynamic relationship between end-tidal sevoflurane concentration and BIS has been evaluated.^{16,17} Liu and colleagues¹⁸ showed that, with increasing sedation with benzodiazepines, there was a progressive decrease in BIS. In the present study, a sedative premedication with a benzodiazepine was given orally 2 h before anaesthesia in both children and adults, ensuring stable sedation at the time of measurement of the baseline values of BIS and CA score. These were at satisfactory high levels in both groups, which shows that premedica-

tion did not disturb the level of consciousness. It has already been shown that benzodiazepines do not shorten the time taken to achieve LOC with inhalational anaesthetic induction with sevoflurane.¹⁹ The pharmacokinetic properties of sevoflurane,⁸ i.e. rapid washout from body tissues and low blood-gas partition coefficient, facilitate control over the depth of anaesthesia, and a rapid and smooth induction of, and emergence from, anaesthesia. This explains why the duration of administration of this potent inhalational agent has little effect on BIS and the depth of anaesthesia at the time of ROC. Moreover, in the present study, although duration of surgery was twice as long in adults as in children, there was no significant difference between the two groups in BIS and CA score at the time of ROC.

In summary, the EEG BIS correlated with the hypnotic component of anaesthesia induced by sevoflurane in children and adult patients.

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