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Abnormally low bispectral index and isoelectric electroencephalogram observed after administration of small doses of propofol during induction of anesthesia

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Abstract
We describe a case in which an unexpectedly, abnormally low bispectral index value (BIS = 4) and an almost isoelectric electroencephalogram (EEG) pattern were observed during typical induction of anesthesia with propofol. Starting 2 min after the beginning of propofol administration (1.26 mg kg^{-1}), the EEG recordings showed burst and suppression pattern for the next 12 min. The EEG during this period was characterized by gradual prolongation of suppression periods until the appearance of the isoelectric line. After that, burst activity returned and eventually the burst suppression pattern disappeared. We excluded the possibility of ischemic brain damage, and the evidence increasingly points toward a greater sensitivity to propofol. The findings described in this case report support the thesis that there is a wide variability in the responses of patients to propofol that cannot be detected without continuous monitoring of cortical electrical activity.

Key words Electroencephalogram · Bispectral index · Burst suppression · Intravenous anesthetics · Propofol

Introduction

There is a wide variability in the responses of patients to propofol. Therefore, the dosage and rate of propofol administration should be titrated appropriately to the individual needs of the patient. Factors that influence the propofol dosage requirements include age, weight, pre-existing medical conditions, type of surgical procedure, and concomitant medical therapy. In the absence of an objective monitor of anesthetic depth, it is common practice to titrate the anesthetic drugs using clinical signs. However, the electroencephalogram (EEG)-based methods of monitoring anesthetic depth can guide the anesthetist in obtaining sufficient anesthesia with a reduced amount of anesthetic. Here, we present a case in which an unexpectedly, unusually low bispectral index (BIS) value and almost isoelectric pattern of the EEG were observed during typical induction of anesthesia with propofol.

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Case report

A 65-year-old male patient, 182 cm in height and 95 kg in weight, and American Society of Anesthesiologists (ASA) II (because of diabetes mellitus and mild hypertension; treated with insulin and enalapril for 10 years) was scheduled for excision of a perivesical tumor during general anesthesia. This patient participated in the study of the new EEG-based method of assessing depth of anesthesia. Informed consent was obtained for the operative, anesthetic, and monitoring procedures, in accordance with protocols approved by the Local Ethics Committee.

Standard oral premedication (7.5 mg midazolam) was administered 30 min before admission to the operating theatre. On arrival in the anesthetic room, monitoring by pulse oximetry ($S_{P_{O_2}}$), end-tidal carbon dioxide tension (Et_{CO_2}), noninvasive blood pressure, and ECG (monitor S/5; Datex-Ohmeda, Helsinki, Finland) was commenced, and an I.V. cannula was inserted, after which the patient's lungs were preoxygenated via a face mask for approximately 5 min. Brain electrical activity was measured continuously with an A-2000 BIS Monitor (Aspect Medical Systems, Newton, MA, USA). The low-impedance electrodes (Zipprep; Aspect Medical Systems) were attached to the patient's temporal area and forehead. The impedance of the electrodes was checked every 3 min and remained below 3 kΩ during the study. The unprocessed EEG signal (sampled at 128 Hz) and the processed EEG derivatives, BIS and burst suppression ratio (BSR), were recorded onto a

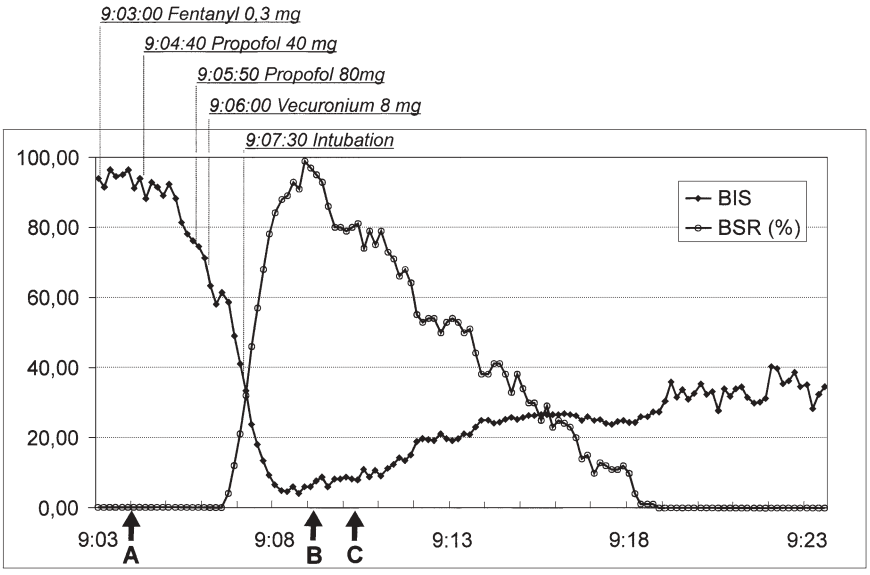

Fig. 1. Changes in bispectral index (*BIS*) and burst suppression ratio (*BSR*) values during induction of anesthesia. *Arrows A–C* indicate the moments at which the electroencephalographic signals shown in Fig. 2 were recorded

portable personal computer using the software Bispectral Analyzer for BIS (BSA for BIS version 3.22B2 for A-2000) [1].

Anesthesia was induced with fentanyl (3 µg kg^{-1}), propofol carefully titrated up to a total dose of 120 mg (1.26 mg kg^{-1}) according to the BIS value, followed by vecuronium (0.08 mg/kg). After obtaining adequate anesthesia (BIS = 40), tracheal intubation was performed. Following intubation, the lungs were ventilated with an oxygen/air mixture ($F_{I_{O_2}} = 0.50$) to achieve normocapnia ($Et_{CO_2} = 38 \pm 2$ mmHg). Dosage and timing of drug administration are shown in Fig. 1.

The recorded EEG was reviewed postoperatively. Two minutes after the beginning of propofol administration, the EEG showed burst and suppression (BS) patterns for the next 12 min (Fig. 1). The EEG during this period was characterized by gradual prolongation of suppression periods until the appearance of an isoelectric line lasting 50 s (Fig. 2B). After that, burst activity returned (Fig. 2C), and finally at 9:18:50 the burst suppression pattern disappeared (Fig. 1). At this time, $S_{P_{O_2}}$ remained greater than 97%, end-tidal CO_2 was 36–38 mmHg, the pulse rate was 60–65 beats min^{-1}, and the blood pressure, which had been 150/90 mmHg at the beginning of induction, dropped to 110/80 mmHg.

When the BIS value returned to 30, maintenance of anesthesia was continued with 50% nitrous oxide in oxygen and 1.2%–1.8% sevoflurane to keep the BIS value between 40 and 60. In addition, intermittent boluses of fentanyl 1 µg/kg and vecuronium 0.01 mg/kg were administered. Surgery lasting 65 min was performed without complications, and the patient tolerated the operation well. After completing the surgery, anesthesia was terminated and muscular block was reversed with 1 mg neostigmine. The BIS value increased gradually, and the patient opened his eyes soon after and responded to commands. After smooth tracheal extubation, the patient returned to the ward in good condition. A detailed neurological examination performed the next day did not show any neurological abnormalities. The postoperative recovery period was uneventful, and the patient was discharged home 6 days later.

Discussion

Burst suppression induced by large doses of anesthetics is associated with reduced cerebral metabolic demand and possible brain protection from ischemia; however this pattern also occurs after head trauma and most characteristically in ischemic brain damage. England reported changes in bispectral index and appearance of burst suppression and flat EEG during transient hypovolemic cardiac arrest [3] that were almost identical to those described in this article. The sudden loss and return of blood pressure after cardiopulmonary resuscitation evoked a parallel changes in the BIS value, with transient electroencephalographic silence (100% burst suppression). The author suggested that the patient was not going to experience permanent ischemic brain injury because of the reversible nature of changes in the electroencephalography [3].

In our case, the most worrisome thought during observation of the flat EEG signal was that this could possibly represent ischemic brain damage. Despite the similar pattern of EEG, it was unlikely that the depression of cortical electrical activity was caused by

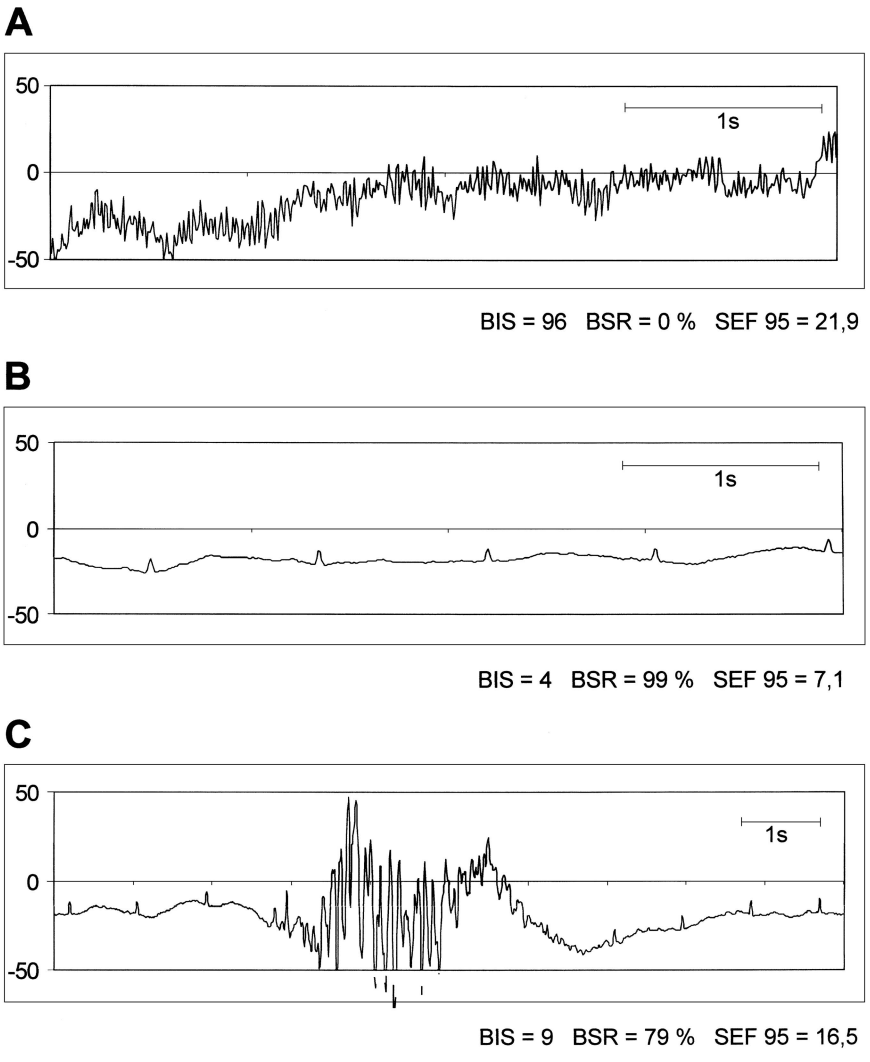

Fig. 2. Raw electroencephalograms (EEG) obtained at the following moments: beginning of the induction of anesthesia (**A**); lowest BIS value (**B**); and typical burst and suppression (**C**). *BIS*, bispectral index; *BSR*, burst suppression ratio; *SEF 95*, spectral edge frequency 95

transient hypotension in the present case. Excluding ischemic brain damage, only one explanation of the observed EEG pattern could be taken into consideration: a greater sensitivity to anesthetics.

Propofol, in common with other hypnotic drugs, induces dose-dependent changes in the EEG. When propofol is infused at a low rate to provide sedation, the most commonly observed EEG change is an increase in beta activity. However, when given at a rate sufficient to produce unconsciousness, propofol produces an increase in delta activity. At even higher infusion rates, propofol can achieve EEG burst suppression [4]. To achieve BS during neuroanesthesia, blood propofol concentrations of $6.3 \pm 1.4\,\mu g\,ml^{-1}$ were required [5]. It is known, from previous studies, that to induce an isoelectric EEG much higher doses of propofol are required [6].

Ravussin and de Tribolet used a continuous infusion of propofol to provide anesthesia for cerebral aneurysm surgery. EEG burst suppression was achieved by increasing the propofol infusion to $500\,\mu g\,kg^{-1}\,min^{-1}$. During this treatment period, volume loading and dopamine infusions were necessary to avoid hypotension [7]. In another study, the propofol infusion rate required to maintain maximal EEG suppression (isoelectric EEG) varied between 250 and $300\,\mu g\,kg^{-1}\,min^{-1}$ and averaged $277 \pm 8\,\mu g\,kg^{-1}\,min^{-1}$. All patients required phenylephrine infusion to support the mean arterial pressure (MAP) [6]. As might be expected, the use of propofol to achieve EEG burst suppression is associated with a reduction in cardiac output and MAP. Propofol $1\,mg\,kg^{-1}$ followed by an infusion of $333\,\mu g\,kg^{-1}\,min^{-1}$ for 30 min, and then $250\,\mu g\,kg^{-1}\,min^{-1}$ was used to produce burst suppression [8]. While maintaining the cardiac filling pressure at baseline levels with supplemental fluids, MAP, cardiac output, and left ventricular stroke work index decreased by 20%, 23%, and 26%, respectively.

In our report, isoelectric EEG was achieved with much lower doses of propofol, which was not associated

with significant changes in hemodynamic parameters. Although high doses of propofol are required to produce EEG suppression, opiates usually combined with a hypnotic allow a propofol-sparing effect. High-dose infusion of sole fentanyl results in slowing of EEG progressing to the formation of delta waves (4 Hz, amplitude 50 mV) but does not produce EEG burst suppression [9]. A supraadditive interaction between fentanyl and propofol has been reported for clinical signs such as loss of consciousness, loss of the eyelash reflex, or regaining consciousness as well as EEG changes [10,11]. Finally, we would like to emphasize that in our case there was no evidence of misinterpretation of data by BIS monitor. Signal quality index persisted at its highest level (100%). Impedance of the electrodes remained below 3Ω. In addition, the whole recorded raw EEG signal was inspected visually afterward. During the period of lowest BIS, it showed an isoelectric line disturbed only by periodic, regular (70 min^{-1}) ECG artifacts (see Fig. 2B).

In summary, the findings described in this case report support the thesis that there is a wide variability in the response of patients to propofol that cannot be detected without continuous monitoring of cortical electrical activity during the operating period.

References

1. Hagihira S, Takasina M, Mori T, Mashimo T, Yashiya I (2001) Practical issues in bispectral analysis of electroencephalographic signals. Anesth Analg 93:966–970
2. Rampil IJ (1998) A primer for EEG signal processing in anesthesia. Anesthesiology 89:980–1002
3. England MR (1999) The changes in bispectral index during a hypovolemic cardiac arrest. Case report. Anesthesiology 91:1947–1949
4. Biebuyck JF, Gouldson R, Nathanson M, White P, Smith I (1994) Propofol: an update on its clinical use. Anesthesiology 81:1005–1053
5. Van Hemelrijck J, Tempelhoff R, White PF, Jellish WS (1992) EEG-assisted titration of propofol infusion during neuroanesthesia: effect of nitrous oxide. J Neurosurg Anesth 4:11–20
6. Matta BF, Mayberg TS, Lam AM (1995) Direct cerebrovasodilatory effects of halothane, isoflurane, and desflurane during propofol induced isoelectric electroencephalogram in humans. Anesthesiology 83:980–985
7. Ravussin P, de Tribolet N (1993) Total intravenous anesthesia with propofol for burst suppression in cerebral aneurysm surgery: preliminary report of 42 patients. Neurosurgery 32:236–240
8. Illievich UM, Petricek W, Schramm W, Weindlmayr-Goettel M, Czech T, Spiss CK (1993) Electroencephalographic burst suppression by propofol infusion in humans: hemodynamic consequences. Anesth Analg 77:155–160
9. Bissonnette B, Swan H, Ravussin P, Un V (1999) Neuroleptanesthesia: current status. Can J Anesth 46:154–168
10. Mi W, Sakai T, Kudo T, Kudo M, Matsuki A (2003) The interaction between fentanyl and propofol during emergence from anesthesia: monitoring with the EEG-bispectral index. J Clin Anesth 15:103–107
11. Nakayama M, Ichinose H, Yamamoto S, Kanaya N, Namiki A (2002) The effect of fentanyl on hemodynamic and bispectral index changes during anesthesia induction with propofol. J Clin Anesth 14:146–149