

- 1 Brown JB, Pedula MS, Barzilay J, Herson MK, Latore P. Lactic acidosis rates in type 2 diabetes. *Diabetes Care* 1998; **21**: 1659–63
- 2 Misbin RI. The phantom of lactic acidosis due to metformin in patients with diabetes. *Diabetes Care* 2007; **27**: 1791–3
- 3 Salpeter S, Greyber E, Pasternak G, Salpeter E. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2002(2): CD002967 (latest version 27 Feb 2002).
- 4 Silvestre J, Carvalho S, Mendes V. Metformin-induced lactic acidosis: a case series. *J Med Case Rep* 2007; **1**: 126
- 5 National Institute for Health and Clinical Excellence. *Quick Reference Guide—The Management of Type 2 Diabetes*. May 2008

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Unusual case of low bispectral index values due to electrocardiographic interferences

Editor—The bispectral index (BIS, Aspect Medical Systems, Newton, MA, USA) is widely used as an accurate measure of the hypnotic effect of anaesthetics and sedative drugs.¹ Values between 40 and 60 are recommended for maintenance of general anaesthesia.² We report a case where BIS values were constantly below expected levels, probably caused by interference with ECG monitoring.

A 59-yr-old man (weight=95 kg, ASA I) underwent laparoscopic partial gastrectomy. Anaesthesia monitoring consisted of three-lead ECG, non-invasive arterial pressure monitoring, peripheral pulse oximetry, and BIS monitoring [BIS-Vista™ (version 1.01) monitoring system, BIS-Quatro-sensor™]. Anaesthesia was induced using propofol

200 mg and fentanyl 250 µg, and endotracheal intubation was facilitated by rocuronium 50 mg. Anaesthesia was maintained by a continuous infusion of propofol titrated to BIS and fentanyl boli of a total of 700 µg throughout surgery. During the first 25 min of anaesthesia, BIS varied between 21 and 27 (Fig. 1); propofol infusion was adjusted according to the BIS value to a minimum value of 90 µg kg⁻¹ min⁻¹. Systolic and diastolic arterial pressure was in the range of 120–140 and 50–75 mm Hg and heart rate was around 60–80 beats min⁻¹ during this period. Since the anaesthetist managing the case (T.H.) had extensive experience with BIS monitoring and interferences with different devices, the BIS sensor was replaced—without improvement of tracing—35 min after beginning of surgery; 90 min after beginning of surgery, another BIS monitor (BIS XP monitoring system) was also applied to verify any monitoring failure. During the surgery, the EMG graph did not indicate any significant activity (<30 dB) and the signal quality index (SQI) showed good to excellent signal quality on any device (>50%, Fig. 1). Approximately 2 h after the beginning of anaesthesia, the patient showed clinical signs of insufficient hypnosis and started to wake up at a BIS of 25 (Fig. 1). Forty milligrams of propofol were immediately injected. A thorough look at the raw EEG trace revealed a pattern that could be most likely attributed to an ECG signal. The three ECG leads were applied on both shoulders and lower left thorax. Propofol dosing continued using solely clinical parameters. The patient was extubated 12 min after the propofol infusion was stopped and did not report awareness when asked after surgery (once immediately, and then 1 month after surgery). EEG signals are known to be

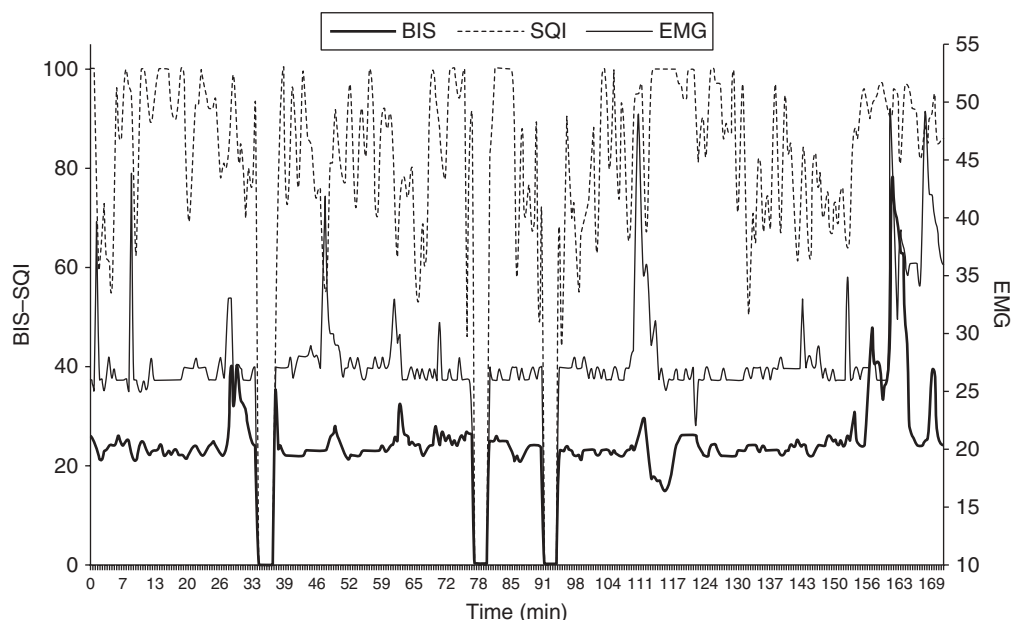


Fig 1 History trends of BIS, SQI, and EMG during maintenance of anaesthesia. SQI and EMG did not indicate poor signal quality (SQI >50%; EMG <30 dB). Thirty-three minutes after beginning of anaesthesia, the BIS sensor was replaced, the monitor was turned off and on 77 min and again 90 min after beginning of surgery. The patient showed clinical signs of awakening 110 min after beginning of anaesthesia.

vulnerable to noise or artifacts situated in the same frequency range as awake EEG and the detection of those artifacts is tricky owing to the variability of the frequency and amplitude of EEGs.³ High-frequency artifacts may be physiological (coming from sources other than the patient's brain) and non-physiological (generated by external devices). Examples of the latter case have been reported to falsely increase the BIS. They include but are not limited to: cardiac pacing devices,^{4,5} cardiopulmonary bypass machine,⁶ warming blankets,⁷⁻⁹ endoscopic shavers,¹⁰ electromagnetic systems,¹¹ and EMG tracheal tubes.¹² Interference of the patient's own ECG with the BIS reading has been scarcely documented. Myles and Cairo¹³ and Puri and Nakra¹⁴ reported cases where the ECG was detected by the BIS monitoring system and not recognized as artifact in patients with severe brain injury. The BIS values were relatively high (38, 45) whereas they were expected to be extremely low due to low cerebral perfusion and neurological damage. Our patient was on no previous medication known to suppress EEG activity, the awake BIS value was more than 90 and the raw EEG appeared normal. We hypothesize that instead of reading EEG, the BIS monitor read ECG tracings, which reflected long isoelectric periods interrupted rhythmically by the ECG signal with relatively high amplitude, thus mimicking a deep anaesthetic state. We recommend that the raw EEG tracing should be thoroughly investigated whenever BIS values seem clinically dubious.

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- 1 Dahaba AA. Different conditions that could result in the bispectral index indicating an incorrect hypnotic state. *Anesth Analg* 2005; **101**: 765–73
- 2 Johansen JW. Update on bispectral index monitoring. *Best Pract Res Clin Anaesthesiol* 2006; **20**: 81–99
- 3 Kelly SD. *Monitoring Level of Consciousness during Anesthesia and Sedation*. Newton, MA, USA: Aspect Medical Systems, Inc., 2003
- 4 Gallagher JD. Pacer-induced artifact in the bispectral index during cardiac surgery. *Anesthesiology* 1999; **90**: 636
- 5 Vretzakis G, Dragoumanis C, Ferdi H, Papagiannopoulou P. Influence of an external pacemaker on bispectral index. *Eur J Anaesthesiol* 2005; **22**: 70–2
- 6 Tewari P, Skinner H. Cardiopulmonary bypass machine can interfere with accuracy of BIS monitor. *Anesth Analg* 2007; **105**: 534–5
- 7 Guignard B, Chauvin M. Bispectral index increases and decreases are not always signs of inadequate anesthesia. *Anesthesiology* 2000; **92**: 903
- 8 Hemmerling TM, Fortier JD. Falsely increased bispectral index values in a series of patients undergoing cardiac surgery using forced-air-warming therapy of the head. *Anesth Analg* 2002; **95**: 322–3
- 9 Zanner R, Schneider G, Kochs EF. Falsely increased bispectral index values caused by the use of a forced-air-warming device. *Eur J Anaesthesiol* 2006; **23**: 618–9
- 10 Hemmerling TM, Migneault B. Falsely increased bispectral index during endoscopic shoulder surgery attributed to interferences with the endoscopic shaver device. *Anesth Analg* 2002; **95**: 1678–9
- 11 Hemmerling TM, Desrosiers M. Interference of electromagnetic operating systems in otorhinolaryngology surgery with bispectral index monitoring. *Anesth Analg* 2003; **96**: 1698–9
- 12 Sloan PA. Interference of bispectral index monitoring with intra-operative use of the electromyograph endotracheal tube. *Can J Anaesth* 2007; **54**: 1028–9
- 13 Myles PS, Cairo S. Artifact in the bispectral index in a patient with severe ischemic brain injury. *Anesth Analg* 2004; **98**: 706–7
- 14 Puri GD, Nakra D. ECG artifact and BIS in severe brain injury. *Anesth Analg* 2005; **101**: 1566–7

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Injection pain due to propofol in children and the ethics of placebo

Editor—I was interested in this study of reducing injection pain due to propofol in children,¹ which is a laudable aim. However, I question the ethics of a placebo-controlled trial design in children below age 7 yr in the light of current guidance and the tenets of the Declaration of Helsinki which seeks to protect the best interests of trial subjects. In particular to have one-quarter of the trial subjects exposed to long chain triglyceride (lct)-propofol with no added lidocaine as one of the control arms seems to me to be completely unacceptable. Indeed, this was so in 1992 when we discussed such a study with our ethics committee and agreed that to deny a control group the most efficacious known treatment was unethical² and therefore adopted a step-down technique to establish the minimum effective dose of lidocaine for this purpose, namely 0.2 mg kg⁻¹. Thus, the authors of this paper have not only denied analgesia to a control population, but have also exposed trial subjects to more than twice the effective dose of lidocaine, 0.5 mg kg⁻¹. It was also interesting that they had to adjust their power calculations and numbers of study subjects and although they do not say so, I suspect this was because of unacceptable pain experiences of their child patients. I fully appreciate the difficulties of conducting paediatric research, but I was surprised that such a trial design achieved IRB approval and survived the peer review process of a major international journal. I think researchers, editors, reviewers, and ethics committees need to be more aware of modern paediatric ethics standards in order to protect the best interests of both trial subjects and control groups.

Declaration of interest

I am the Editor-in-Chief of the journal *Pediatric Anesthesia*.