J Anesth (2008) 22:300–303
DOI 10.1007/s00540-008-0632-4

Journal of
Anesthesia

Marked reduction in bispectral index with severe bradycardia without hypotension in a diabetic patient undergoing ophthalmic surgery

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Abstract
A 75-year-old female patient underwent right vitrectomy under total intravenous anesthesia with propofol, ketamine and fentanyl. During the surgery sudden severe bradycardia (heart rate, 33 beats per min), without hypotension, occurred, which was relatively atropine-insensitive. This event was accompanied by a marked decrease in the bispectral index (BIS), from 70 to 40, and an elevation in the suppression ratio (33). Following the initiation of an isoproterenol infusion, the BIS promptly returned to 70, along with an increase in the heart rate. At the end of surgery the patient emerged from anesthesia without neurological sequelae. Severe bradycardia during anesthesia will cause cerebral hypoperfusion and this may affect cerebral function. We conclude that a BIS monitor may be a useful tool for the detection of bradycardia-related cerebral hypoperfusion.

Key words Bradycardia · Bispectral index · Isoproterenol

Introduction

The bispectral index (BIS) is widely used in the evaluation of sedation during general anesthesia [1]. This monitor has also been reported to be useful in the detection of anesthesia-related cerebral hypoperfusion [2–5].

We experienced a case of bradycardia-related reduction in BIS accompanied by an elevation of the suppression ratio (SR). Here we present this case and discuss the relationship of the event with heart rate, cerebral blood flow, and BIS.

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Received: January 21, 2008 / Accepted: March 30, 2008

Case report

A 75-year-old female patient (body weight, 55.2 kg; height, 152.8 cm) was scheduled for right vitrectomy due to proliferative diabetic retinopathy. She had hypertension and diabetes mellitus, which were well controlled with oral antihypertensive agents (calcium channel blocker, angiotensin receptor inhibitor, and α_1-blocker) and subcutaneous insulin, respectively.

On the patient's arrival in the operating theater, regular noninvasive monitoring, including blood pressure, electrocardiogram, pulse oximetry, end-tidal carbon dioxide, and BIS were started. Blood pressure was 160/80 mmHg, and heart rate was 53 beats·min^{-1} (bpm). Anesthesia was induced with fentanyl 100 μg, ketamine 60 mg, and propofol 30 mg. Following muscle relaxation with i.v. suxamethonium 40 mg, endotracheal intubation was performed. Anesthesia was maintained with propofol 4–6 mg·kg^{-1}·hr^{-1}, ketamine 0.3–1 mg·kg^{-1}·hr^{-1} and fentanyl (total, 200 μg). Muscle relaxation was maintained with intermittent vecuronium (total, 5 mg). Surgical stimulation slightly increased the blood pressure (175/90 mmHg) and heart rate (60 bpm). The heart rate gradually decreased to 40 bpm 20 min after the start of surgery, but the BIS was stable (around 70). The heart rate transiently increased to around 50 bpm in response to i.v. atropine 0.5 mg, but decreased again to 33 bpm. At this point there was a sudden unexpected fall in the BIS, to 40, and an increase in the SR, to 33. Despite the administration of atropine 1.0 mg i.v. the heart rate did not increase. Isoproterenol was therefore given i.v. at 0.005 μg·kg^{-1}·min^{-1} a following a 4-μg bolus. As soon as the heart rate recovered, the BIS returned to 70 (Fig. 1). When the heart rate was judged to be stable the isoproterenol infusion was stopped, and there was no further decrease in the BIS. The surgery was performed successfully, and the patient emerged from anesthesia without neurological sequelae.

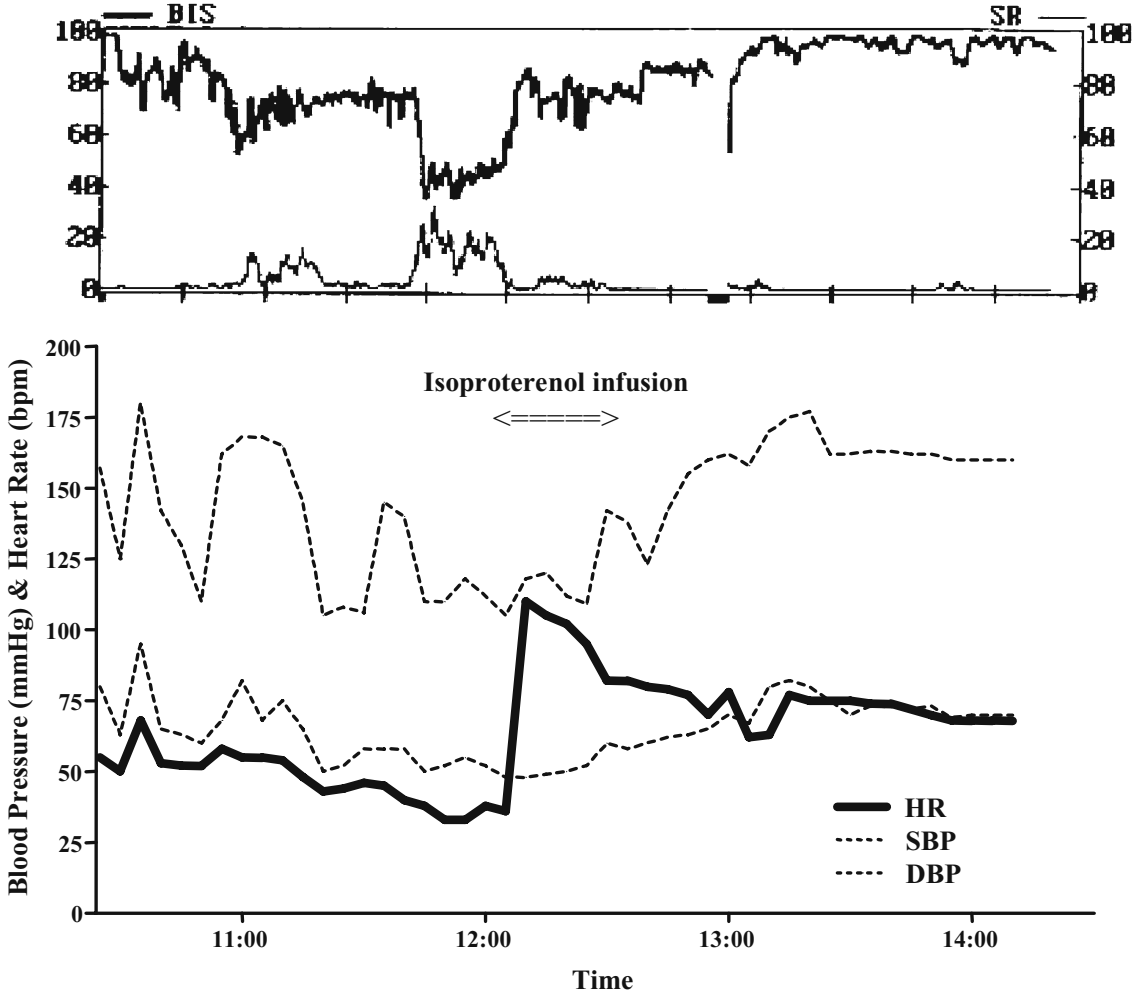

Fig. 1. A sudden decrease in the bispectral index (*BIS*) corresponding with severe bradycardia (*SB*; 33 beats per min). Following an isoproterenol infusion, the BIS and heart rate (*HR*) returned to values recorded at the start of surgery. *SBP*, Systolic blood pressure; *DBP*, diastolic blood pressure

Discussion

In the present patient, the BIS decreased following severe bradycardia and returned following an isoproterenol-induced increase in the heart rate. While we often experience bradycardia during ophthalmic surgery, due to activation of the oculocardiac reflex, an accompanying decrease in the BIS has not been observed. In general, a reduction in the BIS during anesthesia suggests deepening sedation. In the present patient, the propofol and ketamine infusion rates were not altered prior to the observed reduction in the BIS. Several reports suggest that cerebral hypoperfusion decreases the BIS [2–5]. Hemmerling et al. [2] reported a case of possible reversible global cerebral hypoperfusion during off-pump coronary artery bypass surgery. They observed that the BIS suddenly decreased from 45–50 to 0 during distal grafting, as a consequence of cerebral hypoperfusion. Hayashida et al. [3] reported the detection of cerebral hypoperfusion, using the BIS, during pediatric cardiac surgery. They reported 14 episodes of a simultaneous decrease in regional cerebral hemoglobin oxygen saturation (Sr_{O_2}) and the BIS during acute hypotension in five children. As an acute decrease in the BIS coincided with a decrease in Sr_{O_2}, these changes may have been due to a reduction in cerebral blood flow. Merat et al. [4] have reported that a BIS monitor may facilitate the detection of severe cerebral ischemia. They noted two cases where BIS decreased in parallel with a decrease in somatosensory evoked potentials during carotid clamping in a patient undergoing carotid endarterectomy. They also noted a reduction in the cardiac index and central venous O_2 saturation in a patient undergoing resection of an aortic aneurysm. Umegaki et al. [5] described a marked decrease in the BIS with an elevation of the SR as a

result of cerebral hypoperfusion. This was caused by marked cervical swelling, secondary to a massive subcutaneous hematoma around a previously mispunctured right carotid artery, extending throughout the whole neck. A cervical relief incision improved both the BIS and SR.

In the present patient, we feel that the decrease in the BIS may have been related to severe bradycardia rather than the depth of anesthesia. It is well known that severe bradycardia causes cerebral ischemia, the so-called Adams-Stokes attack. In addition, it has been reported that pacemaker implantation improves cerebral blood flow (CBF) [6,7], mental performance [8], and electroencephalogram findings [9] in patients with a decrease in CBF due to bradycardia. Normalization of the heart rate is important for cerebral function. Koide et al. [10] suggested that there may exist an optimal range of heart rates to minimize vascular resistance and maximize blood flow, as they found a significant correlation between changes in heart rate and CBF or cerebral vascular resistance, but not cardiac output, in 14 patients with severe bradycardia undergoing pacemaker implantation. Moreover, cognitive function in these patients was improved following the implantation. In the present patient, as the BIS decreased from 70 to 40 following bradycardia and increased following isoproterenol treatment, depression of cerebral activity may have occurred in response to a decrease in CBF.

Another possible reason for a reduction in the BIS is an increase in propofol concentrations. Kurita and colleagues [11] found an inverse relationship between plasma propofol and cardiac output during a continuous infusion. Thus, if, in the present patient, the bradycardia had reduced cardiac output without hypotension, then the reduction in the BIS could have been due to an increase in plasma propofol resulting from a decrease in cardiac output. We did not, however, monitor cardiac output.

Why did severe bradycardia occur in the present patient? Several case reports suggest that the incidence of undesirable cardiovascular effects, including bradycardia, during anesthesia is higher in diabetic patients [12–14]. In a diabetic patient, Murakawa et al. [13] reported an episode of atropine-resistant severe bradycardia following the induction of anesthesia; the bradycardia was treated with urgent temporary pacing. Horng and colleagues [14] reported that intraoperative hypotension and bradycardia did not respond to ephedrine and atropine in diabetic patients. These patients were later diagnosed with cardiac autonomic dysfunction. It is known that diabetic autonomic neuropathy can contribute to the impairment of cerebrovasular reactivity and autoregulation [15]. Thus, CBF may easily decrease during anesthesia in patients with diabetic autonomic neuropathy.

In the present patient, the BIS was maintained at around 70 as ketamine was infused continuously. As we previously reported, ketamine infusion increased the BIS by around 15 [16]; thus, in the present patient, the BIS would have been around 55 if ketamine had not been used. Therefore, a BIS of 70 would have been sufficient for general anesthesia in the present patient.

In conclusion, severe bradycardia during anesthesia will cause cerebral hypoperfusion and this may affect cerebral function. A BIS monitor may be a useful tool for the detection of bradycardia-related cerebral hypoperfusion.

Acknowledgments. The authors thank Professor D.G. Lambert (University Department of Cardiovascular Sciences [Pharmacology and Therapeutics Group], Division of Anaesthesia, Critical Care and Pain Management, Leicester Royal Infirmary, UK) for his valuable comments.

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