

Use of bispectral index monitoring for a patient with hepatic encephalopathy requiring living donor liver transplantation: a case report

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Abstract We report the use of perioperative bispectral index (BIS) monitoring in a patient who underwent living donor liver transplantation (LDLT). Hepatic encephalopathy featuring extreme excitement developed in a 42-year-old male and was diagnosed as acute hepatitis. Sedation with continuous infusion of midazolam was necessary. BIS value gradually decreased and reached 0 17 h after commencement of continuous infusion of midazolam. Midazolam infusion was stopped but BIS value remained 0. Brain CT scan revealed an almost normal image. Multi-lead electroencephalogram was recorded revealing almost no electrical activity. Administration of flumazenil did not improve his consciousness and BIS value. Adequate spontaneous respiration was maintained and the possibility of brain death was excluded. LDLT was performed on the 5th ICU day. BIS value remained 0 throughout surgery. BIS value suddenly increased 2 h after surgery and reached 60 11 h after surgery. It became possible to communicate with the patient and his trachea was extubated on the 4th postoperative day. We believe that, with BIS, we were able to follow preoperative exacerbation of the “pathological” process of hepatic encephalopathy, and predict postoperative emergence from general anesthesia, suggesting normal graft function.

Keywords Bispectral index · Hepatic encephalopathy · Living donor liver transplantation

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Introduction

Degree of hepatic encephalopathy ranges from euphoria/depression or mild confusion to unresponsive coma, and is graded with the West Haven criteria and psychometric tests [1]. In Japan, living donor liver transplantation (LDLT) is one of the major therapeutic options for patients with end-stage hepatic failure, because organ donation from brain-dead people is limited. For ethical reasons, the indication of LDLT is very strict including preoperative evaluation of the central nervous system of the patients. According to this environment, deciding the needs of, selection of, and dosage of sedatives is critical during preoperative care of patients with end-stage hepatic failure. We report a patient who underwent LDLT for whom, by monitoring perioperative bispectral index (BIS), we were able to follow and predict the dramatic changes in the level of consciousness.

Case report

A 42-year-old male (height 170 cm and weight 70 kg) was diagnosed as acute hepatitis after 1 week of sudden fever (39°C). His serum hepatitis B virus (HBV) antigen was positive and he was diagnosed as acute HBV hepatitis. His plasma aspartate aminotransferase and alanine aminotransferase were 11010 and 11700 IU/L, respectively, prothrombin activity was 13% when he was transferred to our hospital. His consciousness level was clear at admission to our hospital but lethargy and flapping tremor developed 3 days later. He became extremely excited and was transferred to the Intensive Care Unit (ICU). He was barely able to communicate with us but refused all the monitoring and it seemed impossible for him to stay calm on bed. Sedation with midazolam was started and his

trachea was intubated on admission to the ICU. BIS value was 38 after bolus intravenous administration of 10 mg midazolam, and continuous intravenous infusion of midazolam (10 mg/h) was started. BIS value before midazolam administration was not obtained because the patient was so excited that signal quality was low. Urgent brain CT scan revealed an almost normal image, and continuous veno-venous hemodiafiltration (CVVHDF) and simultaneous plasma exchange were initiated. BIS values gradually decreased and reached 0 17 h after the commencement of continuous infusion of midazolam. Continuous infusion of midazolam was stopped but BIS values remained 0 throughout the preoperative periods. On the 3rd ICU day, urgent follow-up CT scan revealed an almost normal image. On the 4th ICU day, a multi-lead electroencephalogram (EEG) was recorded, revealing almost no electrical activity. Administration of 1 mg intravenous flumazenil did not improve his consciousness and BIS values. Adequate spontaneous respiration with PaCO₂ around 40 mmHg was maintained throughout his stay in the ICU and the possibility of brain death was excluded. His family requested LDLT, with his son as donor, and the operation was performed on the 5th ICU day.

Total intravenous anesthesia with continuous infusion of propofol and ketamine and bolus infusion of fentanyl and rocuronium was used during surgery. Duration of surgery was 586 min and duration of anesthesia was 615 min. Intraoperative drug consumption was: 3000 mg propofol, 600 mg ketamine, 800 µg fentanyl, and 250 mg rocuronium. BIS values remained 0 throughout anesthesia. Continuous infusion of propofol and ketamine was stopped at the end of surgery. BIS value that was 0 at re-admission to the ICU suddenly increased to 40 2 h after surgery. Rocuronium (50 mg) was administered intravenously to exclude the interference of BIS values from electromyographic activity [2], with the same result. Increases in heart rate, blood pressure, perspiration, and swallowing appeared as BIS values reached 50, 11 h after surgery. The patient had no response to verbal commands but purposeless movement of the upper extremities appeared at this time. We thought that tracheal intubation was still necessary and decided to sedate him. On the other hand, evaluation of the recovery from hepatic encephalopathy was also necessary. Administration of dexmedetomidine (0.4 µg/kg/h) was started and BIS values remained between 50 and 75 when no stimulation was applied to the patient. Verbal stimulation of the patient did not affect those values and he did not respond to verbal commands until 78 h after surgery. After that time, it became possible to communicate with the patient and BIS values increased to approximately 90 on verbal stimulation. CVVHDF was resumed on the 3rd postoperative day. Other vital signs were stable and his trachea was extubated on the 4th postoperative day. His

liver function was almost normal after surgery and his level of consciousness returned alert after continuous infusion of dexmedetomidine was stopped.

Discussion

BIS monitoring evaluates the “pharmacological” effects of anesthetics or sedatives and it was originally developed to monitor the depth of general anesthesia to prevent intraoperative awareness [3]. In some groups of patients with reduced consciousness from “pathological” causes, for example during cardiopulmonary resuscitation, it is reported that the BIS value is a poor indicator of neurological recovery [4].

In this case report, we monitored BIS in a patient with hepatic encephalopathy, which is a “pathological” process. Sudden decrease in BIS value after the initiation of midazolam infusion could be a result of midazolam per se. It has been reported that midazolam reduced BIS values depending on the degree of sedation. Sedation during regional anesthesia could be managed with midazolam at BIS values around 75 [5]. General anesthesia could be induced with intravenous bolus injection of midazolam 0.2–0.3 mg/kg, resulting in BIS values between 60 and 70 [6]. The BIS value, which remained 0 after cessation of midazolam infusion, could be regarded as reflecting deterioration of hepatic encephalopathy, because it was not reversed by administration of flumazenil. Moreover, preserved adequate spontaneous respiration with PaCO₂ around 40 mmHg throughout the preoperative period when the BIS value remained 0 is not consistent with an overdose of midazolam. In previous reports, midazolam induced respiratory depression in a dose-dependent manner [7] and 20% of patients developed apnea after induction of anesthesia with midazolam [8]. Almost no electrical activity in a preoperative multi-lead EEG support the validity of BIS monitoring. Dahaba et al. [9] reported that mean BIS values differed significantly between patients with West Haven grade 1 (90.2 ± 2.5 ; mean \pm SD), grade 2 (78.4 ± 6.6), grade 3 (63.2 ± 4.8), and grade 4 (45.4 ± 5.0) in 64 awake patients with chronic liver disease. Our patient had acute hepatic failure and experienced very rapid changes in the level of consciousness from excitement to deep coma. We believe that BIS monitoring was able to follow these rapid preoperative “pathological” changes. We did not observe the triphasic wave EEG which is considered to be characteristic of hepatic encephalopathy. It might be because the amplitude of raw waveform displayed in our monitor was set to minimum and was not suitable for observing this kind of precise waveform. When multi-lead EEG was recorded, EEG was isoelectric already.

There are two case reports in which patients with flat EEG recovered without any neurological complications after LDLT [10, 11]. It is also reported that mean BIS values increased with reperfusion of the graft in the 46 non-initial poor graft function (IPGF) patients but not in the 7 IPGF patients during liver transplant surgery [12]. They concluded that BIS monitoring could be an early intraoperative indicator of the vitality of the transplanted graft. Reeves et al. [13] examined pre and post-liver transplantation EEG in 14 patients and reported a good correlation between improvement of liver function and improvement of EEG findings. Our patient had no intraoperative increase in BIS value after reperfusion of the graft and the rapid increase in BIS value occurred 11 h after surgery. This might be because of the difference in the severity of preoperative hepatic encephalopathy because postoperative liver function was almost normal and there was no evidence of IPGF in our patient. We must also consider the possibility that the intraoperative anesthetic agents had affected the delayed increase in BIS values. Dexmedetomidine was administered after LDLT when the patient showed signs of emergence from coma. We judged that the patient still needed tracheal intubation and mechanical ventilation. He seemed to need adequate sedation to tolerate tracheal intubation, but it was also necessary to evaluate the level of consciousness at the same time. Dexmedetomidine was administered to the patient because it is possible to evaluate the level of consciousness under sedation with dexmedetomidine. It has been reported that dexmedetomidine reduced BIS values as sedation was deepened [14]. In patients with normal central nervous function, BIS values increased as they were aroused even under sedation with dexmedetomidine. In our patient, BIS values were not affected by verbal stimulation until 78 h after surgery. This means that the effects of hepatic encephalopathy and/or the effects of intraoperative anesthetic agents remained till that time.

In conclusion, we used BIS monitoring for a patient with hepatic encephalopathy who underwent LDLT. We believe we were able to follow the preoperative exacerbation of hepatic encephalopathy although the effects of midazolam were not completely excluded until flumazenil was administered. We were also able to predict the postoperative emergence from general anesthesia with BIS, which suggests normal graft function.

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