Online Submissions: wjg.wjgnet.com
wjg@wjgnet.com
doi:10.3748/wjg.15.595

World J Gastroenterol 2009 February 7; 15(5): 595-598
World Journal of Gastroenterology ISSN 1007-9327

Usefulness of bispectral monitoring of conscious sedation during endoscopic mucosal dissection

Kazunori Hata, Akira Andoh, Kiyoyuki Hayafuji, Atsuhiro Ogawa, Tamio Nakahara, Tomoyuki Tsujikawa, Yoshihide Fujiyama, Yasuharu Saito

Kazunori Hata, Akira Andoh, Kiyoyuki Hayafuji, Atsuhiro Ogawa, Tamio Nakahara, Tomoyuki Tsujikawa, Yoshihide Fujiyama, Department of Medicine, Shiga University of Medical Science, Seta-Tukinowa, Otsu 520-2192, Japan
Yasuharu Saito, Division of Endoscopy, Shiga University of Medical Science, Seta-Tukinowa, Otsu 520-2192, Japan
Author contributions: Hata K, Hayafuji K, Ogawa A, Nakahara T, Tsujikawa T, and Saito Y performed endoscopic resection of tumors; Andoh A wrote the manuscript; Fujiyama Y arranged the final version of the manuscript.
Correspondence to: Akira Andoh, MD, PhD, Department of Medicine, Shiga University of Medical Science, Seta-Tukinowa, Otsu 520-2192, Japan. andoh@belle.shiga-med.ac.jp
Telephone: +81-77-5482217 Fax: +81-77-5482219
Received: April 21, 2008 Revised: May 25, 2008
Accepted: June 1, 2008
Published online: February 7, 2009

Abstract

AIM: To assess the usefulness of bispectral index (BIS) monitoring in order to carry out endoscopic submucosal dissection (ESD) safely and with patients' satisfaction.

METHODS: Three hundred sixty-six patients with an early-stage neoplasm of the digestive tract were enrolled. The BIS monitor (A-1050: Aspect medical systems/NIHON KOHDEN, Tokyo, Japan) was used. The appropriate sedative condition was set at 55 to 75 BIS levels (BIS value) during the endoscopic procedures.

RESULTS: Among 366 cases, 13 were accompanied by adverse events during and/or after ESD. All episodes occurred in cases with BIS value between 56 and 65. Hypotension was observed in four cases, and bradycardia in six. Respiratory distress was observed in two cases with chronic pulmonary obstructive disease. All patients with adverse events were able to leave the hospital without extension of the hospitalization.

CONCLUSION: BIS monitoring is useful to safely perform ESD. A BIS value of 70 to 75 is suitable for ESD.

Key words: Endoscopy; Cancer; Sedation; Propofol; CO_2

Hata K, Andoh A, Hayafuji K, Ogawa A, Nakahara T, Tsujikawa T, Fujiyama Y, Saito Y. Usefulness of bispectral monitoring of conscious sedation during endoscopic mucosal dissection. *World J Gastroenterol* 2009; 15(5): 595-598 Available from: URL: http://www.wjgnet.com/1007-9327/15/595.asp DOI: http://dx.doi.org/10.3748/wjg.15.595

INTRODUCTION

Endoscopic submucosal dissection (ESD) has recently been developed for *en bloc* resection of gastric cancer, which results in high tumor eradication rates, as well as a modality for the precise histological evaluation of the entire lesion[1,2]. Furthermore, recent studies have reported that ESD is useful for selected localized neoplasms of the esophagus and the colon[3,4]. However, ESD is a highly complex endoscopic technique and sometimes needs long time to be performed. So, conscious sedation is the standard of care for the majority of ESD cases to perform a safe procedure and to minimize complications.

The bispectral index (BIS) is a quantitative parameter of the hypnotic effects of anesthetic drugs on the central nervous system (CNS)[5,6]. BIS is not an instrument just for the frequent analysis of electroencephalogram, but it analyzes the relationship among the different components of the electroencephalogram in various phases. BIS also takes into account the correlation between the electrocardiogram and the CNS suppression. BIS is a dimensionless number ranging from 0 to 100, with 0 representing no cortical activity and 100 representing fully awake state. BIS has been utilized in guiding dosing of anesthetics, including decreasing the amounts of drug use and enhancing faster emergence and recovery[5]. To avoid excessive administration of propofol, we introduced the monitoring of the sedation depth by BIS, which enables the objective evaluation of the sedation.

It is desirable to make an objective judgment of the depth of the conscious sedation during ESD and to maintain a sedation that does not affect the cardiorespiratory dynamics. BIS monitoring is expected to avoid excessive administration of anesthetic drugs

during ESD. In this study, we investigated the usefulness of BIS monitoring while using propofol in the course of ESD. Propofol has been reported to afford a higher comfort and satisfaction to patients and to reduce the time to recovery, compared to previously reported drugs such as benzodiazepines and opiates[7,8].

MATERIALS AND METHODS

Patients

Three hundred sixty-six patients with early-stage esophagus cancer, gastric cancer and/or colorectal cancer, treated with ESD from May, 2004 to April, 2007 at the Hospital of the Shiga University of Medical Science (Otsu, Japan), were enrolled into the study. The baseline features and history of these patients are reported in Table 1.

Anesthesia

An anesthesist or a specialist in endoscopy trained in anesthesiology performed the procedure, including the administration of a sedative drug during operation. Two BIS sensors were put on the forehead of each patient and another sensor was placed on the outer side of an eyebrow. The BIS monitor (A-1050: Aspect medical systems/NIHON KODEN, Tokyo, Japan) was used. As soon as the sedative drug started its effects, oxygen (2 L/min) was given through a nasal cannula. Three-lead electrocardiogram, pulse oximetry and blood pressure were monitored.

Just before the sedation started, intravenous drip infusion of pentazocine (15 mg/body) was given. An initial 40-mg bolus of propofol was administered intravenously to all patients, followed by continuous infusion of propofol (3 mg/kg per hour). The appropriate sedative condition during endoscopic procedures was set at 55 to 75 BIS levels (BIS value). From May, 2004 to September, 2005, the BIS level was set between 56 and 65, while later on (i.e. from October, 2005 to April, 2007) it was set between 70 to 75. In order to maintain suitable BIS levels, the dosage of continuous infusion of propofol was adjusted.

Adverse events during and after ESD were recorded. We observed delayed awakening (i.e. the patient failed to awake 15 min after the stop of propofol administration), hypotension (systolic blood pressure < 90 mmHg), bradycardia (heart beats < 50/min) and respiratory failure (patient needing a mandatory ventilation).

RESULTS

Among the 366 cases, 13 were accompanied by adverse events during and after ESD (Table 2). The adverse events occurred during the period in which BIS value was set between 56 and 65 (12 cases out of 139 cases, 9%), but no adverse events occurred as long as the BIS value was set between 70 and 75.

Hypotension was observed in four cases. One of them occurred immediately after the administration of propofol, but in the other three it occurred at a later phase during ESD. These four patients recovered quickly when propofol was decreased or stopped, together with an adjustment of infusion of fluids.

Respiratory depression was observed in two cases, both of which had chronic obstructive pulmonary disease (COPD.) One patient had a history of chronic bronchial asthma, the other of pulmonary emphysema. During ESD, 2 to 5 L/min of oxygen was given and adjusted at a timely basis in order to maintain a $SpO_2 > 92\%$. The latter case developed CO_2 narcosis after ESD, but gradually recovered.

Bradycardia was observed in six patients. All of them recovered with an adjustment of fluid infusion.

All patients with an adverse event were able to leave the hospital without extending the duration of the hospitalization.

Table 1 Backgrounds of patients (number of cases)

BIS value	56-64 (May/2004 -Sep/2005)	70-75 (Oct/2005 -April/2007)	Total
Esophageal cancer	13	36	49
Gastric cancer	100	149	249
Colon cancer	26	42	68
Total	139	227	366

Table 2 Adverse events (number of cases)

BIS value	56-64 (May/2004 -Sep/2005)	70-75 (Oct/2005 -April/2007)	Total
Delayed awakening	1	0	1
Decreased blood pressure	4	0	4
Bradycardia	6	0	6
Respiratory depression	2	0	2
Total	13	0	13

DISCUSSION

The standard protocol of conscious sedation is generally determined by the experience of doctors at the respective medical institutions. Ideal conditions of conscious sedation are as follows: (1) rapid and short acting, (2) no accumulation and rapid recovery after operation, (3) no modulation of respiratory and cardiovascular dynamics, and (4) no hepatic or renal toxicity. In Japan, midazolam is widely used, while flumazenil is given as an antagonist after the operation[7]. However, because of the different half-life of these two drugs (midazolam, approximately 120 min; and flumazenil, approximately 50 min), there is a high risk of a new period of unconsciousness after the treatment.

Propofol is the most frequently used intravenous anesthetic in the field of intensive cares. The most important feature of propofol is its short half-life. Thus, even after prolonged administration, it does not bring about the repeated sedation once the administration is stopped. In a controlled study of propofol versus

midazolam, it has been reported that patients showed a higher level of satisfaction with propofol than with midazolam[7-9]. In the guidelines of endoscopy under sedation issued by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), it is recommended to use propofol for endoscopic treatments of long duration, due to its dual advantage of a deep sedation and a quick awakening, compared to benzodiazepines and narcotic drugs. However, propofol may cause cardiorespiratory suppression. Since there are no appropriate antagonists available, it is necessary, in case of cardiorespiratory suppression induced by excessive propofol administration, to carry out cardiorespiratory supportive care with a ventilator until propofol is fully metabolized.

To avoid excessive administration of propofol, we introduced monitoring by BIS, which enables the objective evaluation of the sedation depth. BIS is not an instrument just for the frequent analysis of electro-encephalogram, but it also analyzes the relationship among the different components of the electroencephalogram at various stages. BIS is equal to 100 when the patient is fully awake and 0 when an isoelectric electroencephalogram is observed. It has been reported that BIS is useful to evaluate the sedation depth during digestive endoscopy or treatment[10].

During surgical operations under general anesthesia, the BIS value is usually set at 45 to 65[11]. Thus, we also set the target BIS during ESD at 56 to 64, at least during the initial period. However, since we experienced cases with adverse events during ESD, we slightly increased the BIS values. Thus, after October 2007, we set a BIS value at 70 to 75. Propofol has sedative effects but it does not possess analgesic properties. Therefore, we added pentazocine (15 to 30 mg) and in most cases we could carry out the ESD without impediments, using these BIS values.

There were four cases of decreased blood pressure during the first period. In one case, this occurred because of the bolus infusion of propofol at the time of induction of sedation. After this case, propofol was given through a syringe pump with constant speed. Also, we administrated propofol from the port which is located close to the peripheral intravenous indwelling needle, in order to minimize the lag time between the start of injection and the actual appearance of a sedative effect. By doing this, we did not experience any additional case of decreased blood pressure after the infusion.

Regarding the other three cases, decreased blood pressure occurred in the second half of ESD. Each of these patients had a history of elevated blood pressure and therefore they had been taking antihypertensive drugs until the day of ESD. Decreased blood pressure might be attributed to the interaction of propofol with antihypertensive drugs. However, all patients recovered quickly when propofol was decreased or stopped, or when the fluid infusion was adjusted. In addition, no additional case of decreased blood pressure was experienced in the later period, i.e. when the BIS value was set higher.

Two cases of respiratory depression were confirmed and one of the patients had a history of chronic bronchial asthma. Respiratory depression was due to accidental aspiration during ESD. This is not considered as an adverse event of propofol, and could be prevented by placing an aspirating cannula in the stomach. The other patient had a history of pulmonary emphysema and developed CO_2 narcosis because of the excessive infusion of oxygen during ESD. Therefore, based on this case, the oxygen infusion was started at 1 liter per minute when dealing with patients with COPD. Also, we made it a rule to carry out an arterial blood gas analysis at least once during ESD. As a consequence, we have not experienced any additional cases of respiratory depression.

Recent studies have reported that ESD is useful for localized esophagus and colon neoplasms[3,4]. ESD for such neoplasms is a much more complex endoscopic technique than that used for gastric neoplasms. So, BIS monitoring with conscious sedation may be useful for safely performing ESD of esophageal and colonic neoplasms.

In conclusion, BIS monitoring of conscious sedation with propofol is considered a very effective method for safe implementation of ESD. A BIS value between 70 to 75 is suitable for monitoring sedation depth during ESD.

COMMENTS

Background

Endoscopic submucosal dissection (ESD) is a highly complex technique for *en bloc* resection of localized neoplasms of the digestive tract, and conscious sedation is the standard of care to perform safe procedures. During ESD conscious sedation is required, but the usefulness of sedation monitoring has not been reported.

Research frontiers

The bispectral index (BIS) is a quantitative parameter of the hypnotic effects of anesthetic drugs on the central nervous system. In this study, we present data supporting the usefulness of BIS monitoring for safely performing ESD with patients' satisfaction.

Innovations and breakthroughs

This is the first study to report that conscious sedation by BIS monitoring is useful for ESD.

Applications

BIS monitoring may be useful during ESD of gastric, esophageal or colonic tumors.

Terminology

Endoscopic submucosal dissection (ESD) is a highly complex technique for *en bloc* resection of localized neoplasms of the digestive tract. BIS is a quantitative parameter of the hypnotic effects of anesthetic drugs on the central nervous system. BIS is not an instrument just for the frequent analysis of electroencephalogram, but it also analyzes the relationship among the different components of the electroencephalogram at various phases.

Peer review

This paper describes a novel method of assessing sedation during endoscopy and as such it should be published.

REFERENCES

1 **Ono H**, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, Hosokawa K, Shimoda T, Yoshida S. Endoscopic mucosal resection for treatment of early gastric cancer. *Gut* 2001; **48**:

225-229
2 **Yamamoto H**, Kawata H, Sunada K, Satoh K, Kaneko Y, Ido K, Sugano K. Success rate of curative endoscopic mucosal resection with circumferential mucosal incision assisted by submucosal injection of sodium hyaluronate. *Gastrointest Endosc* 2002; **56**: 507-512
3 **Fujishiro M**, Yahagi N, Kakushima N, Kodashima S, Ichinose M, Omata M. En bloc resection of a large semicircular esophageal cancer by endoscopic submucosal dissection. *Surg Laparosc Endosc Percutan Tech* 2006; **16**: 237-241
4 **Yamamoto H**, Kawata H, Sunada K, Sasaki A, Nakazawa K, Miyata T, Sekine Y, Yano T, Satoh K, Ido K, Sugano K. Successful en-bloc resection of large superficial tumors in the stomach and colon using sodium hyaluronate and small-caliber-tip transparent hood. *Endoscopy* 2003; **35**: 690-694
5 **Gan TJ**, Glass PS, Windsor A, Payne F, Rosow C, Sebel P, Manberg P. Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. BIS Utility Study Group. *Anesthesiology* 1997; **87**: 808-815
6 **Song D**, Joshi GP, White PF. Titration of volatile anesthetics using bispectral index facilitates recovery after ambulatory anesthesia. *Anesthesiology* 1997; **87**: 842-848
7 **Sipe BW**, Rex DK, Latinovich D, Overley C, Kinser K, Bratcher L, Kareken D. Propofol versus midazolam/meperidine for outpatient colonoscopy: administration by nurses supervised by endoscopists. *Gastrointest Endosc* 2002; **55**: 815-825
8 **Koshy G**, Nair S, Norkus EP, Hertan HI, Pitchumoni CS. Propofol versus midazolam and meperidine for conscious sedation in GI endoscopy. *Am J Gastroenterol* 2000; **95**: 1476-1479
9 **Tohda G**, Higashi S, Wakahara S, Morikawa M, Sakumoto H, Kane T. Propofol sedation during endoscopic procedures: safe and effective administration by registered nurses supervised by endoscopists. *Endoscopy* 2006; **38**: 360-367
10 **Bower AL**, Ripepi A, Dilger J, Boparai N, Brody FJ, Ponsky JL. Bispectral index monitoring of sedation during endoscopy. *Gastrointest Endosc* 2000; **52**: 192-196
11 **Johansen JW**, Sebel PS. Development and clinical application of electroencephalographic bispectrum monitoring. *Anesthesiology* 2000; **93**: 1336-1344

S- Editor Cheng JX **L- Editor** Negro F **E- Editor** Zheng XM