Original Article

Correlation of bispectral index and Richmond agitation sedation scale for evaluating sedation depth: a retrospective study

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Background: This study aims to verify the correlation of bispectral index (BIS) and Richmond agitation sedation scale (RASS) for evaluating these and explore possibility of replacing RASS with BIS.

Methods: This retrospective cohort study consisted of 74 patients who were collected from the third Intensive Care Unit (ICU) ward of XXX Hospital between May 2012 and June 2015 in this retrospective study. Sedation levels were evaluated using the 10-grade RASS and were continuously monitored with a BIS monitor during the procedure every 5 minutes. BIS values and RASS scores were recorded.

Results: Patients were divided into dexmedetomidine (n=31) and midazolam (n=43) groups, and 342 paired data were collected. A statistically significant correlation existed between BIS values and RASS scores either in all patients undergoing flexible fiberoptic bronchoscopy (FFB) or in dexmedetomidine and midazolam groups at different time points. Correlation coefficient was higher in midazolam group compared with dexmedetomidine group at different time points ($P<0.05$).

Conclusions: A correlation was observed between BIS and RASS for evaluating depth of sedation in ICU patients undergoing FFB ($P<0.05$). Study results indicated that BIS monitoring is a meaningful tool, which can be applied as an adjunctive and alternative method to assess sedation, especially for high-risk patients who are prone to be under- or over-sedation.

Keywords: Bispectral index (BIS); Richmond agitation sedation scale (RASS); deep sedation; flexible fiberoptic bronchoscopy (FFB); midazolam; dexmedetomidine

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Introduction

With continuous improvement of flexible fiberoptic bronchoscopy (FFB) technique, FFB has been increasingly applied in intensive care unit (ICU) patients, which is considered to be a novel and ideal diagnostic and therapeutic method in a variety of lung diseases (1,2). FFB had become a routine and safe operation with low mortality about 0.019% (3), which was considered as the gold standard for observing airway diseases (4). However, along with increasing number of critically ill, elderly and high-risk patients undergoing FFB, safety issues have become

more and more concerned. Meanwhile, the proportion of bronchoalveolar lavage and complicated treatment of FFB is getting higher and higher than simple diagnosis, which makes safety issues more prominent. Noxious stimulation from FFB, which could cause adverse influence and be life-threatening condition occasionally, made sedation to be a requisite for a satisfactory condition, except when there are contraindications. Therefore, appropriate sedation is necessary to attenuate physiologic response, prevent complications and improve security, patients' tolerance and comfort (4-7).

Assessing and adjusting the depth of sedation play crucial roles in sedation management (8).

Richmond agitation sedation scale (RASS), as a conventional clinical subjective sedation scale based on patient response to stimulation, has been proven to be valid and reliable assessment tool in adult ICU patients for more than ten years (9,10). Given the limitations of RASS to monitor sedation level, a new method was required. bispectral index (BIS) is an objective and non-invasive indicator based on electroencephalographic (EEG) analysis (11,12) to evaluate sedation level and aid in achieving optimal titration of sedatives, which quantifies the depth of sedation by dimensionless numerical parameter between 0 (isoelectric EEG activity) and 100 (fully awake). Applying BIS to monitor the depth of anesthesia had been widely accepted and gained popularity. Several researches have reported that BIS values are significantly correlated with RASS scores for evaluating sedation in ICU patients (13-16). However, supportive evidence in application of BIS during FFB are still lacking. Thus, current study aimed to assess the correlation of BIS with RASS for evaluating sedation in ICU patients undergoing FFB and explore the possibility of replacing RASS with BIS.

Methods

Study population

Seventy-four patients were collected from the third ICU ward of the Second Affiliated Hospital of Harbin Medical University between May 2012 and June 2015. The inclusion criteria included: (I) ICU patients who receive invasive mechanical ventilation and require FFB; (II) monitoring BIS using BIS module of BeneView T8Mindray monitoring device; (III) aged >18 years; (IV) with stable hemodynamics, while the exclusion criteria included: data not competed. Patients were divided into two groups according to the sedatives used, and sedation levels were evaluated using the 10-grade RASS and were monitored continuously with a BIS monitor throughout the procedure every 5 minutes. The study was approved by the Ethics Committee of the Institutional Research Board of Harbin Medical University, and all clinical data were collected with the patients' and the healthy control group' s informed consent.

Medical team

An experienced bronchoscopist, assisted by a respiratory therapist (RT) and a senior nurse, performed FFB who were in charge of operation, assessing sedation level (all participants were trained on how to assess sedation level) and adjust sedatives and record data, drug administration and technical assistance, respectively. All participants were familiar with sedation protocol, operating processes and symptomatic treatment.

Sedation protocol

Drug selection

Fentanyl citrate injection [2 mL (0.1 mg)/ampoule, Renfu Pharmaceutical Co., Ltd., Yichang, China] was used as the analgesia and following drugs were used for sedation: dexmedetomidine hydrochloride injection [2 mL (200 μg)/ampoule, Hengrui Pharmaceutical Co., Ltd., Jiangsu, China]; midazolam injection [2 mL (10 mg)/ampoule, Enhua Pharmaceutical Co., Ltd., China]; and propofol injection [50 mL (1 g)/ampoule, Fresenius Kabi pharmaceutical Co., Ltd., Beijing, China].

Sedation protocol

All drugs were administered after consciousness recovery of patients or RASS score reaching zero. Endoscopic dripping of 2% lidocaine (3–5 mg/kg) was performed for topical anesthesia, and then intravenous injection of fentanyl citrate (2.0 μg/kg) was administered. The patients received a standard sedation protocol consisting of intravenous pumping a loading dose of dexmedetomidine 0.8 μg/kg or midazolam 0.05 mg/kg for 10 min followed by maintenance dose of dexmedetomidine or midazolam ranging from 0.2–0.7 μg/kg/h or 0.02–0.2 mg/kg/h, respectively to a require target score between RASS-3 (subject is moderately sedated, with some movement or eye opening. no eye contact.) and -4 (subject is deeply sedated, with no response to voice, but movement or eye opening to physical stimulation) as satisfactory deep sedation level. Bronchoscopists inserted bronchoscopy when reaching

required sedation level. Propofol injection with a loading dose of 2.0 mg/kg could also be used for intravenous injection and can be switched to 0.5–4 mg/kg/h for remedial sedation if necessary. RASS scores were obtained every 5 minutes during FFB, and simultaneously BIS values were continuously assessed and documented, but not for sedation control. BIS was monitored using BIS module of BeneView T8 Mindray monitoring device (Mindray International Medical Co., Ltd., Shenzhen, China), BIS sensor and disposable electrode (Aspect Medical Systems Inc, Newton, Mass., USA). After clearing the frontal-temporal region with alcohol swab for skin preparation, a disposable BIS electrode was positioned on it and then connected to BIS sensor, module and monitoring device. The data and waveform of BIS were continuously recorded. BIS data were excluded if electromyogram (EMG) index was above 55 decibels and/or signal quality index was below 50%. After completion of FFB, further sedation and analgesia could be continued after patient's conditions were evaluated. For patients with severe adverse reactions during FFB, procedure was discontinued and symptomatic treatment was provided. The therapeutic devices and drugs were easily available. Conditions were then evaluated to determine whether the procedure could be continued.

Vital signs monitoring and invasive mechanical ventilation

All patients received electrocardiogram, invasive artery blood pressure, respiratory rate (RR) and SpO_2 monitoring (Mindray monitoring device, BeneView T8), and invasive mechanical ventilation prior to FFB. Ventilator parameters were set to keep SpO_2 >90% during FFB, otherwise examinations were discontinued.

Bronchoscopy

A fiberoptic bronchoscope (Olympus LF-TP, Japan) was used in accordance with standardized procedures.

Data collection

Baseline data

Gender, age, height, weight, acute physiology and chronic health evaluation (APACHE) II score, and indications for FFB were obtained from patient medical records.

Sedative effects

RASS score, BIS value, heart rate (HR), invasive artery blood pressure, RR, and SpO_2 were recorded every five minutes during FFB. Frequencies of remedial sedation by propofol, total sedation time, time of FFB, and incidence of adverse events (including cough, nausea, and bronchospasm) were collected. All measurements were terminated at the end of FFB. After completion of FFB, bronchoscopist sedation satisfaction scores were recorded for all patients ("0" indicated very unsatisfied and "10" indicated very satisfied). Complications including nausea, tachycardia, bradycardia, arrhythmia, SpO_2 decrease, hypotension, hypertension and others were also recorded.

Statistical analyses

Data were analyzed using SPSS 22.0 (SPSS Inc., Chicago, USA). Quantitative and qualitative data were expressed as means ± standard deviations (SD) and numbers or percentages, respectively. Student's *t*-test and Chi-squared test were used to compare quantitative and qualitative data between groups, respectively. Pearson correlation analysis was applied to correlate BIS value with RASS score, total sedation time, time of FFB and satisfaction score of the bronchoscopists, while Spearman correlation analysis was used to correlate BIS value with cough, bronchospasm and oxygen desaturation. $P<0.05$ was considered to be statistically significant.

Results

Patient characteristics

A total of 342 paired data of 74 patients were obtained. Patients were divided into dexmedetomidine (n=31) and midazolam (n=43) groups accordingly. The characteristics of study population are shown in *Table 1*.

Correlation between BIS value and RASS score

A correlation existed between BIS values and RASS scores in all patients undergoing FFB in dexmedetomidine and midazolam groups at different time points ($P<0.05$, respectively). Correlation coefficients were higher in the midazolam group compared with dexmedetomidine group at different time points. Correlation coefficients between BIS values and RASS scores are shown in *Table 2*.

Discussion

RASS, a 10-level numerical rating scale, is one of the most

Table 1 Characteristics of the study population

Parameter	All patients (N=74)	Dexmedetomidine group (N=31)	Midazolam group (N=43)
Gender (male/female)	42/32	18/13	24/19
Age (year)	58.8±12.2	57.2±11.8	59.9±12.5
Height (cm)	168.20±9.04	168.61±9.09	167.91±9.10
Weight (kg)	66.30±9.55	67.55±9.19	65.40±9.81
APACHEII score	16.84±4.62	16.71±4.79	16.93±4.54
Indications for fiberoptic bronchoscopy (examination diagnosis/bronchoalveolar lavage)	24/50	10/21	14/29
Remedial sedation by propofol (yes/no)	37/37	22/9	15/28
Total sedation time (min)	25.20±4.35	27.87±4.10	23.28±3.44
Time of FFB (min)	18.37±3.78	19.77±3.79	17.36±3.48
Satisfaction score of the bronchoscopists	7.36±1.88	7.03±2.07	7.60±1.71
Cough (yes/no)	29/45	17/14	12/31
Nausea (yes/no)	13/61	5/26	8/35
Bronchospasm (yes/no)	33/41	19/12	14/29
Tachycardia (yes/no)	26/48	11/20	15/28
Bradycardia (yes/no)	7/67	3/28	4/39
Arrhythmia (yes/no)	6/68	3/28	3/40
Oxygen desaturation (yes/no)	26/48	15/16	11/32
Hypotension (yes/no)	12/62	5/26	7/36
Hypertension (yes/no)	13/61	6/25	7/36

APACHE II score, acute physiology and chronic health evaluation II score; Satisfaction score, consistency between respiratory therapist and nurse on the comments of the bronchoscopists. FFB, flexible fiberoptic bronchoscopy.

Table 2 Correlation coefficients between BIS values and RASS scores

Parameter	5 min	10 min	15 min	20 min
All patients	0.724**	0.598**	0.681**	0.600**
Midazolam group	0.826**	0.801**	0.775**	0.708**
Dexmedetomidine group	0.643**	0.424**	0.482**	0.459**

**, means P<0.05. BIS, bispectral index; RASS, Richmond agitation sedation scale.

commonly used conventional sedation agitation scales in clinical practice (17), deduced from the response to auditory and physical stimulation and observation of patients like other subjective tools. When application of subjective tools is impractical due to their above-mentioned disadvantages, objective indicators are essential to be an adjunctive or alternative method.

In present study, a statistically significant correlation existed between BIS values and RASS scores in all patients undergoing FFB and dexmedetomidine and midazolam groups at different time points. And it may indicate for the potential validity, reliability and practicability of BIS in the process of FFB. In addition, it may support the idea of replacing RASS with BIS due to its advantages including objectivity, continuity, non-invasion and simplicity. Correlation coefficients were higher in the midazolam group compared with dexmedetomidine group at different time points. There were no significant differences in terms of patient baseline characteristics between groups, whereas total sedation time and time of FFB were significantly shorter in the midazolam group, with a lower percentage of these patients requiring propofol for remedial sedation during FFB. In addition, the number of patients of detected data was significantly more in the dexmedetomidine group

compared with the midazolam group at 20, 25 and 30 min. Furthermore, the incidence of cough, bronchospasm, and oxygen desaturation was significantly higher in the dexmedetomidine compared with midazolam group. All these mean that dexmedetomidine had a poorer sedation effect during FFB in agreement with our previous finding, which could lead to overestimated BIS values (18) and might be associated with lower correlation coefficients. Dexmedetomidine is more effective in conscious and light sedation (19), not in deep sedation. Although BIS values were merely documented, but not used for sedation control, it could still give operators hints to adjust sedation level, which might lead to no significant difference in terms of satisfaction score of the bronchoscopists between groups in contrast to our previous finding.

Also there are some limitations in the current study. First this study is a single-center retrospective study with relatively small sample size. Secondly, although no research has revealed the differences between special BIS monitor and BIS module of BeneView T8 Mindray monitoring device, lacking special BIS monitor may affect the accuracy of data. Thirdly, FFB was performed by different bronchoscopists, therefore the results could be affected by operator experience and tendentiousness, this could be improved in future study. Future studies comprising larger sample size are needed to verify our findings.

In addition, we should also pay attention to some factors, which can affect accuracy of the numerical BIS scale, including hepatic or renal failure with associated encephalopathy, inadequate sedation and analgesia, EMG interference, circulation inhibition, and blood glucose level (20-27). Under- or over-estimating BIS value can affect the correlation with clinical subjective sedation score, as shown in our study, which should be attached much weight to in clinical practices.

Conclusions

In summary, the present study showed that there was a correlation between BIS and RASS for evaluating depth of sedation in ICU patients undergoing FFB, which testified its validity, reliability and practicability in clinical setting. Our study demonstrates that BIS monitoring is a meaningful and objective tool, which can be applied as a adjunctive or alternative method to assess sedation, especially for high-risk patients who are prone to be under- or over-sedation.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Ethics Committee of the Institutional Research Board of Harbin Medical University (No. HMUIRB20170008), and all clinical data were collected with the patients' and the healthy control group' s informed consent.

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