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Auditory evoked potentials index versus bispectral index during propofol sedation in spinal anesthesia

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Abstract
Purpose. It is still controversial whether an electroencephalogram could be a useful monitor of sedation levels. The present study was performed to compare the bispectral index (BIS) and the auditory evoked potentials index (AAI) during light sedation with propofol infusion in spinal anesthesia.
Methods. Eighty patients, aged 20 to 70 years, scheduled for surgery of the lower extremities under spinal anesthesia were assigned to one of four groups (20 patients each). Patients in the AAI propofol and BIS propofol groups were sedated with propofol infusion at an initial rate of 2 $mg \cdot kg^{-1} \cdot h^{-1}$. Propofol infusion was controlled to try to keep the observer's assessment of alertness/sedation (OAAS) scale at 3 or 4. Patients in the AAI control and BIS control groups did not receive propofol.
Results. The OAAS scales and the AAI or BIS decreased significantly in all groups during surgery, while the decrease was larger in the AAI propofol and BIS propofol groups. The AAI was significantly lower along with lower OAAS scales. There was no overlap in the AAI between OAAS scale 3 and scale 5 in the AAI propofol group, while in the BIS propofol group, no difference was observed in the BIS among OAAS scales 2, 3, 4, and 5.
Conclusion. The AAI, but not the BIS, could discriminate slight changes of consciousness during light sedation with propofol infusion in patients with spinal anesthesia.

Key words Conscious sedation · Propofol · Spinal anesthesia · Bispectral index · Auditory evoked potentials index

Introduction

For the comfort of patients during spinal, epidural, or local anesthesia, sedation is often requested. To evaluate sedation levels, many scores have been used, but they need verbal or touch stimuli, which may cause discomfort to the patients, and sedation scores are not continuous monitorings. Recently, the electroencephalogram (EEG) has been applied to monitor sedation levels, and many EEG indices have been studied. The bispectral index (BIS) is a representative of the extracted cortical EEG, while the auditory evoked potential (AEP) is an EEG response to external stimuli.

The BIS is reported to correlate well with the level of responsiveness and provides an excellent prediction of the loss of consciousness. Therefore, the BIS is thought to be a valuable monitor of sedation level and loss of consciousness induced by propofol [1]. However, Ibrahim et al. [2] showed that individual BIS scores demonstrated significant variability, making it difficult to predict sedation levels. The auditory evoked potentials index (AAI) correlated well with changes of the sedation level, as measured by the response to verbal command, during induction with propofol [3]; however, AAI values are reported to have interindividual variations that are too great to predict wakefulness [4]. Thus, it is still controversial whether the BIS or the AAI could be a useful monitor of sedation levels, especially in light sedation. Therefore, the present study was performed to investigate the relation between BIS or AAI and sedation scores during light sedation with propofol infusion in spinal anesthesia.

Subjects and methods

After obtaining approval from the ethics committee of the hospital and gaining informed consent from the patients, 80 patients (aged 20 to 70 years) American Society of Anesthesiologists (ASA) physical status I or II, scheduled for surgery of the lower extremities under spinal anesthesia were enrolled in the present study. They were randomly divided into four groups by an

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envelope method; BIS control, AAI control, BIS propofol, and AAI propofol groups, of 20 patients each. Patients who had neurological disorders, hearing disturbance, liver or renal disease, mental impairment, or obesity (body mass index >30) and those taking any drugs affecting cerebral function, such as hypnotics or antidepressants were excluded.

Midazolam 2–3 mg and atropine 0.5 mg were intramuscularly administered as a routine premedication 15 min before the patients entered the operating room. Spinal anesthesia was performed with the patient in the lateral position with 0.5% hyperbaric tetracaine 2 ml (10 mg) at the L4–5 level. The patients were then immediately returned to the supine position. Anesthesia level was checked by a cold test 5 and 10 min after spinal anesthesia and it was confirmed that the level was adequate for surgery.

For the AAI and BIS monitoring, we used the A-Line AEP (version 1.4; Danmeter, Odense, Denmark), and BIS (version 3.4; A-2000; Aspect Medical Systems, Newton, MA, USA), respectively. The electrodes of the A-Line AEP (AAI control and AAI propofol groups) or BIS (BIS control and BIS propofol groups) were positioned as recommended by the manufacturers after the skin had been prepared with alcohol. The headphone of the AEP was attached to the patients in the AAI control and AAI propofol groups. Electrode impedances were considered acceptable if they were below 5 and 10 kOhm for AEP and BIS, respectively.

Patients in the AAI propofol and BIS propofol groups were sedated with propofol infusion at an initial rate of 2 $mg \cdot kg^{-1} \cdot h^{-1}$ after the start of surgery. No sedatives were administered to the patients in the AAI control and BIS control groups during surgery. The propofol infusion rate was controlled to try to keep the observer's assessment of alertness/sedation (OAAS) scale at 3 or 4 (Table 1), by increases and decreases of 0.5 $mg \cdot kg^{-1} \cdot h^{-1}$. The OAAS scale was checked before sedation; at 1, 3, 5, and 10 min after starting sedation; and every 10 min thereafter. Oxygen 6 $l \cdot min^{-1}$ was administered by a mask to all patients.

Statistical analysis was performed with the χ^2 test, and factorial analysis of variance (ANOVA) was used for demographic data. The OAAS scale was compared between two groups with the χ^2 test. Changes in the BIS, AAI, and propofol infusion dose were analyzed with repeated-measures ANOVA followed by the Student Newman Keuls test as a post-hoc analysis. Nine patients in the AAI propofol and 8 patients in the BIS propofol group showed OAAS scales 2 to 5, except for the data at 1, 3, and 5 min after starting sedation. The other patients showed only OAAS scales 3, 4, and 5. To compare the indexes among the different OAAS scales, those who showed OAAS scales of 2 to 5 were used thereafter. In each patient, the mean index at each OAAS scale was obtained and the BIS or AAI was compared among the different OAAS scales by the Friedman test followed by the Wilcoxon signed rank test as a post-hoc analysis. A P value less than 0.05 was considered to be statistically significant.

Results

Demographic data were not different among the four groups (Table 2). The OAAS scale decreased in all groups during surgery, and the decrease was bigger in the AAI propofol and BIS propofol groups than in the AAI control and BIS control groups (Table 3). The OAAS scales at 20, 30, and 60 min were significantly lower than the scale at 5 min in the AAI propofol and BIS propofol groups. The propofol infusion dose was not different between the AAI propofol and BIS propofol groups (Table 3). The AAI and BIS decreased significantly in all groups during surgery (Fig. 1), with

Table 1. Observer's assessment of alertness/sedation (OAAS) scale

5	Awake
4	Sedated, but is still normally oriented, responds normally to verbal commands
3	Responds only to repeated and loud commands
2	Does not respond to verbal commands, but reacts to prodding and shaking
1	Reacts only to pain
0	Does not react even to pain

Table 2. Demographic data

	AAI control	BIS control	AAI propofol	BIS propofol
Age (years)	55 ± 10	52 ± 9	56 ± 10	53 ± 8
Male/Female	14/6	16/4	11/9	10/10
Height (cm)	158 ± 9	160 ± 8	162 ± 7	161 ± 7
Body weight (kg)	58 ± 9	60 ± 10	61 ± 7	60 ± 7
Anesthesia level	T6 (5–10)	T7 (5–9)	T6 (5–10)	T6.5 (4–9)
Duration of anesthesia (min)	120 ± 28	125 ± 20	130 ± 24	124 ± 26

Values are means ± SD, numbers of patients, or medians and ranges (in parentheses)
AAI, auditory evoked potentials index; BIS, bispectral index; control, no sedation; propofol, propofol infusion; T, thoracic nerve

Table 3. OAAS scale and propofol dose

	Before surgery	5	10	20	30	60	At the end of surgery
OAAS scale							
BIS propofol	5	4.5 (4–5)*,***	4 (2–5)*,***	4 (2–5)*,**,***	4 (2–5)*,**,***	3 (2–5)*,**,***,$	5
BIS control	5	5	5 (4–5)	4.5 (4–5)*	4.5 (4–5)*	5 (4–5)	5
AAI propofol	5	4 (4–5)*,***	4 (2–5)*,***	4 (2–5)*,**,***	3.5 (2–5)*,**,***,$	3 (2–5)*,**,***,$	5
AAI control	5	5	5 (4–5)	4.5 (4–5)*	4.5 (4–5)*	4.5 (4–5)*	5
Propofol dose ($mg \cdot kg^{-1} \cdot h^{-1}$)							
BIS propofol	0	2.23 ± 0.26	2.28 ± 0.30	2.30 ± 0.38	2.30 ± 0.38	2.18 ± 0.24	0
AAI propofol	0	2.23 ± 0.26	2.23 ± 0.26	2.35 ± 0.40	2.33 ± 0.34	2.33 ± 0.41	0

* $P < 0.05$ vs the scale before surgery and after surgery; ** $P < 0.05$ vs the scale in the control group; *** $P < 0.05$ vs the scale at 5 min
The OAAS scale is shown as the median value, with ranges, in parentheses; the propofol dose is shown as the mean ± SD

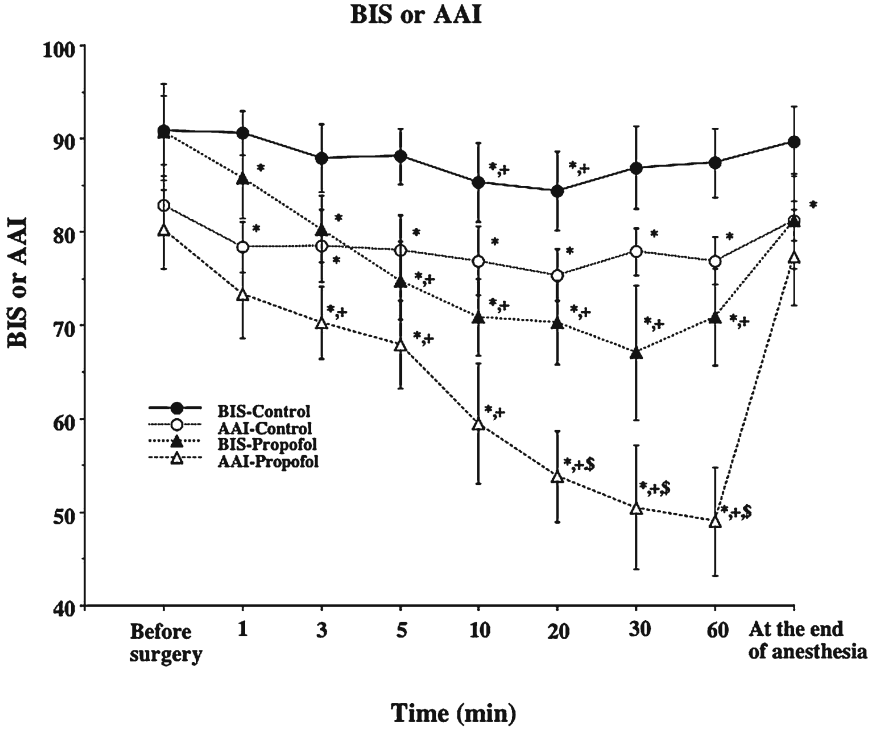

Fig. 1. Changes in the bispectral index (*BIS*) and the auditory evoked potentials index (*AAI*) are shown as means ± SD. The BIS-Propofol and AAI-Propofol groups received propofol infusion and the BIS-Control and AAI-Control groups received no sedatives during the study. *$P < 0.05$ vs the value before surgery; $^{+}P < 0.05$ vs the value at the end of anesthesia; $^{\$}P < 0.05$ vs the value at 5 min

the decrease being more prominent in the AAI propofol and BIS propofol groups. The AAI was significantly lower along with lower OAAS scales. There was no overlap in the AAI between OAAS scales 3 (AAI: minimum, 42; maximum, 67) and 5 (AAI: 69, 92) and these values were significantly different, while no differences were observed in the BIS among OAAS scales 2 (BIS: minimum, 58; maximum, 84), 3 (BIS: 57, 88), 4 (BIS: 58, 90), and 5 (BIS: 73, 97) (Figs. 2, 3).

Discussion

The important finding of this study was the different changes between the BIS and the AAI. Although both the BIS and AAI were decreased by light sedation with propofol infusion during spinal anesthesia, only the AAI could discriminate OAAS scale 3 from OAAS scale 5.

The present study was performed in patients with spinal anesthesia. A high spinal block with a higher dose of bupivacaine was associated with a faster onset, delayed recovery, and lower doses of propofol for sedation compared with a low spinal block with the same drug [5]. However, we used the same dose of tetracaine (0.5% 2 ml [10 mg]) in all patients and the anesthesia level was not different among the groups. Therefore, the influence of different anesthesia levels and different doses of local anesthetic did not exist. The OAAS scales were not different between the BIS control and AAI control groups or between the BIS propofol and AAI propofol groups. In addition, the propofol infusion

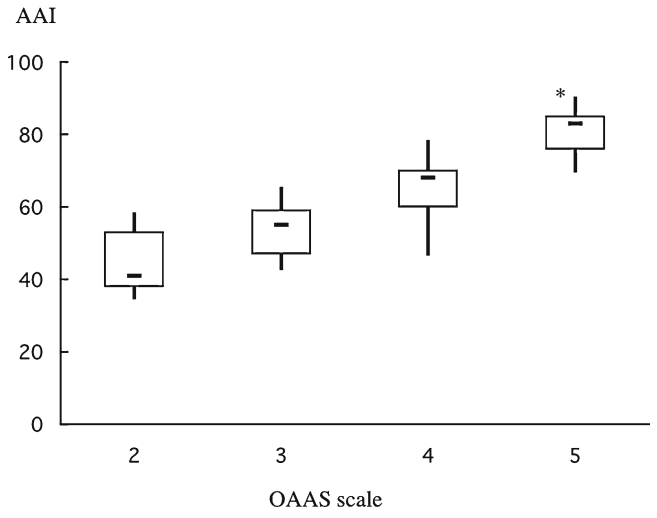

Fig. 2. The auditory evoked potentials index (*AAI*) in the AAI-Propofol group. Nine patients showed OAAS scales 2 to 5. In each patient, the mean values of the AAI at each OAAS scale were obtained, and medians with first and third quartiles (*boxes*) and maximum and minimum values (*bars*) of the nine patients at each OAAS scale are shown. *$P < 0.05$ vs scales 2 and 3

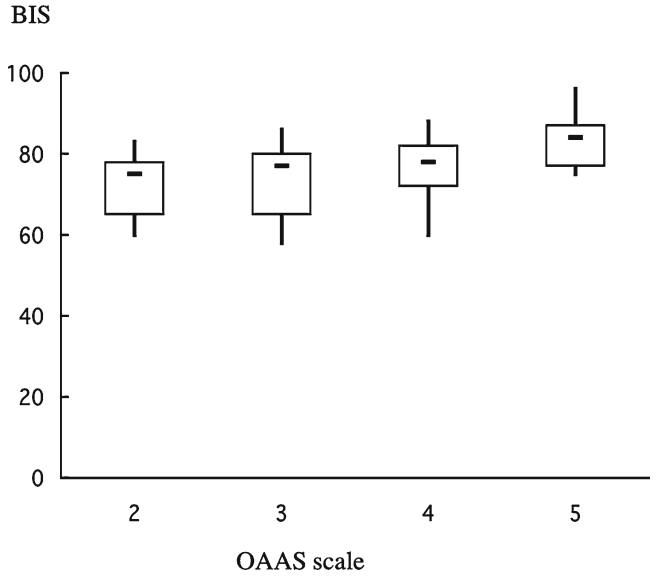

Fig. 3. The bispectral index (*BIS*) in the BIS-Propofol group. Eight patients showed OAAS scales 2 to 5. In each patient, the mean values of the AAI at each OAAS scale were obtained, and medians with first and third quartiles (*boxes*) and maximum and minimum values (*bars*) of the eight patients at each OAAS scale are shown

doses were not different between the BIS propofol and AAI propofol groups. Therefore, the sedation levels were not different between the BIS control and AAI control groups or between the BIS propofol and AAI propofol groups.

We did not use the BIS and AEP in the same patients because we already knew that the click sounds of the AEP have some effects on the BIS [6].

Spinal anesthesia itself was reported not to cause measurable sedation in terms of decreased BIS values [5], although Gentili et al. [7] reported that spinal anesthesia may have sedative properties, as shown by a decrease in BIS levels [8]. The most likely mechanism for sedation during spinal anesthesia is a deafferentation phenomenon. The loss of facilitatory input to the reticular activating system renders it more susceptive to the actions of sedative drugs. The present results showed decreases in the BIS and AAI and OAAS scale during spinal anesthesia without propofol.

However, we administered midazolam as a premedication. Therefore, its sedative effects may have been added, although both the BIS and AAI were high and all patients were awake before surgery. The dose of propofol necessary to cause loss of consciousness is reduced by 43% following pretreatment with midazolam 0.1 $mg \cdot kg^{-1}$ [9]. In our previous study [10], to keep the OAAS scale at 3 or 4 during spinal anesthesia after premedication with midazolam 0.04 $mg \cdot kg^{-1}$, the mean propofol infusion dose was 2.5 $mg \cdot kg^{-1} \cdot h^{-1}$, which is consistent with the present results. Atropine was also administered as a premedication in the present study. Atropine increases delta power and decreases alpha power and beta and theta frequencies [11], but its effects on the BIS and AAI are not clear. However, the BIS and AAI had the same tendency in our control groups. Therefore, the effects of atropine on the BIS and AAI may have no influence on the difference between the BIS and AAI. Considering these effects of midazolam and atropine, it appears that these agents should not be administered to study sedation by propofol. However, these were our standard premedications because even if the patients were awake before sedation, shown by high BIS or AAI values, they were comfortable without memory of spinal puncture, and the study purpose was to investigate the usefulness of the EEG indices in the clinical situation. Therefore, we used premedication in the present study.

Auditory input is considered the last sensory modality to be blunted during anesthesia [12]. A dose-dependent impairment of the central processing of auditory information after propofol administration has been observed [13]. However, propofol did not totally blunt primary cortical responses to acoustic stimulation, indicating that patients may process auditory information under general anesthesia [13]. The AEP signal obtained during surgery appears to represent a balance between central nervous system depression caused by anesthetic drugs and activation induced by noxious stimuli [14]. There are two different types of AEP index, the AAI used in the present study, and another AEP index. In an

autoregressive model with exogenous input, the estimated AEP (for the AAI) was significantly faster than a moving time average estimated AEP (another AEP index) in tracing the transition from consciousness to unconsciousness during propofol induction [15]. Therefore, we used the AAI, because the AAI may be better than the AEP index noted above [15] to predict slight changes of consciousness during light sedation.

Barr et al. [4] reported that the transition to loss of response occurred at a mean AAI value of 46 and a mean BIS value of 58, although neither index was able to discriminate subtle changes in wakefulness. Very sedated patients had BIS values ranging from 35 to 98, and mildly sedated patients had BIS values ranging from 67 to 91 in a study by Nasraway et al. [16]. Thus, large variability and overlap in the BIS at distinct depths of anesthesia would make differentiation of these anesthetic depths difficult [17, 18]. In the present study, the BIS did not have as much variation as that shown in the previous studies [16–18], but it could not discriminate OAAS scale 2 from OAAS scale 5. In contrast, the AAI could discriminate OAAS scale 3 from OAAS scale 5, although it could still be possible that AAI values would overlap at OAAS scales 3 and 5 if the number of patients were to be increased. BIS and AAI correlated well with loss of consciousness defined by OAAS scale 2 in a study by Hadzidiakos et al. [19]. However, their results showed great overlap among OAAS scales 1, 2, and 3 in both the BIS and AAI (measured by a newer monitor, AEP2; Danmeter, Odense, Denmark); therefore, it seems to be impossible to distinguish loss of consciousness using their method. Regarding the AAI, the new monitor (AEP2) uses a composite index based on both AEP and EEG. The AEP2 uses the EEG component in deep sedation levels, while in light sedation levels, it may use the AEP component. However, the better capacity for distinguishing the OAAS scale shown by the AAI in our study compared with the distinguishing of AAI by the AEP2 in the study of Hadzidiakos et al. [19] shows that the EEG components may obscure slight changes in consciousness at the light sedation level. Our present result, that the BIS was not different among OAAS scales 2, 3, 4, and 5, might also lead to the speculation that the EEG component obscured slight changes in consciousness at the light sedation level.

For measuring AAI, a headphone is required, and this might be uncomfortable for lightly sedated patients. However, in our interviews of the patients, only some patients responded that they felt slightly noisy click sounds before sedation, but not thereafter. Therefore, it seems that the AAI is suitable for patients with light sedation. In conclusion, the AAI but not the BIS could discriminate slight changes in consciousness during light sedation with propofol infusion in patients with spinal anesthesia.

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