

Composite auditory evoked potentials index is not a good indicator of depth of anesthesia in propofol-fentanyl anesthesia: Randomized comparative study

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Abstract

Background: The composite auditory evoked potentials index (cAAI) was considered a measure of overall balance between noxious stimulation, analgesia, and hypnosis; while bispectral index (BIS) shows only hypnosis, and auditory evoked potentials index (AAI) shows response to stimuli. The present study compared the performance of cAAI, BIS, and AAI in propofol-fentanyl anesthesia.

Materials and Methods: Forty-five patients for abdominal surgery aged 30-65 years with ASA physical status I or II were randomly divided into three groups by an envelope method. Anesthesia was induced with midazolam, propofol, and fentanyl along with an epidural block. When hemodynamics were stable during surgery, propofol infusion rate was fixed at 4 mg/kg/h for 10 min, then increased to 6 mg/kg/h and kept it for 10 min. AAI (AEP version 1.4), cAAI (AEP version 1.6), or BIS (A-2000) was monitored in each 15 patients, and the performance of three indices was compared.

Results: All three indices decreased significantly before intubation. Only the AAI increased significantly by intubation. During anesthesia except for at propofol 6 mg/kg/h, the cAAI was significantly higher than the AAI. Only the AAI was significantly lower at propofol 6 mg/kg/h than at 4 mg/kg/h. The cAAI had the largest and AAI had the smallest inter-individual variations. The cAAI was higher than the manufacturer's recommended range of general anesthesia.

Conclusion: In propofol-fentanyl anesthesia, AAI might be better to discriminate anesthetic depth than cAAI and BIS.

Key words: Auditory evoked potentials, bispectral index, electroencephalogram, fentanyl, propofol

Introduction

During anesthesia, electroencephalographic (EEG) index is now one of the routine monitoring. Mainly, there are two kinds of EEG indices available in anesthesia, one uses cortical EEG such as bispectral index (BIS), and another uses subcortical EEG response to stimuli, in which only the auditory evoked potentials (AEP) index (AAI) is available. The BIS and AAI measure different aspects of brain activity. BIS measures hypnotic component of anesthesia, while AAI shows the information of both analgesia and hypnosis.^[1] Recently, a new index has been

developed, a composite AAI (cAAI), which uses both cortical EEG and AEP. In the cAAI, active measurement is based on the AEP, and passive measurement during deep anesthesia is based on spontaneous EEG. In case of low AEP signal quality, cAAI is calculated from the spontaneous EEG activity. This prevents mis-interpreting low cAAI values.^[2] The cAAI is considered to be a measure of total balance between analgesia and hypnosis.^[3] Therefore, cAAI might be better than BIS and AAI as a monitor of anesthetic depth. The present study compared the performance of cAAI, BIS, and AAI in propofol-fentanyl anesthesia with an epidural block.

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Materials and Methods

Ethical approval for this randomized controlled non-blind study (No. 1573) was provided by the Institutional Ethical Committee. After informed consent from patients, 45 patients for abdominal surgery aged 30-65 years were equally allocated to one of the three groups (AAI, cAAI, or BIS group) randomly by an envelope method. Those who had neurological disorders, hearing disturbance, liver or renal disease, mental impairment, alcohol abuse, or taking any drugs affecting

cerebral function such as hypnotics, antidepressants, etc., before surgery were excluded.

As a premedication, midazolam 0.05 mg/kg was intramuscularly administered 30 min before entering the operation room as a routine practice. An epidural catheter was inserted in an appropriate interspinal space. Besides usual noninvasive blood pressure, heart rate, and percutaneous oxygen saturation; AAI (AEP version 1.4, Danmeter, Odense, Denmark), cAAI (AEP version 1.6, Danmeter, Odense, Denmark), or BIS (A-2000, Aspect Medical Systems, Newton, MA, USA) was monitored (15 patients each). Anesthesia was induced with midazolam 0.05 mg/kg, propofol 2 mg/kg, and fentanyl 4-5 μ g/kg; and endotracheal intubation was facilitated with vecuronium 0.15 mg/kg. Anesthesia was maintained with propofol infusion, fentanyl, and intermittent epidural administration of 1.5% mepivacaine 4-6 mL. When hemodynamics were stable during surgery, propofol infusion rate was fixed at 4 mg/kg/h for 10 min, then increased to 6 mg/kg/h and kept for 10 min. During this period, epidural mepivacaine was not administered. The AAI, cAAI, and BIS as well as blood pressure and heart rate were compared before induction, just before and after intubation, 10 min after fixed propofol infusion rate at 4 and 6 mg/kg/h, and just after extubation.

Power analysis was performed to detect power of 0.95 for the indices analyzed by repeatedly measuring analysis of variance (ANOVA) using the G Power™ (ver. 3.03, University Mannheim, Germany), and showed that a total of 36 patients were necessary. Therefore, 15 patients in each group were enrolled considering some patients with protocol failure. Statistical analysis was performed with factorial ANOVA and chi-square test for demographic data; and factorial and repeated measures ANOVA for blood pressure, heart rate,

and electroencephalographic indices. A *P*-value less than 0.05 were considered to be statistically significant.

Results

Demographic data were not different among the three groups [Table 1]. Blood pressure and heart rate significantly decreased by anesthesia induction, returned to the baseline (before surgery) after intubation, decreased at propofol 4 and 6 mg/kg/h, and increased after extubation. However, no significant differences were observed among the three groups (data is not shown).

All three indices decreased significantly before intubation. Only the AAI increased significantly by intubation. During anesthesia except for at propofol 6 mg/kg/h, the cAAI showed significantly higher values than the AAI. The AAI at propofol 6 mg/kg/h was significantly lower than that at 4 mg/kg/h, while the cAAI and BIS were not different. The cAAI had the largest and AAI had the smallest interindividual variations [Figure 1]. The cAAI was higher than the manufacturer's recommended range of general anesthesia.

Discussion

The present study compared the performance of AAI, cAAI, and BIS in propofol-fentanyl anesthesia with an epidural block. The AAI had the smallest inter-individual variation, and only the AAI increased by intubation and was significantly different between different propofol infusion rates. The cAAI had the largest inter-individual variation without any difference between different propofol infusion rates.

To compare different indices, it is better to measure all in the same patient simultaneously. However, it is impossible to

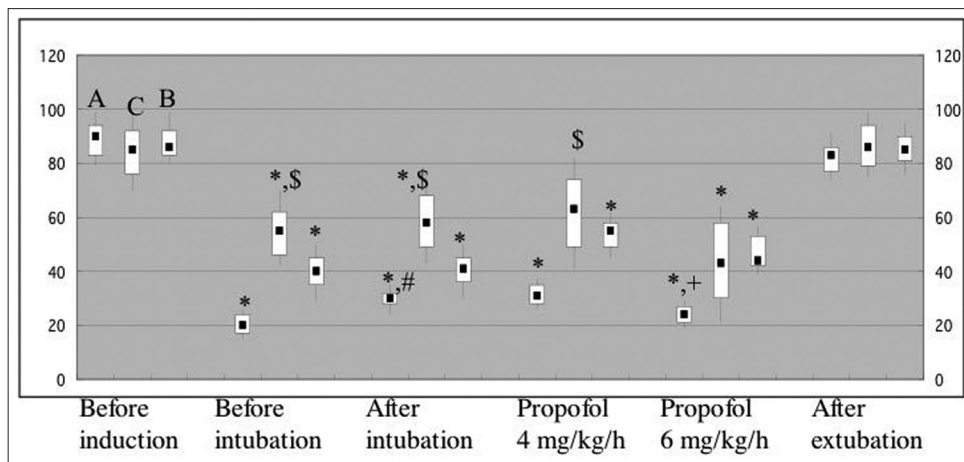


Figure 1: Changes in auditory evoked potentials index (AAI), composite AAI, and bispectral index (BIS). A = AAI, C = composite AAI, B = BIS. Mean (black square) with first and third quartile (white square) are shown. Bars indicate maximum and minimum values. **P* < 0.05 vs before induction, ^{\$}*P* < 0.05 vs AAI (A), +*P* < 0.05 vs propofol 4 mg/kg/h, #*P* < 0.05 vs before intubation

Table 1: Demographic data

	BIS	AAI	cAAI
Gender (male/female)	7/8	9/6	5/10
Age (years)	52±10	55±9	50±11
Body weight (kg)	61±11	66±9	59±10
Height (cm)	162±14	166±11	159±12
Duration of surgery (min)	215±73	243±55	224±48
Type of surgery			
Partial gastrectomy	9	7	8
Colectomy	6	8	7
Epidural catheter insertion			
T6-7	7	5	6
T7-8	2	2	2
T9-10	4	5	5
T10-11	2	3	2
Total consumption of mepivacaine (mL)	62±26	55±32	57±29
Total consumption of fentanyl (µg)	445±60	424±55	398±48

BIS=Bispectral index group, AAI=Auditory evoked potentials index group, cAAI=Composite AAI, Number of patients or mean±standard deviation is shown

measure cAAI and AAI simultaneously in the same patient, and we already showed that the click sound of the AEP affects the BIS,^[4] therefore we used only one monitor in one patient. All indices are simple numbers, therefore, it might not have introduced any bias. In addition, it would be better to include only one type of surgery with the same site of epidural catheter insertion to avoid the effects of surgical stimuli and epidural anesthesia. We included two types of surgery and different epidural catheter insertion sites. However, there were no differences among the groups in the type of surgery, site of epidural catheter insertion, blood pressure, and heart rate. Therefore, three groups were comparable.

We kept propofol infusion rate for 10 min before measurements. We could not find any studies describing how long it takes to stabilize anesthetic condition if we change the infusion rate. However, in 10 min all indices became constant, which suggested that three indices might be comparable.

The cAAI greater than 50-60 indicated fully awake or under minimal sedation, 40-50 or 60 were suggestive of moderate sedation, 30-40 were associated with moderate to deep sedation, and less than 30 showed deep sedation like general anesthesia in the studies by Huang *et al.*,^[5] and by Lu *et al.*^[6]

However, present study showed that cAAI was between 20 and 80 when patients were fully anesthetized with propofol and fentanyl. Our study was performed during surgery in general anesthesia with an epidural block, while the study by Huang *et al.*,^[5] was in sedation during endoscopy and that by Lu *et al.*,^[6] was in sedation and an epidural block in intensive care unit. Epidural lidocaine produced a reduction of cAAI.^[7] Therefore, cAAI in the study by Lu *et al.*,^[6] and ours should

be lower than that in the study by Huang *et al.*,^[5] at similar hypnotic level. However, the cAAI in our study showed higher values than the other two studies.^[5,6] The reason of this discrepancy was not known. In our previous study,^[8] manufacturer's recommended range of general anesthesia fitted better with the AAI than with the BIS.^[8] The present study showed both BIS and AAI fitted well, but cAAI did not fit at all.

The AEP measures output of the central nervous system to a controlled input. AEP provides information about the function of the brainstem and subcortical and cortical components, showing the overall anesthetic state.^[9] Because BIS measures cortical function, it is only able to monitor hypnotic state and is a poor indicator of the sensitiveness to pain.^[10] Therefore, the AAI and not the BIS increased by intubation in the present study as in our previous studies.^[8,11] The cAAI uses AEP as a base measurement and add cortical EEG in deep hypnosis, which seems better than the AAI or BIS. The cAAI had a better correlation with calculated propofol effect site concentration than AAI in the previous study.^[12] However, our present study showed that the AAI and neither cAAI nor BIS was significantly different between different propofol infusion rates.

During induction of anesthesia by propofol-remifentanyl, BIS performed better than cAAI, but cAAI was statistically a better discriminator of the consciousness during the wake-up test and emergence, although these differences did not appear to be clinically meaningful.^[13] Rehberg *et al.*,^[14] reported that lightening of anesthesia before recovery could be noticed earlier with BIS than cAAI, although consciousness was detected with a significantly higher pK values by cAAI. These results suggest that in light hypnosis, cAAI is better than BIS probably due to the factor of AEP. The AAI followed rapid changes from awake to sleep,^[15] and showed no overlap between awake and asleep values.^[16]

The variability of cAAI was higher than the BIS in comparison with the difference between median index values during anesthesia and the threshold recommended by the manufacturer.^[14] The cAAI was higher and had larger inter-individual variation than AAI and BIS during propofol-fentanyl anesthesia, especially in deep anesthesia in the present study. Hadzidiakos *et al.*,^[17] showed that the EEG components of cAAI may obscure slight changes in consciousness at light sedation level. Therefore, adding cortical EEG might obscure the fine changes of AAI.

In conclusion, in propofol-fentanyl anesthesia with an epidural block, AAI might be better to discriminate anesthetic depth than cAAI and the BIS.

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