Comparison of entropy and bispectral index values during propofol induction

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Abstract

Introduction: We aimed to identify the entropy levels that would correspond to bispectral index (BIS) levels during general anaesthesia induction in patients who will undergo elective lumbar disc surgery.

Material and methods: 30 cases in American Society of Anesthesiology classification groups I-II who underwent lumbar disc surgery under general anaesthesia were included in our study between January 1, 2004, and December 31, 2005. BIS and entropy electrodes were applied at the same time in 30 cases in the study group. Non-invasive mean arterial pressures (NMAP), heart rates (HR) and peripheral oxygen saturation (SpO_2) were measured in all cases before induction. During induction, measurements of these parameters every 30 seconds were also recorded. In order to assess the level of sedation during anaesthesia, 'Observer's Assessment of Alertness/Sedation' (OAA/S) scale was used. BIS, entropy and OAA/S values were recorded simultaneously.

Results: Induction OAA/S scores were in correlation with BIS and entropy values. Together with the decreases in OAA/S scores, BIS and entropy values decreased as well, but the decrease in entropy values was more rapid. A significant difference was found between BIS and entropy induction values ($p<0.05$). Induction MAP and HR values at 30, 60, 90, 120 seconds were lower than the values of the control, which was statistically significant ($p<0.05$).

Conclusions: During the induction of general anaesthesia, we found entropy values to be more sensitive and they demonstrated a more rapid decrease than BIS. Based on this observation, induction agents that might cause severe hypotension could be more safely administered under entropy monitoring.

Key words: bispectral index, entropy, anaesthesia, induction.

Introduction

Currently there is no standard method for measuring the hypnotic component of anaesthesia. Electroencephalography (EEG) was introduced to the field of anaesthesiology as a means of assessing levels of hypnosis during anaesthesia. Bispectral analysis is one EEG-based technique for determining hypnotic levels during anaesthesia and sedation. This method yields a bispectral index (BIS) that reflects interfrequency phase relations of EEG [1, 2]. BIS values range from 0 (absence of brain activity) to 100 (fully awake state), and bispectral analysis allows continuous measurement

of a patient's hypnotic state [3, 4]. Specifically, it reveals mathematical relationships between EEG signal components (phase couplings) at different wave speeds. The bispectral index was first used in 1992 [5] and is a practical method for directly measuring sedative effects in the brain [6-12]. BIS is widely used to monitor depth of sedation [11].

Entropy measurement is another EEG-based method for determining hypnotic levels [10, 12-15]. Compared to BIS, entropy is considered to be a more accurate and reliable indicator of the hypnotic effects of anaesthetic and sedative drugs. Entropy values reflect EEG signals that are irregular, complex and unpredictable [3]. This parameter is recorded from EEG of the frontal cortex using a low-impedance sensor [14] and the signals can be interpreted in 2 separate ways: state entropy (SE) is the calculated form of the frequencies between 0.8 and 32 Hz, and response entropy (RE) covers the range from 0.8 to 47 Hz [4, 14]. A number of studies have used approximate entropy and Shannon entropy to describe EEG changes [4, 12, 13]. The Datex-Ohmeda S/5 Entropy Module (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland) was the first commercial entropy monitor ever produced. Most studies of EEG entropy have focused on the use of this method for assessing depth of hypnosis during general anaesthesia; however, entropy can also be used to assess depth of sedation [4, 15]. During sedation or anaesthetic induction, entropy reflects the degree of change in EEG signals from irregular to more irregular as the patient loses consciousness.

Several groups of researchers have induced hypnosis with various agents (sedatives and anaesthetics) and recorded BIS and entropy values to compare these two methods. Entropy is a newer method, and the aim of our study was to compare its utility to that of the BIS index (the most widely used method) for monitoring hypnotic levels during anaesthetic induction.

Material and methods

This prospective study was carried out in the Afyon Kocatepe University Department of Anaesthesiology between January 1, 2004, and December 31, 2005. The ethics committee of our medical school approved the protocol and all participants provided informed consent. The study group comprised 30 patients aged 20 to 60 years who were classified as American Society of Anesthesiologist grading system (ASA) I-II risk [16]. All underwent lumbar disc surgery. Individuals with chronic pulmonary disease, renal failure, history of coronary artery disease, morbid obesity (body weight ≥110 kg), history of alcohol abuse, or history of anaesthesia in the seven days prior to the study were excluded.

Table I. Observer's Assessment of Alertness/Sedation scale (OAA/S)

0 Does not respond to noxious stimulus
1 No response to gentle shaking
2 Responds to gentle shaking
3 Responds when name is called loudly or repeated
4 Lethargic response when name is called at normal volume
5 Responds when name is called at normal volume

Each patient underwent a preoperative evaluation in our Anaesthesiology Outpatient Clinic and was seen again the day before surgery. Every individual fasted for 8 hours before transfer to the operating room. No premedication was administered in order to avoid confounding the sedation scores. All the patients were admitted to the operation room and intravenous infusion of a balanced solution was administered and maintained throughout the operation time. Before induction of anaesthesia, the frontal cortex area was cleansed with alcohol swabs and BIS and entropy electrodes were placed. Immediately prior to administering the anaesthetic, we recorded baseline BIS, RE, and SE values with the patient fully awake.

For induction, propofol was infused by perfusion pump (Braun GmbH Kronberg, Germany) at a rate of 20 µg/kg×min and scores for Observer's Assessment of Alertness/Sedation (OAA/S) were monitored (Table I). Once the OAA/S score was ≤2, the propofol infusion was stopped. Rocuronium bromide 1 mg/kg was then administered for muscular relaxation and endotracheal intubation. The maintenance of anaesthesia was performed with sevoflurane (0.6 to 1.75%) in a 50:50 air and O_2 mixture. Rocuronium bromide 0.1 mg/kg was administered as needed to maintain muscular relaxation. Fentanyl 3 µg/kg was also administered after induction and repeated as needed. At the end of the surgery, anaesthesia was discontinued and atropine and neostigmine were administered to reverse the muscular relaxation. The patient was extubated and was allowed to leave the recovery room once the Aldrete post-anaesthesia recovery score was ≥9.

BIS and entropy values were recorded using a Datex-Ohmeda S/5 Entropy Module (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland). Electrocardiography (ECG) traces were obtained using a Datex Ohmeda S/5 ECG monitor (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland).

The following data were collected for each patient at a series of time points: BIS, RE, SE, ECG, non-invasive mean arterial pressure (MAP), heart rate (HR), and peripheral oxygen saturation (SpO_2). Each parameter was recorded at baseline (as detailed above) and then at 30-second intervals during induction (30, 60, 90, 120 seconds after the

start of propofol infusion) and throughout the operation time. The MAP was recorded from both arms of the patients so it could be measured at 30-second intervals. But we cared only about induction period values because the study interval is the induction period. We also recorded demographic features (age, weight, height). If a patient's MAP was lower than 70 mmHg he/she was excluded from the study.

Statistical analysis

Data were statistically analyzed using the Statistical Package for the Social Sciences v. 10.0 (SPSS 10.0) for Windows (Microsoft Corp. USA). The Kruskal-Wallis test was used to compare the findings for non-parametric data at different time points (baseline vs. other time points). Student's t-test was used to compare results for parametric data at each time point. Results are expressed as mean ± standard error (mean ± SE). P values <0.05 were considered statistically significant.

Results

Table II shows the study group means for age, height and body weight. Figure 1 and Table III list the results for OAA/S, BIS, RE and SE at each of the time points investigated during induction. Comparison of the BIS, RE and SE values at each of these stages revealed a significant difference at all four time points (30, 60, 90 and 120 seconds after the start of propofol infusion). At each time point, RE and SE were both significantly lower than the BIS value ($p<0.5$). As expected, the mean OAA/S score at baseline was significantly higher than the corresponding means at each of the later time points ($p<0.05$). The MAP and HR values at 30, 60, 90 and 120 seconds were all significantly lower than the corresponding baseline values ($p<0.05$ for all) (Table IV). In our study, during the first 30 seconds of induction when BIS values were compared with RE and SE, a significant difference was identified. In the first 60 seconds OAA/S, BIS, RE and SE values were significantly decreased at the same level. For the values at 30 seconds of induction BIS values were quite a lot higher than RE and SE values.

Table II. Demographic characteristics of the study group (n=30) (mean ± SE)

Age (years)	45.60±1.95
Weight (kg)	64.86±0.89
Height (cm)	169.30±1.05

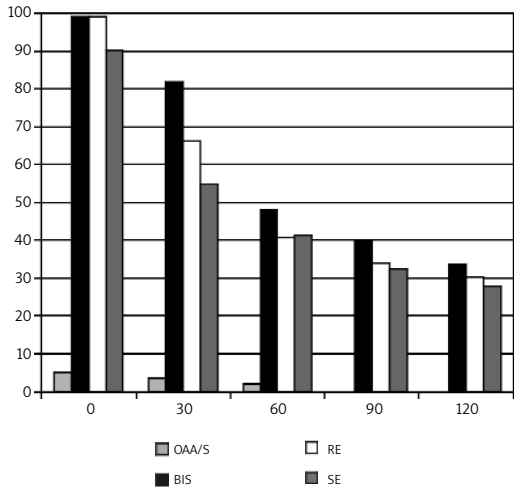

Figure 1. Results shown as bar graph; X axis shows the times in seconds

Discussion

In clinical practice, entropy and bispectral analysis provide numerical representations of hypnosis levels achieved with various anaesthetic agents. Monitoring of BIS or entropy can help clinicians to determine whether the appropriate proper dose of a certain agent has been given. This is especially valuable when using anaesthetics such as propofol, which can induce severe hypotension [3].

In our study, we found that for the MAP values obtained at 30, 60, 90 and 120 seconds of induction,

Table III. OAA/S, BIS, (RE) and (SE) results for the study group (n=30) at each time point (mean ± SE)

	OAA/S	BIS	RE	SE
Baseline	5.00±0.00	99.13±0.13	99.16±0.18	90.36±0.12
30 s	3.50±0.48*	82.03±0.28*	$66.16\pm0.43^{\&,\#}$	$54.83\pm0.78^{\alpha,\#}$
60 s	2.00±0.36*	48.26±0.41*	$40.70\pm0.87^{\&,\#}$	$41.26\pm1.08^{\alpha,\#}$
90 s	0.0±0.0*	39.96±0.78*	$34.03\pm0.72^{\&,\#}$	$32.36\pm0.49^{\alpha,\#}$
120 s	0.0±0.0*	33.53±0.77*	$30.43\pm0.94^{\&,\#}$	$27.90\pm0.40^{\alpha,\#}$

**p<0.05 for comparison with corresponding baseline value*
$^{\&}$p<0.05 for comparison with corresponding baseline value of RE
$^{\alpha}$p<0.05 for comparison with corresponding baseline value of SE
$^{\#}$p<0.05 for comparison with corresponding value of BIS and RE and SE
OAA/S: Observer's Assessment of Alertness/Sedation scale
BIS – bispectral index, RE – response entropy, SE – state entropy

Table IV. MAP and HR results (mean ± SE) for the study group (n=30) at each time point studied

	MAP (mmHg)	HR (beats/min)
Baseline	96.40±0.83	74.33±0.35
30 s	88.76±0.81*	66.36±0.38*
60 s	84.13±0.86*	64.63±0.24*
90 s	80.43±0.93*	64.60±0.27*
120 s	78.26±0.89*	64.63±0.24*

**p<0.05 for comparison with baseline values*
MAP – mean arterial pressure, HR – heart rate

the ones obtained before the intubation were all lower than the baseline values and this difference was identified to be statistically significant. In correlation with low MAP values, entropy and BIS values were also low during induction. The difference between entropy and BIS values was significant. A patient's level of hypnosis is clinically monitored during anaesthesia. Numerical BIS and entropy values are helpful because hypnosis level can be monitored as numeric values. Our results suggest that entropy is more sensitive and reliable than BIS for adjusting doses of propofol as an induction agent. As noted previously, entropy and bispectral analysis are both EEG-based methods of monitoring. SE is based on EEG alone and these values range from 0 to 91. RE is based on both EEG and electromyography, and these values range from 0 to 100. The advantage of RE is that it can reveal more rapid alterations in activity of the frontal cortex.

In our study, anaesthesia induction was achieved with propofol infused at a standard rate. At equivalent OAA/S values, equivalent BIS, entropy SE and RE values together with MAP and PR were evaluated in the same patients. At the end of the study, the BIS and entropy SE and RE scores corresponding to OAA/S scores were identified. We used OAA/S scores to evaluate levels of sedation in our patients, and this method has been validated by several previous studies [14]. During induction we observed that BIS, RE, SE, MAP and HR all declined as OAA/S scores dropped.

Vakkuri et al. [4] reported that monitoring anaesthetic effects with entropy is more useful than monitoring with BIS during recovery from anaesthesia. Our data collected during propofol induction revealed that RE and SE values declined more rapidly than BIS values as the level of sedation increased. It appears that RE and SE are more sensitive than BIS for detecting different levels of sedation. We believe that entropy monitoring might be very valuable for safe anaesthesia when administering induction doses of hypnotic/sedative agents that can cause severe hypotension.

When monitoring entropy, 2 signals are detected with a single sensor and this is efficient. The same is true for bispectral analysis. As noted, entropy monitoring yields two numerical indicators (SE and RE) that represent the degree of irregularity of the EEG signal. SE indicates levels of low-frequency band EEG activity in the frontal cortex as this parameter shows the hypnotic effects of anaesthetic agents on the brain [15]. SE values are resistant to sudden reactions of facial muscles, and this is a reason why SE is used to assess hypnotic effects on the brain during general anaesthesia [14, 15].

Based on our results we think that RE and SE values are more sensitive to the deepening of anaesthesia than BIS values. Similar to the findings in our study, several other studies have demonstrated that entropy values show more rapid decreases than BIS values [13]. After observing more rapid decreases in entropy, we think that it is more sensitive in identifying the degree of hypnosis. In our study, we also had a more rapid decline in entropy values. In one of these studies Soto et al. [12] tried simultaneous evaluations of BIS and entropy values on a single patient and found the entropy values to be very reliable. However, this study was performed on a single patient. In our study simultaneous measurements of BIS and entropy values were performed on 30 patients and simultaneous comparisons were carried out. Relying on our results, we believe that monitoring entropy is more reliable than monitoring BIS.

In several studies, entropy values corresponding to BIS measurements have been identified for different agents used for general anaesthesia. Iannuzzi et al. [14] measured BIS and SE values for loss of consciousness (LOC) and loss of verbal contact (LVC) at effective dose concentrations of propofol. Loss of verbal contact BIS was reported as 70.2 (70.2-90.2) and SE as 60.3 (60.3-75.5), BIS for loss of consciousness was 38.2 (38.2-70.4), while SE was 42.2 (42.2-60.4) [17]. At the end of their study, they reported SE values to be more sensitive at effective concentrations of propofol [17]. Schmidt et al. [3] compared monitoring entropy and BIS during propofol and remifentanyl anaesthesia and reported that both could be used to monitor the depth of anaesthesia. Ellerkmann et al. [11] reported that entropy (RE and SE) could be used when monitoring the depth of anaesthesia. In patients administered with sevoflurane anaesthesia they compared BIS and RE and SE values. They stated that BIS and RE and SE values decreased in parallel with the increases in sevoflurane concentrations. They concluded that monitoring RE and SE could be used in assessing the effects of sevoflurane [11]. Anderson et al. [15] investigated the entropy values at wakefulness levels during propofol hypnosis. At the end of their study, they reported that the use of entropy monitors would be applicable in staging the clinical hypnotic effects. Bruhn et al. [17] evaluated airway during laryngeal

mask and laryngoscopy practices in healthy volunteers. At different doses of propofol and remifentanyl they compared BIS and entropy values. They concluded that monitoring entropy could be as reliable as BIS [17]. The intravenous agents used in anaesthesia induction have well-known hypotensive effects. It is therefore recommended that their dose titration should be done very attentively [18-21]. Muncaster et al. [20] reported that the depth of anaesthesia could be monitored with entropy. Bruhn et al. [21] underlined the fact that entropy could be useful in evaluating the effects of anaesthetic agents. Similar to the findings of the previously performed studies, we think that entropy can be used in identifying the level of hypnosis achieved by different agents. Depending on these measurements medications could be reliably used without the need to administer high doses that would result in severe hypotension.

In conclusions in the evaluation of induction sedation level in general anaesthesia induction entropy correlates with OAA/S scores and shows a more rapid decline than BIS values. Based on our results, we think that monitoring of entropy could be reliably used as BIS monitoring in general anaesthesia induction because entropy shows a more rapid reaction than BIS monitoring. But this must be supported with more studies.

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