Determining entropy values equivalent to the bispectral index values during sevoflurane anaesthesia

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Abstract

Introduction: We aimed to identify the entropy levels that would be equivalent to the bispectral index (BIS) levels in sevoflurane anaesthesia in patients who are to undergo elective lumbar disc surgery.
Material and methods: Thirty cases in ASA groups I-II who underwent lumbar disc surgery under general anaesthesia were included in our study after obtaining the consent of the patients and Ethics Committee of our medical school between January 1, 2005 and October 30, 2006. BIS and entropy electrodes were applied at the same time in 30 cases in the study group. The depth of the anaesthesia was regulated so that 10 min after beginning the general anaesthesia the BIS values were between 40 and 60. At the same time equivalent entropy values corresponding to BIS values were obtained.
Results: At the end of the study, entropy values corresponding to general anaesthesia BIS values were identified. General anaesthesia BIS and RE/SE values at 10 min were lower than the values of the control, which was statistically significant ($p < 0.05$). Equivalent entropy values were obtained lower than the BIS values during general anaesthesia and these values were found to be statistically significant ($p < 0.05$). The blood pressure (BP) values obtained were very low at equivalent BIS values and when these BP values were compared with the initial BP values they were found to be statistically significant ($p < 0.05$).
Conclusions: Based on this observation, we think that general anaesthetic agents that might cause severe hypotension could be more safely administered under entropy monitoring.

Key words: general anaesthesia, bispectral index, entropy.

Introduction

Electroencephalography (EEG) was introduced to the field of anaesthesiology as a means of assessing levels of hypnosis during anaesthesia. Currently there is no standard method for measuring the hypnotic component of 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. 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 [1, 2]. Specifically, it reveals mathematical relationships between EEG signal components (phase couplings) at different wave speeds. The bispectral index was first used in 1992 [3] and is a practical method for directly measuring sedative effects in the brain [4-9]. Today, it is widely used to monitor depth of sedation [9].

Entropy measurement is another EEG-based method for determining hypnotic levels [10-13]. 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 [1]. This parameter is recorded from EEG of the frontal cortex using a low-impedance sensor [12] 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 Hz to 47 Hz [12]. A number of studies have used approximate entropy and Shannon entropy to describe EEG changes [2, 11]. 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 [2, 13]. Several groups of researchers have induced hypnosis with various agents (sedatives and anaesthetics) and recorded BIS and entropy values to compare these 2 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 general anaesthesia.

Material and methods

This prospective study was carried out in the Afyon Kocatepe University Department of Anaesthesiology between January 1, 2005 and October 30, 2006. The ethics committee of our medical school approved the protocol and all participants provided informed consent. The study group comprised 30 patients aged 25 to 60 years who were classified as ASA I-II risk. 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 7 days prior to the study were excluded. Each patient underwent a preoperative evaluation in our Anaesthesiology Outpatient Clinic and was seen again the day before surgery. Every individual fasted for 8 h before transfer to the operating room. Premedication was administered as 0.01 mg/kg midazolam. 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 per 2 mg/kg. We then administered fentanyl 2 µg/kg and rocuronium 0.6 mg/kg IV to facilitate tracheal intubation. The maintenance anaesthesia was 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. After intubation we instituted mechanical ventilation to maintain $PETCO_2$ at 34–38 mmHg. The tip of the CO_2 probe was placed at the tracheal end of the endotracheal tube. We randomly assigned 30 patients to BIS-guided anaesthesia (target BIS range, 40 to 60). 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 after 10 min, 20 min, 25 min, 30 min, 60 min and 90 min during anaesthesia. We also noted demographic features (age, weight, height). Each parameter was recorded at 5 min during general anaesthesia.

Statistical analysis

Data were statistically analysed using the Statistical Package for the Social Sciences v. 10.0 for Windows (SPSS 10.0) (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). Values of $p < 0.05$ were considered statistically significant.

Results

Table I shows the study group means for age, height, and body weight. Mean arterial pressure (MAP) and heart rate (HR) values were found statistically significant when they were compared with initial values ($p < 0.05$) (Table II). Comparison of the BIS, RE and SE values at each of these stages revealed a significant difference at all 4 time points (during general anaesthesia at 5 min). At each time point, RE and SE were both significantly lower than the BIS value ($p < 0.05$) (Table III).

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

Age [years]	47.70 ±1.94
Weight [kg]	66.96 ±0.80
Height [cm]	165.30 ±1.25

Table II. Mean arterial pressure (MAP) and heart rate (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
10 min	86.75 ±0.71*	65.36 ±0.38*
15 min	84.13 ±0.86*	63.63 ±0.14*
20 min	80.43 ±0.93*	62.60 ±0.17*
25 min	76.16 ±0.89*	61.63 ±0.34*
30 min	83.43 ±0.83*	64.40 ±0.27*
60 min	78.43 ±0.83*	65.50 ±0.37*
90 min	79.33 ±0.73*	66.30 ±0.17*

**p < 0.05 for comparison with baseline values*

Table III. Bispectral index (BIS), response entropy (RE) and state entropy (SE) results for the study group (n = 30) at each time point (mean ± SE)

	BIS	RE	SE
Baseline	99.10 ±0.12	99.15 ±0.17	90.26 ±0.11
10 min	60.03 ±0.22*	45.36 ±0.32$^{\&,\#}$	35.88 ±0.68$^{\alpha,\#}$
15 min	60.26 ±0.40*	42.71 ±0.77$^{\&,\#}$	35.26 ±1.18$^{\alpha,\#}$
20 min	40.86 ±0.55*	36.23 ±0.71$^{\&,\#}$	30.23 ±0.37$^{\alpha,\#}$
25 min	40.23 ±0.76*	32.43 ±0.94$^{\&,\#}$	29.90 ±0.41$^{\alpha,\#}$
30 min	40.53 ±0.75*	31.33 ±0.84$^{\&,\#}$	30.90 ±0.31$^{\alpha,\#}$
60 min	40.43 ±0.65*	32.53 ±0.74$^{\&,\#}$	27.90 ±0.31$^{\alpha,\#}$
90 min	40.33 ±0.56*	32.33 ±0.84$^{\&,\#}$	28.90 ±0.21$^{\alpha,\#}$

**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 of RE and SE with corresponding value of BIS

Discussion

In clinical practice, entropy and bispectral analysis provide numerical representations that help clinicians determine whether the appropriate dose of a certain agent has been given. Generally, entropy has been studied for quantification of the anaesthetic drug effect for various GABA-ergic *i.v.* induction agents and volatile anaesthetics such as propofol and sevoflurane, and overall was found to be comparable to the current clinical gold standard, BIS [14, 15].

In our study, during general anaesthesia equivalent BIS values (40-60) determined RE and SE. The difference between entropy and BIS values was significant. Our results suggest that entropy is more accurate and reliable than BIS for adjusting doses of an anaesthetic agent as general anaesthesia. As noted previously, entropy and bispectral analysis are both EEG-based methods of monitoring. State entropy is based on EEG alone and these values range from 0 to 91. Response entropy 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 frontal cortex activity.

At equivalent BIS, entropy SE and RE values together with MAP and HR were evaluated on the same patients. At the end of the study, the BIS scores corresponding to entropy scores were identified. We used BIS scores to evaluate levels of deep anaesthesia in our patients, and this method has been validated by several previous studies [12]. 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 2 numerical indicators (SE and RE) that represent the degree of irregularity of the EEG signal. State entropy 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 [13]. State entropy 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 [12-16].

Vakkuri *et al.* [2] reported that monitoring anaesthetic effects with entropy is more useful than monitoring with BIS during recovery from anaesthesia. Our data collected during general anaesthesia revealed that RE and SE values were lower than BIS values. It appears that RE and SE are more sensitive than BIS for detecting different levels of general anaesthesia. We believe that entropy monitoring might be very valuable for safe anaesthesia when the depth of anaesthesia requires doses of hypnotic/sedative agents that can cause severe hypotension. We obtained higher BIS values than entropy values, which was in accordance with sedation scores in another study by us [17]. In that study while sedation scores decreased the BIS values decreased but at the same time we found that the entropy values decreased faster and were more sensitive [17]. We declared that to avoid serious hypotension during anaesthesia induction, entropy monitoring could be used safely with sedation scores in our study. In this study we aimed to obtain equivalent entropy values to BIS (60-40) values to avoid serious hypotension for the necessary depth of anaesthesia during general anaesthesia. In this study we obtained entropy values that were lower than the

equivalent values of BIS, as in our preceding study. Hypotension was obtained at equivalent BIS values. Like the preceding study we decided in this study when comparing the entropy values with equivalent BIS values and blood pressure obtained at these BIS values that the necessary anaesthesia depth could be provided by entropy values while avoiding hypotension.

Based on our results we think that RE and SE values are more sensitive to the deepening of anaesthesia compared to BIS values. Similar to the findings in our study, several other studies have demonstrated that entropy values show more rapid decreases than BIS values [11]. After observing more rapid decreases in entropy, we think that it is more sensitive in identifying the degree of hypnosis. In one of these studies, Soto *et al*. [10] tried simultaneous evaluations of BIS and entropy values on a single patient and found 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. Based 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*. [12] 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 LOC was 38.2 (38.2-70.4) while SE was 42.2 (42.2-60.4) [14]. At the end of their study, they reported SE values to be more sensitive at effective doses during general anaesthesia [14]. Schmidt *et al*. [1] compared monitoring entropy and BIS during propofol and remifentanil anaesthesia and reported that both could be used for following the depth of anaesthesia. Ellerkmann *et al*. [9] reported that entropy (RE and SE) could be used when monitoring the depth of anaesthesia. In patients administered sevoflurane anaesthesia they compared BIS and RE and SE values. They found that BIS and RE and SE values decreased in parallel with increases in sevoflurane concentrations. They concluded that monitoring RE and SE could be used in assessing the effects of sevoflurane [9]. At the end of their study, they reported that the use of entropy monitors would be applicable in staging clinical hypnotic effects. Muncaster *et al*. [15] reported that the depth of anaesthesia could be monitored with entropy. Bruhn *et al*. [16-20] 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 conclusion, based on our results, we think that monitoring of entropy could be reliably used as BIS monitoring of depth of anaesthesia in general anaesthesia.

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