Comparison of entropy and bispectral index values during propofol induction

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ABSTRACT

الهدف: تحديد مستويات الطاقة اللامتاحة التي سنطابقها مع مؤشر مستويات بيسبكتريا (BIS) في التخدير العام (GA) لدى المرضى الذين سيخضعون لعملية جراحية اختيارية في القرص القطني (LDS).

الطريقة: شملت الدراسة 30 حالة خضعت لعملية جراحية في القرص القطني تحت التخدير العام بعد الحصول على موافقة المرضى ولجنة أخلاق المهنة بمستشفى جامعة كوساتيب الطبي التعليمي في الفترة ما بين 2004/1/1م إلى 2005/12/31م. تم تطبيق الطاقة اللامتاحة والمسرى الكهربائي في نفس الوقت على 30 حالة في مجموعة الدراسة. من أجل تقييم مستوى التسكين خلال التخدير والشفاء، تم استعمال نقاط (التقييم الملاحظ لليقظة/والتسكين) و (OAA/S). تم تسجيل قيم بيسبكتريال والطاقة اللامتاحة و (OAAS/S) بالتوافق.

النتائج: نقاط (OAAS/S) بالإرتباط مع (BIS) وقيم الطاقة اللامتاحة عند 30 حالة. تبين وجود فرق ملحوظ بين (BIS) وقيم الطاقة اللامتاحة (p=0.0398). كانت قيم تحريض (MAP) و(HR) عند 120.90.60.30 دقيقة أقل من قيم مجموعة التحكم والتي كانت ملحوظة إحصائيا (p=0.0412).

خاتمة: أثناء تحريض التخدير العام، وجدنا أن قيم الطاقة اللامتاحة أكثر حساسية وأنها تسيطر بزيادة مطردة أكثر من (BIS). بناءً على ضوء نتائجنا، قد يكون أكثر أماناً في مراقبة الطاقة اللامتاحة أثناء استعمال عوامل التحريض التي قد تسبب انخفاض شديد في ضغط الدم. أن عوامل التحريض التي قد تسبب الهبوط الشديد في ضغط الدم من الممكن أن تكون أكثر أماناً تحت مراقبة الطاقة اللامتاحة.

Objectives: To identify the entropy levels that would correspond to bispectral index (BIS) levels in general anesthesia (GA) induction in patients who will undergo elective lumbar disc surgery (LDS).

Methods: Thirty cases who underwent LDS under GA were included in our study after obtaining patient consent and approval of the Ethics Committee of Afyon Kocatepe University Medical School, Afyonkarahisar, Turkey, between January 01, 2004 to December 31, 2005. Bispectral index and entropy electrodes were applied at the same time to 30 cases in the study group. In order to assess the level of sedation during anesthesia and recovery, 'Observer's Assessment of Alertness/Sedation' (OAA/S) scale was used. Bispectral index, state-entropy (SE), response-entropy (RE), and OAA/S values were recorded simultaneously.

Results: Induction OAA/S scores were in correlation with BIS and entropy values (RE-SE) in 30 cases. A significant difference was found between BIS and entropy induction values (p=0.0398). Induction mean arterial pressure and heart rate values at 30, 60, 90, and 120 seconds were lower than the values of the control, which was statistically significant (p=0.0412).

Conclusion: During the induction of GA, we found entropy values to be more sensitive and they demonstrated a more rapid increase than BIS. Therefore, it would be safer to monitor entropy while using agents of induction that might cause severe hypotension. Induction agents that might cause severe hypotension could be more safely administered under entropy monitoring.

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Currently there is no standard method for measuring the hypnotic component of anesthesia. An EEG was introduced to the field of anesthesiology as a means of

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assessing levels of hypnosis during anesthesia. Bispectral analysis is one EEG-based technique for determining hypnotic levels during anesthesia and sedation. This method yields a bispectral index (BIS) that reflects interfrequency phase relations of EEG.[1] Bispectral index 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.[2,3] Specifically, it reveals mathematical relationships between EEG signal components (phase couplings) at different wave speeds. The BIS was first used in 1992[4] and is a practical method for directly measuring sedative effects in the brain.[5-11] Today, it is widely used to monitor depth of sedation.[10] Entropy measurement is another EEG-based method for determining hypnotic levels.[9,11-14] Compared to BIS, entropy is considered to be a more accurate and reliable indicator of the hypnotic effects of anesthetic and sedative drugs. Entropy values reflect EEG signals that are irregular, complex, and unpredictable.[2] This parameter is recorded from EEG of the frontal cortex using a low-impedance sensor[13] and the signals can be interpreted in 2 separate ways: State-entropy (SE) is the calculated form of the frequencies between 0.8-32 Hz, and response-entropy (RE) covers the range from 0.8-47 Hz.[3,13] A number of studies have used approximate entropy and Shannon entropy to describe EEG changes.[3,11,12] 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 anesthesia, however, entropy can also be used to assess depth of sedation.[3,14] During sedation or anesthetic induction, entropy reflects the degree of change in EEG signals from irregular to more irregular as the patient loses consciousness. Entropy and bispectral analysis are both EEG-based methods of monitoring. State-entropy is based on EEG alone and these values range from 0-91. Response-entropy is based on both EEG and electromyography, and these values range from 0-100. The advantage of RE is that it can reveal more rapid alterations in activity of the frontal cortex. Several groups of researchers have induced hypnosis with various agents (sedatives and anesthetics), 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 BIS index (the most widely used method) for monitoring hypnotic levels during anesthetic induction.

Methods. This prospective study was carried out in the Afyon Kocatepe University, Department of Anesthesiology, Afyonkarahisar, Turkey, between January 1, 2004 to 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 20-60 years who were classified as American Society of Anesthesiologist grading system (ASA) I-II risk.[15] 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 anesthesia in the 7 days prior to the study were excluded. Each patient underwent a preoperative evaluation in our Anesthesiology 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. Before induction of anesthesia, the frontal cortex area was cleansed with alcohol swabs and BIS and entropy electrodes were placed. Immediately prior to administering the anesthetic, we recorded baseline BIS, RE, and SE values with the patient fully awake. For induction, propofol was infused at a rate of 20 μg kg^{-1} min^{-1} and scores for OAA/S were monitored (**Table 1**).[1] Once the OAA/S score was ≤2, the propofol infusion was stopped. Rocuronium bromide 1 mg kg^{-1} was then administered for muscular relaxation and endotracheal intubation. Maintenance anesthesia was sevoflurane (0.6-1.75%) in a 50:50 air and O_2 mixture. Rocuronium bromide 0.1 mg kg^{-1} was administered as needed to maintain muscular relaxation. Fentanyl 3 μg kg^{-1} was also administered after induction and repeated as needed. At the end of the surgery, anesthesia 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-anesthesia recovery score was ≥9. Bispectral index and entropy values were recorded using a Datex-Ohmeda S/5 Entropy Module. (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland) An EEG traces was obtained using a Datex Ohmeda S/5 (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland) ECG

Table 1 - Observer's Assessment of Alertness/Sedation scale.

Score	Response
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

monitor. 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, and 120 seconds after the start of propofol infusion). We also noted demographic features (age, weight, height).

Statistical analysis. Data were statistically analyzed using the Statistical Package for Social Sciences version 10.0 for Windows (SSPS 10.0)(Microsoft Corp. USA). The Kruskal-Wallis test was used to compare the findings for non-parametric data at different time points (baseline versus 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*-value of < 0.05 was considered statistically significant.

Results. The mean ± SE age of the study group was 45.60 ± 1.95, the weight was 64.86 ± 0.89, and the height was 169.30 ± 1.05. **Table 2** lists 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 4 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=0.0398). As expected, the mean OAA/S score at baseline was significantly higher than the corresponding means at each of the later time points (p=0.0457). The MAP and HR values at 30, 60, 90 and 120 seconds were all significantly lower than the corresponding baseline values (p=0.0412) (**Table 3**). In our study, during the first 30 seconds of induction when BIS values were compared with RE and SE, a significant difference was identified. At first 60 seconds OAA/S, BIS, RE, and SE values were significant. For the values at 30 seconds of induction, BIS values were higher than RE and SE values

Table 2 - The OAA/S, BIS, RE and SE results for the study group (n = 30) at each time point (mean±SE).

Time	OAA/S	BIS	RE	SE
Baseline	5.00±0.00	99.13±0.13	99.16±0.18	90.36±0.12
30 secs	3.50±0.48*	82.03±0.28*	66.16±0.43†§	54.83±0.78 ‡§
60 secs	2.00±0.36*	48.26±0.41*	40.70±0.87†§	41.26±1.08‡§
90 secs	0.0*±0.0	39.96±0.78	34.03±0.72†§	32.36±0.49‡§
120 secs	0.0*±0.0	33.53±0.77*	30.43±0.94†§	27.90±0.40‡§

*p< 0.05 - comparison with corresponding baseline value,
†p<0.05 - comparison with corresponding baseline value of RE, ‡p<0.05 - comparison with corresponding baseline value of SE, §p<0.05 - comparison with corresponding value of BIS, RE and SE,
OAA/S - Observer's Assessment of Alertness/Sedation scale,
BIS - Bispectral index, RE - Response entropy, SE -State entropy

Table 3 - The MAP and HR results (mean±SE) for the study group (n = 30) at each time point studied.

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

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

Discussion. In clinical practice, entropy and bispectral analysis provide numerical representations of hypnosis levels achieved with different anesthetic agents. Monitoring of BIS or entropy can help clinicians determine the appropriate proper dose of a certain agent has been given. This is especially valuable when using anesthetics such as propofol, which can induce severe hypotension. In our study, we found that the MAP values obtained at 30, 60, 90, and 120 seconds of induction and those 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 were significant. Our results suggest that entropy is more accurate and reliable than BIS for adjusting doses of propofol as an induction agent. In our study, anesthesia 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 HR were evaluated on 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.[13] During induction we observed that BIS, RE, SE, MAP and HR all declined as OAA/S scores dropped. Vakkuri et al[3] reported that monitoring anesthetic effects with entropy is more useful than monitoring with BIS during recovery from anesthesia. 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 valuable for safe anesthesia when administering induction doses of hypnotic/sedative agents that can cause severe hypotension. Based on our results, RE and SE values are more sensitive to the deepening of anesthesia 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.[12] After observing more rapid decreases in entropy, 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[11] tried simultaneous evaluations of BIS and entropy values on a single patient and found entropy value 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, 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 anesthesia. Iannuzzi et al[13] have 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).[15] At the end of their study, they have reported SE values to be more sensitive at effective concentrations of propofol.[16] Schmidt et al[2] compared monitoring entropy and BIS during propofol and remifentanyl anesthesia and reported that both could be used for following the depth of anesthesia. Ellerkmann et al[10] reported that entropy (RE and SE) could be used when monitoring the depth of anesthesia. In patients administered with sevoflurane anesthesia they compared BIS, RE, and SE values. They stated that BIS, RE, and SE values decreased in parallel with the increase in sevoflurane concentrations. They concluded that monitoring RE and SE could be used in assessing the effects of sevoflurane.[10] Anderson et al[14] 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[16] evaluated the airway response 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.[16] The intravenous agents used in anesthesia induction have well-known hypotensive effects. It is therefore recommended that their dose titration should be carried out very attentively.[17-20] Muncaster et al[19] reported that the depth of anesthesia could be monitored with entropy. Bruhn et al[20] underlined the fact that entropy could be useful in evaluating the effects of anesthetic 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, the evaluation of induction sedation level in GA induction entropy correlates with OAA/S scores and shows a more rapid decline than BIS values. Based on our results, monitoring of entropy could be reliably used as BIS monitoring in GA induction.

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