ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

# Comparison of the depth of anesthesia in sevoflurane and halothane anesthesia with bispectral index and 95% spectral edge frequency

Bispektral indeks ve %95 spektral edge frekans ile halotan ve sevofluran anestezi derinliklerinin karşılaştırılması

Günhan Gökahmetoglu<sup>1</sup>, Elvan Tercan<sup>2</sup>, Cihangir Bicer<sup>3</sup>, Recep Aksu<sup>3</sup>, Adem Boyaci<sup>3</sup>

#### ABSTRACT

**Objective:** The aim of the present study was to evaluate the depth of anesthesia provided by halothane or sevoflurane by using the bispectral index (BIS) and 95% spectral edge frequency (SEF) monitoring systems.

**Methods:** Forty patients, between the ages of 20-60 years, scheduled for gynecological surgery under general anesthesia were studied between the years 2001-2002. Anesthesia induction was maintained by conventional spontaneous inhalation induction method with sevoflurane in the group I patients (n=20), with halothane in the group II patients (n=20). SEF and BIS index values were recorded.

**Results:** In both groups, SEF values recorded before intubation, after intubation, before and after skin incision were significantly lower compared with values recorded at baseline (p<0.05). Also, SEF values in both groups recorded after anesthesia induction were significantly higher compared with baseline values (p<0.05). Regarding the recorded SEF values after extubation, there were statistically significant differences between the two groups (p<0.05). In both groups, BIS values recorded after anesthesia induction, before intubation, after intubation, before and after skin incision were significantly lower compared with values recorded at baseline and after extubation (p<0.05). Regarding the recorded BIS values before intubation and 1 min after intubation, there were statistically significant differences between the two groups (p<0.05).

**Conclusion:** We conclude that BIS index and SEF values will only be helpful in the evaluation of the hypnosis component of anesthesia and it is not sufficient in showing the autonomous response, which is formed against the perioperative sympathetic and surgical stimulations.

**Key words:** Bispectral index, halothane, sevoflurane, anesthesia depth, hemodynamic responses

#### ÖZET

**Amaç:** Bu çalışmanın amacı, bispektral indeks (BIS) ve % 95 spektral edge frekans (SEF) monitorizasyon sistemleri kullanarak, halotan ve sevofluran anestezi derinliklerinin değerlendirilmesidir.

**Yöntemler:** 2001-2002 yılları arasında, yaşları 20 ile 60 arasında değişen, genel anestezi altında jinekolojik operasyon geçiren 40 hasta çalışmaya dahil edildi. Anestezi indüksiyonu Grup I hastalarda (n=20) halotan, Grup II hastalarda sevofluran ile konvansiyonel spontan inhalasyon indüksiyon metodu ile sağlandı. SEF ve BIS indeks değerleri kaydedildi.

**Bulgular:** Her iki grupta entübasyon öncesi ve sonrası, cilt insizyon öncesi ve sonrası SEF değerleri, bazal değerlerine göre anlamlı derecede düşüktü (p<0,05). Aynı zamanda, her iki grupta anestezi indüksiyonu sonrası kaydedilen SEF değerleri anlamlı olarak bazal değerlerden yüksekti (p<0,05). Ekstübasyon sonrası kaydedilen SEF değerleri kıyaslandığında, iki grup arasında istatistiksel olarak anlamlı fark bulundu (p<0.05). Her iki grupta da, anestezi indüksiyonu sonrası, entübasyon öncesi, entübasyon sonrası, cilt insizyon öncesi ve sonrası kaydedilen BIS değerleri, bazal ve ekstübasyon sonrası kaydedilen değerlere kıyasla anlamlı derecede düşüktü (p<0.05). Entübasyon öncesi ve entübasyondan bir dakika sonra kaydedilen BIS değerlerine bakıldığında, her iki grup arasında istatistiksel olarak anlamlı fark bulundu (p<0,05).

**Sonuç:** Sonuç olarak BIS ve SEF değerleri anestezinin hipnotik komponentini değerlendirmede yardımcı olabilir ve bunlar peroperatif sempatik ve cerrahi uyaranlara karşı otonomik cevapların gösterilmesinde yeterli değildir.

Anahtar kelimeler: Bispectral indeks, halotan, sevofluran, anestezi derinliği, hemodinamik değişiklikler

<sup>1</sup> Kayseri Eğitim Araştırma Hastanesi, Anestezi Bölümü Kayseri, Turkey
<sup>2</sup> Medipol university Medical Faculty Department of Anaestesiology and Reanimation, İstanbul, Turkey
<sup>3</sup> Erciyes University Medical Faculty Department of Anaestesiology and Reanimation, Kayseri, Turkey **Yazışma Adresi /Correspondence:** Günhan Gökahmetoğlu,
Kayseri Eğitim Araştırma Hastanesi, Anestezi Bölümü Kayseri Email: gunhangok@gmail.com
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# INTRODUCTION

The purposes of general anesthesia are to provide hypnosis, analgesia and appropriate surgical area (immobility, muscle relaxation). Unfortunately, the difference between hypnosis and analgesia is deleted in the operation room and patient replies (such as hypertension or movement) cannot be said to demonstrate the analgesic or hypnotic demands. The clinicians using anesthetic and sedatives need to direct the hypnotic status of their patients. For many years, monitoring the effects of the central nervous system (CNS) in an objective and reliable way has been a purpose for anesthesiology [1]. By discovering that the brain produces electrical activity, the fact was regained regarding that the anesthetic agents change electroencephalography (EEG). Analgesic medicines have effects on both the cerebral physiology and the EEG patterns. Insufficient anesthesia generally causes EEG activation. EEG may be considered as a criterion of the anesthetic depth due to many reasons [2]. Despite the dramatic developments in anesthesia safety, it is not accurately clear whether these benefits are due to more intense monitoring or due to new monitoring standards. Bispectral index (BIS) is an EEG parameter, which has been specifically developed to measure the patient responses during anesthetics and sedatives administration. The opportunity to arrange and develop better hypnotic drug administration doses are provided for the anesthesia operators. The results show that BIS monitoring during anesthetic administration provides various benefits, both clinically and economically [1].

In this study, we aimed to evaluate the anesthesia depth provided by halothane and sevoflurane by using the BIS and 95% spectral edge frequency (SEF) monitoring systems during the general anesthesia induction, maintenance and wakeup periods.

# **METHODS**

After Erciyes University Medical Faculty Ethics Committee approval, 40 patients of ASA I-II group, between the ages of 20-60 years, scheduled for gynecological surgery under general anesthesia were studied between the years 2001-2002. All patients gave their informed consent. Surgical interventions which may possibly take more than two hours, patients with intelligence problem which may cause cooperation difficulty or who had a history of neurologic disease, patients who had taken inhalation anesthesia until 6 months ago, age below 20 or over 60 years and the patients who did not accept this technique when explained were excluded from the study.

Patients did not receive any sedative, hypnotic or analgesic premedication. Forty patients were randomly divided into two groups. Twenty were assigned to the sevoflurane group (group I) and 20 to the halothane group (group II). After the patients in both groups were taken into the operation room, iv serum physiologic infusion was started before induction. Anesthesia was given to all patients by the same team. All patients were monitored in order to monitor their continuous heart rates (HR), noninvasive artery blood pressure, oxygen saturation  $(SpO_{2})$  and the gas ratios in the inspiration and expiration mixture (Hewlett Packard Monitor and Anaesthesia Viridiazuc). After skin preparation, disposable BIS sensor (Aspect Medical Systems, Natick, MA, USA) was attached to the patient's forehead according to a standard montage and BIS and 95% SEF were monitored continuously using A-2000 BIS monitor (Aspect Medical Systems International B.V., Leiden, Netherlands) for display of the Bispectral Index processed data and real-time EEG waveforms.

The mixtures of each anesthetic agent together with oxygen were delivered by an Ohmeda Vapor vaporizer into the circle system of an Ohmeda anesthesia machine. The inspiratory and expiratory limbs of the circle were attached to a Y connector. Respiratory gases were sampled into the multi-gas monitor (Datex), between the Y connector and the elbow connector with the mask attached to it. The patients were told to breath with the conventional spontane inhalation induction technique and anesthesia induction was provided by volatile anesthetic inhalation. In Group I (n=20) patients, the anesthesia induction was provided by sevoflurane starting from 1% within 6L/min O<sub>2</sub> and by increasing 1% in every 3 breathes and lastly at 7% concentration. The period from the beginning of the induction until the perishment of the eye lash reflex which we controlled at every 10 seconds was recorded as the duration of induction. 0.1 mg/kg iv vecuronium bromide was given in order to facilitate the tracheal intubation. Then, volatile anesthetic agent concentration was decreased with 1% at every 3 breathes to 2% concentration and endotracheal intubation was performed. The anesthesia induction in Group II patients was started with the same conditions with Group I. However, the halothane concentration was increased to 5%. Once again, the period from the beginning of the induction until the perishment of the eye lash reflex which we controlled at every 10 seconds was recorded as the duration of induction. Neuromuscular blocking agent was given at the same doses. In induction; complications such as coughing, bucking, laryngospasm, bronchospasm, nausea vomiting, extremity movements, secretion increase, excitation, agitation, and arrhythmia were recorded.

Laryngoscopy quality was assessed by tracheal intubation scoring system as: excellent (easy passage of endotracheal tube without coughing; vocal cords relaxed and abducted), good (passage of endotracheal tube with slight coughing or bucking; vocal cords relaxed and abducted), poor (passage of endotracheal tube with moderate coughing or bucking; vocal cords moderately abducted) and not possible (unable to intubate) [3]. Excellent and good tracheal intubation conditions were accepted as clinically sufficient.

After the tracheal intubation, all patients were mechanically ventilated with 10-12 ml/kg of tidal volume to maintain end-tidal carbon dioxide pressure (ETCO<sub>2</sub>) 30-35 mmHg. Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), heart rate (HR), BIS index, SEF value, SpO<sub>2</sub> and ETCO<sub>2</sub> values were recorded before anesthesia induction; after the anesthesia induction; before intubation; at minutes 1, 2 and 3 after intubation; before skin incision, after skin incision and at the end of the tracheal extubation.

In order to have a BIS index value in the range of 55 - 60 within the last 10-15 minutes of the surgery, the volatile anesthetic concentrations were reduced by titration. After skin closure at the end of the surgery, residual neuromuscular blockade was reversed and the anesthetics discontinued. The period from this moment till extubation was recorded as the duration of extubation. The response time to the command 'open your eyes' and the time at which the patient was oriented to time and place were recorded as duration of recovery.

Data are presented as mean  $\pm$  SD. Data between the treatment groups were analyzed using Student's t-test or multiple analysis of variance (ANOVA). Nonparametric data were analyzed by Chi square test. Pearson correlation test was applied to assess the recorded anesthesia depth parameters and hemodynamic parameters and p values <0.05 considered statistically significant.

#### RESULTS

There was no statistically significant difference between the groups, in terms of age, weight, type of surgery and duration of surgery (p>0.05). The mean times for induction of anesthesia, extubation and recovery were significantly shorter with sevoflurane than with halothane (p<0.05) (Table 1). There were statistically no significant differences between the groups regarding to the recorded complications observed during the anesthesia induction (p>0.05).

There were statistically no significant differences in the SAP and DAP values between the two groups (p>0.05), however, SAP values in groups I and II and DAP values in group I were significantly lower at all recorded times except after extubation period compared with baseline values (p<0.05) (Table 2). Regarding the recorded HR and SpO<sub>2</sub> values, there were statistically no significant differences between the two groups (p>0.05).

In both groups, SEF values recorded before intubation, at 1., 2. and 3. minutes after intubation, before and after skin incision were significantly lower compared with values recorded at baseline, after anesthesia induction and after extubation (p<0.05) (Table 3). Also SEF values in both groups recorded after anesthesia induction were significantly higher compared with baseline values (p<0.05) (Table 3). Regarding the recorded SEF values after extubation, there were statistically significant differences between the two groups (p<0.05) (Table 3).

In both groups, BIS values recorded after anesthesia induction, before intubation, at 1., 2. and 3. minutes after intubation, before and after skin incision were significantly lower compared with values recorded at baseline and after extubation (p<0.05) (Table 3). Regarding the recorded BIS values before intubation and 1 min after intubation, there were statistically significant differences between the two groups (p<0.05) (Table 3).

There was no statistically significant correlation observed between the SEF and BIS index values recorded in both Groups and the cardiovascular parameters (p>0.05).

**Table 1.** Patients andsurgical characteristics

**Table 2.** Systolic (SAP) and diastolic (DAP) arterial pressures.

	Group I (sevoflurane) (n=20)	Group II (halothane) (n=20)	t	р
Age (yr) Type of surgery (AH/VH/M)	48.2 ± 7.6 9/7/4	48.2 ± 10.4 11/6/3	0.017	>0.05
Weight (kg) <sup>*</sup> Duration of induction (sec) <sup>*</sup>	$\begin{array}{c} 67.6 \pm 10.5 \\ 119.8 \pm 7.3 \end{array}$	$\begin{array}{c} 67.6 \pm 11.3 \\ 152.1 \pm 9.3 \end{array}$	0.014 12.09	>0.05 <0.05
Duration of surgery (min) <sup>*</sup> Duration of extubation (min) <sup>*</sup> Duration of recovery (min) <sup>*</sup>	$\begin{array}{c} 103.1 \pm 12.3 \\ 8.1 \pm 0.5 \\ 6.8 \pm 1.0 \end{array}$	$\begin{array}{c} 102.9 \pm 14.1 \\ 9.6 \pm 0.8 \\ 9.8 \pm 1.0 \end{array}$	0.03 6.86 8.8	>0.05 <0.05 <0.05

\*Data are presented as mean ± SD. AH/VH/M=abdominal hysterectomy, vaginal hysterectomy, myomectomy

	Group I (sevoflurane) (n=20) SAP	Group II (halothane) (n=20) SAP	Group I (sevoflurane) (n=20) DAP	Group II (halothane) (n=20) DAP
Preoperative (baseline)	$131.1\pm11.2$	$131.3\pm14.6$	$78.1\pm10.0$	$74.0\pm7.1$
After induction	$121.1\pm11.4^{\star}$	$118.0\pm10.9^{\ast}$	$74.8\pm8.7^{\star}$	$72.0\pm7.2$
Before intubation	$112.3 \pm 12.9^{\ast}$	$106.4\pm23.9^{\star}$	$\textbf{71.4} \pm \textbf{8.7*}$	$70.2\pm7.2$
After intubation 1.min	$115.5\pm12.6^{\ast}$	$116.3\pm8.1^{\star}$	$76.2\pm8.9^{\star}$	$73.8\pm7.3$
After intubation 2.min	$112.4\pm10.8^{\star}$	$113.1\pm7.3^{\star}$	$74.0\pm8.9^{\star}$	$72.4\pm7.2$
After intubation 3.min	$107.9\pm7.6^{\star}$	$109.5\pm7.5^{\ast}$	$\textbf{72.3} \pm \textbf{8.6}^{\textbf{*}}$	$71.6\pm6.5$
Before skin incision	$104.0\pm5.8^{\star}$	$107.9\pm7.4^{\star}$	$71.5\pm8.6^{\star}$	$71.2\pm6.8$
After skin incision	$108.0\pm5.7^{\star}$	$110.6\pm8.0^{\star}$	$74.8\pm8.4^{\star}$	$\textbf{72.9} \pm \textbf{6.4}$
After extubation	135.6 ± 9.0	131.1 ± 11.4	$80.2\pm9.3$	$76.8\pm6.8$

Data are presented as mean ± SD, \*p < 0.05 vs. baseline

Table	3.	Bisp	ectral		
index	(BIS)	and	95%		
Spectral Edge Fre-					
quency (SEF) values					

	Group I (sevoflurane) (n=20) SEF	Group II (halothane) (n=20) SEF	Group I (sevoflurane) (n=20) BIS	Group II (halothane) (n=20) BIS
Preoperative (baseline)	$17.8\pm1.7$	17.1 ± 1.1	96.7 ± 1.3	96.4 ± 1.1
After induction	$19.7 \pm 1.5^{\text{\#}}$	$19.0 \pm 1.5^{\text{\#}}$	$53.6\pm5.5^{\scriptscriptstyle +}$	$52.4\pm7.5^{\scriptscriptstyle +}$
Before intubation	$15.1 \pm 1.2^{\star}$	$14.5 \pm 1.4^{\star}$	$45.1 \pm 5.0^{+\$}$	$42.1\pm4.2^{\scriptscriptstyle +}$
After intubation 1.min	$14.1 \pm 1.7^{\star}$	$13.4\pm2.0^{\star}$	$44.5 \pm 5.3^{\rm +\$}$	$39.1\pm5.6^{\scriptscriptstyle +}$
After intubation 2.min	$14.2\pm1.8^{\star}$	$14.2 \pm 1.8^{\star}$	$42.9\pm5.7^{\scriptscriptstyle +}$	$40.6\pm6.2^{\scriptscriptstyle +}$
After intubation 3.min	$14.4 \pm 1.4^{\star}$	$14.5 \pm 1.5^{\ast}$	$42.4\pm5.8^{\scriptscriptstyle +}$	$40.4\pm6.3^{\scriptscriptstyle +}$
Before skin incision	$14.5 \pm 1.4^{\star}$	$14.6 \pm 1.2^{\star}$	$43.0\pm5.7^{\scriptscriptstyle +}$	$40.6\pm4.9^{\scriptscriptstyle +}$
After skin incision	$15.6 \pm 1.9^{\star}$	$14.7 \pm 1.6^{\ast}$	$43.2\pm5.6^{\scriptscriptstyle +}$	$41.4\pm5.5^{\scriptscriptstyle +}$
After extubation	$18.7\pm1.7^{\$}$	$17.6 \pm 1.0$	$86.5\pm4.5$	$\textbf{85.4} \pm \textbf{4.3}$

\*p < 0.05 vs. baseline and after induction, # p < 0.05 vs. baseline

 $^{\rm s}$  p < 0.05 vs. group II,  $^{\rm +}$  p < 0.05 vs. baseline and after extubation

# DISCUSSION

In the modern application; anesthesia is generally induced rapidly and safely in adults through iv agents. Induction by inhalation is frequently used in children but prolonged anesthesia induction can frighten both the children and the adults [4]. Thus, generally both the patients and the anesthetists avoid from induction by volatile agents. However, in recent years, the discovery of the new volatile anesthetics with less adverse effects, having lower blood: gas solubility ratios and providing rapid anesthesia induction, easy control for anesthesia depth, popularized the usage of inhalation induction method again in general anesthesia application both in children and in adults. [3-8]. In our study, we have used conventional inhalation induction method for the adults. The time elapsed as the anesthesia induction was  $119.8 \pm 7.3$  sec. for Group I; and  $152.0 \pm 9.3$  sec. for Group II. Smith et al. [9] have found the anesthesia induction time with sevoflurane as 109 seconds, and they have stated that the reason of the shortness of that time was giving the inhalation induction agent from 5% concentration up to the completion of the induction. In the study of Oguz et al. [10], the period in sevoflurane induction performed by the conventional method was determined as 107 seconds. Here, using the N<sub>2</sub>O-O<sub>2</sub> mixture in 2:1 ratio has shortened this period with respect to the periods which we have obtained.

In this study, we found shorter extubation and recovery times in the sevoflurane group compared with halothane group. In rats, cerebral sevoflurane concentration was shown to decrease two times faster than the halothane [11]. Also, sevoflurane is more rapidly taken and eliminated faster than halothane [12]. These studies demonstrate the reason of why the extubation times and recovery times are shorter in sevoflurane and longer in halothane.

All inhalation agents have irritation risk for the respiratory tract and this risk increases with longer induction periods. Coughing is accepted as a good indicator of respiratory tract irritation. In our study, we observed 5% coughing in the sevoflurane group and 10% in the halothane group. We did not see bucking, laryngospasm or bronchospasm in both groups. In a study which compares vital capacity rapid inhalational induction of anesthesia with sevoflurane and isoflurane, Yurino et al [13] reported extremity movements in 12% of the patients in

sevoflurane group, and they observed no cough, laryngospasm, breath holding or a secretion increase. Oguz et al [10] reported that the length of the induction period leads patient to anxiety and extremity movements. We have only encountered extremity movements in 1patient in the halothane group. The movements were in the form of moderate extremity movements joined by the wrist joint. Immamura et al [14] reported that in patients having sevoflurane anesthesia, the risk of arrhythmia inducted with the adrenaline discharge under hypoxic and hypercarbic conditions was less than in halothane. Sevoflurane and halothane were reported as the most suitable agents in terms of cardiovascular parameters in anesthesia induction with mask [15]. We observed arrhythmia in 2 patients in the halothane group, while there was no arrhythmia in any case among the sevoflurane group.

In a study conducted by Hall et al [16], anesthesia induction was performed with sevoflurane in concentrations of 3% and 8%; mean arterial pressure after the loss of consciousness was found to be lower than the baseline value. Tanaka et al [15] reported that sevoflurane and halothane caused minimal change in SAP and DAP values compared to other volatiles. The decrease of SAP in the halothane group in our study was more than the decrease in DAP but it was not statistically insignificant.

Glass et al [17] conducted a series of volunteer studies in order to show the effect of BIS monitoring in the measurement of hypnotic drug effects. Propofol, midazolam, isoflurane, midazolam-alfentanil, propofol-alfentanil or propofol-nitrous oxide combinations were administered to healthy subjects in gradual doses; the anesthetic agent doses were gradually increased and decreased and BIS index was constantly recorded. Clinic measurement for sedation, hypnosis and memory were also carried out. It was proven that BIS is a very good determinant of the hypnotic state.

In a study conducted by Flaishan et al [18], in which the benefits of BIS monitorization were researched in the return of consciousness after the anesthesia induction with propofol and tiopental, the consciousness was regained when the BIS values exceeded 60, and the changes in blood pressure and heart rate failed to reflect those. No statistical significance was found in our study during the correlation test with HR and blood pressure changes in the intraoperative assessment of BIS and SEF values.

SEF is a frequency, where the total EEG power is below 95%. It was suggested that SEF can be used in order to measure the anesthesia depth. In a study conducted by Schwander et al [19], SEF decreased during general anesthesia inducted by isoflurane or propofol compared to the conscious state, and it increased similarly to the conscious state values during the periods, where the effects of the isoflurane or propofol anesthesia disappear, or during intraoperative spontaneous movements. We have observed an increase of SEF during our post-induction measurements in our cases. SEF values did not show a relationship with the intraoperative hemodynamic changes. In a study conducted by Sawtelle et al [20], SEF 95% values of patients were compared with BIS, and the hypnotic state of the patients were determined with BIS at least 15 minutes before SEF 95%. We have observed no such correlations in our study. The SEF value in the moment of extubation was significantly higher in sevoflurane group compared to halothane group. There was no such difference between the groups in terms of BIS values.

The idea of finding a reliable index of the anesthesia depth has changed toward the finding of various indexes for different anesthesia components. Therefore, a monitor can only measure one of the general anesthesia components. We especially think that the BIS index is associated with the hypnotic component of the anesthesia. In our study; the following results were obtained: anesthesia induction is faster with sevoflurane than halothane; during the anesthesia induction and the peroperative period, the hemodynamic differences in both halothane and sevoflurane treated patients are similar; the complications regarding to the usage of halothane or sevoflurane in anesthesia induction and maintenance are similar; postoperative extubation and recovery periods are shorter in the sevoflurane group than halothane group; BIS index and SEF values which are recorded during the surgery show a similar change in both groups; the numerical values of SEF, obtained after the induction and extubation are higher than the basal values and they are insufficient parameters in showing the anesthesia depth; there is no correlation between the hemodynamic data and the recorded BIS index and the SEF values.

With these results, it is considered that BIS index and SEF values will only be helpful in the evaluation of the hypnose component of anesthesia and it is not sufficient in showing the autonomous response which is formed against the peroperative sympathetic and surgical stimulations.

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