Using Entropy in the General Anesthesia Managements

*Elif Büyükerkmen, Remziye Gül Sivaci and Elif Doğan Baki**

Departement of Anesthesiology and Reanimation, Afyon Kocatepe University, Afyonkarahisar, Turkey

Abstract

Purpose: We aimed to investigate the effects of three general anesthesic management on depth of anesthesia, anesthesic quality, agent consumption and postoperative recovery.

Materials and Methods: 90 patients scheduled for elective tympanoplasty and septoplasty surgery with American Society of Anesthesiologist (ASA) pysical status between I-III were included in this study. Neuromuscular transmission (NMT), surgical pleth index (SPI) and entropy were monitorized in addition to standart monitoring. Entropy was recorded as state entropy (SE) and response entropy (RE). After standart anesthesia induction, patients were divided into three groups according to maintenance of anesthesia using a sealed envelope system. Propofol 3-5 mg/kg/h iv infusion was performed to Group 1 (Group P, n=30), Desflurane 1MAC was used to Group 2 (Group D, n=30) and Sevoflurane to Group 3 (Group S, n=30). Also, rocuronium and remifentanyl infusion were used in maintenance. While desflurane and sevoflurane consumption were recorded from the anesthesia directly, propofol consumption was calculated through the consumption of perfusors and recorded at the end of the surgery. Total cost of anesthetics that used were calculated by multiplying the unit price with their consumption. Apart from these, hemodynamic values of all patients, recovery time, alertness levels in the recovery room (according to Ramsey Scale) were recorded.

Results: Significant differences were found between the three groups in terms of cost. While the cost of propofol was significantly lower, it was significantly higher in desfluane group. Also awareness and postoperative hemodynamics were observed to be more stable in propofol and sevoflurane group patients.

Conclusıon: We concluded that propofol anesthesia decreased the cost significantly.

Keywords: Propofol; Desflurane; Sevoflurane; Entropy; Cost; Recovery

OPEN ACCESS

Correspondence:
Elif Doğan Baki, Departement of Anesthesiology and Reanimation, Afyon Kocatepe University, Campus of Ali Çetinkaya, Afyon-İzmir Karayolu, 8 km, Afyonkarahisar, 03200, Turkey, Tel: +90 5308739908; Fax: +90272228s1181; E-mail: elifbaki1973@mynet.com

Received Date: *25 Apr 2017*
Accepted Date*: 27 Jun 2017*
Published Date*: 07 Jul 2017*

Citation:
Büyükerkmen E, Sivaci RG, Baki ED. Using Entropy in the General Anesthesia Managements. Clin Surg. 2017; 2: 1549.

Introduction

The evaluation of anesthetic depth during general anesthesia is an ongoing problem and quite a complex issue [1,2]. Conventionally, anesthetic depth is evaluated according to clinical symptoms such as eyelash and corneal reflexes, pupil size and reaction to light, blood pressure, pulse rate, and respiratory depth and rythym [3]. However, all these clinical findings may not always suffice in showing the anesthetic depth. Awareness of the under- or over-dosage of anesthetics used, as well as the related economic loss, have led to the increased use of different new techniques and devices for determining the anesthetic depth [4].

One of the monitorization techniques used for assessing the degree of anesthetic hypnosis is entropy monitoring [5,6]. Entropy relies on a method of assessing the degree of irregularity, complexity and uncertainty in electroencephalogram (EEG) signals [7]. The principle is based on calculation of the spectral entropy of raw EEG and frontal electromyelographic (EMG) data [8]. Entropy monitors produce two numbers (RE: Response Entropy and SE: State Entropy), which are related to the frequency bandpass used [9]. Entropy is the measurement of EEG signal irregularity. The irregularity within an EEG signal decreases with increasing brain levels of anaesthetic drugs. If we relate the irregularity to the entropy within the signal, then an entropy scale can be assigned [10]. There are only a few studies in the literature on the effect of entropy monitoring on anesthetic depth, consumption of anesthetic agent, and postoperative recovery. The purpose of this study was to assess the effects of three general anesthesia methods on anesthetic depth and quality, anesthetic agent consumption, and postoperative recovery, using the entropy monitoring.

Material and Methods

Patient selection

This study was carried out in the operation rooms of the Medical Faculty Hospital of Afyon

Table 1: Demographic features of the patients.

	Group D (n=30)	Group S (n=30)	Group P (n=30)	p
Gender (F/M), n	16/14	14/16	17/13	0.732€
Age (years)	49.00 ± 18.62	41.00 ± 15.22	39.87 ± 12.62	0.054*
Weight (kg)	77.63 ± 14.84	75.63 ± 12.86	70.17 ± 12.53	0.090*
Height (cm)	162 (150-185)	168 (115-185)	170 (150-182)	0.361#
BMI	26.37 (18.59-40)	26.03 (19.95-64.27)	24.18 (16.36-31.24)	0.055#
Duration of anesthesia (min)	132.53 (64-235)	130.00 (65-240)	152.50 (65-240)	0.280#
Duration of surgery (min)	120.00 (60-217)	112.50 (60-220)	117.50 (60-230)	0.669#
Cost of agents	40.37 ± 16.65	30.62 ± 12.46	9.67 ± 4.01	0.001*

Patients' data are expressed as mean ± SD (standard deviation) and median (minimum – maximum). *One-way variance analysis (ANOVA), #Kruskal-Wallis,€Chi-square, p<0.05 is accepted as statistically significant.

Table 2: Surgical Pleth Index (SPI) values of the patients.

	Group D (n=30)	Group S (n=30)	Group P (n=30)	p
SPI T1	47.50±19.80	46.27±21.19	44.97±16.38	0.878*
SPI T2	25.50 (15-55)	29.01 (10-85)	27.00 (6.84)	0.865#
SPI T3	32.50 (8-72)	25.00 (4-77)	26.50 (11-77)	0.271#
SPI T4	47.10±20.04	47.13±20.18	39.60±16.31	0.213*
SPI T5	67.07±12.97	64.18±17.07	54.50±17.66	0.009*
SPI T6	75.00 (30-98)	69.00 (21-98)	66.50 (37-98)	0.868#

Surgical Pleth Index (SPI). Patients' data are expressed as mean ± SD (standard deviation) and median (minimum – maximum). *One-way variance analysis (ANOVA), #Kruskal-Wallis. p<0.05 is accepted as statistically significant.

Kocatepe University after acquiring the approval of the Faculty Ethics Committee (approval date, 15 August 2013; approval number, 2013/10-60) and informed written consent of the patients included in the study. A total of 90 adult patients with an age range between 18 and 70 were included in the study. Elective surgery had been planned for the patients who were in the I-III risk group of ASA (American Society of Anesthesiologists), and the patients had undergone tympanoplasty and septoplasty surgery lasting between 60 and 240 min.

The criteria for exclusion from the study were the following: ASA IV risk group, postoperative intensive care, need for ventilation, pregnancy, age of under 18, inappropriate psychiatric state for giving consent, and refusal of consent.

After anesthesizing the patients with the standard anesthetic technique, the patients were divided into three groups according to anesthetic maintenance. The groups were randomly determined using the sealed envelope method. Group 1 (Group P) received propofol 3-5 mg/kg/h i.v. infusion; Group 2 (Group D) received Desflurane 1MAC, and Group 3 (Group S) received Sevoflurane 1 MAC.

Protocol of study

1. For hemodynamic follow-up; electrocardiography (EKG), non-invasive systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), and peripheral oxygen saturation (SpO_2) were monitorized.

2. The anesthetic depth was monitorized with entropy (Carescape Monitor B650 GE Healthcare, Finland). For this purpose, SE and RE values measured via a forehead-mounted sensor were noted. After cleansing the skin with alcohol, the entropy sensor was placed on the fronto-temporal region and pressed for 5 seconds to provide skin-sensor contact. Since RE is affected by response of facial muscles, whereas SE reflects the effect of the hypnotic agent on the brain, the SE values were noted as essential values.

3. Neuromuscular monitorization (NMT) was performed by exciting the ulnar nerve at about 2 cm proximal to the volar wrist joint and observing the response of the m. adductor pollicis.

Vascular access was established with a 20 gauge-intraket, and after calculating the hourly fluid requirement, crystalloid solution infusion was started.

For induction; midozolam 0.01 mg/kg, fentanyl 2 mcg/kg, lidocaine 1 mg/kg, propofol 2 mcg/kg, and rocuronium 0.6 mg/kg were used. The patients were pre-oxygenated with a face mask using O_2 100% 4 L/min. Following a 2-min controlled mask ventilation, the patients were intubated with an orotracheal intubation tube appropriate for age and weight. For anesthetic maintenance; 2 lt/min fresh gas flow with O_2/air 50/50%, the vaporizer was set at 2% for Group S, at 6% for Group D, and at propofol 5 mcg/kg/h infusion for Group P. Remifentanyl 0.1 mcg/kg/min infusion was started after induction, and, as myorelaxant, rocuronium 0.1 mg/kg/h was administered to all three groups. During surgery, the quantities of desflurane, sevoflurane, and propofol were decreased or increased so as to maintain RE and SE values between 40 and 60. Ventilation with tidal volume 8-10 ml/kg and frequency of 12/min was started. The end-tidal CO_2 levels in all patients were continuously monitorized during surgery and kept between 35 and 40 mmHg.

The following values of the patients at pre-induction (T1), post-intubation (T2), and at hours 1st (T3), 2nd (T4), pre-extubation (T5), and post-extubation (T6) were noted: Systolic pressure, diastolic pressure, mean arterial pressure, pulse rate, saturations, SPI value, NMT value, and RE and SE values. At the end, desflurane and sevoflurane consumptions were directly calculated over the used anesthesia device (Datex-Ohmeda Avance Config, 3030 Ohmeda Drive USA) and the propofol consumption was calculated over the perfusor. Subsequently, the total cost of anesthetic agents was calculated by multiplying the unit price of each agent with the quantity used. Furthermore, the total anesthesia and surgery durations and the Ramsey scores at post-extubation minute 1 and post-op min 30 of all patients were noted.

Statistical analyses

For the statistical evaluation of the obtained data, the SPSS 20.0 Program (Statistical Package for the Social Sciences Inc, Chicago, IL, USA) was used. The Kolmogorov-Simirnov test was performed for the control of normal distribution of the data. The frequency analysis was performed to assess the gender distribution in the groups. The

Table 3: Neuromuscular transmission (NMT) values of the patients perioperatively.

	Group D (n=30)	Group S (n=30)	Group P (n=30)	P
Pre-induction NMT	86.17 ± 8.47	85.53 ± 8.15	86.23 ± 10.44	0.947*
Pre-extubation NMT	75.00 (14-96)	67.50 (12-98)	75.00 (41-55)	0.482#
Post-extubation NMT	88.50 (48-100)	88.50 (28-100)	90.00 (63-100)	0.271#

Neuromuscular transmission (NMT). Patients' data are expressed as mean ± SD (standard deviation) and median (minimum –maximum). *One-way variance analysis (ANOVA), #Kruskal-Wallis. p<0.05 is accepted as statistically significant.

Table 4: Ramsey scores of patients postoperatively.

Ramsey scores	Group D (n=30)	Group S (n=30)	Group P (n=30)
Post-extubation 1st minute			
Ramsey 1 (n)	0	1	1
Ramsey 2 (n)	15	18	7
Ramsey 3 (n)	9	7	13
Ramsey 4 (n)	4	4	9
Ramsey 5 (n)	2	0	0
Post-extubation 30th minute			
Ramsey 2 (n)	26	30	30
Ramsey 3 (n)	4		

continuous variables according to their normal distribution were expressed as mean ± standard deviation or as median (minimum-maximum). The difference analysis of the categorical variables between groups was performed using the chi-square test. The difference analysis of continuous variables according to the normal distribution between the groups was performed using the One-Way ANOVA or the Kruskal-Wallis test. The Post-Hoc Tukey test was performed to determine the group with variables causing a significant difference.

The Spearman's or the Pearson's correlation analyses were performed in terms of distribution of the total cost, the quantity of consumed anesthetic agent, BMI, and RE and SE entropies within each group. A p value of <0.05 was accepted as statistically significant.

Results

A total of 90 adult patients who had undergone tympanoplasty and septoplasty surgery lasting between 60 and 240 minutes completed the study. There was no significant difference between the groups in terms of gender, age, weight, BMI, duration of anesthesia, and duration of surgery (p>0.05) (Table 1). Pre-extubation SPI values of Group P were significantly lower than Group D (p<0.05) (Table 2). There was no significant difference in neuromuscular transmission (NMT) values between the three groups (p>0.05) (Table 3). The Ramsey scores of the study groups at post-extubation at minute 1st and 30th minute in the recovery room were seen in Table 4, no significance was seen between them. There was a significant and positive correlation between the duration of anesthesia and total consumption of the anesthetic agents in all groups (p<0.05). And there was a significant and positive correlation between the body mass index (BMI) and the cost (r=0.256, p=0.015). There was a positive and significant correlation between the duration of anesthesia and cost, too (r=0.962, p<0.05). The cost of the propofol group was significantly lower than the other groups (p<0.05). MAP measured before and just after extubation were significantly lower in Group P than the others (p<0.05) (Table 5).

Discussion

Measurement of anesthetic depth is a critical issue in routine anesthesia pratice. EEG is used for measurement of the anesthetic depth, that is, to follow the electrical activity of brain; however, application and interpretation of EEG during anesthesia is quite difficult. Newly developed monitorization techniques like EEG, BIS, and entropy have been introduced into routine use. Entropy is a monitorization technique used to follow-up the anesthetic depth, which presents EEG measurements in a simple, easy, non-invasive and numerical manner. Entropy allows the easy follow-up of anesthetic maintenance of the patient by momentary measurements. Hence, a correlation between entropy and anesthetic agents can be made. Using entropy monitoring, we assessed the effects of three general anesthesia methods on the anesthetic depth and quality, consumption of anesthetic agent, and post-operative recovery. In our study were the following the most important findings: 1) The cost of propofol was significantly lower than the cost of inhalation anesthetics, 2) propofol and sevoflurane provided a better post-operative hemodynamic stability and awareness than dessflurane.

Rapidly increasing health expenditures and high costs of modern inhalation anesthetics have reviewed cost control in anesthesia [10]. Several studies on the cost comparison of inhalation anesthetics and propofol, some have reported TIVA (total intravenous anesthesia) to be more expensive and some have reported no cost difference in between. It has been reported that depending on the used volatile agent and fresh gas flow, TIVA is about 2 to 6 times more expensive than inhalation anesthesia and therefore, should be used only for short surgical interventions [11]. It has been determined that the cost of the new anesthetic desflurane or sevoflurane combined with fresh gas flow 2 L/min is similar to that of sufentanyl infusion, thus TIVA is more expensive [12,13]. In their study on application of O_2 100% with desflurane or propofol infusion 100-200 µg/kg/min, Rosenberg et al. [14] have found that TIVA with propofol is more expensive than anesthesia with desflurane. Another study [15] compared TIVA

Table 5: Mean arterial pressures of the patients perioperatively (mmHg).

	Grup D (n=30)	Grup S (n=30)	Grup P (n=30)	p
MAP T1(mmHg)	101.00 (91-145)	95.00 (80-119)	93.00 (72-121)	0.001#
MAP T2(mmHg)	89.73 ± 14.96	90.43 ± 18.43	82.70 ± 15.08	0.131*
MAP T3(mmHg)	84.00 ± 16.79	81.37 ± 16.50	78.17± 18.53	0.429*
MAP T4(mmHg)	94.00 (47-116)	88.00 (64-113)	76.00 (60-132)	0.065#
MAP T5(mmHg)	99.87 ± 19.26	99.97 ± 28.69	87.43 ± 13.47	0.038*
MAP T6(mmHg)	117.00 (85-143)	104.00 (71-139)	98.50 (65-126)	0.007#

MAP; mean arterial pressure. Patients' data are expressed as mean ± SD (standard deviation) and median (minimum –maximum). *One-way variance analysis (ANOVA), #Kruskal-Wallis,€Chi-square, p<0.05 is accepted as statistically significant.

using propofol and remifentanyl with that using desflurane and fentanyl plus high fresh gas flow in long surgical interventions and reported that in the desflurane-fentanyl group, the recovery time was shorter and the anesthesia cost wass lower, and that in both groups, the return of cognitive functions and the duration of stay in post-surgery unit were similar time-wise. Consistent with the findings of our study, in septorhinoplasty cases, no significant difference in terms of cost and recovery profiles was determined between TIVA using propofol and remifentanyl and anesthesia with desflurane and remifentanyl infusion applied with high rate of fresh gas flow [16]. In the study [17] they compared the cost of remifentanyl combined with propofol with the cost of sevoflurane and desflurane applied with fresh gas flow 6 L/min used in total abdominal hysterectomy operations and found no significant difference in between. When we compare our study with the above-mentioned two studies, we think that the lower consumption of propofol could be due to the use of entropy monitoring in our study.

When we evaluated the hemodynamic data, we determined that hemodynamically, propofol anesthesia is a safe and stable method. We observed no increase in the mean values of arterial blood pressure when compared with the control values. Smith et al. [18] have reported that the post-induction mean arterial pressure was lower in patients under propofol anesthesia than in those under sevoflurane anesthesia. Özköze et al. [19] have determined that the post-induction mean arterial pressure was significantly lower in the propofol group than in the sevoflurane and isoflourane groups. In our study, there was an elevation in the pre- and post-extubation MBP values in all three groups; however, this elevation was significantly lower in the propofol group (MBP 5; $p<0.038$, MBP 6; $p<0.007$). There was no difference between the three groups in terms of pre-intubation, post-intubation, and intra-operative pulse values; the pulse values were found to be higher than the pre-extubation basal values, however, but this increase showed no difference between the propofol and desflurane groups, whereas it was significantly high in the sevoflurane group ($p<0.029$).

Various tests have been used to assess the patients' hypnotic status and cognitive functions during the recovery period [20]. In our study, in order to determine the level of consciousness, we used the Ramsey scale at post-extubation minutes 1 and 30. The Ramsey score at minute 1 was 2 in 60% of the patients in Group S, in 50% in Group D, and in 23% in Group P. The Ramsey score(s) at minute 30 were 2 in all patients in Groups P and S; and in Group D, 2 in 26 patients and 3 in 4 patients. This meant that in the postoperative period, patients in Groups S and D were more conscious, and patients in Group P were more sedatized and tranquil. However, there was no significant difference in the level of consciousness at minute 30 between all patients of the three groups.

The surgical pleth index (SPI) has been developed to numerically express the nociceptive physiological responses during general anesthesia. The index has a scoring system between 0 and 100. High scores are associated with high stress. The optimal score has not been determined yet, however, when balanced with nociceptive and anti-nosciceptive factors, 50 is considered as the average stress score [21]. In our study, when compared with the basal values, the extubation SPI values decreased in all three groups. Intraoperatively, the propofol group had a more stable course, but this was statistically insiginificant. However, while the pre-extubation SPI values increased in all groups, this increase was significantly lower in the propofol group ($p<0.009$). There was no significant difference between the three groups in terms of pre-extubation and post-extubation NMT values.

Entropy monitoring is based on the irregularity of EEG waves caused by different frequencies [22]. When the patient loses conciousness, EEG waves tend to be more regular and provide continuous data on the hypnosis level during anesthesia [23]. The EMG of facial muscles coincides with classical EEG frequencies. This coincidence causes problems in the analysis of the cortical activity. The EMG waves of facial muscles change with the consciuosness level of the patient and use of myorelaxant agent. In the entropy module first developed by Datex-Ohmeda, EEG waves are evaluated by SE and EMG waves are evaluated by RE. Both SE and RE values increase as the patient is relieved of the effect of myorelaxant and starts to gain consciousness. Balcı et al. [24] have reported that entropy monitoring can be safely used to follow-up the hypnosis level during anesthesia and the recovery period. In our study, we also used the SE and RE levels to determine the anesthetic level in all of our patients. There was no significant difference between the three study groups in terms of SE and RE values.

Conclusion

With anesthetic depth kept fixed by entropy in all groups, there was a significant difference in anesthesia cost between the groups. We think that entropy and SPI are good alternatives to BIS in measuring the anesthetic depth.

1. The cost of propofol anesthesia was clearly low, whereas the cost of desflurane anesthesia was significantly high.

2. The patients in the propofol group were more stable in terms of hemodynamics and post-operative conciousness level.

For more reliable and significant results, studies on larger patient populations are required.

References

1. Kissin I. General anesthetic action: An absolute notion. Anesth Analg. 1993; 76: 215-8.
2. Glass PS. Anesthetic drug interactions: an insight into general anesthesia--its mechanism and dosing strategies. Anesthesiology. 1998;88(1):5-6.
3. Coloma M, Chiu JW, White PF, Armbruster SC. The Use of Esmolol as an Alternative to Remifentanil During Desflurane Anesthesia for Fast-Track Outpatient Gynecologic Laparoscopic Surgery. Anesth Analg. 2001;92(2): 352-7.
4. Heier T, Steen PA. Assessment of anaesthesia depth. Acta Anaesthesiol Scand. 1996 ;40(9):1087-100.
5. Bruhn J, Lehmann LE, Röpcke H, Bouillon TW, Hoeft A. Shannon entropy applied to the measurement of the electroencephalographic effects of desflurane. Anesthesiology. 2001;95(1):30-5.
6. Pensado Castiñeiras A, Rama Maceiras P, Molins Gauna N, Fiqueira Moure A, Vásquez Fidalgo A. [Immediate anesthesia recovery and psychomotor function of patient after prolonged anesthesia with desflurane, sevoflurane or isoflurane]. Rev Esp Anestesiol Reanim. 2000;47(9):386-92.
7. Schmidt GN, Bischoff P, Standl T, Hellstern A, Teuber O, Schulte EJ. Comparative evaluation of the Datex-Ohmeda S/5 Entropy module and the Bispectral IndexR monitor during propofol–remifentanil anesthesia. Anesthesiology. 2004;101(6):1283-90.
8. Bruhn J, Ropcke H, Hoeft A. Approximate entropy as an electroencephalographic measure of anesthetic drug effect during desflurane anesthesia. Anesthesiology. 2000; 92(3):715-26.

9. Viertio-Oja H, Maja V, Sarkela M Talja P, Tenkanen N, Tolvanen-Laakso H, Paloheimo M, et al. Description of the Entropy algorithm as applied in the Datex-Ohmeda S/5 Entropy Module. Acta Anaesthesiol Scand. 2004; 48(2):154-61.
10. Hanci V, Yurtlu S, Ayoglu H, Okyay RD, Erdogan G, Abdusoglu M, et al. Effect of low-flow anesthesia education on knowledge, attitude and behavior of the anesthesia team. Kaohsiung J Med Sci. 2010;26(8):417-23.
11. Tomatir E. Düsük Akimli Anestezi ve Maliyet. Anestezi Dergisi. 2002;10:149-56.
12. Bach A, Böhrer H, Schmidt H, Motsch J, Martin E. Economic aspects of modern inhalation anesthetics with sevof lurane as an example. Anaesthesist. 1997;46(1):21-8.
13. Boldt J, Jaun N, Kumle B, Heck M, Mund K. Economic considerations of the use of new anesthetics: A comparison of propofol, sevoflurane, desflurane, and isoflurane. Anesth Analg. 1998;86(3):504-9.
14. Rosenberg MK, Bridge P, Brown M. Cost comparison: A desflurane-versus a propofol-based general anesthetic technique. Anesth Analg. 1994;79(5):852-5.
15. Röhm KD, Piper SN, Suttner S, Schuler S, Boldt J. Early recovery, cognitive function and costs of a desflurane inhalational vs. a total intravenous anaesthesia regimen in long-term surgery. Acta Anaesthesiol Scand. 2006;50(1):14-8.
16. Gokce BM, Ozkose Z, Tuncer B, Pampal K, Arslan D. Hemodynamic effects, recovery profiles, and costs of remifentanil-based anesthesia with propofol or desflurane for septorhinoplasty. Saudi Med J. 2007;28(3):358-63.
17. Tüfek A, Bilgin H, Özcan B. Sevofluran, desfluran or propofal anesthesia combined with remifentanyl: composition properties, complications and comparison of anesthetic drug cost. Journal of Turkish Anesthesia Reanimation. 2006;34:103-10.
18. Smith I, Ding Y, White PF. Comparison of induction, maintenance and recovery characteristics of sevoflurane-N2O and propofol-sevoflurane-N2O with propofol-isoflurane-N2O anesthesia. Anesth Analg. 1992;74(2): 253-9.
19. Ozkose Z, Ercan B, Unal Y, Yardim S, Kaymaz M, Dogulu F, et al. Inhalation versus total intravenous anesthesia for lumbar disc herniation: comparison of hemodynamic effects, recovery characteristics and cost. Neurosurg Anesthesiol. 2001;13(4):296-302.
20. Ellerkmann RK, Liermann VM, Alves TM, Wenningmann I, Kreuer S, Wilhelm W, et al. Spectral entropy and bispectral index as measures of the electroencephalographic effects of sevoflurane Anesthesiology. 2004;101(6):1275-82.
21. Ilies C, Ludwigs J, Gruenewald M, Thee C, Hanf J, Hanss R, et al. The effect of posture and anaesthetic technique on the surgical pleth index. Anaesthesia. 2012;67(5):508-13.
22. Butterworth JF, Mackey DC, Washnick JD. Nonkardiovaskuler moniterizasyon. Morgan&Mikhail Clinical Anesthesiology, 5th edition, McGraw-Hill Education, United States. 2013;123-42.
23. Bein B. Entropy. Best Pract Res Clin Anaesthesiol. 2006;20(1):101-9.
24. Balci C, Akbulut G, Ibis AH, Arikan Y. Determination of entropy values towards bispectral indeks values in the duration of recovery. J Anesth. 2006;14:264-8.