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Research Article

Evaluation of BIS Monitorization Using Sevoflurane Versus Desflurane During Extracorporeal Circulation in Cardiovascular Surgery Anesthesia

Kardiovasküler Cerrahi Anestezisinde Ekstrakorporeal Dolaşımda Sevofluran ve Desfluran Kullanımının BIS Monitorizasyonu ile Değerlendirilmesi

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Abstract: The risk of awareness in cardiac surgery is 5 times higher than in other surgeries. The use of cardiopulmonary bypass pump may lead to inadequate anesthesia depth. In this study we aimed to evaluate the awareness and the depth of anesthesia with BIS monitorization in cardiovascular anesthesia. This study was designed as a propective randomised controled trial. Sixty patients who underwent coronary artery bypass grafting and heart valve surgery were included in the study. The patients were divided into 2 groups randomly. Maintenance of anesthesia provided by 2-4% sevoflurane to Group 1 and 5-8% desflurane to Group 2 including extracorporeal circulation period. Anesthesia depth adjusted according to hemodynamic and clinical values. Patients in both groups were followed with BIS monitoring. In all study groups, fixed dose of remifentanil infusion was initiated following induction of anesthesia. Patients hemodynamic data, BIS measurements were recorded during the operation. Considering the ease of recognitions and recall, from the beginning of extracorporeal circulation, the dog barking was constantly listened with earphones by patients to assess alertness and awareness. On the second postoperative day, patients were asked whether they remember anything about operation and dog barking. The obtained data were evaluated with SPSS package program. Similar hemodynamic data and BIS measurements were obtained in both groups in our study. Postoperative awareness and remembrance were not found in either group. In cardiovascular surgery, it was observed that the depth of anesthesia determined by hemodynamic data is correlated with BIS, but shifted to deeper levels of anesthesia. Although complications were not seen in the patients, it was concluded that the adjusting the level of anesthesia with BIS could be safer.

Key Words: awareness, BIS monitorization, sevoflurane, desflurane valve surgery, cardiopulmonary bypass.

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Özet: Kardiyovasküler cerrahide anestezi sırasında farkındalık diğer cerrahilere göre 5 kat fazladır. Kalp akciğer pompası kullanımı yetersiz anestezi derinliğine sebep olabilir. Çalışmamaızda sevofloran ve desfloran ile uygulanan kardiak anestezide BİS eşliğinde farkındalık ve anestezi derinliğini belirlemeyi amaçladık. Prospektif ve randomize olarak tasarladığımız çalışmamız koroner arter ve kalp kapak cerrahisi geçirecek 60 kişi dahil edildi. Rastgele 2 gruba ayrılan hastalara sevofloran ve desfloran ile inhalasyon anestezisi ile analjezi için sabit doz remifentanil infuzyonu uygulandı. Hemodinamik veriler ve BİS değerleri kaydedildi. Kolay hatırlanabilmesi nedeniyle tanıdık ses olan köpek havlaması ekstrakorporeal dolaşım boyunca hastalara dinletildi. Post operatif 2. günde farkındalık ve uyanıklık için hastalarla görüşme yapıldı ve kaydedildi. Elde edilen veriler SPSS ile incelendi. Hastalarda benzer hemodinamik veriler ve BİS değerleri olduğu görüldü. Hastalarda farkındalık ve uyanıklığa rastlanılmadı.Kardiyovasküler anestezi uygulamasında anestezi derinliğinin hemodinamik veriler ile belirlenmesinin BİS ile korele olmasına rağmen anestezinin daha derin seviyeye doğru kaydığı görüldü. Bu nedenle BİS ile anestezi derinliğinin güvenli şekilde belirlenebileceği kanısına varıldı.

Anahtar Kelimeler: farkındalık, BİS monitorizasyonu, kardiyopulmoner bypass

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1. Introduction

Awareness is defined as waking the brain with a stimulus while under general anesthesia and storing in memory to be recalled in the future. (1) Under general anesthesia, awareness seen in 0.1% to 0.2%. It is an uncommon but well defined undesirable condition (1, 2).

Patients who experienced intraoperative wakefulness or awareness may have complaints such as behavioral disability, nightmares, anxiety during the day, and recall in the early postoperative period, in some cases long-term psychological sequelae can be seen (3,4,5).

The risk of awareness in cardiac surgery is 5 times higher than in other surgeries. Historically, up to 23% awareness has been reduced to 1% today. Comorbidities of cardiac surgery patients and hemodynamic instability during surgery may preclude from ideal anesthesia depth, also the use of cardiopulmonary bypass pump may lead to inadequate anesthesia depth.(6)

The reliability of clinical parameters used to follow the depth of anesthesia is poor. This situation has led to the need for devices such as bispectral index (BIS) that allow the depth of anesthesia to be determined via the electroencephalogram (EEG). Monitoring with EEG and variants, prevention of complications that may be caused by anesthesia overdose, prevention of awareness and awakeness, and early discharge are aimed.(7) However, despite the technological progress, these devices did not fully meet expectations and caused the emergence of different opinions in the prevention of awareness. (8,9,10)

In this study we tried to investigate alertness and awareness and the effectiveness of BIS monitoring in volatile anesthetic based cardiac surgery.

2. Method

After the approval of ethics committee no. 12 dated 31/05/2011 at ESOGU Medical Faculty, 60 patients, aged 18-85, 22 female, 38 male, who will undergo coronary artery bypass grafting and heart valve surgery scheduled for elective surgery with extracorporeal circulation. The size of the study group was determined according to previous studies. The informed constent of patients was taken. American Society of Anesthesiogy (ASA) II-III, were included. Patients with uncontrolled diabetes, advanced renal insufficiency, allergic response to any of the previously known agents were not included in the study.

During the preoperative patient visit, information was given to the patients about the study. It was explanined that they will continuously listen the dog barking during the extracorporeal circulation which is a stimulating voice and easy to remember, from the mp3 player earphones to evaluate the intraoperative awareness.

One hour before the operation, 0.01 mg / kg morphine was administered intramuscularly. Patients who were taken to the operating table were monitored with BIS XP ASPEKT PLATFORM. BIS monitor was placed away so the anesthesiologist could not follow. Before the induction, invasive arterial pressure monitoring, peripheral oxygen saturation (SpO2) and electrocardiogram (ECG) monitoring were performed to the patients. After intubation, central venous cannulation was performed and central venous pressure was monitored.

For each patient, induction of anesthesia made with etomidate 0.1-0.2 mg/kg, muscle relaxation achieved with rocuronium bromur 1 mg/kg. Patients were randomly divided into 30 patients as the sevoflurane group (group 1) and 30 patients as the desflurane group (group 2).

The maintenance of anesthesia adjusted according to the clinical and haemodynamic values of the patient. Volatile anesthetics applied 2-4% sevoflurane concentration in group 1 and 5-8% desflurane concentration in group 2. Remifentanil infusion was administered with the highest dose which was 0.1 mcg/ kg / min adjusted according to hemodynamic values. The extracorporeal circulation was performed with the Stockert S3 model roller pump after classical cannulation. During extracorporeal circulation, anesthesia was maintained by perfusionist and anesthetist cooperativly. Anestehesia manintained by vaporisator on cardiopulmonary bypass pump (CPBP) with sevoflurane concentration 0.5-1% and desflurane concentration 1-3% and constant remifentanil infusion continued. Hypothermia was performed with 30-320 C at the extracorporeal circulation. During the entire duration of the extracorporeal circulation, all of the patients listened to the dog barking with the earphone from the mp3 player. Anesthesia depth was measured according to hemodynamic and clinical findings. Anesthesia was maintained with a mean arterial pressure of 50-60 mmHg and norephinephrine as vasopressor agent was started when necessary. Volatile anesthetic and remifentanil infusion were stopped at the end of skin closure. The patient was transferred to the cardiovascular intensive care unit with endhotracheal tube (ETT) in a monitored manner.

On the second postoperative day, patients were asked to remember any sounds, dog sounds, any event about the operation, and a dream that included a dog during the operation. The interview was performed on the second day to avoid amnestic effects of anesthetic agents and premedication.

Demographic characteristics of the patients were recorded. Awareness, BIS measurements, hemodynamic data and consumption of remifentanil, sevoflurane and desflurane groups were compared.

Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (OAP), peripheral oxygen saturation (SpO2), central venous pressure (CVP) and heart rate (HR) values, which are the hemodynamic parameters of the patients, were recorded before and after induction, after the intubation, after the incision, during the sternotomy, at the 1st, 10th and 30th minutes on heart-lung pump, after the aortic clamp was removed and at the 1st, 10th and 30th minutes after the heart-lung pump stoped, at the end of the sternum closure and at the end of the skin closure. BIS values were recorded at the indicated times by an observer who did not participate in the study. The duration of extracorporeal circulation, duration of anesthesia and operation time were recorded.

The obtained data were evaluated with SPSS statistical package program. The Kolmogorov-Smirnov distribution test was used to examine the normal distribution. The Pearson Chi-square test was used to compare the qualitative data. In the comparison of quantitative data, Mann Whitney U test was used for the comparison of parameters between groups in the case of two groups. Wilcoxon signed test was used for intra-group comparison of parameters. All the findings were evaluated bidirectionally as $p<0.05$ significance level and $p <0.01$ significance level.

3. Results

This study was performed on a total of 60 patients aged between 18 and 83 years. (Table 1)

Table 1.
Demographic Characteristics

		Group 1		Group 2		*p*
		M	**SD**	**M**	**SD**	
Age (year)		62,8	15,1	57,1	14,6	**0,068**
Weight (kg)		73,8	14,2	69,5	9,5	**0,060**
Duration of Anesthesia (min)		271,8	68,0	299,5	68,0	**0,093**
Duration of surgery (min)		234,7	66,7	264,5	70,6	**0,094**
Duration of Crossclemp (min)		98,0	54,1	90,4	47,9	***0,813***
Duration of Extracorporeal circulation(min)		113,8	56,1	130,8	49,2	***0,099***
Remifentanil Consumption (micg)		1442,06	785,93	1413,19	897,01	***0,722***
		n	**%**	**n**	**%**	
Gender	**Male**	18	60%	20	67%	**0,205**
	Female	12	40%	10	33%	

Intraoperative wakefulness and awareness were not seen in both groups during the postoperative 2nd day visit which was the main research topic of our study. (Table 2)

Table 2.
İntraoperative Awereness

Awareness	Group 1	Group 2
Clinical finding	Not seen	Not seen
Dream	Not seen	Not seen
intraoperative voice	Not seen	Not seen
Awareness / recall	Not seen	Not seen

No postoperative history of bad recall was found. Sweating, pupil reaction, which was evaluated as intraoperative alertness symptom, was not observed with our patients. There was no statistically significant difference in BIS measurments between group 1 and 2 ($p>0.05$) but there are differences in intra group comprasions. (Figure 1, table 3)

Table 3.
BIS values

	Group 1		Group 2		p
	Mean	SD	Mean	SS	
Before induction	96,517	3,302	97,290	1,811	0,525
After induction	41,483	13,963	41,677	11,982	0,594
After intubation	42,931	10,219	39,355	7,521	0,248
After insicion	38,483	8,551	39,161	7,866	0,594
Sternotomia	37,448	7,619	47,097	58,395	0,773
Heart-lung pump 1.min	38,517	7,642	40,065	5,785	0,241
Heart-lung pump 10.min	36,724	5,769	36,968	7,186	0,959
Heart-lung pump 30. min	36,586	5,335	39,710	7,189	0,057
After aortic clemp removal	43,448	11,179	46,548	12,463	0,245
After heart-lung pump stopped 1. min	43,690	10,880	46,097	11,329	0,558
After heart-lung pump stopped 10. min	38,448	10,084	42,097	8,807	0,129
After heart-lung pump stopped 30. min	36,655	5,918	40,387	10,154	0,185
After sternum closure	37,414	6,489	38,677	8,352	0,728
After skin closure	38,897	5,821	39,484	7,650	0,818

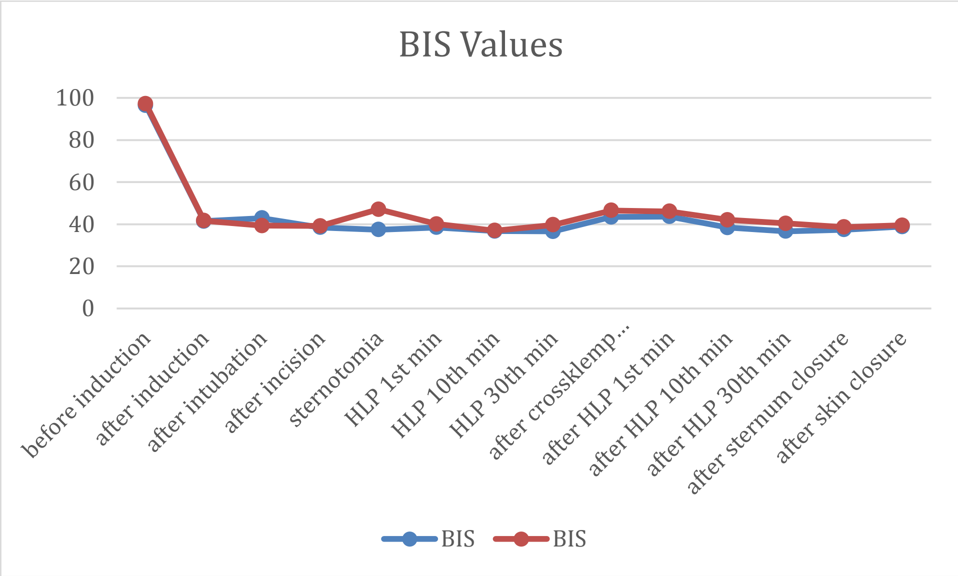

Figure 1. *Group 1 and Group 2 BIS measurement graphics*

There were no significant differences between the the haemodynamic values that we used to determine our depth of anesthesia in our study. The values of HR, SAP, DAP, MAP, CVP, SPO2 recorded in different time periods of both groups are seen in the table 4. The results of both groups were similar. Although there were statistically significant differences between the values of the two groups recorded at different times, they were not considered significant because of differences that were not clinically significant.

Table 4.
Haemodynamic variables

	HR				*P*	MAP				*P*	SAP				*P*	DAP				*P*
	1		2			1		2			1		2			1		2		
	M	SD	M	SD		M	SD	M	SD		M	SD	M	SD		M	SD	M	SD	
BI	**83,3**	**17,7**	**83,3**	**13,9**	**0,859**	**99,1**	**17,7**	**97,3**	**21,8**	**0,579**	**135,2**	**34,0**	**133,3**	**30**	**0,544**	**76,4**	**15,7**	**75,2**	**18,1**	**0,700**
AI	88,1	23,2	88,1	16,8	0,343	87,3	16,5	98,1	20,8	**0,028***	11,7	24,7	132,4	26,1	**0,018***	67,6	14,1	77,8	19,7	**0,025***
AIn	**98,4**	**22,7**	**98,4**	**19,4**	**0,293**	**105,2**	**29,3**	**106,2**	**25,1**	**0,865**	**145,9**	**41,8**	**144,5**	**31,6**	**0,959**	**83,5**	**22**	**84,7**	**24,4**	**0,959**
AIns	81,9	20,6	81,9	16,9	0,355	90,0	20,5	92,9	17,1	0,375	127,5	30,3	130,5	24,6	0,355	69,2	16,4	73,5	14,7	0,203
S	**85,1**	**21,4**	**85,1**	**23,3**	**0,277**	**82,1**	**14,7**	**82,4**	**12,6**	**0,853**	**118,6**	**20,8**	**117,9**	**18,31**	**0,912**	**64**	**12,5**	**64,2**	**11**	**0,739**
HLP 1	69,3	26,1	62	31,4	0,138	57	10,6	56,9	12,1	0,651	63	12,8	79,5	99,2	0,657	53	10,5	51,8	13	0,935
HLP 10	**x**	**x**	**x**	**x**	**X**	**57,5**	**9,4**	**51,5**	**10,8**	**0,023***	**x**	**x**	**x**	**x**	**X**	**x**	**x**	**X**	**x**	**X**
HLP 30	x	x	x	x	*X*	63	12,4	59,2	11,9	0,190	x	x	x	x	X	x	X	x	X	X
A Aort CC	**65,7**	**24,6**	**70,1**	**28,5**	**0,290**	**56**	**10,6**	**56,0**	**11,9**	**0,599**	**65,7**	**16,9**	**69**	**23,3**	**0,510**	**50,88**	**9,03**	**49,29**	**10,5**	**0,728**
KAP AYRI LMA 1	69,8	18,7	82	18,9	**0,031***	58	10,8	62,6	14,7	0,118	79,2	18,9	82,0	26,7	0,784	47,9	9,03	51,3	12,5	0,190
A HLP 10	**705**	**15,8**	**89,1**	**19**	**0,000****	**62**	**9,3**	**62,4**	**12,0**	**0,684**	**89,8**	**17,4**	**89,8**	**20,5**	**0,976**	**48,4**	**8,1**	**49,2**	**10,4**	**0,382**
A HLP 30	80,1	17,7	93	19,1	**0,004****	66	10,5	67,0	11,4	0,876	98,1	13	96,8	18,4	0,784	50,1	9,1	52,8	10,0	0,311
A S	**82,7**	**16,3**	**92,9**	**17,6**	**0,032***	**70,4**	**12,5**	**69,3**	**10,8**	**0,824**	**100,1**	**22,6**	**101,3**	**16,7**	**0,745**	**55,3**	**12,3**	**53,4**	**9,9**	**0,894**
A S Ins	83,7	15,6	93	15,7	**0,027***	703	10,1	69,3	8,9	0,636	102,4	10,1	10,2	14,1	0,767	54,9	11,4	54,3	10,5	0,859

List of Abbreviations

EEG: Electroencephologram
BIS: Bispectral mIndex
ASA: American Society of Anesthesiology
SpO_2: Peripheric Oxygen Saturation
ECG: Electrocardiogram
l/min: Litre/minute
micg/kg/min: Microgram/kilogram/minute
CPBP: Cardiopulmonary By-pass Pump
mp3: MPEG layer 3
ETT: Endhotracheal tube
SAP: Systolic Arteriel Pressure
MAP: Mean Arteriel Pressure
DAP: Dystolic Arteriel Pressure
CVP: Central Venous Pressure
HR: Heart Rate
Kg: Kilogram
min: Minute
micg: Microgram

4. Discussion

Intraoperative awareness is a rare complication of general anesthesia which can lead to serious sequelaes. Cardiac surgery patients have more intraoperative awakening and awareness than other operations. It is thought that dilutional effects of extracorporeal circuit on anesthetics and hypothermia causes this complication.

The traditional clinical findings which are used to assess the depth of anesthesia during surgery may be insufficient to prevent awareness.(11) In addition, it has been reported in some publications that tachycardia and hypertension are not observed in the case of awareness and end tidal anesthetic gas monitoring may not be effective enough (12,13).

Awerness with recall is a rare result of general anesthesia. Although relatively uncommon, it can lead to serious sequelae. People who experienced awareness during anesthesia were reported to experience postraumatic stress disorder at rates of 50% within two years of the onset of symptoms, although there were no complaints during the initial period (11,12).

Previous studies have shown that cerebral monitoring provides rapid recovery from the general anesthesia (14). Studies with EEG-based cerebral monitors show that better titration of intravenous and inhalation anesthetics is achieved during general anesthesia. Also these studies have reported that use of these monitoring devices accelerate the recovery (15). Another known fact is that anesthesiologists use volatile anesthetics at lower concentrations when using cerebral monitors (16). However, it has not yet been clear that the risk of intraoperative awareness is low under BIS monitoring.

When volatile agent based cardiac anesthesia technique is used, the concentration of volatile anesthesia is often determined by the perfusionist via vaporiser attached to by-pass pump and is usually reduced with the aim of preventing myocardial depression during the termination from CPB. This increases the risk of alertness of the patient when it is concurrent with the rewarming period. Compared with opioid-benzodiazepine combination, when volatile anesthetics used the incidence of alertness clinical findings is lower (17).

While it is said that the most accurate method for the investigation of awareness is the interview in the postoperative period, the right time for this interview is still a matter of debate. While some researchers are advising to interview patients as soon as the state of consciousness returns to normal, this option may not be reliable in every patient since patients may still be asleep. One group argues that patients should be assessed at least one week after the operation (18). We aimed to meet with our patients on the 2nd postoperative day. This period was chosen because patients are routinely followed up in the intensive care unit for 2 days postoperatively in our cardiovascular surgery clinic. The effects of anesthetic agents were completely weared of after two days and the surgical intensive care is relatively quite enviroment then ward. Also we tought that remembrance could be easier. Non of our patient describe awareness or recall in our interview. It was also thought that the lower BIS values among the groups correlated with these expressions and there was no statistically significant difference between BIS values in two groups. ($p > 0.05$)

According to the BIS value of the heart-lung pump 30th minute and aortic clamp removed in intra-group comparisons, the increase in the BIS value is statistically significant in both groups. ($p < 0.05$). These results were attributed to the low concentration of the anesthetic agent given by the perfusionist at CPB termination and rewarming. However, even though the BIS value was measured higher, it was concluded that this value is not clinically significant because it is in the BIS measurement range, which is considered as the deep hypnotic level. Also our patiets did not report anything about their operation period. But we did not measure blood concentration or end tidal volatile agent concentrations which can explain the varying levels of blood concentrations of volatile anesthetics at this time window.

When hemodynamic results of both groups were evaluated, there were statistically significant results in groups and between the groups. But it was thought that the values recorded at different times did not make a clinical difference because of the similar range in clinical practice. Puri (19), stated that the use of BIS monitoring during CPBP carries value because it reduces the incidence of hemodynamic instability, but it also adds that BIS values show wide variations during CPBP. In our study, the depth of anesthesia was provided according to hemodynamic and clinical data. Therefore, we can not comment on the effect of BIS monitoring on the hemodynamic results. However, our data has been shown that the depth of anesthesia determined by haemodynamic changes causes us to keep our patients below the deep hypnotic level (<40), which may be dangerous. In a study (20), mortality increased in patients whose BIS vlaues below 40 for more than 5 minutes. Although we did not see any intraoperative complication in our patients we did not questioned the long-term effects of this condition.

In our study, we tried to asses the intraoperative awareness and recall and their correlation with BIS monitoring which anesthesia depth adjusted with hemodynamical variables. Our patients did not experienced awareness and recall in both groups. We assumed that patients do not have such an experience because group 1 and group 2 BIS values are consistent with the deep hypnotic level. In both groups, the BIS measurement values during the operation were found at the range indicated as the necessary level for the adequate depth recommended in the literature. Nitzschke, in his (21) study, showed that in volatil-based anesthesia applied with the BIS guideline, less gases are applied and less vasopressors are needed. However, we have not been able to make a clear assessment of these statement. Because we could not measure the end tital volatile concentration, which is the main limitation of our study, and the blood volatile agent concentration measurement, which is not feaseable and applicable in clinical practice. In addition, we didn't manage to make medium and long round interviews with our patients, we could not evaluate the long-term mortality and morbidity of deep anesthesia levels.

Studies with EEG-based cerebral monitors showed that better titration of intravenous and inhalation anesthetics is achieved during general anesthesia. It is thought that the evaluation of alertness with clinical findings is not enough when anesthesia is performed with volatile anesthetics and BIS monitoring should provide safer and more comfortable conditions for patient and anesthesiologist.

5. Conclusion

We found similar BIS values and haemodynamic values in our groups in which we did not experience intraoperative alertness and awareness. We observed that the depth of anesthesia maintained with hemodynamic data points to deep anesthesia levels in BIS values. It is concluded that maintance of anesthesia and also adjusting the depth of anesthesia with BIS is rational.

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