Med. J. Cairo Univ., Vol. 86, No. 3, June: 1699-1706, 2018
www.medicaljournalofcairouniversity.net

The Impact of Bispectral Index on Isoflurane Consumption and Recovery Profile in Patients Undergoing Upper Abdominal Surgery

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Abstract

Background: Isoflurane requires careful administration and monitoring. Its excessive usage in patients may cause significant morbidity because of hypotension, tachycardia and delay in recovery. The Bispectral index (BIS) monitoring may be useful for titration of volatile anesthetic agents more precisely than what is possible by usual clinical parameters.

Aim: Our aim is to evaluate the effect of BIS monitoring on isoflurane consumption and recovery profile with monitoring of heamodynamic changes in adult patients undergoing upper abdominal surgery.

Patients and Methods: This study was carried out on 90 patients, 18-60 years, ASA I-II, scheduled for upper abdominal surgery under general anesthesia. Patients were randomized into two equal groups (45 patients in each group): Group I: SP group: Patients in the SP group had continuous assessment by standard clinical practice. Group II: BIS group: Patients in the BIS group had continuous assessment of BIS monitoring. The following parameters were compared between the two groups: Intraoperative hemodynamics, intraoperative isoflurane consumption, the time taken to extubate the patients, recovery duration using modified aldrete score.

Results: There was statistically significant decrease in isoflurane consumption in BIS group as compared to SP group, while there was significant negative correlation between BIS and both time to extubate the patients and recovery time in BIS group. the heamodynamic changes showed insignificant difference between both groups.

Conclusions: The use of BIS index, in adult patients undergoing upper abdominal surgery under general anaesthesia, significantly decreases isoflurane consumption and improves recovery profile.

Key Words: *Bispectral index – Isoflurane – Depth of anaesthesia.*

Introduction

ANAESTHESIA is a balance between the amount of anaesthetic drug (s) administered and the state of arousal of the patient. Given that the intensity of surgical stimulation varies throughout surgery, and the haemodynamic effects of the anaesthetic drugs may limit the amount that can be given safely, it is not uncommon for there to be critical imbalances between anaesthetic requirement and anaesthetic drug administration **[1]**.

Depth of anesthesia (DOA) may be conceptualized as a continuum spanning from an anesthetized patient approaching consciousness (light anesthesia) to one with dramatically reduced brain activity (deep anesthesia). It is assumed that assessing depth of anesthesia with brain monitors will prevent instances of awareness, while allowing safe reduction in anesthetic administration **[2]**.

The BIS processes a single frontal electroencephalograph signal to calculate a dimensionless number intended to reflect the patient's level of consciousness. BIS values range from 0 to 100, reflecting the absence of detectable brain electrical activity and brain electrical activity during the awake state, respectively. Targeting a BIS range between 40 and 60 has been advocated for awareness prevention and the avoidance of excessive anesthesia **[3,4]**.

Under general anesthesia approximately 2 out of 1000 patients experience an intraoperative awareness. The Bispectral index (BIS) is currently the only technology for monitoring the state of consciousness that can reduce the incidence of intraoperative risk in adults by about 80% **[5]**.

Isoflurane requires careful administration and monitoring. Its excessive usage in patients may cause significant morbidity because of hypotension, tachycardia and delay in recovery **[6]**.

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The aim of this study was to evaluate the effect of BIS monitoring on isoflurane consumption and recovery profile with monitoring of hemodynamic changes in adult patients undergoing upper abdominal surgery.

Patients and Methods

After obtaining the research ethics committee approval (approval code: (39145) and an informed written consent was taken from every patient, this prospective randomized blind study was carried out in Tanta University Hospitals in General Surgery Department from January to September 2017, on 90 patients of both sex, 18-60 years old, ASA I and II, scheduled for elective upper abdominal surgery. Patients with history of any psychiatric illness, stroke with residual neurologic deficits or altered mentation, alcohol abusers and Long-term use of central nervous system (CNS) activator drugs, benzodiazepines or opiates therapy were excluded from the study.

Patients were randomized into two equal groups by using ninety slips of paper.

Forty-five patients were labeled as standard practice (SP) group and the other 45 patients as Bispectral Index (BIS) group. These slips were placed in an envelope and taken out for every patient before the start of procedure by a nurse who has no subsequent role in the study. Group I: SP group: Patients in the SP group had continuous assessment by standard clinical practice, Group II: BIS group: Patients in the BIS group had continuous assessment of BIS monitoring (Covidien, Mansfield, MA, USA) by applying BIS XP sensors Zipprep TM four electrodes to the forehead and temple regions before the induction of anesthesia.

Preoperative assessment was done by: History taking, clinical examination, laboratory investigations including: CBC, prothrombin time activity, liver & renal functions and electrolytes. On the arrival to O.R., routine standard monitoring in the form of pulse oximetery, electrocardiogram, end tidal carbon dioxide and non-invasive blood pressure were instituted in both groups. The spectrophotometer analysis of inspired and expired composition of the gases and isoflurane were also employed. An intravenous (I.V) line was inserted by 20G cannula. All patients were premedicated with intravenous midazolam 0.03mg/kg. After preoxygenation with 100% oxygen for 3-5 minutes, general anesthesia was induced in both groups with propofol 1.5mg/ kg, fentanyl 1 [redacted]g/k[redacted] and cisatracurium 0.15mg/kg of body weight. Endotracheal intubation was performed after 2-3 minutes of giving the muscle relaxant. All patients were mechanically ventilated to keep end tidal carbon dioxide of 32-35mmHg. Anaesthesia was maintained by isoflurane, 80% oxygen and 20% air with total flow of 2 liters. Isoflurane was delivered through TEC 6 vaporizer (GE health care, Avance CS2, Datex Ohmeda, USA) by regulating its concentration through the dial setting in percentage and by monitoring the MAC value on the anesthesia monitor. In Group I (SP group), it was started by 1 minimum alveolar concentration (MAC) and was titrated by monitoring the standard clinical parameters like heart rate, blood pressure and end tidal vapor concentration in the form of MAC. In group II (the BIS Group), isoflurane delivery was aided by keeping the BIS value between the numerical value of 40-60. Intermittent bolus of cisatracurium 0.03mg/kg intravenously were delivered to keep at least 1-2 twitch using train of four stimuli as guided by the nerve stimulator. The isoflurane was used in all the patients to maintain adequate DOA. Intraoperative hypotension (MAP <20% below baseline) was treated with boluses of ephedrine 6 mg. Bradycardia (HR<50 beats minutes) was treated with atropine 0.01mg/kg in both the groups. The patients in both groups were extubated when they are fulfilling the subjective and objective criteria for extubation. Neuromuscular blockade was reversed with neostigmine 0.04mg/kg and atropine 0.01mg/kg.

Measurements: Patient's demographic data and other relevant information were recorded. Hemodynamic variables including mean arterial blood pressure (MAP) and heart rate (HR) were recorded from baseline (pre-anaesthetic) and at 15, 30, 45, 60 minutes and at the end of surgery. The BIS score was recorded after induction and at 15, 30, 45, 60 minutes and at closure of skin in the BIS group. Our primary outcome was to measure intraoperative isoflurane consumption in milliliters starting from induction and till closure of skin incision in both groups and was recorded as described by Dion and as given below:

"Usage of Isoflurane (ml) = Dialed concentration x Fresh gas flow x Duration at that concentration x Molecular weight divided by 2412 x Density"

The variables were the vaporizer concentration (%) P, the fresh gas flow F (L/min), the duration of anaesthesia (min), lsoflurane Molecular weight (g)=184.4, Density (g/ml)=1.50.

The time taken to extubate the patient in minutes (after discontinuation of isoflurane) was recorded.

Recovery duration, which was the time taken for the patient to achieve modified Aldrete score >9 as expressed in Table (1), was recorded in minutes.

Table (1): Modified Aldrete Scoring System [8].

Item	Structure	Points
Activity	Able to move volantarily or on command	
	4 extremities	2
	2 extremities	1
	0 extremities	0
Respiration	Able to deep breath and cough freely	2
	Dyspnea, shallow or limited breathing	1
	Apneic	0
Circulation	BP±20mmHg of preanesthetic	2
	BP±20-50mmHg of preanesthetic	1
	BP±50mmHg of preanesthetic	0
Consiousness	Fully awake	2
	Arousable on calling	1
	Not responding	0
O2 Saturation	Able to maintain O2 saturation 92% on room air	2
	NeedsO2 inhalation to maintain O2 saturation 90%	1
	O2 saturation 90% even with O2supplementation	0

A score ≤ 9 is required for discharge.

The sample size calculation was found as N > 45 based on the following criteria:

95% confidence limit, 80% power of the study and expected effect on isoflurane consumption ranging between 50-80% between the two studied groups. 1:1 ratio of group I to group II.

Statistical presentation and analysis was conducted by SPSS V.24. Results were expressed as means±standard deviation (SD). Student paired *t*-test: For statistical analysis within the same group. Unpaired *t*-test: Used for comparison of parametric data (age, weight, BMI, duration of anaesthesia, HR, MAP, Isoflurane consumption, recovery duration, time taken to extubate patients) between the two studied groups. Modified chi-square test for small numbers: for comparison between two groups as regards qualitative data (sex, ASA status & type of surgery).

Results

There was no statistical significant difference between the two groups as regard demographic data (age, sex, weight, BMI, duration of anaesthesia, ASA status & type of surgery) (Table 2). HR and MAP at different time of operation (Fig. 1A,B).

As regard comparison of isoflurane consumption between the two groups our results showed that BIS monitoring reduced consumption of isoflurane by 30% in the BIS group less than SP group. Also there was significant decrease in recovery time and time for extubation in BIS group (Table 3). As regard the relationship between the BIS index and recovery profile our study there was a significant negative correlation between BIS and both time to extubate the patients and recovery time. (Fig. 2A,B).

Data presented as mean ± SD as regard age, weight, BMI and duration of anaesthesia.

Data presented as number percent as regard sex, ASA status and type of surgery.

Table (2): Comparison of the demographic data and patients' characteristics between the groups.

		SP Group (n=45)	BIS Group (n=45)	*p*-value
Age (Years)	Mean ± SD	27.5±7.1	29.1±6.9	0.28
Weight (Kg)	Mean ± SD	79.3±9.5	82.15±9.50	0.16
BMI	Mean ± SD	24.3±2.9	24.9±2.5	0.32
Duration of anaesthesia	Mean ± SD	75.4±8.9	77.4±8.9	0.28
ASA status:				
ASA I	N (%)	31 (69%)	24 (53%)	0.83
ASA II	N (%)	14 (31%)	21 (47%)	
Sex:				
Female	N (%)	29 (64%)	31 (69%)	0.65
Male	N (%)	16 (36%)	14 (31%)	
Type of Surgery:				
Cholecystectomy	N (%)	21 (47%)	19 (42%)	0.82
Splenectomy	N (%)	4 (9%)	6 (13%)	
Epigastric hernia	N (%)	10 (22%)	8 (18%)	
Paraumbilical hernia	N (%)	10 (22%)	12 (27%)	

Table (3): Isoflurane consumption (ml) and recovery profile (minutes) in both groups.

	SP Group (n=45)	BIS Group (n=45)	*p*-value
Isoflurane consumption (ml)	27.7±1.9	19.3±1.9	<0.001 *
Time to extubate (minutes)	12.6±1	7.1±1	<0.001 *
Recovery time (minutes)	10.8±1	6.1±1	<0.001 *

*Data presented as mean ± SD.

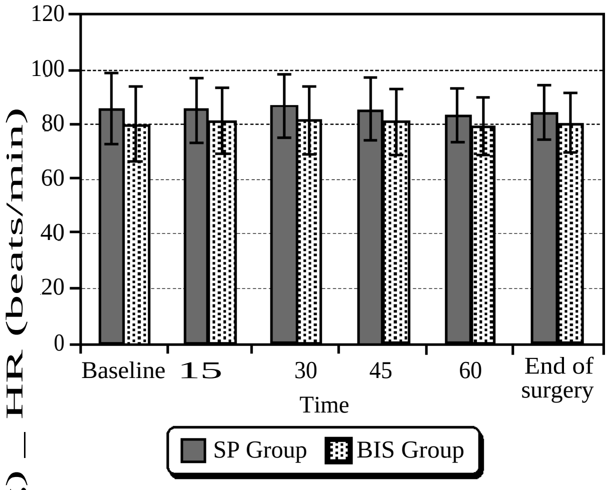

Fig. (1A): HR changes (beats/min) in the two groups.

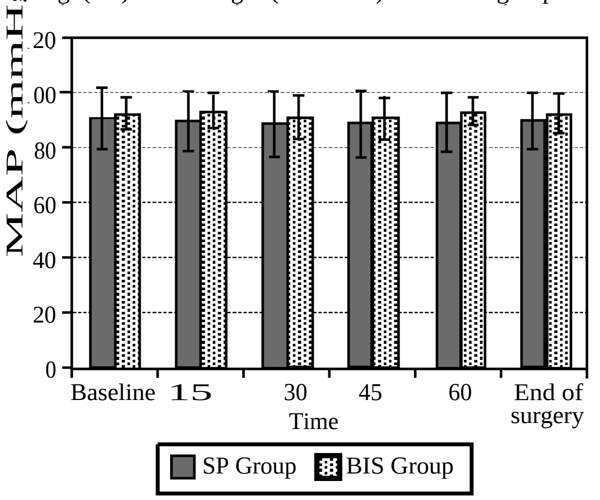

Fig. (1B): MAP changes (mmHg) in the two groups.

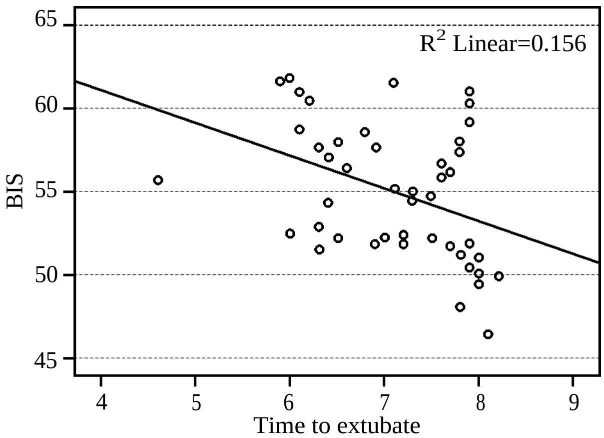

Fig. (2A): Scatter plot of time to extubate patients in BIS group.

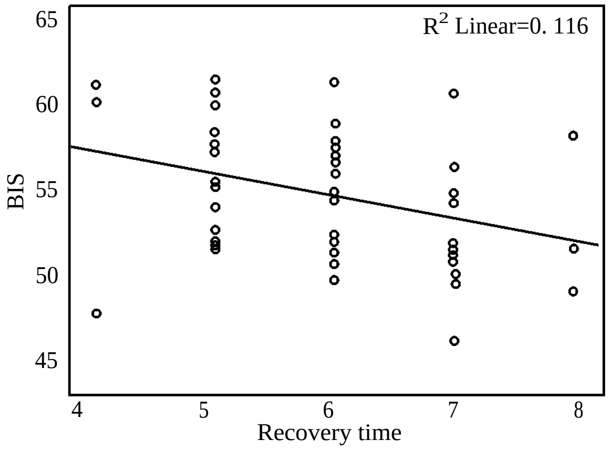

Fig. (2B): Scatter plot of recovery time in BIS group.

Discussion

Many anaesthesiologists rely on somatic signs (motor responses, changes in respiratory pattern) and autonomic signs (tachycardia, hypertension, lacrimation, sweating) to guide the dosages of anaesthetic agents in order to achieve the basic goals of anaesthetic management; that is unconsciousness (hypnotic effects), blockade of somatic motor responses, and suppression of autonomic responses to noxious stimulation. However, these clinical signs are not reliable measures of the conscious state of anaesthetized patients **[7]**. The use of these clinical signs in judging the dosages of anaesthetic agents can lead to either overdosage or underdosage, which can result in adverse effects due to too deep or too light anaesthesia **[7]**.

In the present study, there were no significant differences in demographic data and patients' characteristics of both groups regarding age, weight, BMI, gender, duration of surgery, ASA classification and type of surgery.

Concerning the comparison of isoflurane consumption between the two studied groups, the present study showed that BIS monitoring reduced consumption of isoflurane by 30 % less than SP group indicating that BIS monitoring is used successfully to titrate isoflurane.

It has been cleared that the Bispectral Index (BIS) may be used to titrate volatile anesthetics more precisely to individual anesthetic requirements than would otherwise be possible by usual clinical methods. This may potentially avoid exposure to unnecessarily high concentrations of anesthetics while at the same time minimizing the likelihood of awareness during anesthesia **[8]**.

In correspondence with our results, Guignard et al., [9] demonstrated 12-25% reduction in isoflurane consumption with bispectral index monitoring. Also, Wong et al., [10] showed 30% reduction in the total isoflurane usage in the BIS group in elderly western population undergoing elective hip or knee replacement. Moreover, Recart et al., [11] demonstrated that the use of an bispectral index monitor to titrate the volatile anesthetic resulted in significant reduction in the anesthetic requirement. Similarly, the meta-analysis of randomized controlled trials about the effect of bispectral index monitoring on ambulatory anesthesia and a cost analysis studied by Liu et al., [6] revealed that BIS monitoring decreased anesthetic consumption. Consistent with our results, Muralidhar et al., [12] observed that the consumption of isoflurane was 35.2% lower when adjusting BIS values between 45-55 in 40 adult patients undergoing elective off-pump CABG (coronary artery bypass graft) procedures. Moreover, Shafiq et al., [13] concluded that the use of BIS in 60 elderly Asian patients undergoing gynecological and general surgical procedures, which were expected to last for 2-6 hours, resulted in 40% reduction of isoflurane usage. Similarly, Chan et al., [14] studied the effect of BIS-guided anesthesia on postoperative delirium and cognitive decline in 60 elderly patients undergoing elective major non-cardiac operations and declared 30% decrease in the administration of volatile anesthetic when BIS was maintained between 40 and 60 during surgery. Also, coincide with our results, Punjasawadwong et al., [7] stated that BIS-guided anaesthesia reduced the requirement for volatile anaesthetics (desflurane, sevoflurane, isoflurane) by 0.65 minimal alveolar concentration equivalents (MAC) in 985 participants. On the contrary to our results, Bruhn et al. [15] investigated the impact of bispectral index (BIS) or middle-latency auditory evoked potential monitoring on recovery times and drug consumption when compared with standard anaesthetic practice during desflurane-remifentanil anaesthesia and concluded that BIS guided titration to the used target ranges did not result in a reduction of desflurane consumption during minor surgery with use of remifentanil compared with standard anaesthetic practice. Their results may be explained by the low mean BIS values used in their study and also, to the use of remifentanyl, moreover the type of surgery is different from our study. Moreover, Persec et al., [16] did not find any significant difference in analgesic consumption and anaesthetic gas delivery between the studied groups. This may be related to the use of fentanyl and nitrous oxide for intra operative analgesia which decreased the anaesthetic requirements in both groups of their study.

Recovery from anesthesia is a critical perioperative period from the perspective of both physiologic stability and patient satisfaction. Faster recovery can accelerate operating room turnover and reduce labor costs in the post-anesthesia care unit (PACU). Thus, delayed or complicated recovery from general anesthesia can have a considerable impact on patient safety, and cost of patient care [17].

As regard the relationship between the BIS index and recovery profile, the present study showed that the mean time taken to extubate the patients and the recovery time in group II (BIS) was significantly less than that in group I (SP) with significant negative correlation between BIS values and both time to extubate and recovery time in group II.

In accordance with our findings, with previous studies by Shafiq et al., [13], Persec et al., [16], Chan et al., [14] and Punjasawadwong et al., [7] suggesting that BIS-controlled anesthesia leads to faster extubation and improves recovery. Moreover, the Systematic review and meta-analysis by Oliveira et al., [18] about the Benefit of general anesthesia monitored by bispectral index compared with monitoring guided only by clinical parameters declared that BIS monitoring significantly decreased time for extubation and recovery duration.

Also, Kamal et al., [19] showed that time to discharge from PACU was faster in BIS group yet there was no difference in time for extubation. Also, our results are consistence.

In the contrary to our results, Ahmad et al., [20] performed their study on laparoscopic gynecological patient demonstrated that the application of the BIS monitor does not have a significant impact on the ability to successfully fast track outpatients. This may be explained by the use of different anaesthetic regime as in the BIS-monitored group, nitrous oxide was added to help to maintain the BIS value below 60, while in the non-BIS-monitored group, nitrous oxide was added if blood pressure and/or heart rate increased to more than 20% of awake values until completion of surgery. Also, Villafranca et al., [21] investigated the impact of bispectral index versus end-tidal anesthetic concentration-guided anesthesia on time to tracheal extubation in fast-track cardiac surgery and revealed that anesthetic management based on BIS guidance does not strongly increase the probability of earlier tracheal extubation in patients undergoing fast-track cardiac surgery. This can be explained by the difference in type of operation (cardiac patients) and different anaesthetic regime as they used sufentanyl and sevoflurane or desflurane. Also, Fritz et al., [17] . studied the postoperative recovery with Bispectral Index versus anesthetic concentration-guided protocols showed that the BIS protocol used in that study was not associated with improved recovery. This can be attributed to the potent volatile anaesthetic used as their trial included only patients at high risk for intraoperative awareness who had one or more of the following risk factors: Preoperative long-term use of anticonvulsants, opiates, benzodiazepines or cocaine, cardiac ejection fraction less than 40%, history of awareness with recall, history of difficult intubation or anticipated difficult intubation; ASA status IV or V, aortic stenosis; end-stage lung disease, marginal exercise tolerance not resulting from musculoskeletal dysfunction, pulmonary hypertension; planned open-heart surgery, and daily alcohol consumption which can explain the recovery delay.

As regard the hemodynamic parameters, there were no significant changes in mean values of HR and MAP in both groups at all-time of the study intervals compared to baseline and also no significant difference between both groups.

In agreement with our study, Guignard et al., [9] who studied the effect of BIS monitoring on isoflurane consumption in 80 patients undergoing various surgical procedures (with a target BIS range of 40-60), showed that the intraoperative HR and MAP values did not differ between the two groups. Also, Recart et al., [9] investigated the effect of cerebral monitoring on recovery after general anesthesia by comparing of the auditory evoked potential and bispectral index devices (with a target BIS range of 45-55) with standard clinical practice in 90 patients undergoing various laparoscopic surgical procedures and demonstrated that there were no significant differences among the three studied groups in the averaged hemodynamic variables during the surgery. Moreover, White et al., [22] studied the effect of Bispectral Index or Auditory Evoked Potential Index monitoring on recovery after desflurane anesthesia in 60 patients undergoing gynecological laparoscopic surgeries and concluded that during the maintenance period, the average hemodynamic variables did not differ significantly among the three study groups. Also, Persec et al., [16] studied the effect of bispectral index monitoring on extubation time and analgesic consumption in 45 patients undergoing major abdominal surgery with target BIS level of 50-60 and reported that there was no significant difference in heart rate and blood pressure levels during the whole investigation time.

The present study has some limitations one of which is that BIS-measurements are susceptible to sources of error. For example due to electromyography activity and electric device interference. Other possible shortcoming of our study was small sample size (n=90), also that it was confined to adults only excluding pediatrics and geriatrics. So, further studies should be performed on a larger sample size of patients and different type of surgeries for generalization of these results.

Conflicts of interest:

No conflicts of interest declared.

Authors' Contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing.

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أثر أستخدام مؤشر البايسبكترال على أستهلاك الأيزوفلوران ودلالات الإفاقة فى المرضى الخاضعين لجراحات تجويف البطن العلوى

مؤشر البايسبكترال أصبح معترف به عالمياً لقياس درجة عمق التخدير ويجب المحافظة عليه بين ٤٠ – ٦٠ لضمان عمق التخدير ومنع حدوث وعى أثناء الجراحة أو إستخدام جرعات زائدة من المخدر.

كان هدف الرسالة تقييم أثر أستخدام مؤشر البايسبكترال على أستهلاك الأيزوفلوران ودلالات الإفاقة فى المرضى الخاضعين لجراحات تجويف البطن العلوى. وتمت هذه الدراسة فى مستشفيات جا معة طنطا بين ٩٠ مريضاً ما بين عمر ١٨ و ٦٠ عا ماً وتم أخذ موافقة كتابية منهم للأشتراك فى البحث وتم تقسيمهم الى مجموعتين كل مجموعة ٤٥ مريضاً عند وصول المرضى غرفة العمليات تم متابعة المرضى برسم القلب الكهربائى وقياس ضغط الدم ومعدل ضربات القلب فى الد قيقة.

كان التخدير العام فى كلتا المجموعتين بإستخدام البروبوفول ١–٢ ملغ/ كغ والفنتانيل ١ميكورغرام/ كغ و سيساتركوريوم ٠.١٥ ملغ/ كغ من وزن الجسم . تم الحفاظ على التخدير بنسبة ٨٠٪ من الأكسجين و٢٠٪ من الهواء مع تدفق إجمالى من ٢ لترات فى المجموعة الاولى: تمت معايرة الأيزوفلوران أعتماداً على الممارسات القياسية للتخدير. فى المجموعة الثانية تمت معايرة الأيزوفلوران عن طريق تثبيت مؤشر البايسبكترال بين ٤٠–٦٠.

النتائج والمنا قشة: لا يوجد فرق معنوى فيما يتعلق بالبيانات الديموغرافية والعلامات الحيوية أثناء الجراحة .

من خلال الدراسة نستنتج أن أستخدام مؤشر البايسبكترال يؤدى الى تقليل أستهلاك الأيزوفلوران وتقليل فترة الأفاقة.