ORIGINAL ARTICLE

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Effects of Bispectral Index Monitoring During On-pump Coronary Artery Bypass Surgery on Intraoperative Opioid Use and Postoperative Recovery

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Abstract

Objective: Bispectral index (BIS) is a processed electroencephalogram that is extensively used to monitor intraoperative anesthetic depth. There have been studies on the effects of BIS monitoring during cardiac surgery on operative and postoperative results. However, these studies have reported different results. This study evaluated the effects of BIS monitoring on opioid use and postoperative recovery in patients undergoing on-pump coronary artery bypass surgery.

Methods: A total of 114 patients who underwent elective on-pump coronary bypass graft surgery were ultimately included in the study and were prospectively randomized into BIS (-) and BIS (+) groups (51 and 63 patients respectively). In BIS (-) group, fentanyl doses were given according to clinical parameters such as hemodynamic changes and follow up pupils. In BIS (+) group, fentanyl doses were adjusted to keep BIS levels between 40 and 50.

Results: There were no differences between the two groups with respect to age, sex, body mass index, smoking history and severity of comorbidities. Intraoperative fentanyl use was significantly lower in BIS (+) group; 2676±527.4 and 1632.5±325.5 in BIS (-) and BIS (+) groups respectively ($p<0.001$). The durations of postoperative intubation (10.5±2.7 vs. 8.05±2.9 h; $p<0.001$), intensive care unit (ICU) (2.8±0.9 vs. 2.4±0.7 days; $p=0.02$) and hospital (5.6±3.7 vs. 4.3±1.7 days; $p=0.03$) stays were also significantly shorter in BIS (+) group.

Conclusion: BIS monitoring during on-pump coronary bypass surgery decreases the need for opioid use during surgery. It is also associated with decreased time to extubation and shorter durations of ICU and hospital stays.

Keywords: Coronary artery bypass surgery, bispectral index, fentanyl, postoperative clinic effects

INTRODUCTION

Bispectral index (BIS) is a processed electroencephalogram (EEG) which is derived from the phase coupling of spontaneous EEG (1) and is extensively used to monitor anesthetic depth (1,2). The measurement of anesthetic depth is important for both titrating anesthetic drugs and for avoiding patient awareness during surgery. It has been suggested that the use of BIS monitoring during surgery decreases hypnotic drug use and results in faster recovery from anesthesia (3). The development of fast

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track cardiac anesthesia techniques has facilitated safe early extubation after cardiac surgery but the role of anesthesia depth monitoring in extubation and length of stay after cardiac surgery has not been well studied (4). There are studies about the effects of BIS monitoring during cardiac surgery on operative and postoperative results such as opioid use, time to extubation and recovery (5). However the evidence for better clinical outcomes is conflicting (1). This study evaluated the effect of BIS monitoring on opioid use and postoperative recovery in patients undergoing isolated on-pump coronary artery bypass surgery.

METHODS

After obtaining approval of University of Health Sciences Turkey, Istanbul Bagcilar Training and Research Hospital, Ethical Committee (ethical approval number: 2011/37) and written informed consent of participants, patients who underwent elective on-pump coronary bypass graft surgery were recruited for this prospective randomized study. The sample size for the study was estimated on the basis of the a previous study (6). Given a 5% two tailed significance level (α: 0.05) and power of 90%, 50 patients for each group were needed to detect differences in intraoperative fentanyl use between two groups. A total of 140 patients who had undergone elective on-pump coronary bypass graft surgery were recruited for this study. Patients requiring emergency operation, those with severe carotid disease, recent cerebrovascular event and renal/hepatic dysfunction (n=8) and who refused to participate (n=2) were excluded from the study. Patients (n=130) were randomized to two groups [65 patients in group BIS (-), 65 patients in group BIS (+)]. Randomization was performed using a sealed envelope method. Patients who required additional procedures such as valvular or aortic interventions (n=6) and intraoperative intraaortic balloon pump (n=10) were also excluded and 114 patients were ultimately enrolled (Figure 1).

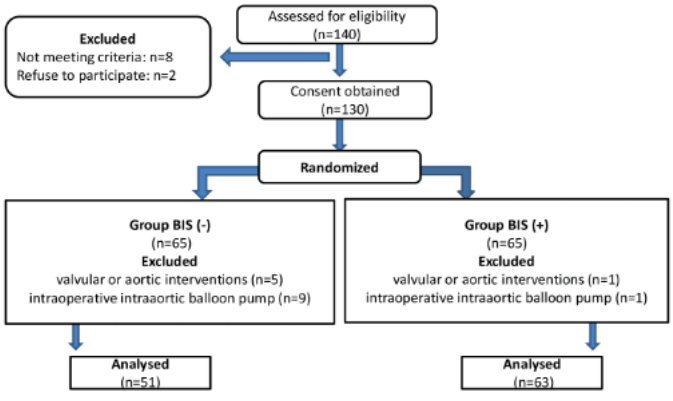

Figure 1. Study flow diagram
BIS: Bispectral index

All patients received oral 10 mg diazepam the night before surgery and premedication was done with midazolam 0.07 mg/kg intramuscularly 30 min before anesthesia induction. Routine monitoring with 12 lead electrocardiogram and pulse oximetry was performed. Additionally, the invasive arterial pressure was measured via a right radial artery catheter and recorded continuously. The BISTM monitor (A-2000 Aspect Medical Systems, Inc. Needham, MA, USA) probe was placed on the patients' foreheads (the proximal end of the BIS probe was placed forehead at the midline of the eyebrows, and the distal end was placed on the temple at eye level) and the basal values were recorded. BIS monitoring continued until the end of operation in BIS (+) group.

In both groups standard anesthesia induction technique was used with 7-10 µg/kg fentanyl, 0.1 mg/kg midazolam, and 1 mg/kg propofol for induction of all patients. Neuromuscular blockade was achieved by administering vecuronium bromide 0.1 mg/kg. Anesthesia maintenance was achieved with 1.5% sevoflurane, 50% oxygen, and 50% medical air. Sevoflurane concentration was adjusted to 1.5% in both groups to determine the difference between the groups in terms of the amount of fentanyl consumed in the perioperative period. Boluse doses of midazolam (0.1 mg/kg) and vecuronium bromide 0.1 mg/kg were repeated at the onset of cardiopulmonary bypass (CPB) and rewarming period. In BIS (-) group, depending on the clinical parameters such as hemodynamic parameters and follow-up pupils, bolus doses of fentanyl 5 µg/kg were administered. Insufficient depth of anesthesia was defined as an increase in systolic blood pressure of more than 15 mmHg, an increase in heart rate of more than 15/min, and concomitant mydriasis in BIS (-) group. However, in the BIS (+) group, bolus doses of fentanyl 5 µg/kg were adjusted to keep BIS levels between 40 and 50. Nitroglycerin (1 mg) was given in case where there was 20% increase in mean blood pressure for both groups if the level of BIS was within the normal range (40 and 50) in BIS (+) group, and despite the additional doses of fentanyl in BIS (-) group. Total amount of fentanyl used was recorded.

A double-lumen central venous catheter was inserted into the right internal jugular vein. Controlled mechanical ventilation was instituted to achieve an end-tidal CO_2 between 35 and 45 mmHg. Temperatures during CPB were maintained between 30 and 32 °C. After median sternotomy, standard methods of extracorporeal circulation and cold blood cardioplegic arrest were employed. Heparin was administered to achieve and maintain an activated clotting time >450 s. After termination of CPB, protamine 1-1.3 mg/100 units heparin was administered. At the end of the operation, the patients were monitored and

transferred to the cardiovascular surgery intensive care unit (ICU) on mechanical ventilation and were extubated after satisfying the criteria for extubation. The team following the patient in the ICU was blinded to the groups.

Statistical Analysis

Statistical analysis was performed using IBM SPSS statistics version 20 (IBM, Armonk, NY, USA). All data are presented as mean ± standard deviation for continuous variables, as numbers with percentage for categorical variables. Differences between categorical variables were tested using the chi-square test and Fisher exact test. In the comparison of two independent groups, the Student t-test was used for numerical variables with normal distribution. A p value of 0.05 or less was considered significant.

RESULTS

A total of 114 patients who underwent elective on-pump coronary bypass graft surgery were included in this prospective randomized study. Group BIS (-) included 51 patients and group BIS (+) included 63 patients. There was no difference between two groups with respect to age, sex, body mass index, smoking history, and severity of comorbidities such as cardiac, pulmonary, vascular and renal disease (Table 1).

The number of bypass grafts was higher and durations of aortic cross clamp and CBP were slightly longer in BIS (+) group although not significantly (Table 2). The inotrope use were not different between groups. The duration of operation (as measured by total anesthesia time) was statistically longer in BIS (+) group. In spite of that, intraoperative fentanyl use was significantly lower in BIS (+) group compared to the BIS (-) group (2676±527.4 vs. 1632.5±325.5, p<0.001). The durations of postoperative intubation, ICU and hospital stays were also significantly shorter in BIS (+) group (p<0.001, p=0.02, p=0.03 respectively, Table 2).

There was no mortality in any patient in the study. There was no difference in terms of drainage or complications. Atrial fibrillation developed in 2 patients in each group and sternal wound drainage was observed in 1 patient in BIS (+) group. Reexploration for bleeding was seen in 1 patient in BIS (-) group. But this patient was taken to the operating room 2 h after extubation and therefore, first extubation time was used for analysis and did not affect results.

Table 1. Demographic characteristics of patients

Variable	Group BIS (-) n=51	Group BIS (+) n=63	p value
Age (years) Ejection fraction BMI	59.3±11.3 50.14±8.3 27.8±4.1	62.06±10.1 49.9±8.1 28.9±4.2	0.1 0.8 0.1
Sex (n) Male Female	 38 13	416	0.5
Hypertension	33 (64.7%)	39 (61.9%)	0.2
Smoking	29 (56.9%)	32 (50.8%)	0.3
Diabetes mellitus	24 (47.1%)	26 (41.3%)	0.1
COPD	20 (39.2%)	22 (34.9%)	0.2
Previous MI	24 (47.1%)	20 (31.7%)	0.1
Peripheral arterial disease	3 (5.9%)	8 (12.7%)	0.4

BMI: Body mass index, BIS: Bispectral index, COPD: Chronic obstructive pulmonary disease, MI: Myocardial infarction

DISCUSSION

Patients undergoing cardiac surgery are a complex group with multiple comorbidities and present a special challenge for anesthesiologists. Extensive monitorization is usually necessary with sophisticated technologies (2). Brain monitoring and assessing depth of anesthesia are important order to decrease the incidence of awareness during surgery, to reduce time to awakening and overall anesthetic consumption and to provide surrogate information on cerebral perfusion. Several parameters have been used to assess the depth of anesthesia which include hemodynamics (7), pupillary reflex, and skin conductivity (8). The most reliable variables were derived from the EEG (9). The BIS is a processed EEG that has been investigated in different studies and is presently the most extensively validated measure of depth of anesthesia (9). The BIS reports a number from 0 to

Table 2. Operative and postoperative data of patients

Variable	Group BIS (-) n=51	Group BIS (+) n=63	p value
Duration of operation (min)	191.1±45.1	217.2±49.7	**0.008**
Duration of ACC (min)	52.9±25.8	62.3±28.01	0.06
Duration of CPB (min)	89.08±33.4	101.9±38.8	0.06
Number of coronary grafts	2.6±0.8	2.9±0.8	0.06
Fentanyl used (µg)	2676±527.4	1632.5±325.5	**<0.001**
Duration of intubation (hrs)	10.5±2.7	8.05±2.9	**<0.001**
Duration of ICU stay (days)	2.8±0.9	2.4±0.7	**0.02**
Duration of hospital stay	5.6±3.7	4.3±1.7	**0.03**
Drainage	565.6±281.8	559.1±215.9	0.05
Mortality	None	None	None

ACC: Aortic cross clamp, CPB: Cardiopulmonary bypass, min: Minutes, hrs: Hours, BIS: Bispectral index

100; 100 represents an awake state and 0 represents complete EEG inactivity.

The use of BIS monitoring during general anesthesia was associated with significantly reduced incidence of awareness (10) and many authors showed a correlation between BIS and level of awareness (11,12). Several studies have demonstrated that BIS monitoring can reduce anesthetic use and, consequently, the time to extubation and other recovery parameters in non-cardiac surgery (13,14). Taş et al. (15) showed that BIS monitorization can help avoid excessive anesthetic agent use and to faster recovery from anesthesia in patients undergoing thyroidectomy. However, in several other studies, BIS monitoring was not associated with better postoperative outcomes (16). In the B-Aware (17), B-Unaware (18), and BAG-RECALL (19) trials, the use of BIS monitoring was not associated with a reduction in the amount of anesthesia administered or a decreased hospital length of stay.

There are studies have examined the use of BIS monitoring in cardiac surgery (5) and there is still controversy about the effects of BIS monitoring on postoperative recovery. Villafranca et al. (20) performed a secondary analysis of the BAGRECALL trial and demonstrated that compared with management based on end-tidal anesthetic concentration, anesthetic management based on BIS guidance does not strongly increase the probability of an earlier extubation in patients undergoing fast-track cardiac surgery. They suggested that the decision for extubation was more influenced by patient characteristics and perioperative course than the assignment to BIS or end-tidal anesthetic concentration monitoring. Similarly, Vance et al. (4) showed no difference in time to extubation between BIS-guided and mean alveolar concentration-guided anesthetics in patients undergoing cardiac surgery. Moreover, their results showed no statistically significant differences in ICU and total post-operative hospital length of stay.

In this study, our results revealed a significant difference in intraoperative opioid use. Additionally, we observed statistically significant differences in time to extubation and durations of ICU and hospital stays. This difference is mainly the result of different anesthetic management techniques between our study group and previous studies. Most of these studies used only mean alveolar concentration in patients who were not monitored by BIS. In our study inhalation anesthetic technique was similar in two groups, whereas intravenous opioid use was based on BIS monitoring. Therefore, instead of hemodynamic parameters, BIS values were used to guide intravenous opioid usage and a significant difference was observed as a result. Another important factor may be a more homogenous patient group that includes only coronary artery bypass surgery. Other studies on patients cardiac surgery included all cardiac surgical procedures (4,5,20).

There are many factors that can affect postoperative recovery following cardiac surgery, including the development of low cardiac output, excessive bleeding, inotrope use, pre-existing comorbidities, prolonged surgical time, and excessive depth of anesthesia. In this study, the two groups were well matched in key areas. There were no significant differences between the groups in terms of preoperative comorbidities, ejection fraction, age, and sex (Table 1). There was also no difference in drainage, inotrope use or postoperative complications. The duration of operation was longer in BIS (+) group. Therefore, management of opioid use based on BIS monitoring remains an important factor for better postoperative results in our patients. Our study show that beneficial effects of BIS monitoring on both extubation times and ICU and total post-operative hospital length of stay.

Study Limitations

There were some limitations to our study. First, although other factors affecting postoperative recovery were similar in our patient group, studies with a higher number of patients must evaluate BIS monitoring as an independent factor for early extubation. Second, different anesthetic management strategies should be compared to determine the best management of cardiac surgery patients.

CONCLUSION

BIS monitoring during on-pump coronary bypass surgery decreases the need for opioid use. It is associated with decreased time to extubation and shorter durations of ICU and hospital stays. Further studies are recommended to evaluate BIS monitoring as an independent factor for early extubation and faster postoperative recovery after cardiac surgery.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Istanbul Bagcilar Training and Research Hospital, Ethical Committee (ethical approval number: 2011/37).

Informed Consent: Consent was received.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.G.Ö., A.P., K.E., Design: F.G.Ö., A.S., V.E., Data Collection or Processing: F.G.Ö., A.P., Analysis or Interpretation: F.G.Ö., N.K., S.D., Literature Search: F.G.Ö., N.K., S.D., Writing: F.G.Ö., N.K., S.N.Ş.

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