The Effects of Bispectral Index and Neuromuscular Blockade Monitoring on the Depth of Anaesthesia and Recovery in Cardiac Patients Under Desflurane Anaesthesia

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Objective: In this study, we aimed to investigate the effects of bispectral index (BIS) and neuromuscular blockade monitoring on the depth of anaesthesia and recovery in cardiac patients, scheduled to undergo open cholecystectomy operation with desflurane anaesthesia.

Methods: After the approval of the Ethics Committee and consent from the patients, patients were randomly divided into two groups. All patients received standard induction drugs, and 4-6% desflurane was used for maintenance of anaesthesia. In Group I, the anaesthesiologist was blind to BIS, and end-tidal volatile agent concentration (ETVAC) of desflurane was titrated according to the patients' hemodynamic changes. In Group II, ETVAC of desflurane was titrated to maintain BIS at 50-60. The hemodynamic data, BIS values, end-tidal volatile agent concentration (ETVAC) and train of four (TOF) values were recorded at pre-induction, post-induction, post-intubation, 1st and 5th minutes after surgical incision and then every 15 min. At the end of the operation, extubation time and the time to reach an Aldrete recovery score ≥ 9 were recorded in each group. Additionally, neuromuscular agent and narcotic agent doses were recorded.

Results: The BIS values were lower for Group I in all times, except pre- and post-induction times ($p < 0.05$). ETVAC values of all times were lower for Group II ($p < 0.05$).

Conclusion: The requirement of volatile agent, which was given according to BIS monitoring, was lower than in the standard technique, but it is considered not to affect the early extubation, recovery and neuromuscular agent requirement dependent on TOF monitoring.

Key Words: Bispectral index, desflurane, anaesthesia, recovery period

Introduction

Generally, clinical parameters, such as lacrimation, sweating and pupil size are used in monitoring the depth of anaesthesia. Some of these parameters are not reliable, as there can be alterations in these parameters by opioid and neuromuscular blocker use (1).

These methods can be considered as subjective measures; the most objective assessment method is electroencephalography (2). Bispectral index (BIS) is a processed electroencephalographic parameter measuring the hypnotic effects of anaesthetic and sedative agents on the brain (3, 4). Theoretically, along with the other parameters and clinical findings, use of BIS monitor to assess hypnosis, is much better to titrate the dose of hypnotic and analgesic drugs. Numerical expression of sedation and hypnosis using BIS provides clinical benefits (3-5).

The level of sedation and hypnosis can be monitored as a numeric value between 0 and 100 using a BIS monitor by the help of a sensor placed over the frontotemporal area; a value of 100 indicates that the patient is fully awake, 80 indicates light sedation, 60 moderate hypnotic state, and 40 deep hypnotic state (6).

Application of anaesthesia, surgical intervention and anaesthetic agents has multi-directional effects on the functions of circulatory system by affecting its various components. While diseases associated with the cardiovascular system affect anaesthesia, anaesthesia has also some effects on the cardiovascular system. This interaction becomes more important in patients with cardiovascular dysfunction (7).

In this present study, we aimed to evaluate the effects of bispectral index and neuromuscular blockade monitoring on the depth of anaesthesia and recovery in patients with cardiovascular dysfunction who had no previous history of cardiac surgery, undergoing elective open cholecystectomy with desflurane anaesthesia.

Methods

The present study was performed on a total of 100, American Society of Anesthesiologists (ASA) II-III patients between the ages of 30-65 years, having a cardiac problem but no previous history of cardiac surgery scheduled for elective open cholecystectomy under general

anaesthesia with desflurane. The study was started after approval was obtained from the Local Ethics Committee of Cumhuriyet University Medical School (Date: 20.06.2006 Decision number: 2006-5/7) and written informed consents were obtained from the patients. ASA III patients with decompensated heart failure or a history of myocardial infarction in the last 6 months, liver failure, chronic renal insufficiency, history of neurological and psychiatric diseases, respiratory system diseases, alcohol and drug use and history of allergy were excluded.

The present study was a double blind randomized controlled study. The patients were randomized into two groups according to the adjustment method of end-tidal concentration of the volatile anaesthetic (ETVAC) by drawing from sealed envelopes, which consisted group assignment during the preoperative assessment. Desflurane (Suprane, Baxter, USA) ETVAC was titrated according to hemodynamic responses in Group I (n=50) while it was adjusted by targeting BIS scores at 50-60 in Group II (n=50). A researcher other than the anaesthetist adjusting the ETVAC of desflurane recorded the BIS values in Group I.

All patients received intramuscular (IM) 0.07 mg kg⁻¹ midazolam (Dormicum, Roche Basel, Switzerland) as premedication 30 minutes before induction. Patients were taken to the operation room and monitoring including ECG, arterial blood pressure, heart rate, and peripheral oxygen saturation (Criticare, 1100, USA) was started. For monitoring the depth of anaesthesia, the skin of the forehead and temporal area was wiped with an alcohol pad and the proximal end of the disposable BIS electrode (BIS XP monitor, Aspect A 2000TM, USA) was applied to the middle of the forehead and the distal part was applied over the temporal area at the eye level. Neuromuscular monitoring (TOF-Watch SX monitor, Organon, Turkey) was performed with train-of-four (TOF) stimulation at 10-second intervals from the arm without the intravenous line, by placing electrodes over the path of the ulnar nerve. Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), peripheral oxygen saturation (SpO₂), end-tidal carbon dioxide pressure (ETCO₂), end-tidal volatile agent concentration (ETVAC), BIS and TOF values, were recorded before induction (BI), after induction (AI), after intubation (AINT), at 1 and 5 minutes after surgical incision and at 15-minute intervals afterwards.

Induction of anaesthesia was accomplished with 1 µg kg⁻¹ fentanyl (Fentanyl-citrate, Abbott, USA), 0.3 mg kg⁻¹ etomidate (Etomidate-Lipuro, Braun, Germany), 0.5 mg kg⁻¹ rocuronium (Esmeron, Organon, Netherlands). Intubation was performed after a neuromuscular blockade level of 0-5% was achieved. Maintenance of anaesthesia was accomplished with 50% O₂ + 50% N₂O + 4-6% desflurane. Controlled mechanical ventilation was adjusted to maintain a respiratory rate of 12-16 min⁻¹ and ETCO₂ of 35-40%. After induction, desflurane ETVAC was titrated according to hemodynamic responses in Group I (n=50). Desflurane ETVAC in Group II (n=50) was adjusted by targeting BIS scores between 50 and 60. Titration of anaesthetic dose was done according to a 20% increase or decrease in baseline HR and MAP values in Group I. In Group II, desflurane ETVAC was increased at BIS scores>60 and continued at this concentration until it was <60. If the BIS score<50, desflurane ETVAC was decreased and continued at this concentration until the score increased to values above 50. Rocuronium injections were applied when the response to TOF stimulation was 2 or above in both groups. Fentanyl was given by 25-50 µg IV bolus if HR and MAP showed 20% increase from the baseline value, provided that desflurane ETVAC was 4%. Total rocuronium and fentanyl doses used during the intervention were recorded.

Anaesthetic gases were discontinued 3 minutes after the last skin suture, and the time from anaesthetic gas discontinuation to extubation (extubation duration) and the time needed to reach an Aldrete recovery score ≥9 were recorded. In both groups, when the response to TOF stimulus was 3, reversal with 0.04 mg kg⁻¹ neostigmine was performed.

Statistical analysis

The data obtained was analyzed by SPSS (version 13.0) program. Student t test, Chi-square test, Fisher's exact Chi-square test, repeated measures analysis of variance with Bonferroni test were used in the statistical analysis. Data are presented as mean±standard deviation, subject number and percentage in the tables. The significance level was set at 0.05.

Results

There was no significant difference between the groups regarding the demographic data of the patients (Table 1).

No significant difference was found between the two groups in terms of anaesthesia duration, total opioid dose, total neuromuscular blocker dose, extubation duration, and the time to reach an Aldrete recovery score ≥9 (Table 2).

There was no significant difference between the two groups regarding MAP, HR, respiratory rate and SPO₂.

When the ETVAC of the two groups were compared, the ETVAC values of Group II at all time points was found to be significantly lower than that of Group I (p<0.05) (Figure 1).

When the groups were compared regarding the BIS values recorded at different time points, there was no significant difference regarding the values recorded before and after induction, however, the BIS values of Group I recorded at the other time points were significantly lower compared to that of Group II (p<0.05) (Figure 2).

In the comparison of the groups regarding the TOF values, no significant difference was found between the groups at any time point (Figure 3).

Discussion

Reduction of the risk of intraoperative awareness, use of hypnotic drugs according to individual patient needs and therefore reduction in the probability of over-dose or insufficient dose can be named among the benefits of using bispectral index. In addition, it has advantages like shortening of the recovery duration by maintaining the hypnotic level at 40-60. Sleight et al. (1), reported the sensitivity and specificity of BIS as 97.3%, and 94.4%, respectively. Kerssens et al. (8), in their study, suggested that the optimal depth of anaesthesia was at a BIS value of 40-60. While Vernon and colleagues (9) reported the mean BIS value as 55, Leslie et al. (10) reported this

Table 1. Demographic data of the groups

	Group I (n=50)	Group II (n=50)	p
Age (years)	55.58±8.24	52.68±8.70	0.568
Height (cm)	165.94±8.68	164.98±9.11	0.825
Body weight (kg)	70.54±12.99	72.28±13.52	0.610
ASA II/III	9/41	8/42	1.000
Gender (M/F)	20/30	19/31	1.000

Table 2. Duration of anaesthesia, total opioid and neuromuscular blocker doses, extubation duration, the time to reach an Aldrete Recovery Score ≥ 9

	Group I (n=50)	Group II (n=50)
Anaesthesia duration (min)	108.08 $\pm$ 42.83	113.74 $\pm$ 39.87
Total opioid amount (mg)	0.07 $\pm$ 0.03	0.08 $\pm$ 0.02
Total neuromuscular blocker amount (mg)	51.90 $\pm$ 15.28	51.70 $\pm$ 15.23
Extubation duration (min)	5.06 $\pm$ 2.45	4.94 $\pm$ 2.52
The time to reach an Aldrete score ≥ 9 (min)	8.00 $\pm$ 4.37	7.98 $\pm$ 3.82

Figure 1. End-tidal volatile agent concentration (ETVAC)

*: p<0.05

Ent.: Intubation, Ins. Son: After incision, dk: minutes

value as 57. BIS value is a single numeric value on a monitor, derived from EEG recordings at 10, 15 and 30 second intervals. As can be understood, BIS value is an indicator, always indicating the level of anaesthesia in the previous 10-30 seconds (1, 11).

In our study, the effects of the depth of anaesthesia and neuromuscular blockade monitoring under desflurane anaesthesia on recovery were evaluated in patients with cardiovascular dysfunction and without a history of heart surgery. The ETVAC values recorded at all time points in Group II patients were lower than that of Group I. This finding was interpreted as indicating that BIS monitor reflects the level of hypnotic depth correctly, allowing the use of appropriate dose of anaesthetic. In other words, it was interpreted that ETVAC determined based on the hemodynamic data in clinical practice may be higher than the patient needs. Ganidağlı et al. (12) found that ETVAC values were significantly lower five minutes after incision and at all the subsequent time points in the group, in which sevoflurane was titrated according to BIS monitoring in comparison to the standard group. Boztuğ and colleagues (13), in the study evaluating the effects of BIS monitoring on the quality of recovery after craniotomy surgery, found that the mean end-tidal sevoflurane concentration was significantly lower in the BIS group than that in the control group. Recart et al. (14), in the study evaluating the

Figure 2. Bispectral index (BIS) values

*:p<0.05

Ind: Induction, Ent.: Intubation, Ins. Son.: After incision, dk: minutes

Figure 3. Train-of four (TOF) values

Ent.: Intubation, Ins. Son: After incision, dk: minutes

effects of cerebral monitoring on volatile anaesthetic requirement and the quality of recovery, determined that the mean end-tidal desflurane concentration was significantly lower in the auditory evoked potential (AEP) and BIS groups than the control group. Pavlin et al. (15), in their study associated with BIS, compared the end-tidal gas concentrations of isoflurane and sevoflurane, and determined a non-significant decrease in isoflurane concentration (2.7%), and a significant decrease in sevoflurane concentration (4.7%).

In our study, Group I BIS values measured at different time points were significantly lower than that of Group II. This finding can be explained by the higher end-tidal desflurane concentration in Group I. The difference in BIS values was attributed to maintaining the BIS values at 50-60 for a long period in Group II. The presence of a significant difference in BIS and ETVAC values, but not in hemodynamic parameters, was interpreted as hemodynamic vari-

ables may not always indicate the depth of anaesthesia. Boztuğ et al. (13) similarly found that the BIS values were significantly higher compared to that in the control group during the maintenance of anaesthesia in patients undergoing craniotomy surgery. Similarly, Ganidağlı et al. (12) determined that the BIS values measured 5 minutes after incision and at the subsequent time points were significantly lower in the standard group, than that in the group that BIS monitoring was used. White and colleagues (16) in the study, in which evaluated the effects of BIS or AEP monitoring on recovery after desflurane anaesthesia, found that the mean BIS and AEP values were significantly lower in the control group, in comparison to BIS and AEP groups. They also indicated that end-tidal desflurane concentration in the BIS group ($2.7\% \pm 0.9\%$) and AEP group ($2.6\% \pm 0.9\%$) was significantly lower when compared to that of the control group ($3.6\% \pm 1.5\%$). Pavlin et al. (17) found similar results to our study.

Kreuer and colleagues (18), in their study which compared Narcotrend or BIS monitoring with the standard technique in desflurane-remifentanyl anaesthesia, contradicting to our results, found similar mean BIS values with the standard group. Recart et al. (14), in a study on the effects of cerebral monitoring on volatile anaesthetic requirement and quality of recovery, found that the mean AEP and BIS values measured during the maintenance of anaesthesia in the AEP and BIS groups were significantly higher in comparison to the control group.

In our study, duration of anaesthesia, total opioid amount, total neuromuscular blocker amount were similar in both groups. there was also a non-significant difference between the groups in terms of extubation duration and the time to achieve an Aldrete recovery score ≥ 9 . The presence of an inter-group differences in the depth of anaesthesia and end-tidal volatile agent concentrations necessitates recovery durations to be different. The absence of a difference between the groups regarding the recovery parameters was interpreted to indicate that neither TOF nor BIS monitoring had an impact on improving recovery. BIS monitoring was thought to be effective in the titration of the inhalation agent. The finding of similar recovery durations in both groups was attributed to TOF monitor-guided pharmacological antagonism in both groups and to the individual differences in the metabolism of desflurane. There are two types of publications in the literature about the effects of BIS monitoring on recovery duration; literature reporting shorter recovery durations and literature reporting similar recovery durations (18). Luginbühl et al. (19), in their study in which evaluated the effects of BIS monitoring on recovery and drug use in desflurane and propofol anaesthesia concluded that BIS monitoring decreased drug use and accelerate recovery in propofol anaesthesia but not in desflurane anaesthesia. Based on the results of our study, we also concluded that BIS monitoring did not improve recovery when compared to the standard technique in desflurane anaesthesia. Pavlin et al. (15) in a retrospective study in an academic medical institution on 1580 patients, found no difference between the BIS group and the control group regarding the recovery parameters, similar to our study. They concluded that the use of BIS monitor had a minimal effect on intraoperative anaesthetic use but not on recovery.

Ganidağlı and colleagues (12), in their study, contradictory to the results of the present study, found that the total neuromuscular blocker dose was significantly higher in the BIS group ($p < 0.05$). They thought that the higher total mivacurium dose in the BIS group might be associated with lower ET/VAC. The significantly lower extubation duration in the BIS group, was thought to be due to rapid ending of the effects of mivacurium, which is a short-acting

neuromuscular blocker, after discontinuation of anaesthetic gases delivered at low end-tidal concentrations. However, an intermediate acting neuromuscular blocker, rocuronium was used in this present study. The lack of a difference between the two groups regarding the total amounts of neuromuscular blockers and opioids was thought to result in similar recovery durations. White et al. (16) concluded that when compared to standard anaesthesia monitoring AEP and BIS monitoring improved desflurane titration and recovery profile during general anaesthesia. Similarly, Röhm et al. (20) found that BIS guided desflurane anaesthesia provided a more rapid recovery when compared to total intravenous anaesthesia technique involving propofol-remifentanyl.

In two other studies, in which bispectral index value was adjusted as 40-60 during the operation and between 60 and 75 at the last 15 minutes of intervention, a more rapid recovery was demonstrated in the BIS group than that in the control group (21, 22). These findings support the fact that mean BIS values during surgery are not correlated with recovery parameters and the BIS values increased at the last 15 minutes of intervention are correlated with the shortening of recovery duration. Cooper and Ebstein (23), in a similar study, emphasized that only BIS monitoring was not sufficient, and the BIS values should be increased at the end of the surgery.

In the present study, we kept the BIS levels at 50-60 in the BIS group and did not change it until the end of the surgery. If we had used higher BIS values near the end of surgery, we could have found that the extubation and recovery durations were shortened. In addition, the finding that end-tidal desflurane concentration was significantly lower in the BIS group would have led us to find a shorter recovery duration in this group. However, adjusting additional neuromuscular blocker dose according to TOF monitoring in both groups and the fact that total amounts of blocker consumption did not differ between the groups explain the similarity in recovery durations.

Conclusion

We suggest that volatile agent dose regulated according to BIS monitoring is lower than the volatile agent dose regulated according to the standard technique in patients with heart diseases undergoing desflurane anaesthesia; however, this discrepancy does not affect the extubation duration, recovery and neuromuscular blocker agent requirement associated with TOF monitoring.

Conflict of Interest

No conflict of interest was declared by the authors.

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Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Cumhuriyet University Faculty of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Author Contributions

Concept - A.P., K.K.; Design - K.K., C.D., İ.Ö.K.; Supervision - K.K., İ.Ö.K.; Funding - A.P., C.M.; Materials - A.P.; Data Collection and/or Processing - A.P., A.C.İ.; Analysis and/or Interpretation - K.K., C.D., İ.Ö.K., S.G., C.M.; Literature Review - A.P., A.C.İ., İ.Ö.K.; Writer - A.P., K.K.; Critical Review - C.D., A.C.İ., İ.Ö.K., S.G., C.M.; Other - C.D., A.C.İ., S.G., C.M.

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