

Original Article

Bispectral Index Monitoring Can Be an Effective Method to Assess Sedation Levels After Open-Heart Surgery

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ABSTRACT

Background: Proper sedation is the main part of patient management in post-cardiac surgery care units. The bispectral index (BIS) monitor is a noninvasive device that can show the sedation level of patients through electroencephalography processing. We aimed to study the role of BIS monitoring to assess sedation levels in patients after cardiac surgery in the post-cardiac surgery care unit.

Methods: This observational prospective cohort study enrolled 110 patients (37 female, mean age: 60 ± 13 y) candidated for open-heart surgery in Rajaie Cardiovascular Medical and Research Center. In the post-cardiac surgery care unit, sedation levels in 55 patients were monitored via BIS monitoring, while in the control group ($n = 55$), sedation levels were assessed via the Glasgow Coma Scale, the visual analog scale, and hemodynamic parameters. Both groups had the same sedation protocol. The primary endpoint of the study was the frequency of the prescription of analgesics, and the secondary endpoint was the duration of mechanical ventilation, intensive care unit (ICU) stay, and hospital stay. Data were collected and analyzed using SPSS software, version 22.

Results: The results showed a decrease in the consumption of dexmedetomidine, midazolam, and morphine in the BIS group ($P < 0.001$), but no significant difference was observed in terms of the use of ketorolac and paracetamol (Apotel) ($P > 0.05$). Also, in the BIS group, the duration of mechanical ventilation ($P < 0.001$), ICU stay ($P < 0.001$), and hospital stay ($P < 0.001$) decreased significantly compared with that in the BIS group.

Conclusions: BIS monitoring decreased the dose of sedative/analgesic drugs in the participants; it can, therefore, be a reliable method to assess sedation levels. (*Iranian Heart Journal 2021; 22(1): 49-56*)

KEYWORDS: Consciousness monitors, Intensive care units, Cardiac surgical procedures, Hypnotics and sedatives, Analgesics

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Sedation in the post-cardiac surgery intensive care unit (ICU) is necessary because all patients after a major surgical procedure need to be tranquilized with combined analgesics and sedatives with the least effects on hemodynamic status. Sedation assists in the control of anxiety and stress and prevents ischemia in the organs, which underscores the significance of striking a balance between over- and undersedation in patients.¹ Undersedation can cause hemodynamic instability, restlessness, anxiety, and post-traumatic stress disorders and may increase catabolism.² Oversedation can bring about hemodynamic instability, lengthened mechanical ventilation, ventilator-associated pneumonia, increased ICU and hospital lengths of stay, and increased medical costs.³ The ideal sedation enables the patient to remain calm, to feel comfortable, and to awake easily; in other words, over- and undersedation have been avoided. The level of optimized sedation differs depending on patients and their procedures.⁴ The measurement of the sufficiency of sedation can be troublesome because its related concepts such as pain, tranquility, restlessness, excitement, and irritability are subjective and difficult to measure.⁵

Thus far, 35 subjective scales have been introduced to measure sedation levels; nonetheless, the validity and reliability of all of them still need proper confirmation.⁶ One of the devices for measuring the depth of sedation is the bispectral index (BIS) monitor.⁴ The BIS monitor is a noninvasive device that utilizes electroencephalography (EEG) processing in order to display sedation levels.⁷ BIS monitoring confers an objective measurement of patients' response to sedation and their brain activity.⁸

Traditionally, intensivists use vital signs, the Glasgow Coma Scale (GCS), hemodynamic status, and clinical judgment to determine sedation levels. Indeed, in the absence of

specific criteria for the objective determination of sedation levels to adjust the dosage of sedative drugs, there may be overly high and low doses of sedation, increasing the side effects of drugs, the duration of mechanical ventilation, hospital and ICU lengths of stay, hospitalization costs, and workload on nurses. Studies have suggested that BIS monitoring provides intensive care personnel with an objective criterion for determining sedation levels with a view to preventing over- or undersedation. This objective monitor can assist physicians and nurses in adjusting the dosage of sedative drugs depending on the patient's need in the ICU by keeping sedation at a certain level. That is why some studies have found this technology helpful, economical, and applicable for easily monitoring sedation levels in the ICU.⁹ Nonetheless, to the best of our knowledge, there is currently a paucity of data on BIS monitoring after cardiac surgery to assess sedation levels and to adjust the dose of sedative drugs. Accordingly, we designed the current study to investigate the possible role of BIS monitoring in assessing sedation levels and decreasing the use of sedative/analgesic drugs in patients after cardiac surgery in the post-cardiac surgery ICU.

METHODS

Study Design

The present observational prospective cohort study was conducted in Rajaie Cardiovascular Medical and Research Center (RCMRC), a large tertiary care hospital in Tehran, Iran. The study protocol was approved by the Research Review Board and the Ethics Committee of RCMRC (code: RHC.AC.IR.REC.1396.19). All the patients signed the informed consent form.

Population

Between June 2017 and January 2018, a total of 110 consecutive patients who were candidates for elective open-heart surgery were enrolled. The inclusion criteria were comprised of age between 30 and 70 years, preoperative left ventricular ejection fraction of 30% or more, no history of previous cerebrovascular events, no history of alcohol addiction or substance abuse, aortic cross-clamp time of 100 minutes or shorter, cardiopulmonary bypass time of 120 minutes or shorter, total anesthesia time of 10 hours or shorter, and a maximum total of 4 vascular grafts (in cases undergoing coronary artery bypass graft surgery). The exclusion criteria consisted of any serious adverse events during and after surgery including the need for intra-aortic balloon pumps, neuro- and cerebrovascular events, reoperation, low output syndrome, severe arrhythmias, acute kidney injuries, re-intubation, pneumothorax, bleeding of 100 mL or more per hour, cardiopulmonary resuscitation, and death.

Exposure and Comparison

In this observational cohort study, exposure was considered to be the assessment of sedation levels by using BIS monitoring in the post-cardiac surgery ICU.

The BIS monitor is a noninvasive device that uses EEG processing so as to display sedation levels under mechanical ventilation. It consists of a flexible sensor placed on the patient's forehead and temporal skull and a monitor that shows the sedation scale. The scale ranges from 0 to 100, with 0 showing the brain inactivity, 95 to 100 complete, 80 to 90 light, 70 to 80 moderate, 60 to 70 deep sedation, and 40 to 60 general anesthesia surgical plans.⁷ In the exposed group (the BIS group), sedation levels were recorded hourly for up to 12 hours. In this study, we used the BIS Quatro (4 electrodes) Sensor (USA).

The comparison was to monitor sedation levels subjectively through a combination of

vital signs, GCS, the visual analog scale (VAS) for pain monitoring, and hemodynamic status.

Outcomes

The primary endpoint of the study was the frequency of the prescription of analgesics, and the secondary endpoint was the duration of mechanical ventilation (intubation), ICU stay, and hospital stay.

Study Conduct

All the candidates for elective cardiac surgery were assessed for the study inclusion criteria the night before the operation by the co-authors (anesthesiologists). Patients were registered, and their demographic data including age, gender, and left ventricular ejection fraction were recorded. They were followed during surgery and in the post-cardiac surgery ICU. In the case of the occurrence of any of the exclusion criteria, the patient was excluded from the study. Ultimately, 110 patients remained in the study, and 55 of them were assessed via BIS monitoring. The application of BIS monitoring for sedation and analgesia assessments was based on the facilities in the post-cardiac surgery ICU and the anesthesiologists' clinical decision.

Anesthesia Protocol

At the anesthesiologist's discretion, promethazine (50 mg) and morphine (10 mg) half an hour before surgery were injected intramuscularly to the patients. All the patients had the same anesthetic protocol and underwent cardiopulmonary bypass for open-heart surgery. The duration of cardiopulmonary bypass, aortic cross-clamping, and anesthesia, as well as the type of surgery, was recorded.

Sedation Protocol

The protocol of analgesia/sedation in the BIS group was 400 µg of dexmedetomidine

(Precedex) and ketorolac infused at a minimum rate of 4 mL per hour upon the arrival of patient at the ICU. Midazolam was also injected at a bolus dose of 10 mg. The mentioned drug protocol was administered until sedation levels reached between 70 and 80. Nevertheless, if the BIS monitor showed more than 80, a 4 mL bolus of dexmedetomidine and ketorolac was injected. If restlessness and pain were not alleviated (ie, the score of VAS was over 3–5 and the BIS score would not decrease), the minimum arterial O₂ saturation was 95%, the mean blood pressure was greater than 65 mm Hg, and there was no significant bleeding, 3 mg of morphine sulfate and 3 mg of midazolam were injected. A day after surgery, in the event of pain, an infusion of 1 g of paracetamol (Aptel) was done every 8 hours.

In the non-BIS group, the injection of dexmedetomidine and ketorolac was done similarly based on the protocol. If pain was not alleviated based on VAS, GCS, and hemodynamic status, in cases without hypoxia, hypotension, and acute anemia, the infusion pump was bolus-injected pro re nata/as required (PRN). If pain and restlessness persisted, 3 mg of morphine and 3 mg of midazolam were injected. A day after surgery, in the event of pain, 1 g of paracetamol was infused every 8 hours PRN. All the patients were extubated according to a standard protocol. If the patient had a stable cardiovascular condition and no bleeding, the fraction of inspired oxygen (FiO₂) was reduced by 40% to 50%; then, the respiratory rate was decreased to 4 breaths per minute and pressure support to 6 to 8. If the aforementioned conditions were met and the patients had stable hemodynamic conditions, they were detached from the device and extubated after suctioning by the anesthesiologist.

Statistical Analysis

The fitness of the interval data to normal distribution was assessed using the one-sample Kolmogorov–Smirnov test. The data were described as the median (interquartile range, IQR) for the interval and the count (%) for the categorical variables. Comparisons between the groups were performed using the Mann–Whitney *U* and the Pearson χ^2 tests. A multivariable analysis was performed using logistic and multiple linear regression models. A *P* value of 0.05 or less was considered statistically significant. The statistical analyses were conducted using IBM SPSS Statistics 22 for Windows (IBM Inc, Armonk, NY).

RESULTS

Background Characteristics

A total of 110 patients (37 female, mean age = 60 ± 13 y, range = 30–70 y) were enrolled and equally distributed into 2 groups: the exposed group (BIS monitoring) and the unexposed group (non-BIS). Overall baseline data were similar between the 2 groups; nevertheless, because of the dissimilarities in the patients' clinical situations, there were differences between the groups concerning operation duration, anesthesia duration, cross-clamp duration, pump duration, and drainage volume were different between the study groups. The data are presented in Table 1.

Sedative Drugs

The primary endpoint of the study was the relative frequency of the use of sedative/analgesic drugs prescribed in the post-cardiac surgery ICU. In Table 2, the use of these drugs is compared between the 2 study groups. It was found that BIS monitoring might lead to a decrease in the frequency of using dexmedetomidine, midazolam, and morphine sulfate significantly ($P < 0.05$). The odds ratios suggested a considerable preventive role for BIS monitoring in the prescription of the

abovementioned drugs (odds ratio [OR]: 0.07 to 0.15). The multivariate analysis showed that potential confounders had no significant effect on this association, and the adjusted OR was similar to the crude OR (Table 2).

Secondary Endpoints

Ventilation (intubation) time and ICU and hospital lengths of stay were the secondary endpoints of the study. Table 3 shows that the median of intubation time and hospital stay was smaller in the BIS group. The difference was also significant for ICU stay,

although it was not clinically important. After adjustments for potential confounders via regression models, *t* was cleared, meaning that the negative association between BIS monitoring and hospital stay was stronger than the association between BIS monitoring and intubation duration ($\beta = -3.1$ vs -1.6). The association between BIS monitoring and ICU stay was negative and significant ($P < 0.05$), albeit weak ($\beta = -0.3$) (Table 3).

Table 1: Comparisons of the background data between the study groups

	BIS Group (n=55)	Non-BIS Group (n=55)	P value
Age (y)	59(50 - 69)	62(58 - 68)	0.25
Ejection fraction (%)	40(35 - 45)	40(40 - 50)	0.173
Gender (F/M)	18/37	19/36	0.840
Type of Operation			0.113
Valve replacement	2(3.6%)	6(10.9%)	
Coronary artery bypass	41(74.6%)	36(65.5%)	
Placement of ventricular aids	2(3.6%)	2(3.6%)	
Repair of congenital abnormalities	3(5.5%)	0(0%)	
Valve replacement + coronary artery bypass	7(12.7%)	11(20%)	
Operation duration (h)	4.3(3.45 - 5.3)	5.2(4.2 - 6.2)	0.01
Anesthesia duration (h)	5(4.2 - 6)	6(5 - 7)	0.005
Cross-clamp duration (min)	33(28 - 42)	40(29 - 54)	0.016
Pump duration (min)	65(50 - 80)	72(55 - 90)	0.12
Drainage volume (cc)	45(30 - 65)	55(35 - 75)	0.028

Data are presented as the median (IQR) or the count (%).
BIS, Bispectral index

Table 2: Comparisons of the sedative/ analgesic drugs prescribed in the post-cardiac surgery care unit between the study groups

	BIS Group (n=55)*	Non-BIS Group (n=55)*	P value	Crude OR	Adjusted OR**
Dexmedetomidine	34(61.8%)	52(94.5%)	<0.001	0.09 (0.03-0.34)	0.12 (0.03-0.45)
Midazolam	20(36.4%)	49(89.1%)	<0.001	0.07 (0.03-0.19)	0.07 (0.03-0.21)
Morphine sulfate	9(16.9%)	31(56.4%)	<0.001	0.15 (0.06-0.37)	0.15 (0.06-0.39)
Ketorolac	54(98.2%)	55(100%)	>0.999	0 (0- ∞)	0 (0- ∞)
Apotel	37(67.3%)	34(61.8%)	0.550	1.27 (0.58-2.78)	1.64 (0.69-1.84)

* Data are presented as the count (%).

** binary logistic regression model adjusted for: operation duration, anesthesia duration, cross-clamp duration, pump duration, and drainage volume
BIS, Bispectral index

Table 3: Secondary endpoints analysis

	BIS Group (n=55)*	Non-BIS Group (n=55)*	P value	Adjusted Coefficient (SE) **
Intubation time	8(6.2 - 9.15)	10.15(9.3 - 11)	<0.001	-1.6 (0.4)
ICU stay	3(3 - 3)	3(3 - 4)	<0.001	-0.3 (0.1)
Hospital stay	11(10 - 14)	15(13 - 18)	<0.001	-3.1 (1)

* Data are presented as the median (interquartile range).

** coefficients in the multiple linear regression model adjusted for: dexmedetomidine use, drainage volume, morphine use, cross-clamp duration, anesthesia duration, and midazolam use
BIS, Bispectral index

DISCUSSION

The findings of the current prospective observational cohort study suggested that the use of BIS monitoring for the assessment of sedation levels in patients in the post-cardiac surgery ICU could decrease the dose of prescribed analgesic/sedative drugs and lower intubation time and hospital stay. These results remained consistent after we made adjustments for the effects of potential confounding factors in the study.

The monitoring for hemodynamic status and the cardiovascular system in patients after cardiac surgery is an important issue because both are affected by sedation levels because over- or undersedation can lead to hemodynamic instability and respiratory and neurological damage. There are standards to guide anesthesiologists for patient management in this regard.¹⁰ All patients after cardiac surgery must be assessed routinely for consciousness levels, pain, and hemodynamics via GCS and VAS. The selection of appropriate sedative and analgesic drugs after major surgeries and their optimization should be performed according to standard protocols. What is deserving of note, however, is that BIS monitoring is not included in standard monitoring systems in ICUs because it cannot definitely determine pain levels in patients. Be that as it may, it appears that monitoring the electrical activity of the brain via BIS monitoring may provide useful data

to keep the patients' sedation levels at an acceptable level and estimate the dose of sedative/analgesic drugs correctly. In this study, we sought to investigate the possible efficacy of BIS monitoring in maintaining sedation levels after cardiac surgery at an optimum level and we obtained satisfactory results.

Some previous studies have evaluated the effects of BIS monitoring on the dose of sedatives, opioids, and non-opioids. A study by Oslon¹¹ on mechanically-ventilated neurologic patients showed that the dose of propofol decreased significantly in a group whose sedation levels were measured via BIS monitoring compared with the control group. An investigation by Kaplan and Baily¹² on the effects of BIS monitoring on the dose of paralytic and sedative drugs showed that the BIS device made the study patients forget traumatic events somehow and lowered the dose and cost of the drugs. Alteba Tena et al¹³ studied the effect of BIS monitoring on the dose of sedatives and concluded that there was no significant difference between BIS monitoring and the Richmond Agitation Sedation Scale (RASS) groups in terms of the dose of propofol, morphine, and midazolam. In a clinical trial performed by Weatherburn et al,¹⁴ it was concluded that BIS monitoring did not decrease the dose of sedative drugs.

The present study suggests a significant decrease in the use of dexmedetomidine, ketorolac, midazolam, and morphine with

the use of the BIS monitor. The cumulative effect of sedatives and metabolites appears commonly in ICUs, especially in the case of liver or kidney failure. The effects of induced opioid drugs usually disappear as an alternative for clearance with redistribution. Consequently, low-clearance drugs prescribed continuously as the form of infusion may cause drug accumulation and oversedation. The excessive increase in sedation may be caused by disusing and misusing a measure for sedation or using an improper measurement. Also, it may be caused by the ongoing use of sedative and analgesic infusions or the intravenous bolus in a large quantity and for a long time.

The simultaneous prescription of several opioid and sedative drugs may exacerbate the synergetic effects of drugs and lead to the loss of consciousness, slow healing of wounds, slow motion of the digestive system, increasing the need for essential tests, and increasing ventilator-dependent pneumonia. Drug accumulation and oversedation can decrease the use of the accurate measurement of sedation such as BIS monitoring, which shows an objective measure of sedation levels. Based on the results of the current study, BIS monitoring reduced the dose of sedative drugs and opioids but did not have an effect on a non-opioid, Apotel. The dose of Apotel was the same in both groups and did not show a significant difference. What should be taken into consideration in this regard is that these kinds of drugs are merely used for alleviating pain and they have no effect on sedation levels, so the measured BIS did not play a dramatic role in changing the dose of Apotel in both groups. Non-opioid sedative drugs may alleviate pain in patients, but they do not play a part in reducing stress and restlessness: it means that they exert no effect on sedation levels in patients. Although ketorolac is a non-opioid sedative drug, its dosage was significant; as a result,

we can conclude that ketorolac in the drug protocol should be injected as a bolus and in combination with dexmedetomidine sedatives. In this regard, the prescription of Apotel depends upon the demanded effect of dexmedetomidine on minimizing restlessness and the BIS scale.

CONCLUSIONS

We observed that BIS monitoring decreased the prescription of sedative/ analgesic drugs in our patient population after cardiac surgery in the ICU. BIS monitoring can, therefore, be a reliable method to assess the patient's sedation levels and conditions. It is necessary to conduct clinical trials in order to provide high-level evidence and apply the findings in the guidelines.

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