

Original Article

Bispectral Index in Poisoning Cases with Multi-drug Ingestion: A Predictable Role for Early Endotracheal Intubation

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INTRODUCTION

Patients with mixed drug poisoning are still a challenging concern for emergency medicine practitioners. Many poisonings result from an intentional and unintentional overdose of neurological and psychiatric drugs and sedatives, and antidepressant drugs are among the most common causes of loss of consciousness and Coma.^[1,2] Accurate assessment of consciousness level in these patients is an important concern in determining the need to endotracheal intubation. To determine the level of consciousness different methods such as Glasgow Coma Scale (GCS) and bispectral index (BIS) can be used. Due to the

ABSTRACT

Objective: Bispectral index (BIS) is one of the several methods used to monitor the depth of anesthesia. Poisoning with ingestion of different drugs is one of the most common poisonings that have different clinical signs from drowsiness to coma. This study was performed to compare the BIS index number in poisoned patients with multi drugs ingestion with or without the need for endotracheal intubation.

Methods: This cross-sectional study was performed on poisoned patients with ingestion of different drugs referring to Clinical Toxicology Department of Noor University Hospital, Isfahan, Iran. The clinical signs and symptoms and the vital signs at the admission time were measured, and the required therapies were given. The endotracheal intubation was done for patients who had the indication of intubation. BIS was monitored and compared for all patients with or without a need for intubation on the admission time and time of endotracheal intubation. Obtained data were analyzed by SPSS software. **Findings:** At the admission time, the mean (standard error [SE]) BIS index value for poisoned patients who needed endotracheal intubation was 66.47 ± 2.57 in comparison with 85.21 ± 1.47 for patients who did not need intubation ($P < 0.001$). The results of receiver operating characteristic curve (mean \pm SE) showed the discrimination was excellent for BIS (0.899 ± 0.04 ; 95% confidence interval: 0.81–0.98) ($P < 0.0001$). BIS < 79.5 had the sensitivity 88% and specificity 87% for endotracheal intubation. **Conclusion:** BIS is an appropriate index for prediction of the need to intubation in poisoned patients with ingestion of different drugs.

KEYWORDS: Bispectral index, coma, consciousness, endotracheal intubation, poisoning

lack of patient's cooperation in the eye and verbal contributions, determination of the consciousness level with GCS may confuse the physicians.^[3] However, this evaluation is important and valuable for considering the need for intubation, sufficient oxygenation, and treatment procedures.^[4]

Bispectral analysis is considered as a signal processing methodology which judges the connections between signal components and records harmonization within

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signals, such as Electrocardiograms (EEGs). By quantifying the correlation between all the repetitions inside the signal, the bispectral analysis allows an additional EEG facet of brain action. The BIS is utilized in association with other physiological monitoring measures such as electromyography (EMG) to assess the depth of anesthesia for minimizing the probable occurrence of intraoperative consciousness.^[5] The BIS monitor presents a single dimensionless figure, which varies from zero (which means EEG silence) to one hundred. A BIS number between forty and sixty represents an appropriate level for general anesthesia.^[6]

Poisoned patients are usually referred to the hospitals with the sign of a decreased level of consciousness. Sedative and/or hypnotic drugs alone or in combination with other drugs can be the most common causes of loss of consciousness and coma. Since by BIS monitoring, there is the possibility of determining the anesthesia depth and titration of drugs, some side effects such as nausea and vomiting can be prevented and the recovery time of patient also can be decreased.^[7] This index has been used as a reliable tool to determine the depth of consciousness, management, and treatment in patients poisoned with Alprazolam.^[8] Sandler and Sparks have previously reported a significant relationship between the objective BIS values and subjective values of Observer's assessment of alertness/sedation scale (OAA/S scale) with sedative and anesthetic medications such as midazolam, fentanyl, and propofol.^[9] It is also reported that BIS monitoring may reveal the effect of oral diazepam premedication.^[10]

Since mixed drug poisoning^[11,12] is the most common cause of poisoning in patients admitted to our clinical toxicology department and there are few studies considering BIS in poisoning cases for determining the level of consciousness,^[13,14] using a method with the ability to assess the consciousness level and determine the need for intubation, is necessary. Therefore, we aimed to evaluate if the BIS score could be used to assess a patient's level of consciousness and to identify the range of BIS scores according to a patient's need to intubation in patients with mixed drug poisoning.

METHODS

We conducted a cross-sectional study in the Toxicology Emergency center of Noor and Ali Asghar University Hospital, Isfahan, Iran, in 2014. Inclusion criteria were adult patients (older than 19 years old), and poisoning due to the ingestion of different types of drugs. Patients who discharged with his own consent were excluded from the study. A written informed consent was obtained from the first-degree family members of the patients.

On admission, endotracheal intubation was undertaken at the discretion of the attending anesthesiologist in accordance with the institutional approach outlined previously.^[15] It was performed for patients with coma who were unable to protect their airway and those with respiratory rate <12 without any response to naloxone administration. Patients were classified into two groups according to the need for endotracheal intubation: Group N: patients who did not require endotracheal intubation; and Group I: Patients who required intubation.^[15] Gastric evacuation and activated charcoal administration were performed for the patient in accordance with our local guidelines as well.^[15]

All patients were monitored by pulse oximetry, EEG, noninvasive blood pressure device, and thermometer. EMG, mean body temperature and the quality of BIS signal perception signal quality index (SQI) were also measured at the times of evaluation.

For all patients, the demographic data, vital signs, and level of consciousness were recorded on admission time. For groups, BIS was measured on admission, and at the time of intubation of Group I. Discrimination was tested using the receiver operating characteristic (ROC) curve and by comparing the area under the curve (AUCs) and its standard error (SE).^[16] AUC between 0.7 and 0.8 was considered "acceptable" and AUC between 0.8 and 0.9 was considered "excellent" discrimination. For BIS the sensitivity, specificity, and the best cutoff point were determined. Data were analyzed using SPSS software version 20 (SPSS, Inc., Chicago IL, USA), for Windows. All continuous quantitative data were reported as mean \pm SE or standard deviation (SD) were appropriate. Statistical analyses were with independent *t*-test, Chi-square, or Fisher's exact test and variance analysis with repetition of observation. $P < 0.05$ was considered as statistically significant.

RESULTS

Fifty-eight patients poisoned with different mixed drugs who were hospitalized in the emergency room of Noor University Hospital during the study. The average age of patients was 33.6 (\pm 8.9 SD) years. Patients' age was ranging from 21 to 68 years old. The majority of patients were male ($n = 34$) and under 40 years old (77.6%). During their hospitalization, 25 patients (43.1%) needed endotracheal intubation [Table 1].

According to the result of *t*-test analysis, there was no significant difference in the mean age mean time interval between drug ingestion and the first treatment intervention between two groups. Furthermore, there was no significant difference in distribution frequency of gender, kind of poisoning, and vomiting after drugs

ingestion between groups. Both groups were similar with respect to frequency of gastrointestinal [Table 1].

The mean (SE) BIS index at the admission time in nonintubated patients was 85.21 ± 1.74 and in those patients received intubation was 66.47 ± 2.57 . According to the *t*-test, this value was significantly lower in intubated poisoned patients ($P < 0.001$) [Table 2]. Patients evaluated for the need to intubation on admission time based on the local guideline. Then, comatose patients received naloxone as coma cocktail. Those who did not respond to naloxone, intubated. Hence, the level of consciousness and respiratory rate and therefore need

to intubation was different between admission time and after naloxone administration. In the Group I, mean (SE) BIS index at the time of intubation was 71.65 ± 2.42 which was significantly more than this value at admission time ($P < 0.001$) [Table 3].

The mean heart rate (SE) at the admission time in the nonintubated group was 87.30 ± 3.02 and in the intubated group was 80.04 ± 5.06 . According to the *t*-test, this difference was significant ($P < 0.001$). At the admission time, mean systolic blood pressure was significantly lower in patients who were intubated later in comparison with nonintubated patients. However, at the time of intubation, these patients had significantly higher systolic blood pressure ($P < 0.001$). Mean diastolic blood pressure was significantly different between two groups at the admission and intubation time ($P < 0.001$).

There was a significant difference in mean EMG index at the admission time between two groups. In addition to the Group I, there was a significant difference in mean EMG index between the time of their admission and intubation time ($P < 0.001$) [Tables 2 and 3].

The results of ROC curve showed the discrimination was excellent for BIS (0.899 ± 0.04 ; 95% confidence interval: 0.81–0.98) ($P < 0.0001$). BIS < 79.5 had the sensitivity 88% and specificity 87% for endotracheal intubation.

With respect to outcome, most patients survived without complications in both groups (78.8% in nonintubated patients vs. 64% in intubated patients. Seven patients died (three in nonintubated and four in intubated patients).

DISCUSSION

The purpose of this study was to compare the BIS index of patients with mixed drugs poisoning with and without the need to endotracheal intubation. We studied 58 patients with different mixed drugs poisoning, and 25 patients needed endotracheal intubation.

Patients in both groups of with and without the need to intubation had no significant difference with respect to their demographic variables, type, and method of poisoning, decontamination, and the time interval between ingestion and admission.

In those patients who needed endotracheal intubation, mean BIS index was significantly lower at the admission time. Therefore, this may suggest that BIS index at the time of admission to hospital may be an appropriate index for prediction of intubation and other therapeutic interventions.

In our study, the significant difference in changes of some parameters such as SQI, EMG, systolic blood pressure,

Table 1: Comparison of different variables between two groups of patients with mixed drug poisoning

Variable	Total (n=58)	Nonintubated group (n=33)	Intubated group (n=25)	P
Age (year)	33.6±9.8	33.1±7.9	34.2±12	0.67*
Gender (male/female) (n)	34/24	21/12	13/12	0.37**
Poisoning				
Intentional	42 (72.4)	26 (78.8)	16 (64)	0.21**
Accidental	16 (27.6)	7 (21.2)	9 (36)	
Vomiting after poisoning				
Yes	4 (6.9)	3 (9.1)	1 (4)	0.57**
No	30 (51.7)	18 (54.4)	12 (48)	
Unknown	24 (41.4)	12 (36.3)	12 (48)	
GID				
Yes	31 (53.4)	19 (57.6)	12 (48)	0.66**
No	3 (5.2)	2 (6.1)	1 (4)	
Unknown	24 (41.4)	12 (36.4)	12 (48)	
The time interval elapsed between ingestion and admission (h)	10.5±2.6	8.09±1.86	13.8±2.73	0.36*

Data are presented as mean±SE or n (%) where applicable. **t*-test, **Chi-squared test. GID=Gastrointestinal decontamination, SE=Standard error

Table 2: Bispectral index, signal quality index, electromyography, and vital signs of poisoned patients in both intubated and nonintubated groups

Variables	Need to intubation		P*
	No	Yes	
BIS	85.21±1.74	66.47±2.57	<0.05
SQI	100.5±1.01	100	>0.05
EMG (%)	64.06±6.18	39.69±7.91	<0.05
SBP (mmHg)	106.38±3.01	94.7±4.47	<0.05
DBP (mmHg)	71.06±1.97	68.30±2.02	<0.05
Respiratory rate (per min)	15.6±0.62	13.05±0.97	<0.05
Heart rate (per min)	87.30±3.02	80.04±5.06	<0.05

Data are presented as mean±SE, **t*-test. BIS=Bispectral index, SQI=Signal quality index, EMG=Electromyography, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, SE=Standard error

Table 3: Bispectral index, signal quality index, electromyography, and vital signs of patients need to intubation on admission time and on the time of intubation

	Patients needed to intubation**		P*
	At the admission time	At the time of intubation	
BIS	66.47±2.57	71.65±2.42	<0.05
SQI	100	100	>0.05
EMG (%)	39.69±7.91	42.81±8.59	<0.05
SBP (mmHg)	94.7±4.47	102.75±5.01	<0.05
DBP (mmHg)	68.30±2.02	75.40±4.90	<0.05
Respiratory rate (per min)	13.05±0.97	15.4±5.21	<0.05
Heart rate (per min)	80.04±5.06	82±6.52	<0.05

Data are presented as mean±SE, **t*-test, **patients evaluated for need to intubation on admission time based on local guideline. Then comatose patients received naloxone as coma cocktail. Those who did not respond to naloxone, intubated. So the need to intubation was different between admission time and after naloxone administration. BIS=Bispectral index, SQI=Signal quality index, EMG=Electromyography, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, SE=Standard error

and the respiratory rate between two groups showed that besides of BIS, at the admission time, other factors may be effective in determining the need for intubation.

Since the majority of drug poisonings is due to the ingestion of psychoneurologic drugs which may have some effects on awareness and consciousness, BIS index may be helpful as an applicable indicator for determination of general condition, decision-making for treatment and need to intubation. In this regard, Sandler and Sparks reported a strong relationship between the quantitative values of BIS index and OAA/S scale with sedative and hypnotic drugs such as midazolam, fentanyl, and propofol.^[9] Hirota *et al.* also reported that BIS monitoring may determine the effect of oral diazepam premedication.^[10] In another study, it is reported that BIS monitoring is useful in the determination of the level of awareness and management of patients with acute Alprazolam poisoning.^[8]

In a study on patients with methadone toxicity, it was shown that the most appropriate BIS cutoff point to predict the need for endotracheal intubation, is BIS equal or <78. Therefore, it may be possible to consider the BIS as an appropriate index for predicting the need for intubation in patients poisoned with opioids. BIS index at the admission time and the time of intubation were significantly lower in patients with opioids poisoning.^[14] In our study, the BIS index measured at the time of admission was an appropriate index for prediction of the need for intubation.

At the time of admission, mean EMG index was lower in the intubated group, and there was a significant

difference between groups in the mean systolic blood pressure. In the intubated group, systolic blood pressure was higher at the time of intubation. It may be due to the intravenous fluid therapy and naloxone administration in addicted comatose patients with respiratory depression.

We found that other parameters and general status of patients at the time of admission had not any significant effect on the need for intubation. Other variables such as EMG, SQI, Systolic blood pressure, and respiratory rate showed a significant difference between two groups. This indicates that other than BIS, other indicators as well, are effective in determining the need for intubation. Thus, if poisoned patients with an ingestion of mixed drugs evaluated by BIS index at admission time to the hospital it is possible to identify high-risk patients who need intensive care. According to our results, it is concluded that BIS index is probably an acceptable index in determining the need for endotracheal intubation in patients with mixed drug overdose and low levels of consciousness.

Our study had some limitations including small number of patients, lack of a control group, and lack of toxicological screening tests for some patients to confirm the type of ingested drug.

BIS is an appropriate index for prediction of the need to endotracheal intubation in poisoned patients with ingestion of different drugs.

AUTHORS' CONTRIBUTION

NEM and AY conceptualized the idea, and AMS proposed and managed the study design and the research protocol. AY, MJ, and LH recruited the patients and gathered the data. NEM analyzed the data and drafted the manuscript, and all of the authors have contributed for corrections and modifications of the manuscript and are accountable for the originality and validity of the data.

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Conflicts of interest

There are no conflicts of interest.

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