Prediction of endotracheal intubation outcome in opioid-poisoned patients: A clinical approach to bispectral monitoring

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BACKGROUND: Some opioid-poisoned patients do not respond appropriately to naloxone; consequently, intubation is required. Although various measures have been used to evaluate the level of consciousness of poisoned patients, no study has assessed the role of the bispectral index (BIS) to ascertain the depth of anesthesia in opioid-poisoned patients who require endotracheal intubation.

OBJECTIVE: To compare BIS scores between opioid-poisoned patients with and without intubation, and to determine the BIS cut-off point for endotracheal intubation in these patients.

METHODS: In the present cross-sectional study, conducted in an Iranian university referral hospital for poisoning emergencies between 2012 and 2013, opioid-poisoned patients (n=41) were divided into two groups according to their requirement for endotracheal intubation. BIS analyses were performed at the time of admission and at the time of intubation for those who required it. In addition, electromyography and signal quality index were evaluated for all patients at the time of admission, and cardiorespiratory monitoring was performed during the hospitalization period. Using ROC curves, and sensitivity and specificity analyses, the optimal BIS cut-off point for prediction of intubation of these patients was determined.

RESULTS: The optimal cut-off point for prediction of intubation was BIS ≤78, which had a sensitivity of 86.7% (95% CI 66.1 to 98.8) and specificity of 88.5% (95% CI 73.9% to 98.8%); the positive and negative predictive values were 81.2% and 92%, respectively.

CONCLUSIONS: BIS may be considered an acceptable index to determine the need for intubation in opioid-poisoned patients whose response to naloxone is inadequate.

Key Words: Bispectral index (BIS); Endotracheal intubation; Naloxone; Opioid poisoning

Various indexes have been evaluated to determine the need for intubation in critically ill patients (6–8). Not only is a Glasgow Coma Scale (GCS) score ≤8 a useful guide for endotracheal intubation in patients with brain injury resulting from respiratory compromise, it also indicates the need for intubation in cases for which the cause of unconsciousness is poisoning (9,10).

Another index used to measure the level of consciousness and depth of anesthesia and sedation is the bispectral index (BIS) (11). In 1996, The United States Food and Drug Administration approved a novel measure of the level of consciousness by algorithmic processing of a patients’ electroencephalographic data for assessing the hypnotic effects of general anesthetics and sedatives (12,13). BIS monitoring was initially used primarily during operative anesthesia. Recently, however, BIS monitoring has become a reasonable approach used in intensive care unit (ICU) patients to assess the depth of sedation, especially among individuals receiving neuromuscular paralysis.
Despite the potential application of the BIS for monitoring the depth of anesthesia, to our knowledge, its role has yet to be evaluated instead of a maintenance opportunity, any inappropriate delays in the decision to intubate poisoned patients is very important because, decreased consciousness and loss of protective airway reflexes, which may result in respiratory failure and aspiration injury (20). As a result, inability to restore normal breathing predisposes opioid-poisoned patients to the major referral medical centre for toxicological emergencies in central Iran, is facilitated, staffed and designed for the management of poisoning patients, of whom approximately 400 are admitted monthly. Patients included in the present study were all opioid-poisoning individuals who were admitted to the ward during the study period. Patients hospitalized for opioid poisoning were randomly selected using a random number table and their identification number. The study protocol was approved by the Institutional Board of Human Studies at Isfahan University of Medical Sciences. In addition, after the study was accurately explained to the patients, informed consent for inclusion was obtained. Discharge and/or death before study commencement were considered to be exclusion criteria.

Fourty-one patients hospitalized for opioid poisoning were recruited for the present study and were followed to measure outcomes. Initially, adequate supportive primary care was performed for all opioid-poisoned patients and treatment to facilitate the recovery process was continued. Demographic data and clinical findings from the patients, including vital signs, hemodynamic parameters, routine blood biochemistry analysis, clinical history at admission, amount of ingested opioids, performed treatment modality (eg, gastric lavage, activated charcoal) and length of hospitalization, were recorded for further analysis. If intubation was necessary to control airway and oxygenation, time of intubation was also documented. This information was collected from patient charts and documented reports of emergency services. Expeditious endotracheal intubation was performed for patients who were unable to protect their airway despite naloxone administration (6).

The outcomes were followed based on BIS measured at admission and before intubation of the included patients. The BIS ranges from 0 (equivalent to electroencephalogram silence) to 100, which indicates complete alertness (17).

In addition, electromyography and signal quality index were evaluated for all patients at the time of admission; cardiac and respiratory monitoring were also performed during the hospitalization period.

All data were analyzed using SPSS version 16 (IBM Corporation USA) and Med-Calc (Med-Calc Software Inc, Belgium) statistical software.


\( \chi^2 \) or Fisher's exact test was applied to compare categorical data between patients with and without endotracheal intubation; \( P<0.05 \) was considered to be statistically significant. In addition, significant differences in continuous data were determined using the Mann-Whitney U test or an independent-samples t test where appropriate. ROC curves were used for discrimination by comparison of areas under the curve (AUC) (22). Acceptable and excellent discrimination were defined as AUC 0.7 to 0.8, and 0.8 to 0.9, respectively (23). Therefore, according to the result of ROC curve analyses, sensitivity, specificity and the optimal cut-off point were determined (24). This BIS cut-off point was used to determine predicted and observed endotracheal intubation in poisoned patients.

**RESULTS**

Endotracheal intubation was required in 15 of the 41 opioid-poisoned patients evaluated in the present study. No patient died during the study and, among patients who completed the study, 10 (66.7%) in the intubation group and 21 (80.8%) in the nonintubation group experienced improvement without complications \((P=0.45)\). In contrast, five patients in each group showed improvement but experienced complications \((33.3\% \text{ versus } 19.2\%; P=0.45)\). Demographic data and clinical findings of patients, including route and cause of poisoning, type and amount of ingested opioid, use of concomitant medication, time to first treatment modality and length of hospitalization, were compared between intubated and nonintubated patients (Table 1). Fisher's exact test and \( \chi^2 \) analyses showed significant differences in employment status, use of concomitant medication, and length of hospitalization between intubated and nonintubated patients \((P=0.038, 0.008 \text{ and } 0.001, \text{ respectively})\). In addition, independent sample t tests showed a longer time to first

**TABLE 1**

**Demographic data and clinical characteristics of the study patients**

| Characteristic                        | Intubated (n=15) | Nonintubated (n=26) | P    |
|--------------------------------------|------------------|---------------------|------|
| Age, years, mean ± SD               | 41.9±3.21        | 33.6±2.40           | 0.046|
| Sex                                  |                  |                     |      |
| Male                                 | 10 (66.7)        | 22 (84.6)           | 0.25*|
| Female                               | 5 (33.3)         | 4 (15.4)            |      |
| Marital status                       |                  |                     |      |
| Single                               | 5 (33.3)         | 10 (38.5)           | 0.74†|
| Married                              | 10 (66.7)        | 16 (61.5)           |      |
| Employment status                    |                  |                     |      |
| Employed                             | 7 (46.7)         | 21 (80.8)           | 0.038†|
| Unemployed                           | 8 (53.3)         | 5 (19.2)            |      |
| Route of poisoning                   |                  |                     |      |
| Oral                                 | 13 (86.7)        | 24 (92.3)           | 0.62*|
| Nonoral                              | 2 (13.3)         | 2 (7.7)             |      |
| Cause of poisoning                   |                  |                     |      |
| Unintentional (accidental)           | 6 (40)           | 18 (69.2)           | 0.07†|
| Intentional                          | 9 (60)           | 8 (30.8)            |      |
| Type of opioid                       |                  |                     |      |
| Methadone                            | 12 (80)          | 21 (80.8)           | 0.09*|
| Heroin                               | 3 (20)           | 1 (3.8)             |      |
| Other opioids                        | –                | 4 (15.4)            |      |
| Using concomitant medication         |                  |                     |      |
| Yes                                  | 11 (73.3)        | 8 (30.8)            | 0.008*|
| No                                   | 4 (26.7)         | 18 (69.2)           |      |
| Time to first treatment modality, h, mean ± SD | 6.38±1.65  | 2.52±0.65           | 0.025|
| Length of hospitalization, h         |                  |                     |      |
| ≤48                                  | 6 (40)           | 26 (100)            | 0.001*|
| >48                                  | 9 (69)           | 0 (0)               |      |

Data presented as n (%) unless otherwise indicated. *Fisher’s exact test; †χ² test
treatment modality among intubated compared with nonintubated patients. Moreover, Mann-Whitney U test analysis was used to compare the mean values of blood biochemistry parameters during the first two days of admission between the two groups (Table 2). This analysis showed significant differences in some factors of arterial blood gases including HCO₃⁻, base excess and PaO₂ (P=0.03, 0.02 and 0.02, respectively). Finally, mean values of hemodynamic indexes, electromyography and BIS were compared between groups using t tests at admission and at intubation (Table 3). The related results demonstrated that mean systolic blood pressure (SBP), electromyography results, signal quality index and BIS were significantly lower among intubated compared with nonintubated patients.

A ROC analysis of data to evaluate the best point of BIS for prediction of intubation was performed. According to this analysis, BIS ≤78 was the best point for intubation prediction, with 86.7% sensitivity (95% CI 66.1% to 98.8%) and 88.5% specificity (95% CI 73.9% to 98.8%), with associated positive and negative predictive values of 81.2% and 92%, respectively.

**DISCUSSION**

Endotracheal intubation may prevent respiratory failure and aspiration in opioid-poisoned patients who fail to respond to naloxone and meet the criteria for intubation (25). The primary purpose of the present study was to determine the optimal BIS cut-off point to predict the need for endotracheal intubation in opioid-poisoned patients. Among the 41 patients (age range 24 to 50 years) recruited during the study period, 36.6% underwent intubation. According to the results of the present study, patient age was a significant factor for intubation. Previous studies have reported that vital signs and hemodynamic parameters are dependent on patient age, and that older patients may experience more acute signs of poisoning (26). Although the reason for poisoning did not significantly affect patient intubation status in the present study, intubated patients had a more prevalent history of intentional poisoning (n=9) than nonintubated patients (n=7). In the current study, time to first treatment modality had an impact on patient intubation. As expected, the first treatment modality was conducted earlier in nonintubated patients (mean [± SD] 2.54±0.65 h versus 6.38±1.65 h). In addition, coadministration of other medications with opioids was another factor that influenced the need for intubation. It appears that this factor was associated with a greater severity of poisoning and predisposed patients to require endotracheal intubation (73.3% in intubation versus 30.8% in nonintubation). Moreover, a previous study showed that the time elapsed from taking the poisoning agent to undergoing the first treatment was one of the most important factors to affect prognosis, morbidity and mortality (8). This result appears to be reasonable because the more time elapsed to initiate treatment leads to greater absorption of the poison and more severe adverse reaction (8,26).

In contrast, arterial blood gas analysis of patients showed significant differences in PaO₂, serum bicarbonate level and SBP at ICU admission between intubated and nonintubated patients. Serum bicarbonate levels were significantly lower at admission in individuals who required intubation during the study period. This result demonstrates that patients with more severe opioid toxicity and lower serum bicarbonate levels would require intubation. In addition, SBP was also lower in this group, which showed worse hemodynamic values on admission in those who required intubation. Lower blood pressure may cause metabolic acidosis and lower serum bicarbonate levels. In contrast, PaO₂ at ICU admission was lower in patients who did not require intubation during their hospital stay. This may have occurred because these patients may have adequately responded to naloxone, which led to improvement in respiratory distress, thereby obviating the need for intubation.
BIS analysis showed that BIS was significantly lower in intubated patients at both admission to the ICU and at intubation. The present study showed that BIS ≤ 8, with specificity of 88.5% and sensitivity of 86.7%, was a proper criterion to predict the need for intubation in opioid-poisoned patients. Another study reported that correlation between GCS and BIS analysis is highest when BIS < 80 and GCS score < 8 are used as cut-off points (19).

CONCLUSION
Because coadministration of other sedatives with opioids occurred in some poisoned patients, they did not respond adequately to naloxone and, consequently, intubation was required. Our study showed that BIS may be an acceptable index to determine the need for intubation in these patients.

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