ORIGINAL RESEARCH

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Predictive Value of Base Excess for Mortality in Methanol Intoxication

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Abstract

Objective: Methanol intoxication is among the common reasons for emergency department admissions, apart from suicide attempts. In this study, we investigated the predictive value of base excess (BE) for methanol-related mortality and its potential use in clinical practice.

Materials and Methods: All patients with a confirmed diagnosis of methanol intoxication in an 8-year retrospective study were included. Cases with in-hospital mortality were included in the mortality group. Blood gas and biochemical parameters of the patients were recorded. Receiver operating characteristic curve and regression analyses were performed for variables with significant differences between the groups.

Results: We found that pH, HCO_3, and BE were significantly lower, whereas lactate levels were significantly higher in the mortality group. According to the cut-off values of the independent variables, we determined the area under the curve values to be 0.852, 0.855, 0.900, and 0.708, respectively. We found that the BE value of <-23.65 had the highest sensitivity, specificity, and odds ratio (OR) values [sensitivity: 86.4%, specificity: 89.47%, OR: 0.780 (95% CI; 0.656-0.929)].

Conclusion: We suggest that BE values can be useful for clinicians in prioritizing patients in mass emergency department admissions, such as those with methanol intoxication.

Keywords: Base excess, intoxication, methanol, predictive

Introduction

Methanol, also known as wood alcohol, is a substance that has been shown to be deadly even in small amounts and is found in various substances (such as cleaning agents, windscreen washer fluids, antifreeze, aviation fuels, solid fuels, copier fluids, and perfume) often used in household or industrial sectors. is an alcohol derivative. Methyl alcohol intoxication is often oral or accidental. However, it has been reported that the consumption of fake drinks, suicide, inhalation, or skin contact also causes toxication [1-5]. Alcohol and aldehyde dehydrogenase enzymes are responsible for the metabolism of methanol and other alcohols [1,6].

In our country, methanol poisoning mostly causes mass applications because of fake alcohol consumption [7]. Although their timing and clinics are different, these cases often cause congestion in the emergency departments. With the introduction of the coronavirus disease-2019 pandemic into our lives, an increase was observed in the number of methanol intoxication cases in neighboring countries in the early periods [8]. According to a synthesis study conducted by 12 major clinical toxicology centers in Iran, the number of applicants with methanol poisoning in February and May 2020 is five times larger than the mass methanol poisonings seen in Libya in 2013. The reason for this has been shown to be the widespread use of alcohol recommended for disinfecting the mouth in social media and the large number of hand disinfectants that do not comply with the standards with high methanol content [8].

High anion gap metabolic acidosis is observed in patients presenting with methyl alcohol poisoning. Low pH and $HC0_3$ values, as well as low base excess (BE), another parameter that can be easily measured in blood gas, have been shown to be associated with mortality [9]. We believe that the BE value

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may be useful for clinicians in assigning priority to patients in collective emergency department admissions such as those with methanol intoxication.

Materials and Methods

This study was conducted retrospectively on patients who applied to the Emergency Department of University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital because of methanol intoxication. University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee approval was obtained for the study (KAEK/2022.04.97) and the Helsinki statement was strictly adhered to throughout the study. Informed consent was not obtained because this was a retrospective study.

Patient records were accessed from archive data and the Data Processing Automation system. The study included 51 patients aged 18 years and over who applied to the emergency department with a prediagnosis of methanol intoxication between May 1, 2014, and May 1, 2022. Ten patients were excluded from the study after ethanol intoxication was detected in 4 of the patients' triggers, and six of them left the hospital by signing a treatment rejection form. Age, gender, clinical follow-up, and in-hospital mortality of the patients were recorded.

From the blood gas analysis of the patients at the time of admission to the emergency service, pH, HCO_3, pO_2, pCO_2, lactate, and BE values and biochemistry parameters, glucose, urea, creatinine, sodium, and potassium values were recorded in the study form. Blood gas samples from the blood samples taken from the patients were studied in the ABL 800 device, and biochemistry samples were studied in the COBAS 501 device. BE is calculated automatically by the device.

Statistical Analysis

Categorical data are expressed as numbers and percentages. The Mann-Whitney U test was used in the analysis of data that did not fit the normal distribution, and the data are shown as median inter quantile range. The cut-off values were determined by performing a receiver operating characteristic (ROC) curve analysis of the variables that were found to be significant between the groups. Binary logistic regression analysis was performed to determine the effect of the independent variables in the mortality group. The obtained data were analyzed using the Statistical Package for the Social Sciences statistics 26.0 (IBM Inc., New York, USA) program. P<0.05 and 95% confidence interval (CI) were used for statistical significance.

Results

A total of 41 patients (4 females and 37 males) were included in the study. We did not find a statistically significant difference between the gender distribution and mean age of the groups with mortality (p=0.639, 0.053, respectively) (Table 1).

When we grouped patients based on mortality, we found that in the group with mortality, pH, HCO_3, and BE values were significantly lower, whereas pO_2, lactate, glucose, and creatinine values were significantly higher. A comparison of other data is shown in Table 2.

The ROC curves of the independent variables where a statistically significant difference was detected between the groups with mortality are shown in Figures 1 and 2. In the ROC analysis of pH, HCO_3, BE, and lactate values, statistical significance was determined, and the area under the curve (AUC) values were 0.852, 0.855, 0.900, and 0.708, respectively, for the determined cut-off values. We observed that BE had the highest sensitivity and specificity values at a value of <-23.65 (86.4% and 89.47%, respectively). The ROC analysis of the independent variables, sensitivity, specificity, negative likelihood ratio, and positive likelihood ratio values are shown in Table 3.

In the univariate logistic regression analysis conducted to verify the accuracy of the independent variables that showed statistical significance and had high AUC values in the ROC analysis for predicting mortality, we found that BE had the highest odds ratio (OR) value [OR: 0.780 (95% CI; 0.656-0.929)] (Table 4).

Table 1. Analysis of general data

		Mortalite n (%)		p
		Absent	Present	
		19 (46.35)	22 (53.65)	
Gender	Woman	2 (50)	2 (50)	0.639[a]
	Man	17 (45.9)	20 (54.1)	
Age median (IQR)		38 (16)	43.5 (14.25)	0.053[b]

[a]Fisher's exact test, [b]Mann-Whitney U test, IQR: Interquartile range

Table 2. Comparison of variables in groups with mortality

	Mortality		p
Parameters	Absent	Present	
pH	7.11 (0.22)	6.87 (0.39)	<0.01
pCO_2 (mmHg)	33.10 (15)	35.25 (21.35)	0.695
pO_2 (mmHg)	47.30 (12.50)	93.15 (121.93)	<0.01
Lactate (mmol/L)	2.9 (3.40)	7.13 (5.61)	0.023
HCO_3 (mmol/L)	9.5 (10)	5.65 (2.98)	<0.01
BE (mmol/L)	-18.60 (14.40)	-25.35 (4.13)	<0.01
Glucose (mg/dL)	116 (41)	185 (166)	0.011
Urea (mg/dL)	30 (24.90)	26 (22.68)	0.320
Creatinine (mg/dL)	1.14 (0.50)	1.41 (0.66)	0.023
Sodium (mmol/L)	135 (11)	136 (6.5)	0.885
Potasium (mmol/L)	5.2 (1.2)	5.35 (1.30)	0.784

*Mann-Whitney U test, BE: Base excess

Discussion

Methanol poisoning is a serious medical emergency that can have lasting effects and can even be fatal. Substances containing methanol can be accidentally or intentionally ingested (suicide attempt) [10]. The severity of the patient's condition determines the priority of treatment. For methanol intoxication, the main principles of treatment are prompt diagnosis and resuscitation. It is also crucial to provide cardiopulmonary support, inhibit the conversion of toxic metabolites (by targeting the alcohol dehydrogenase enzyme), correct any existing metabolic acidosis, and remove toxic metabolites from the body [11,12].

In our study, we found that patients diagnosed with methanol intoxication in the emergency department who had hospital mortality had significantly lower pH, HCO_3, and BE values than those who did not experience mortality. The conversion of the toxic metabolite formic acid, which is responsible for toxicity and metabolic acidosis in methanol poisoning, can be facilitated by high-dose folate or folinic acid treatment. This treatment leads to its conversion to carbon dioxide and water

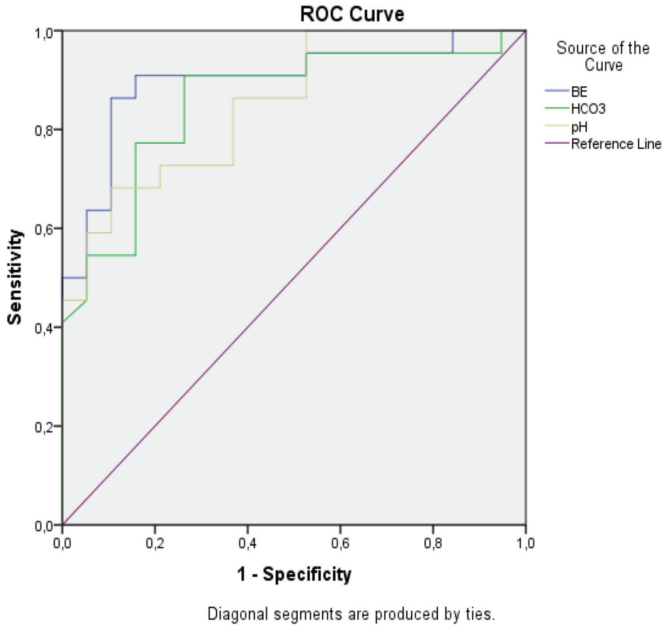

Figure 1. ROCs of BE, HCO_3, and pH values

ROC: Receiver operating characteristic, BE: Base excess

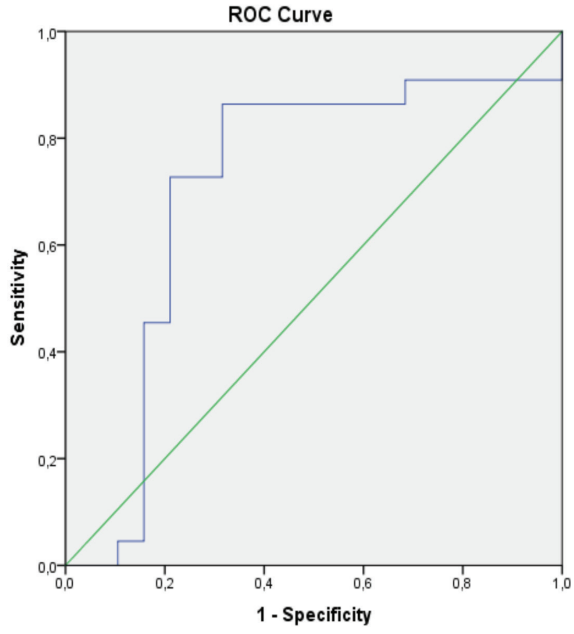

Figure 2. ROC of lactate value

ROC: Receiver operating characteristic

Table 3. ROC analysis results of significant independent variables

Test result variables	Area	Sensitivity	Specifity	NLR	PLR	p	Asymptotic 95% CI	
							Lower	Upper
pH <6.99	0.852	68.2	80.95	0.39	3.58	0.000	0.739	0.965
HCO_3 <7.15 (mmol/L)	0.855	77.3	84.21	0.27	4.89	0.000	0.736	0.974
BE <-23.65 (mmol/L)	0.900	86.4	89.47	0.15	8.20	0.000	0.799	1.000
Lactate >4.25 (mmol/L)	0.708	86.4	68.42	0.20	2.73	0.023	0.530	0.887

NLR: Negative likelihood ratio, PLR: Positive likelihood ratio, BE: Base excess, CI: Confidence interval, ROC: Receiver operating characteristic

Table 4. Univariate logistic regression results

	B	p	OR	95% CI	
				Lower	Upper
pH	-8.808	0.002	0.000	0.000	0.036
HCO_3	-0.298	0.008	0.743	0.595	0.927
BE	-0.248	0.005	0.780	0.656	0.929
Lactate	0.098	0.163	1.103	0.951	1.266

CI: Confidence interval, OR: Odds ratio, BE: Base excess

[11]. HD is the best method for rapidly removing both toxic acid metabolites and parent alcohols and plays a fundamental role in treating severely poisoned patients [13]. A study conducted by Kute et al. [14] reported that a pH value ≤6.9 was highly associated with mortality [9]. Additionally, it was determined that coma, seizures, and severe metabolic acidosis during presentation predicted a poor prognosis [14]. Our study also yielded similar results, with pH values below 6.9 in the mortality group.

Patients with methanol intoxication may develop life-threatening complications such as gastrointestinal involvement, central nervous system involvement, acute kidney failure, and metabolic acidosis (with an increased anion gap). In a retrospective study conducted in our country, 31 patients were admitted to the emergency department because of methanol poisoning. This condition was more common in men and those with a history of chronic alcohol use. In addition, low pH, HCO_3, and BE values, and high sodium values, were associated with mortality [10]. Our study is supported by the results found in the literature.

In the study conducted by Smuszkiewicz et al. [15], it was reported that both BE and lactate have prognostic value in determining mortality in patients in the intensive care unit (ICU). Similarly, Smith et al. [16] found that both lactate and BE were correlated with mortality in 148 patients admitted to the ICU for various reasons. In the literature, lactate and BE have been reported as biomarkers of traumatic shock and as significant predictors of mortality in trauma and sepsis patients [17]. In our study, the statistically significant differences in pH, lactate, and BE values between the group with and without mortality were consistent with these findings.

In our study, we retrospectively analyzed 41 patients who presented to the emergency department with a suspected diagnosis of methanol poisoning based on their history and clinical evaluation, including 37 men and 4 women, as methanol levels were not measured in our center. We did not detect a statistically significant difference in the gender distribution and mean age between the mortality groups. In the study by Kute et al. [14], it was reported that all methanol intoxication cases were men with a mean age of 40±8.5 years. We believe that these results may be related to the fact that men are more likely to produce alcohol at home and generally consume more alcohol. Our results are consistent with the literature.

Study Limitations

We had no possibility of using fomepizole because it is not available in our country. The retrospective design of our study, the inability to determine methanol levels in patients, and the relatively small number of cases can be considered limitations.

Conclusion

In conclusion, many people who consume counterfeit alcohol hide their stories because of guilt, shame, or potential legal problems, which makes it difficult for clinicians to evaluate and delays diagnosis and treatment. Despite advanced treatments, morbidity and mortality in methanol poisoning remain high, mostly due to late diagnosis. In our study, we found that lower BE values in patients with methyl alcohol poisoning were associated with mortality. We believe that more comprehensive studies will provide more effective results.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee approval was obtained for the study (KAEK/2022.04.97) and the Helsinki statement was strictly adhered to throughout the study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.F.B.K., R.Y., S.F., S.D., Concept: A.F.B.K., R.Y., M.U., S.D., Design: A.F.B.K., S.F., M.U., Data Collection or Processing: A.F.B.K., B.Y., S.T.F., U.M.K., Analysis or Interpretation: A.F.B.K., B.Y., U.M.K., S.D., Literature Search: S.F., B.Y., S.T.F., Writing: A.F.B.K., R.Y., S.T.F., U.M.K., S.D.

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