

## PAPER DETAILS

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# Methanol poisoning in the emergency department: a retrospective study

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## ABSTRACT

**Aim:** Massive methanol poisonings have occurred in the past decades, resulting in a large number of deaths. In this study, our aim is to retrospectively analyze methanol poisoning cases admitted to the emergency department between 2019-2021, to evaluate their demographic characteristics, causes of poisoning, clinical and laboratory findings, treatments applied and mortality, and to contribute to the poisoning data of our country.

**Material and Method:** The cases of methanol poisoning who applied to the emergency department in a 3-year period were analyzed retrospectively. Medical files of patients aged 18 years and older were reviewed. Patients diagnosed with 'methanol poisoning' as a result of the examination were included in the study.

**Results:** A total of 59 patients were included in the study. 88% (n=52) of the patients with a mean age of 53±10 were male. The presence of neurological symptoms and GCS were associated with mortality among the symptoms of patients presenting to the emergency department (p=0.017, p<0.001, respectively), it was seen that low pH and NaHCO<sub>3</sub>, and high lactate, serum sodium and anion gap were associated with mortality (p<0.001, p=0.003, p<0.001, p=0.022, respectively, p=0.001)

**Conclusion:** Methanol poisoning is a disease with high mortality despite the improved treatment possibilities. Lactate level was found to be an independent factor for mortality, and increased lactate levels are associated with poor clinical outcome. There was no difference in mortality between patients treated with ethanol and fomepizole.

**Keywords:** Methanol intoxication, mortality, emergency department

## INTRODUCTION

Toxic alcohol poisoning is a multifaceted clinical picture that occurs with mild gastrointestinal (nausea, vomiting, abdominal pain) and neurological (headache, change in consciousness, visual disturbance) symptoms, which can result in severe metabolic acidosis, cardiovascular shock, seizures, coma and death (1). The most common ones we encounter as toxic alcohol poisoning are; methanol, isopropyl alcohol and ethylene glycol (1). Methanol is found as a solvent in many household products such as antifreeze, cleaning solutions, paints and paint removers. Consumption of illegally produced or homemade alcoholic beverages containing relatively high levels of methanol carries another risk. In this way, mass methanol poisonings that resulted in many deaths in the past decades have occurred (2).

In the absence of nonspecific symptoms and a reliable anamnesis, diagnosis in the emergency department can be quite difficult (3). Accidental or intentional ingestion

of substances containing methyl alcohol may result in high rates of mortality and morbidity. Some survivors may develop permanent blindness, kidney dysfunction and chronic brain damage. However, even with high intakes, a positive outcome is possible if the patient arrives at the hospital early enough and the poisoning is detected in time and treated appropriately (4). In the treatment steps; vital support, the use of antidotes, and hemodialysis (2). Early diagnosis and treatment steps are of great importance in preventing clinical complications and mortality (4).

In this study, our aim is to retrospectively analyze methanol poisoning cases admitted to the emergency department between 2019-2021, to evaluate their demographic characteristics, causes of poisoning, clinical and laboratory findings, treatments applied and mortality, and to contribute to the poisoning data of our country.

## MATERIAL AND METHOD

The study was carried out with the permission of İzmir Katip Çelebi University Non-interventional Clinical Researchs Ethics Committee (Date: 18.11.2021, Decision No: 0506). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

### Study Design and Settings

This single-center, retrospective cohort study was conducted in the adult emergency department of a tertiary university hospital in the city center of Izmir, located in the west of Turkey. The cases of methanol poisoning admitted to the emergency department during the 3-year period between January 1, 2019 and December 31, 2021 were analyzed retrospectively.

### Study Population

According to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), among patients admitted to the emergency department, at least one of the diagnostic codes (F10, T51, X45, X65, Y15) containing the word 'alcohol and/or methanol poisoning' Medical files of patients aged 18 years and over, one of which was coded, were reviewed. Patients diagnosed with 'methanol poisoning' as a result of the examination were included in the study. Cases with a definite history of methanol exposure, and patients with suspected methanol intake and diagnosed with methanol intoxication due to clinical findings of methanol intoxication such as unexplained metabolic acidosis, acute kidney failure, neurologic dysfunction, and increased anion gap were included in the study. Patients who did not have a history of methanol intake or whose diagnosis of methanol intoxication was definitively excluded, and patients with missing data were excluded from the study.

### Data Collection and Processing

Age, gender, vital signs at admission, symptoms at admission, glasgow coma score (GCS), chronic disease history, mechanism of intoxication (intentional, unintentional, drunkenness), how long after methanol intake, laboratory tests, applied treatments of the patients included in the study and clinical outcomes (admission, discharge, referral, death) will be evaluated. Information about the clinical outcomes of the referred patients was obtained by contacting the institution to which they were sent.

From laboratory tests, pH, lactate and bicarbonate ( $\text{HCO}_3^-$ ) in blood gas, glucose, blood urea nitrogen (BUN), potassium (K), sodium (Na), chlorine (Cl) levels from biochemical parameters were measured and recorded. With these data obtained, the anion gap was calculated using the formula 'Anion gap =  $(\text{Na} + \text{K}) - (\text{HCO}_3^- + \text{Cl})$  (mmol/L)' (5).

## Outcome Measures

The primary outcome of this study was the mortality rate in methanol poisonings admitted to the emergency department. The effects of clinical characteristics and laboratory findings on mortality were investigated.

### Data Analysis

Data obtained in the study were analyzed using IBM SPSS Statistics for Macos, Version 26.0. Armonk, NY: IBM Corp. Categorical variables were expressed as numbers and percentages, while numerical variables were expressed as mean and standard deviation when presenting the descriptive statistics. Histogram curves, kurtosis -skewness values and a Shapiro-Wilks test were used to test the normal distribution of the data. Mean and standard deviation values were presented since the data were distributed normally. A Student's t-test was used for the comparison of two independent groups. A Chi-square test were used for the comparison of two categorical variables. The results were expressed at a 95% confidence interval. A p value less than 0.05 was considered statistically significant.

## RESULTS

A total of 59 patients were included in the study. 88% (n=52) of the patients with a mean age of  $53 \pm 10$  were male. It was determined that the patients applied to the emergency department  $18 \pm 13$  hours after ingestion of methanol, 75% (n=44) of them were poisoned for the purpose of intoxication, and 51% (n=29) had a history of chronic disease. In the physical examination performed at the time of admission, 80% (n=47) of the patients had GIS symptoms, 78% (n=46) had neurological symptoms, and the mean GCS was  $12 \pm 4.4$  points. Ethyl alcohol was given to 81% (n=48) of the patients and fomepizole was given to 19% (n=11) as antidote treatment. Hemodialysis was applied to 76% (n=45) of the patients and bicarbonate was applied to 78% (n=46) of them. Of the patients, 53% (n=31) were hospitalized in the inpatient service, 47% (n=28) in the intensive care unit, and 37% (n=22) were intubated. Morality rate was determined as 25.4% (n=15). Sociodemographic and clinical characteristics of the patients are shown in **Table 1**.

It was observed that the gender, age, admission to the hospital after methanol intake, the presence of chronic disease and the type of poisoning were not associated with mortality ( $p=0.259$ ,  $p=0.838$ ,  $p=0.412$ ,  $p=0.576$ ). While only the presence of neurological symptoms and GCS were associated with mortality among the symptoms of patients presenting to the emergency department ( $p=0.017$ ,  $p<0.001$ , respectively), GIS symptoms were not associated with mortality ( $p=0.435$ ) (**Table 2**)

**Table 1.** Sociodemographic and clinical characteristics of the patients

		Number (n)	Percentage (%)
Gender	Female	7	12
	Male	52	88
Form of poisoning	Willful	15	25
	inebriation	44	75
Chronic disease	Yes	30	51
	No	29	49
Hospitalization status	Service	31	53
	Intensive care	28	47
Hemodialysis	Yes	45	76
	No	14	24
Entubation	Yes	22	37
	No	37	63
Mortality	Yes	15	25
	No	44	75

**Table 2.** Effects of gender, age, symptoms and type of intoxication on mortality mortality

		Number (%)	Available	None	p
Gender	Female	7 (12)	3 (43%)	4 (57%)	0.259
	Male	52 (88)	12 (23%)	40 (76%)	
Gastrointestinal symptom	Yes	47 (80)	13 (28%)	34 (72%)	0.435
	No	12 (20)	2 (17%)	10 (83%)	
Neurological symptom	Yes	46 (78)	15 (33%)	31 (67%)	0.017*
	No	13 (22)	0 (0%)	13 (100%)	
Chronic disease	Yes	30 (51)	9 (30%)	21 (70%)	0.412
	No	29 (49)	6 (21%)	23 (79%)	
Form of poisoning	Intentional	15 (25)	3 (12%)	20 (80%)	0.576
	Unintentional	44 (75)	12 (27%)	32 (73%)	
Age	(Mean±SD)	NA	54±11	53±10	0.838
GCS (point)	(Mean±SD)	NA	6.2±4	14±2.3	<0.001
Application time (hour)	(Mean±SD)	NA	18.3±9.5	18.5±14	0.952

Chi-square test was applied, \* p&lt;0.05, NA: Not applicable.

When the effect of vital signs measured at the first admission to the emergency department on mortality was investigated; Systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, and oxygen saturation measured by pulse oximetry were found to be unrelated to mortality ( $p=0.840$ ,  $p=0.404$ ,  $p=0.204$ ,  $p=0.576$ ,  $p=0.596$ , respectively) (**Table 3**).

When the mortality rates of the patients were compared according to the laboratory values checked in the emergency department, it was seen that low pH and  $\text{NaHCO}_3$ , and high lactate, serum sodium and anion gap were associated with mortality ( $p<0.001$ ,  $p=0.003$ ,  $p<0.001$ ,  $p=0.022$ , respectively). ,  $p=0.001$ ). It was observed that blood glucose, BUN, potassium and chlorine values were not associated with mortality ( $p=0.062$ ,  $p=0.500$ ,  $p=0.084$ ,  $p=0.336$ ), respectively (**Table 4**). According to the logistic regression analysis performed with the factors found significant from the laboratory values, only lactate level was found to be an independent indicator in terms of mortality ( $p=0.042$ ).

**Table 3.** Relationship between vital signs and mortality

	Mortality (Mean±SD)		P
	Yes	No	
Systolic TA (mmHg)	138±36	137±25	0.840
Diastolic TA (mmHg)	75±20	79±12	0.404
Pulse (beat/dk)	103±22	96±14	0.204
Respiration rate (min)	22±6	23±5	0.576
Saturasyon ( $\text{SO}_2$ %)	98±2	97±3	0.596

**Table 4.** The Relationship of Laboratory Parameters with Mortality

	Mortality (Mean±SD)		P
Test name	Yes	No	
pH	6.9±0.2	7.2±0.2	<0.001
$\text{NaHCO}_3$	8.7±5.6	15±7	0.003
Lactate	9±3.7	3±2.3	<0.001
Glucose	244±117	176±110	0.062
BUN	12.7±5.2	15.3±14.3	0.500
Potassium	4.9±1.5	4.3±0.8	0.084
Sodium	138±4.4	134±6.3	0.022
Clor	100.3±5.5	98±9	0.336
Anion Gap	34±9.8	25.2±7.6	0.001

There was no correlation between ethyl alcohol and fomepizole given as antidote treatment in the emergency department in terms of mortality ( $p=0.549$ ).

## DISCUSSION

Although methanol poisoning is not seen very frequently in the emergency department, it is an important and requires urgent treatment because the cases usually apply collectively from a common source of poisoning and have high mortality and morbidity (6,7). This study is one of the most recent studies on methanol poisoning with a large case series in our country. In our study, clinical features and laboratory findings that may be associated with mortality were investigated retrospectively and some important results were obtained.

Neurological symptoms and GCS (respectively  $p=0.017$ ,  $p<0.001$ ) from clinical findings, low pH and  $\text{NaHCO}_3$  among laboratory findings, and high lactate, serum sodium and anion gap were associated with mortality (respectively;  $p<0.001$ ,  $p=0.003$ ,  $p<0.001$ ,  $p=0.022$ ,  $p=0.001$ ). Low GCS, pH and  $\text{NaHCO}_3$ , high lactate and anion gap levels are clinically expected to increase mortality and are not unique to methanol poisoning. In addition, according to logistic regression analysis, only lactate level was found to be an independent factor in terms of mortality. The data of this study alone may not be sufficient to determine the precise threshold value of serum lactate level in terms of mortality, but a serum lactate level  $>3\pm2.3$  is a warning for negative results.

Although the difference between serum sodium levels is statistically significant, the value in one group was found to be within the normal range (135-145 mEq/L) and the



other was found to be very close to the normal range and is not considered clinically significant. Although some studies have reported a relationship between high sodium value and mortality (8,9,10,11), according to the logistic regression analysis performed in our study, sodium alone was not an independent factor. The emergence of neurological symptoms and the decrease in GCS are interrelated and have been shown to increase mortality (12,13). However, the time between methanol exposure and hospital admission was quite similar in both groups, and its relationship with mortality could not be demonstrated. This suggests that the occurrence of neurological symptoms is not only related to time but also probably to the amount of methanol ingested.

In our study, ethanol was administered to 81% (n=48) of the patients and fomepizole was administered to 19% (n=11) as an antidote. In a study conducted in our country, it was reported that 58% of the patients were treated with ethanol, and fomepizole was not used in any of the patients (14). In international studies, it has been reported that 80% of ethanol and 16% of fomepizole are used, quite similar to our study (15,16). There was no correlation between ethyl alcohol and fomepizole used as antidotes in terms of mortality ( $p=0.549$ ). This situation is similar to previous studies (2,10,17). Bicarbonate treatment was applied to 78% (n=46) of the patients, and hemodialysis was applied to 76% (n=45) of them. In a study conducted in our country, it was reported that 87% of the patients were treated with bicarbonate and 84% of them were treated with hemodialysis (10,11). In the USA, the rate of patients undergoing hemodialysis is about half of that in our country (10,11).

In our study, the mortality rate was determined as 25.4% (n=15). This rate is similar to the studies conducted in Turkey (7,14), but it is considerably higher than the studies conducted abroad (10,11,15). Such a high mortality rate may be related to the number of patients who need hemodialysis and mechanical ventilation. The rate of patients undergoing hemodialysis and intubated in our study is approximately twice that of the aforementioned study (10,11,17). More research is needed to determine the factors affecting mortality and the level of impact.

### Limitations

It is not possible to directly measure methanol concentrations or their toxic metabolites in our hospital and in any hospital within the borders of our province. For this reason, history, clinical features and laboratory findings were used instead of direct measurement in the diagnosis of patients.

## CONCLUSION

Methanol poisoning is a disease with high mortality despite the improved treatment possibilities. Lactate level was found to be an independent factor for mortality, and increased lactate levels are associated with poor clinical outcome. There was no difference in mortality between patients treated with ethanol and fomepizole.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of İzmir Katip Çelebi University Non-interventional Clinical Researchs Ethics Committee (Date: 18.11.2021, Decision No: 0506).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version they have no conflicts of interest to report regarding the present study

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