ORIGINAL ARTICLE

Evaluation of Electrocardiogram Changes in Patients with Methanol Poisoning

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Abstract

Introduction: Methanol is the simplest yet toxic alcohol found in many households and industrial materials. Exposure to methanol can be hazardous, and if left untreated, can result in mortality or severe morbidity. Methanol poisoning is mostly accidental, but it can result in mortality and severe morbidity. Due to the high prevalence of ECG changes in patients with methanol poisoning, this study aimed to evaluate the relationship of these ECG changes with methanol poisoning in determining the prognosis of the patients.
Methods: This cross-sectional study was conducted on 114 patients with acute methanol poisoning at the Shahid Rajaei Hospital in Karaj, Alborz Province, Iran. Clinical, laboratory and ECG variables were evaluated. Furthermore, the gathered data were analyzed with SPSS software.
Results: 1.8% of patients had a PR interval of less than 121ms, and 3.5% had more than 200ms. Among various ECG changes, only PR intervals of more than were significantly associated with mortality. Patients with short QT intervals had the highest PCO2, PH, and HCO3. On the other hand, people with long QT had the lowest amount of PCO2, PH, and HCO3, which was statistically significant. Laboratory tests showed significant differences in serum potassium level and blood PH between died and survived patients.
Discussion and conclusion: In our study, the most common finding in ECG was sinus tachycardia, and short QT was the second most common finding, which is consistent with other studies. Our study found that in ECGs, only PR intervals more than 200 have a significant relationship with mortality, which supports previous studies. Finally, it was that mortality in patients with methanol poisoning is significantly associated with PR interval prolongation, acidosis, and hyperkalemia.

Keywords: Electrocardiography, Methanol poisoning, Acidosis

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INTRODUCTION

Methanol is the simplest yet toxic alcohol found in many households and industrial materials [1]. Exposure to methanol can be hazardous, and if left untreated, can result in mortality or severe morbidity [1, 2]. Methanol poisoning is mostly accidental (ingesting low-quality homemade liquor due to errors in the distillation and fermentation process or contamination [1, 3], and suicide and intentional use of methanol are not as common [2]. Moreover, the same low-quality liquor can cause epidemic poisoning since some are produced in mass and used for gatherings. The toxicity of methanol is due to its metabolite and formic acid, which can disrupt the mitochondrial cytochrome c oxidase resulting in hypoxia and, in turn, metabolic acidosis [4].

Furthermore, methanol and its metabolite have direct toxic effects on some tissues; for example, methanol toxicity can damage the optic nerve [2]. Another effect of methanol can be attributed to its cardio-toxic property that has been reported in several studies in patients with methanol poisoning [5, 6]. Some of these cardio-toxic effects are presented as electrocardiograph (ECG) changes. Although methanol poisoning causes various changes in patients' ECGs, studies found no ECG change specifically for “methanol poisoning” [7]. Since alcoholic beverages are illegal in Iran, most alcohols are self-made in a substandard environment; hence, methanol toxicity is common. Due to the high prevalence of ECG changes in patients with methanol poisoning and the high mortality, this study aimed to evaluate these patients' ECGs and see whether there exists a relationship between ECG changes and prognosis.

METHODS

Research Context

This cross-sectional study was conducted on patients with acute methanol poisoning referred to Shahid Rajaei Hospital of Karaj, Alborz Province, Iran, in 2019-2020.

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Ethical Consideration

This study has been approved by the ethics in research committee of Alborz University of medical sciences with the approval code of IR.ABZUMS.REC.1399.118. Furthermore, the study was explained to the participants, and written consent regarding their data usage for the study and publication purposes was obtained. The participants were assured that their personal information and contact or any data that would lead to their identification would not be shared under any circumstance. Moreover, all methods were carried out based on relevant guidelines and regulations. All stages of this study have been carried out in compliance with the Helsinki Declaration on Research Projects provisions.

Sample Size

The study's sample size was calculated using G-power software and the data from other studies. With consideration of **α** of 0.05 and a β of 80%, the sample size was estimated to be 106.

Inclusion and Exclusion Criteria

All patients with acute methanol poisoning referred to Shahid Rajaei Hospital between the years 2019 to 2020 were eligible to enter the study. These patients had to be diagnosed with acute methanol poisoning by having all of the following criteria; the use of homemade and substandard alcohol beverages within the past four days, the presence of high osmolar gap metabolic acidosis that no other underlying cause was found, and the presence of similar signs and symptoms in those who used the same beverages if available. Our exclusion criteria were the lack of a proper ECG evaluation or patient dissatisfaction regarding participating in the study and any history of heart disease and the use of other substances.

Electrocardiography

A conventional 12 lead ECG alongside precordial ECG was obtained from the patients while laying down for 30 minutes and after correct positioning using CardioCare 2000- 12 Channel ECG(Bionet Co., Ltd.South Korea)

Data Collection

The initial information of patients was extracted from the patients' files and given history. Demographic, relevant medical examinations, para-clinic, and lab test data were gathered (Age, Sex, Systolic blood pressure, Diastolic blood pressure, Venous blood pH, Blood Co2 pressure, Serum bicarbonate, Serum Potassium, PR interval, QRS duration, ST-segment changes, T wave changes, Heart rate, Heart axis, Corrected QT interval and outcome).

Statistical Analysis

Statistical analysis was done using SPSS software version 20; the normal distribution of the variables was first investigated using a one-sample Kolmogorov–Smirnov test. Afterward, due to the normal distribution of the variables, appropriate parametric methods such as t-test were used; for variables without a normal distribution, the Mann-Whitney test was used. Spearman correlation test was used to analyze the correlation between mortality and ECG parameters. In all tests, a p-value < 0.05 was considered as statistically significant.

RESULTS

In total, 114 patients with methanol poisoning were included in the study. The demographics, clinical, and laboratory characteristics of the patients included in the study are presented in Table 1.

The age of the participants ranged from 15 to 57 years; most patients were 21 to 29 years (43%) and 31 to 39 years old (28.9 %). The mean duration of methanol consumption to emergency referral was between 24 to 40 hours. The majority of the patients had a Glasgow Coma Scale (GCS) score of 15 (%82.5) out of 15 points; few had a GCS score lower than 10 (%7.9). Systolic blood pressure at baseline ranged from 70 mmHg to 182 mmHg. Moreover, an association between systolic blood pressure and PR interval was observed, as in participants with PR intervals greater than 200 had lower systolic blood pressures. 27.2% of patients had a high systolic blood pressure (above 135 mmHg). 28.9% had high diastolic blood pressure (above 90 mmHg), 27.2% had a heart rate greater than 100 beats per second. There were no significant differences between those who survived or passed away regarding their blood pressure, heart rate, PCO2, and HCO3. However, significant differences regarding their serum potassium level and blood PH were observed (P-value < 0.05) (see Table 2). 88.6% of the patients had a pH less than 7.35, 63.2% had a PCO2 less than 35 mmHg, 78.9% had an HCO3 less than 21mEq/L. Finally, 7.9% had hyperkalemia

Table 1. Demographic, clinical and laboratory characteristics of the patients included in the study

Variable	Mean ± SD or number (%)
Age	28.93 ± 9.21
Male	100 (87.7)
Female	14 (12.3)
Time of Consumption to Hospital (hours)	40.59 ± 17.42
GCS	13.99 ± 2.73
Systolic BP	128.45 ± 18.01
Diastolic BP	84.15 ± 17.79
Heart Rate	85.21 ± 18.90
PH	7.16 ± 0.18
PCO2(mmHg)	32.99 ± 12.53
HCO3(mEq/L)	13.51 ± 6.46
Serum Potassium (mmol/L)	4.43 ± 0.68

Table 2. Comparison of different variables between the deceased and survived groups

Variable	Survived	deceased	P value
Systolic BP	129.24 ± 16.692	120.30 ± 28.367	0.135
Diastolic BP	84.67 ± 17.595	78.80 ± 19.915	0.566
Heart Rate	84.58 ± 18.745	91.80 ± 20.308	0/35
PH	7.19 ± 0.158	6.92 ± 0.229	<0.001*
PCO2(mmHg)	32.77 ± 11.563	35.32 ± 20.881	0.988
HCO3(mEq/L)	13.67 ± 6.290	11.85 ± 8.304	0.202
Serum Potassium (mmol/L)	4.35 ± 0.569	5.35 ± 1.046	0.003*

(potassium levels above 5.5 mEq/L) hemodynamic and laboratory variables had no significant correlation with ST-segment, QRS, T wave, R wave, and Axis changes. Nonetheless, patients with short QT had the highest PCO2, PH, and HCO3. On the other hand, patients with long QT had the lowest amount of PCO2, PH, and HCO3, which was statistically significant (P-value < 0.05). 1.8% of the patients had a PR interval of less than 121 milliseconds (ms), and 3.5% had a PR interval of more than 200ms. A PR interval of more than 200ms was associated with significant mortality risk. Yet, other ECG changes were not significantly associated with mortality (Table 3). Moreover, Spearman correlation test revealed a significant correlation between PR interval prolongation and mortality (P-value= 0.0059).

Table 3. Comparison of ECG changes in survived and deceased patients with methanol poisoning

Variable		Survived n (%)	Deceased n (%)	P value
PR	<120	2 (100)	0	0.045*
	120-200	100 (92.6)	8 (7.4)	
	>200	2 (50	2 (50.0)	
QRS	Narrow	89 (92.7)	7 (7.3)	0.193
	Wide	15 (83.3)	3 (16.7)	
ST-segment	Normal	97 (92.4)	8 (7.6)	0.179
	Elevated	5 (83.3)	1 (16.7)	
	Depressed	2 (66.7)	1 (33.3)	
T wave	Flat	7 (87.5)	1 (12.5)	0.156
	Normal	85 (93.4)	6 (6.6)	
	Tall	12 (80.0)	3 (20.0.)	
R wave in lead 2	Low amplitude	24 (88.9)	3 (11.1)	0.719
	Normal	63 (92.6)	5 (7.4)	
	High amplitude	17 (89.5)	2 (10.5)	
Axis	Normal	89 (90.8)	9 (9.2)	0.794
	RAD	7 (87.5)	1 (12.5)	
	LDA	7 (100)	0	
	EAD	1 (100)	0	
QT	Short	27 (96.4)	1 (3.6)	0.58
	Normal	71 (88.8)	9 (11.2)	
	Prolonged	6 (100.0)	0	

DISCUSSION

Based on the results of the study, the mortality rate due to methanol poisoning in the studied population was 8.8%, which is in line with the results of other studies. In Iran, the mortality rate of methanol poisoning has been reported to vary from 7 to 51 % [8-11]. Furthermore, in other countries, the mortality of methanol poisoning varies from 3.3 to 34% [9-11]. This difference in methanol poisoning mortality rates in different studies may be due to differences in the geographical area, race, methanol consumption pattern, timely diagnosis of intoxication, standard supportive care, and correction of metabolic acidosis, and other underlying factors [12]. However, it is difficult to compare the outcome of different studies because methanol poisoning can easily be missed at early stages resulting in treatment delay [13]. In our study, it was found that among all the ECG parameters, only a PR interval of more than 200ms had a significant association with mortality. This finding is in line with those of Navabi et al., who ran a retrospective descriptive-analytical study on the factors influencing the prognosis of hospitalized patients with acute methanol poisoning and found a significant relationship between non-sinus rhythms and mortality [14]. Our study found that low blood pH is a significant risk factor for mortality in patients, which is consistent with many other studies [15-17]. Our study found no association of mortality with bicarbonate and carbon dioxide levels. However, a significant association between hyperkalemia, low pH levels, prolonged PR interval, and mortality was seen. Contrary to our study, in some studies, bicarbonate and carbon dioxide (PCO2) levels were significant values and were considered as screening factors in determining the stage of the disease and the outcome of the patient [18]. The reason for this discrepancy in our study and the results of other studies may be due to differences in the sample size, controlling the effect of confounders, and demographic characteristics.

One study found that although the prevalence of cardiac complications in methanol poisoning was high, ECG abnormalities could not predict the incidence of mortality [4]. The findings of our study also showed that despite a high prevalence of various electrocardiographic changes in patients with methanol poisoning, only PR interval was significantly associated with mortality. In our study, the most common finding in ECGs was sinus tachycardia and short QT, which was consistent with other studies. Similarly, in another study, ECG changes included sinus tachycardia (%44), alongside PR interval prolongation (%11), QT prolongation (%22), nonspecific T-wave changes (%66), and the development of Brugada type 1 ECG pattern in one patient [6].

LIMITATIONS

Among our limitations, the relatively small sample size was the most significant; however, despite the small sample size, we considered potential confounders, especially the use of other substances that could affect our results.

CONCLUSION

Our study showed that the prevalence of mortality in patients with methanol poisoning is significantly associated with PR interval prolongation, acidosis, and hyperkalemia. It was also noted that the most common ECG abnormalities include sinus tachycardia and short QT, and only short QT was significantly associated with acidosis. Finally, more extensive studies are needed to determine the relationship of ECG findings as indicators with the prognosis of patients with methanol toxicity

Declarations

Ethics approval and consent to participate

This study has been approved by the ethics in research committee of Alborz University of medical sciences with the approval code of IR.ABZUMS.REC.1399.118. The study was explained to the participants, and written consent regarding the usage of their data for the study and publication purposes was obtained. The participants were assured that their personal information and contact or any data that would lead to their identification would not be shared under any circumstance. Moreover, all methods were carried out based on relevant guidelines and regulations. All stages of this study have been carried out in compliance with the Helsinki Declaration on Research Projects provisions.

Availability of data and materials: All data generated or analyzed during this are available from the corresponding author upon reasonable request.

Consent to publish: Not applicable.
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Authors' contributions: HFD and LSA conceived and designed the study, MRT, SY collected the data and gathered the patients, and wrote the manuscript, MQ analyzed and interpreted the data.

REFERENCES

1. Kraut JA, Mullins ME. Toxic Alcohols. N Engl J Med. 2018 Jan 18;378(3):270-280. doi: 10.1056/NEJMra1615295. Erratum in: N Engl J Med. 2019 Jan 10;380(2):202. PMID: 29342392.
2. Allister Vale, Ethanol,Medicine, Volume 35, Issue 11, 2007, Pages 615-616, ISSN 1357-3039, https://doi.org/10.1016/j.mpmed.2007.08.015.
3. Chan APL, Chan TYK. Methanol as an Unlisted Ingredient in Supposedly Alcohol-Based Hand Rub Can Pose Serious Health Risk. Int J Environ Res Public Health. 2018 Jul 9;15(7):1440. doi: 10.3390/ijerph15071440. PMID: 29987197; PMCID: PMC6069146.
4. Liesivuori J, Savolainen H. Methanol and formic acid toxicity: biochemical mechanisms. Pharmacol Toxicol. 1991 Sep;69(3):157-63. doi: 10.1111/j.1600-0773.1991.tb01290.x. PMID: 1665561.
5. Sanaei-Zadeh H, Emamhadi M, Farajidana H, Zamani N, Amirfarhangi A. Electrocardiographic manifestations in acute methanol poisoning cannot predict mortality. Arh Hig Rada Toksikol. 2013 Jun;64(2):79-85. doi: 10.2478/10004-1254-64-2013-2285. PMID: 23819935.
6. Cavalli A, Volpi A, Maggioni AP, Tusa M, De Pieri G. Severe reversible cardiac failure associated with methanol intoxication. Postgrad Med J. 1987 Oct;63(744):867-8. doi: 10.1136/pgmj.63.744.867. PMID: 3447111; PMCID: PMC2428610.
7. Jaff Z, McIntyre WF, Yazdan-Ashoori P, Baranchuk A. Impact of methanol intoxication on the human electrocardiogram. Cardiol J. 2014;21(2):170-5. doi: 10.5603/CJ.a2013.0053. Epub 2013 May 15. PMID: 23677726.
8. Carolyn V. Coulter, Sarah E. Farquhar, Claire M. McSherry, Geoffrey K. Isbister & Stephen B. Duffull (2011) Methanol and ethylene glycol acute poisonings predictors of mortality, Clinical Toxicology, 49:10, 900-906, DOI: 10.3109/15563650.2011.630320
9. Kute VB, Godara SM, Shah PR, Gumber MR, Goplani KR, Vanikar AV, Munjappa BC, Patel HV, Trivedi HL. Hemodialysis for methyl alcohol poisoning: a single-center experience. Saudi J Kidney Dis Transpl. 2012 Jan;23(1):37-43. PMID: 22237216.
10. Zakharov S, Pelclova D, Urban P, Navratil T, Diblik P, Kuthan P, Hubacek JA, Miovsky M, Klempir J, Vaneckova M, Seidl Z, Pilin A, Fenclova Z, Petrik V, Kotikova K, Nurieva O, Ridzon P, Rulisek J, Komarc M, Hovda KE. Czech mass methanol outbreak 2012: epidemiology, challenges and clinical features. Clin Toxicol (Phila). 2014 Dec;52(10):1013-24. doi: 10.3109/15563650.2014.974106. Epub 2014 Oct 25. PMID: 25345388.
11. Lee CY, Chang EK, Lin JL, Weng CH, Lee SY, Juan KC, Yang HY, Lin C, Lee SH, Wang IK, Yen TH. Risk factors for mortality in Asian Taiwanese patients with methanol poisoning. Ther Clin Risk Manag. 2014;10:61-7. doi: 10.2147/TCRM.S51985. Epub 2014 Jan 17. PMID: 24465131; PMCID: PMC3900329.
12. Shadnia S, Rahimi M, Soltaninejad K, Nilli A. Role of clinical and paraclinical manifestations of methanol poisoning in outcome prediction. J Res Med Sci. 2013 Oct;18(10):865-9. PMID: 24497857; PMCID: PMC3897070.
13. Zahra Nekoukar, Zakaria Zakariaei, Fatemeh Taghizadeh, Fatemeh Musavi, Elham Sadat Banimostafavi, Ali Sharifpour, Nasrin Ebrahim Ghuchi, Mahdi Fakhar, Rabeeh Tabaripour, Sepideh Safanavaei, Methanol poisoning as a new world challenge: A review, Annals of Medicine and Surgery, Volume 66, 2021, 102445, ISSN 2049-0801, https://doi.org/10.1016/j.amsu.2021.102445.
(https://www.sciencedirect.com/science/article/pii/S2049080121003952)
14. Navabi SJ, Eivazi M, Beiranvand B. An epidemiological study of patients with methanol poisoning and the factors affecting the prognosis of patients in imam khomeini hospital Kermanshah 2010-2015. Scientific Journal of Forensic Medicine. 2018;24(3):175-84. http://sjfm.ir/article-1-793-en.html [in persian]
15. Hovda KE, Hunderi OH, Tafjord AB, Dunlop O, Rudberg N, Jacobsen D. Methanol outbreak in Norway 2002-2004: epidemiology, clinical features and prognostic signs. J Intern Med. 2005 Aug;258(2):181-90. doi: 10.1111/j.1365-2796.2005.01521.x. PMID: 16018795.
16. Paasma R, Hovda KE, Tikkerberi A, Jacobsen D. Methanol mass poisoning in Estonia: outbreak in 154 patients. Clin Toxicol (Phila). 2007;45(2):152-7. doi: 10.1080/15563650600956329. PMID: 17364632.
17. Hassanian-Moghaddam H, Pajoumand A, Dadgar SM, Shadnia Sh. Prognostic factors in methanol poisoning. Hum Exp Toxicol. 2007 Jul;26(7):583-6. doi: 10.1177/0960327106080077. PMID: 17884962.
18. Rzepecki J, Krakowiak A, Fiszer M, et al. [Acute methanol poisoning among patients of Toxicology Unit, Nofer Institute of Occupational Medicine in Łódź, during the period 2000-2009]. Przeglad Lekarski. 2012 ;69(8):431-434. PMID: 23243901.