

Research Paper: Visual Disturbances in Patients With Acute Methanol Poisoning: A Cross-sectional Study.



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ABSTRACT

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Background: Methanol poisoning is a serious problem in public health, especially in developing countries. The present study aimed to evaluate the incidence of visual disturbances in patients with acute methanol poisoning in the south of Iran.

Methods: This cross-sectional study (from 21/March/2014 to 21/March/2019) was conducted on all adult patients' medical records who were referred to Ali-Asghar Hospital in Shiraz City, Iran, with acute methanol poisoning. The required data were collected using a data-gathering form and were then analyzed.

Results: Twenty male patients were enrolled in this research, with Mean±SD age of 33.15±10.40 years. Visual disturbances were observed in 15(75%) of the study subjects, as the most common clinical manifestations. Blurred vision (40%) and blindness (35%) were the most frequent visual disturbances in the study participants. None of the study subjects reported photophobia. The explored variables did not differ between patients with visual disturbances and those without visual disturbances. Only one patient who encountered blindness was expired.

Conclusion: The incidence of visual disturbances in the study patients with acute methanol poisoning was higher than that of similar studies.

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1. Introduction

Methanol is an alcohol that causes high toxicity among humans; mostly by direct consumption and rarely through inhalation or skin absorption. As little as 30 mL of pure methanol can cause permanent blindness and 30-240 mL of it may cause death. Methanol has little toxicity; however, when metabolized into products, such as formaldehyde and formic acid, it is highly toxic [1]. Methanol poisoning carries high morbidity and mortality, even after hospital discharge [2, 3]. Treatment options for methanol poisoning include correcting acidosis, active charcoal, and stomach washing. Hemodialysis is the last treatment option that increases patients' survival and prevents visual damage [2].

Metabolic acidosis, optic nerve neuropathy, and the complications of the central nervous system are the most serious and debilitating consequences of methanol poisoning. Formic acid is the main cause of optic nerve neuropathy [4]. Ophthalmological signs and symptoms of methanol poisoning range from blurred vision and visual field changes to complete blindness. Most patients with methanol poisoning manifest some clinical signs of ophthalmological abnormalities, even in the absence of visual dysfunction [5]. The prevalence of visual disturbances after methanol poisoning ranges from 29% to 64% [1, 2, 6-8].

Methanol poisoning remains a serious problem in developing countries, including Iran, which causes irreversible complications and even death. Alcohol poisoning may be due to suicide; however, in Iran, methanol is considered a cheap and more accessible substitute for ethanol, i.e., resulted in increased methanol poisoning. Based on recently conducted studies, alcohol poisoning is on the rise [2].

This study aimed to evaluate the incidence of visual disturbances in patients with acute methanol poisoning in the south of Iran.

2. Materials and Methods

This retrospective cross-sectional study (from 21/March/2014 to 21/March/2019) evaluated the archived data from all medical records of patients with methanol poisoning who were referred to Ali-Asghar Hospital, affiliated with the Shiraz University of Medical Sciences, and a central Hospital in Shiraz City, Iran, for poisoning patients. The inclusion criteria of the study were patients

aged ≥ 16 years old with methanol poisoning and available medical records in the archives of the hospital. The diagnosis of methanol poisoning was based on the patients' medical history, the level of methanol in blood, or the physician's final diagnosis. Patients with unavailable or incomplete medical files were excluded from the study.

The necessary data were collected using a data-gathering form. This checklist included 3 parts; a. sociodemographic characteristics (e.g., age, gender, marital status, place of residence); b. medical history (e.g., smoking, substance use, alcohol consumption, psychological disorders, & suicide); c. hospital admission data (e.g., vital at the time of admission, signs and symptoms, laboratory findings, received treatment, & therapeutic outcomes). Then, the study patients with and without visual disturbances were compared.

All data analyses were performed in SPSS v. 26 using Chi-squared and Fisher's Exact tests for proportions, as well as Independent Samples t-test and Mann-Whitney U test respecting the mean values. The collected results were presented as Mean \pm SD for continuous variables and summarized in frequency(percentage) for categorical ones. Two-Sided $P < 0.05$ and Confidence Interval (CI) of 95% were considered to be statistically significant. Furthermore, the missing data were considered in the statistical analysis and recorded as not determined.

The current study was approved by the Vice-Chancellor of Research and Technology, as well as the Ethics Committee of Shiraz University of Medical Sciences (IR.sums.med.rec.1398.150). To observe the ethical issue, the collected data were not revealed to anyone, except for the researchers.

3. Results

Totally, 20 medical records were evaluated; all of the explored cases were male, with the Mean \pm SD age of 33.15 ± 10.40 (range: 16-61) years. Moreover, 17(85%) of them were single and 9(45%) lived in the urban regions. Besides, 6(30%) presented a history of smoking, 2(10%) reported a history of substance dependence, and most of them (70%) stated no history of psychological disorders. Only 1(5%) patient who was admitted to the Intensive Care Unit (ICU) was expired. Visual disturbances were detected in 15(75%) of the research subjects. The Mean \pm SD interval between consumption and arrival to the hospital was 3.13 ± 2.85 hours, and the duration of hospitalization was 3.94 ± 3.98 days (Table 1).

Visual disturbances were the most common clinical manifestations (75%), compared with respiratory and gastrointestinal problems. Furthermore, 10(50%) study participants reported a history of alcohol consumption. Only one patient who lost vision was expired.

As per Table 2, 7(35%) patients encountered blindness and 8(40%) manifested blurred vision. None of the study subjects reported photophobia. In the eye examination, 2(10%) of the study participants presented miosis and 2(10%) experienced mydriasis. Additionally, 3(15%) of the study subjects presented no pupil reactivity. Metabolic acidosis was observed in only 2(10%) patients. The studied variables did not differ between patients with and without visual disturbances.

4. Discussion

The present study data suggested that visual disturbances (75%) were the most common clinical manifestations in adult patients with acute methanol poisoning. Totally, 35% of the examined patients encountered blindness and 40% had blurred vision.

Hovda et al. reported that 55%, 43%, and 41% of patients presented visual disturbances, gastrointestinal symptoms, and shortness of breath, respectively [3]. Hassanian-Moghaddam et al. studied 25 patients with methanol poisoning and reported that 23% of them had blindness [6], i.e., lower than the current study findings. Shadnia et al. reported that 64% of the explored participants experienced visual disturbances [1].

As per Mostafazadeh and Eghbali, 14.3% of patients encountered visual complications at discharge [7]. Mirzaei et al. reported a prevalence of 39.7% for vision problems, i.e., mentioned as the most common complication [8]. However, in the study by Massoumi et al., 71% of the examined patients manifested nausea and vomiting. They reported that blindness was observed in 2% of the study participants, blurred vision in 41.2%, mydriasis in 27%, and miosis in 2%; similar to the present study, most of the explored patients (71%) had a normal pupil size [2].

Sanaei-Zadeh et al. argued that methanol poisoning causes various degrees of visual disturbances; it indicates a significant individual variation in sensitivity to methanol poisoning [9]. Elkhamary et al. evaluated the association between visual and neurological damages in patients with methanol poisoning using MRI images. Optic nerve problems and atrophy were observed in

56.9% of patients and bilateral putamen necrosis and visual nerve destruction in 36.2% of them [10].

In the current study, all patients were male, i.e., consistent with the study by Shadnia and associates [1]. In studies by Mostafazadeh and Eghbali [7] as well as Sanaei-Zadeh et al. [9], 82.1% and 96% of the explored patients were male, respectively. Moreover, Hovda et al. [3], Navabi et al. [11], and Massoumi et al. [2] reported that most of the studied patients were male. Therefore, methanol poisoning is more common in men.

The obtained results suggested that the Mean±SD of the study subjects' age was 33.15±10.40 (range: 16-61) years. Most of the study participants were single, lived in urban areas, had a diploma, and were employed. Furthermore, most of them reported a history of alcohol consumption. However, these factors did not differ between patients with and without visual disturbances. Massoumi et al. declared that 13.7% of patients were under 20 years of age, 86.3% lived in urban areas, 11.8% had a history of suicide, and 13.7% had a history of substance dependence [2]. Mostafazadeh and Eghbali reported a mean age of 29.3 years in this respect [7]. Hassanian-Moghaddam et al. reported a mean age of 38.5 years in this regard [6]. Accordingly, methanol poisoning further occurs at younger ages and in urban areas.

This study disregarded specifying the method of methanol consumption; however, Mostafazadeh and Eghbali mentioned drinking as the main method [7]. Additionally, in most cases of the present study, the blood levels of methanol were not recorded. Shadnia et al. reported a median consumption of 20 mg/dL; thus, 37% of the examined patients consumed 20-50 mg/dL methanol and 23% over 50 mg/dL [1]. Massoumi et al. reported that 74.5% of patients were intoxicated by industrial alcohol [2].

In the present study, only one patient was admitted to the Intensive Care Unit (ICU), and was expired. This patient was in a coma when admitted to the hospital. Shadnia et al. reported that 8 patients were admitted to the ICU [1]. In the study by Massoumi et al., only 37.3% of patients were alert when admitted to the hospital [2].

In the present study, there was no difference concerning the blood levels of glucose, potassium, and pH between the study groups; these factors were not considered as prognostic factors. Shadnia et al. reported that 60% of patients developed leukocytosis. Moreover, the prevalence of hyperglycemia was reported as 70%, and 40% of patients manifested hyperkalemia [1]. Sanaei-Zadeh et al. found a significant correlation between blood glucose

Table 1. The patients' characteristics

Variables		Total	With Visual Disturbances (n=15)	Without Visual Disturbances (n=5)	P
Age (y) (Mean±SD)		33.15±10.4	33.47±9.92	32.20±12.76	0.788
Gender No. (%)	Men	20 (100)	15 (100)	5 (100)	-
	Women	0 (0)	0 (0)	0 (0)	
Marital status No. (%)	Single	17 (85)	13 (86.7)	4 (80)	0.468
	Married	2 (10)	1 (6.7)	1 (20)	
	Not determined	1 (5)	1 (6.7)	0 (0)	
Place of live No. (%)	Urban	9 (45)	6 (40)	3 (60)	0.585
	Rural	7 (35)	6 (40)	1 (20)	
	Not determined	4 (20)	3 (20)	1 (20)	
Educational level No. (%)	Illiterate	1 (5)	1 (6.7)	0 (0)	0.712
	Primary	1 (5)	1 (6.7)	0 (0)	
	Middle school	2 (10)	2 (13.4)	0 (0)	
	Diploma	6 (30)	5 (33.3)	1 (20)	
	Not determined	10 (50)	6 (40)	4 (80)	
Having job No. (%)	Yes	8 (40)	8 (53.3)	0 (0)	0.141
	No	1 (5)	1 (6.7)	0 (0)	
	Not determined	11 (55)	6 (40)	5 (100)	
Having underlying disease No. (%)	Yes	3 (15)	3 (20)	0 (0)	0.541
	No	14 (70)	10 (66.6)	4 (80)	
	Not determined	3 (15)	2 (13.4)	1 (20)	
History of alcohol consumption No. (%)	No. (%)	10 (50)	9 (60)	1 (20)	0.182
	Yes	1 (5)	0 (0)	1 (20)	
	No	9 (45)	6 (40)	3 (60)	
	Not determined				
History of smoking No. (%)	Yes	7 (35)	6 (40)	1 (20)	0.491
	No	4 (20)	2 (13.4)	2 (40)	
	Not determined	9 (45)	7 (46.6)	2 (40)	
History of addiction No. (%)	Yes	2 (10)	2 (13.4)	0 (0)	1.0
	No	12 (60)	8 (53.3)	4 (80)	
	Not determined	6 (30)	5 (33.3)	1 (20)	
History of psychological diseases No. (%)	No. (%)	1 (5)	1 (6.7)	0 (0)	1.0
	Yes	14 (70)	11 (73.3)	3 (60)	
	No	5 (25)	3 (20)	2 (40)	
History of suicide No. (%)	Yes	0 (0)	0 (0)	0 (0)	-
	No	13 (65)	10 (66.7)	3 (60)	
	Not determined	7 (35)	5 (33.3)	2 (40)	
Transfer to hospital No. (%)	By himself	4 (20)	4 (26.6)	0 (0)	0.679
	Individual acquaintances	10 (50)	7 (46.6)	3 (60)	
	Emergency medical service	2 (10)	2 (13.4)	0 (0)	
	Not determined	4 (20)	2 (13.4)	2 (40)	
Duration between consumption and arrival to the hospital (hour) (Mean±SD)		3.13±2.85	3.28±3.04	2.0±0.1	0.429
Duration of hospitalization (day) (Mean±SD)		3.94±3.98	4.29±4.61	3.0±0.71	0.094
Outcome No. (%)	Discharged	19 (95)	14 (93.3)	5 (100)	1.0
	Death	1 (5)	1 (6.7)	0 (0)	

Table 2. The patients' signs, symptoms, and laboratory data at the time of admission to the hospital

Variables	Total	With Visual Disturbances (n=15)	Without Visual Disturbances (n=5)	P	
Vital signs (Mean±SD)	Systolic blood pressure (mmHg)	138.20±17.16	140.20±18.18	132.20±13.50	0.102
	Diastolic blood pressure (mmHg)	74.95±31.41	73.40±34.92	79.60±19.58	0.875
	Heart rate (/minutes)	96.80±20.28	92.60±17.05	109.40±25.91	0.783
	Respiratory rate (/minutes)	19.21±1.51	19.13±1.51	19.50±1.73	0.580
	Temperature (°C)	36.53±0.86	36.52±0.94	36.57±0.67	0.674
	GCS (/15)	14.41±2.65	14.15±3.17	15.0±0.0	0.357
CNS No. (%)	Alert	19 (95)	14 (93.3)	5 (100)	1.0
	Coma	1 (5)	1 (6.7)	0 (0)	
Ophthalmic No. (%)	Blindness	7 (35)	7 (46.6)	0 (0)	0<0.001*
	Blurred vision	8 (40)	8 (53.3)	0 (0)	
	Photophobia	0 (0)	0 (0)	0 (0)	
	No symptom	5 (25)	0 (0)	5 (100)	
Pupil No. (%)	Miosis	2 (10)	1 (6.7)	1 (20)	0.090
	Mydriasis	2 (10)	2 (13.4)	0 (0)	
	Normal size	8 (40)	8 (53.3)	0 (0)	
	Not determined	8 (40)	4 (26.6)	4 (80)	
Pupil reactivity No. (%)	Reactive	8 (40)	7 (46.6)	1 (20)	0.296
	Not reactive	3 (15)	3 (20)	0 (0)	
	Not determined	9 (45)	5 (33.3)	4 (80)	
Respiratory No. (%)	Dyspnea	1 (5)	1 (6.7)	0 (0)	1.0
	Depression	1 (5)	1 (6.7)	0 (0)	
	No symptom	18 (90)	13 (86.7)	5 (100)	
Gastrointestinal No. (%)	Nausea/vomiting	4 (20)	4 (26.6)	0 (0)	0.530
	No symptom	16 (80)	11 (73.3)	5 (100)	
Laboratory tests (Mean±SD)	White blood counts 10 ⁹ /L	9.74±2.42	9.88±1.91	9.28±4.15	0.118
	Lymphocyte 10 ⁹ /L	20.60±9.98	21.68±10.42	17.08±8.66	0.796
	Blood sugar (mg/dL)	114.25±35.40	115.77±38.25	107.67±23.18	0.981
	Serum sodium (mEq/L)	137.37±3.41	137.56±3.10	136.75±4.79	0.928
	Serum potassium (mEq/L)	4.25±0.91	4.26±0.94	4.20±0.95	0.515
	BUN (mg/dL)	11.41±4.81	11.23±4.99	12.0±4.83	0.836
	Creatinine (mg/dL)	1.24±0.21	1.19±0.19	1.40±0.23	0.247
	PT (Second)	14.57±1.79	14.21±1.77	15.75±1.50	0.211
	PPT (Second)	29.24±4.35	28.85±4.38	30.50±4.65	0.584
	INR	1.26±0.21	1.22±0.19	1.37±0.25	0.058
Vein blood gas	PH (Mean±SD)	7.23±0.11	7.23±0.10	7.25±0.15	0.215
	PCO ₂ (Mean±SD)	26.73±9.41	28.14±10.17	22.15±4.71	0.432
	HCO ₃ (Mean±SD)	21.40±39.30	24.95±44.69	9.88±4.09	0.466
	O ₂ saturation (Mean±SD)	90.27±22.72	88.36±26.53	95.50±3.70	0.432
	Metabolic acidosis No. (%)	2 (10)	2 (13.4)	0 (0)	1.0
	Respiratory alkalosis No. (%)	1 (5)	1 (6.7)	0 (0)	1.0
Treatment No. (%)	Gastric lavage	0 (0)	0 (0)	0 (0)	-
	Active charcoal	1 (5)	1 (6.7)	0 (0)	1.0
	Hemodialysis	17 (85)	12 (80)	5 (100)	0.539
	Sodium bicarbonate	12 (60)	10 (66.7)	2 (40)	0.347
	Folic acid folinate	16 (80)	12 (80)	4 (80)	1.0
	Fompizol	0 (0)	0 (0)	0 (0)	-
Number of hemodialysis (Mean±SD)	1.45±0.94	1.40±1.06	1.60±0.55	0.492	
The time interval between arrival to the hospital and first hemodi	Alysis (hour) (Mean±SD)	5.46±2.0	5.25±1.84	6.08±2.62	0.163

* Statistically significant

SD: standard deviation; GCS: Glasgow Coma Scale; CNS: Central Nervous System; BUN: Blood urea nitrogen; PT: Prothrombin Time; PTT: Partial thromboplastin time; INR: The international normalized ratio.

levels and pH and base deficit; however, no correlation was found between blood glucose levels and the duration of treatment, age, or serum bicarbonate concentration. Finally, they concluded that hyperglycemia can be a new prognostic factor in patients with methanol poisoning; however, further studies are required in this respect [9].

Desai et al. addressed pH as the strongest predictor for final visual acuity and its improvement. The risk of transient visual impairment is high in patients with a $\text{pH} < 7.2$ [5]. Ma et al. found that, at the initial stages of acute poisoning, all patients presented transient systemic symptoms (the vision ability of 0.1 or even less). After receiving treatment, the study patients' visual function was improved to different degrees at the one-year follow-up, but it was not satisfactory [12]. However, Shadnia et al. and Hassanian-Moghaddam et al. reported a similar level of pH between those who expired and those who survived [1, 6]. In line with the results of this study, Sanaei-Zadeh et al. reported no difference concerning pH concentration and the time interval between consumption and arrival to the hospital between the patients with and without visual disturbances [9].

The mortality rate was measured as 5% in our study; however, Shadnia et al. [1] and Sanaei-Zadeh et al. [9] reported mortality rates of 30% and 28%, respectively. Hassanian-Moghaddam et al. reported a mortality rate of 48%; 77% of them were fully recovered without any complications. For patients with a comma, the mortality rate was reported as 90%; while for other patients, it was reported as 20%, and this difference was statistically significant [6]. Mostafazadeh and Eghbali stated that approximately 18% of patients died in hospitals despite receiving appropriate treatment [7]. In the study by Massoumi et al., 4 patients died, also 15 patients with complications and 32 without complications, were survived [2].

In the study by Hovda et al., 8/59 patients with definite methanol poisoning died out of the hospital, and 9/59 died inside the hospital [3]. Ten percent of patients with the sequel and 73% without sequel survived. The authors reported that late hospital admission is the main cause of high morbidity and mortality. Prognostic factors for poor outcomes included respiratory arrest, coma, and severe metabolic acidosis at the time of admission. Finally, they argued that rapid admission, respiratory compensation, and metabolic acidosis were associated with patients' survival [3]. Paasma et al. identified $\text{pH} < 7$, coma [Glasgow Coma Scale (GCS) < 8], and insufficient hyperventilation at the time of hospital admission, as the strong predictors of the final therapeutic outcomes [13].

Shadnia et al. found that coma, respiratory depression, PaCO_2 , and hyperglycemia were strong prognostic factors for undesirable survival in these patients [1]. Furthermore, Hassanian-Moghaddam concluded that $\text{pH} < 7$ and coma at the time of admission, as well as delayed hospital admission (> 24 hours), are associated with a poor prognosis [6].

In this study, Computed Tomography (CT) scan findings of all patients were not recorded; thus, their exact investigation was impossible. However, Taheri et al. declared that 66.6% of patients with acute methanol poisoning manifested abnormal brain CT scan findings. They stated that in addition to clinical and laboratory findings, the presence of putamen hemorrhage and subcortex white matter necrosis, i.e., detectable in the brain CT scans of patients with acute methanol poisoning, are associated with poor outcomes. Therefore, this modality can be useful for physicians [14]. Sefidbakht et al. stated that CT scans and MRI data reveal changes in patients with methanol poisoning which can be helpful for physicians [15].

There was no significant difference between the research groups concerning the provided treatment. Shadnia et al. reported that treatment methods provided to both patients who either expired or survived were statistically the same. Besides, the treatment type did not affect the prognosis of patients [1]. Moghadami et al. found that folinic acid infusion provided no protective effect and only reduced acidosis in patients receiving folate [16]. Massoumi et al. recommended the rapid use of sodium bicarbonate in patients with methanol poisoning [2].

In developing countries, identifying methanol poisoning has limitations. Thus, active case finding and developing guidelines are beneficial interventions for reducing morbidity and mortality induced by methanol poisoning [17]. Increasing population' and healthcare providers' awareness about the complications of methanol poisoning and their prevention methods would be useful. Early diagnosis and treatment can prevent long-term complications. Additionally, the time interval between methanol intake and hospital admission is critical for preventing complications and death [2].

This was a retrospective study; accordingly, not recording methanol poisoning in the patients' medical records was expected to be a major problem, i.e., also found during the study. Most of the examined cases were recorded as alcohol poisoning; therefore, methanol poisoning was identified through evaluating the medical history sheets or physicians' notes. Thus, the speed of data collection was very slow. Meanwhile, several patients' medical

records may have been missed. Furthermore, the limited number of investigated patients per year, the high frequency of incomplete records, and the inadequacy of data were among the main limitations, which may have influenced the prognostic factors. Additionally, the low number of identified patients in the present study can be because some patients with methanol poisoning are referred to other centers. Therefore, multicenter, prospective studies can provide more precise information for physicians and policymakers. Establishing a registry system for patients with poisoning can provide further data in this regard.

Conclusion

In the present study, the incidence of visual disturbances in patients with acute methanol poisoning was higher than that in similar studies. Healthcare managers and policymakers should pay more attention to preventing methanol poisoning.

Ethical Considerations

Compliance with ethical guidelines

The current study was approved by the Vice-Chancellor of Research and Technology, as well as the Ethics Committee of Shiraz University of Medical Sciences (IR.sums.med.rec.1398.150). To observe the ethical issue, the collected data were not revealed to anyone, except for the researchers.

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Conflict of interest

The authors declared no conflicts of interest.

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