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Neurologic Complications of Methanol Poisoning: A Clinicoepidemiological Report from Poisoning Treatment Centers in Tehran, Iran

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Abstract

Background: In this study we sought to investigate clinical findings (with a focus on neurologic effects) and also to analyze outcomes of a series of patients with methanol poisoning admitted to two poisoning treatment centers in Tehran, Iran.
Methods: In this prospective cross-sectional study, methanol-poisoned patients admitted to departments of forensic medicine and toxicology of Loghman Hakim and Baharloo hospitals in Tehran during October 2010 to October 2011 were included; and their data were recorded in predesigned checklists.
Results: Twenty-eight methanol poisoned patients (82.1% men) with mean age of 29.3±4.6 years were studied. Most patients (67.9%) had metabolic acidosis at presentation. On admission, all patients had different degrees of decrease in consciousness, who the majority of them (57.1%) were admitted with mildly reduced consciousness (grade I of Grady coma scale). Headache and vertigo were observed in 7.1% and 17.9% of patients, respectively. Most patients (53.6%) had no ocular effects, while 46.6% of patients developed blurred. All patients received sodium bicarbonate. Ethanol as antidote and folic acid were given to 18 patients (64.2%) and 16 patients (57.1%), respectively. Six patients (21.4%) underwent hemodialysis. Over half of the patients (53.6%) fully recovered and were discharged without complications. Four patients (14.3%) developed total blindness. Four patients (14.3%) left the hospital against medical advice by self-discharge (they had no significant complication at the time of discharge). Five patients (17.9%) died; who compared to survived cases had significantly lower blood pH (P=0.028), higher coma grade (P<0.001) and more delayed presentation to hospital (P=0.004). Age had no significant impact on mortality.
Conclusion: Methanol poisoning causes major neurologic effects such as coma and blindness. It is also responsible for high mortality.

Keywords: Blindness; Methanol; Mortality; Neurologic Manifestations; Poisoning

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INTRODUCTION

Methanol poisoning has remained a common problem in many parts of the world. It may occur as a result of accidental consumption of methanol-contaminated alcoholic beverages, deliberate or accidental ingestion of methanol containing products and (rarely) inhalation of methanol fumes in chemical industries (1,2). The outbreaks of methanol poisoning most commonly arise from the consumption of adulterated counterfeit or informally-produced alcoholic drinks, especially in countries where alcohol use is banned (2,3).

Methanol, also known as methyl alcohol is a colorless, volatile, flammable and poisonous liquid with the chemical formula of CH_3OH. The lethal dose of methanol for humans is not clearly known, but is reported to range from 0.3 to 1 g/kg or blood methanol concentrations above 1500-2000 mg/L (2,4). Methanol is well absorbed through the gastrointestinal track and its peak serum concentration usually occurs within 30-90 minutes following oral intake. Methanol distributes widely in body fluids with a volume distribution of 0.6-0.7 L/kg (4). The highest concentration of methanol occurs in kidneys, liver and gastrointestinal track. Its concentration is also high in vitreous body (1).

Initial effects of methanol poisoning include central nervous system depression, headache, dizziness and ataxia. The patients may also suffer from nausea, vomiting, severe abdominal pain, tachycardia and tachypnea (1,5). After a latent period which usually lasts 12 to 24 hours, metabolic acidosis, kidney failure, optic neuritis, retinal edema and coma may develop depending upon the methanol dose ingested (5). Timely diagnosis and treatment of methanol poisoned patients has an essential role in reducing the mortality and preventing the debilitating complications such as blindness.

In this study we sought to investigate clinical findings (with a focus on neurologic effects) and also to analyze

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Table 1. Grady Coma Scale (6)

Grade	State of awareness	Responds appropriately to: Calling name	Light pain	Deep pain
I	Confused, drowsy, lethargic, indifferent and/or uncooperative; does not lapse into sleep when left undisturbed	Yes	Yes	Yes
II	Stuporous; may be disoriented to time, place, and person; will lapse into sleep when not disturbed; or belligerent and uncooperative	No	Yes	Yes
III	Deep stupor; requires strong pain to evoke movement	No	No	Yes
IV	Exhibits decorticate or decerebrate posturing to a deep pain stimulus	No	No	No
V	Does not respond to any stimuli; flaccid	No	No	No

outcomes of a series of patients with methanol poisoning admitted to two poisoning treatment centers in Tehran, Iran.

METHODS

In this prospective cross-sectional study, methanol-poisoned patients admitted to departments of forensic medicine and toxicology of Loghman Hakim and Baharloo hospitals in Tehran, Iran during October 2010 to October 2011 were included; and their demographic characteristics, poisoning circumstances, clinical manifestations, pH level and outcomes in addition to therapeutic interventions performed for them were recorded in predesigned checklists. The diagnosis of patients was confirmed based on positive toxicologic laboratory test for methanol in blood samples. The patients' level of consciousness has been determined according to the Grady coma scale (Table 1) (6).

Data were analyzed using SPSS for windows version 14 (SPSS Inc., Chicago, USA). Results are presented with frequency and percentage in tables. The mortality analyses were performed by comparing the clinical variables between dead and survived cases with chi squared test for categorical variables and with independent samples t-test for a normally distributed continuous variable. In addition, for comparison of categorical variables between two genders, chi squared test was done. P values less than 0.05 were considered statistically significant.

RESULTS

Demographic features and circumstances of poisoning

During the 12-month study period, 43210 poisoning cases (due to various toxic agents) were admitted to departments of forensic medicine and toxicology of Loghman Hakim and Baharloo hospitals, of which, 28 cases (0.06%) were due to methanol poisoning.

Most of the methanol-poisoned patients were men (23, 82.1%). Mean age of patients was 29.3 ± 4.6 years. The majority of patients (35.7%) aged over 35 years (Table 2). Considering the intention of poisoning, 92.9% of patients were poisoned accidentally due to drinking alcoholic beverages contaminated with methanol (in adults) or drinking methanol containing liquids (in children). Only two cases (7.1%) with suicidal purpose were observed. Most patients (35.7%) were transferred to the hospital within less than 4 hours after poisoning.

Clinical findings

Most patients (67.9%) had metabolic acidosis at presentation (Table 2). The most common gastrointestinal (GI) effects were nausea (35.7%) and vomiting (25%). GI effects were generally more common in women. Tachypnea was seen in 8 patients (28.6%).

Table 2. Demographic and on-admission clinical findings of methanol poisoned patients according to gender

Variables	Total (n = 28)	Men (n = 23)	Women (n = 5)
Age group (year), n (%)			
< 15	3 (10.7)	3 (13.1)	0 (0.0)
16-25	7 (25.0)	7 (30.4)	0 (0.0)
26-35	8 (28.6)	6 (26.1)	2 (40.0)
> 35	10 (35.7)	7 (30.4)	3 (60.0)
Intention of poisoning, n (%)			
Accidental	26 (92.9)	22 (95.7)	4 (80.0)
Suicidal	2 (7.1)	1 (4.3)	1 (20.0)
Gastrointestinal effects, n (%)			
Without manifestation	12 (42.8)	11 (47.8)	1 (20.0)
Nausea	10 (35.7)	7 (30.4)	3 (60.0)
Vomiting	7 (25.0)	5 (21.7)	2 (40.0)
Abdominal pain	5 (17.9)	2 (8.7)	3 (60.0)
Respiratory effects, n (%)			
Without manifestation	19 (67.9)	15 (65.2)	4 (80.0)
Tachypnea	8 (28.6)	8 (34.8)	0 (0.0)
Bradypnea	1 (3.5)	0 (0.0)	1 (20.0)
Blood pH imbalance, n (%)			
Normal	9 (32.1)	7 (30.4)	2 (40.0)
Metabolic acidosis	19 (67.9)	16 (69.6)	3 (60.0)

Neurologic effects

On admission, all patients had different degrees of decrease in consciousness, who the majority of them (57.1%) were admitted with mildly reduced consciousness (grade I of Grady coma scale) (Table 3). Headache and vertigo were observed in 7.1% and 17.9% of patients, respectively. Most patients (53.6%) had no ocular effects, while 46.6% of patients developed blurred vision. Blurred vision was more common in men compared to women, though the difference was not significant (P = 0.191).

Table 3. On-admission neurologic effects of methanol poisoned patients according to gender

Variables	Total (n = 28)	Men (n = 23)	Women (n = 5)
Level of consciousness (Grady coma scale), n (%)			
Grade I	16 (57.2)	12 (52.2)	4 (80.0)
Grade II	9 (32.1)	9 (39.1)	0 (0.0)
Grade III	3 (10.7)	2 (8.7)	1 (20.0)
Ocular effects, n (%)			
Without manifestation	15 (53.6)	11 (47.8)	4 (80.0)
Blurred vision	13 (46.4)	12 (52.2)	1 (20.0)
Headache, n (%)	2 (7.1)	2 (8.7)	0 (0.0)
Vertigo, n (%)	5 (17.9)	5 (21.7)	0 (0.0)

Table 4. Mortality analysis in patients with methanol poisoning

	Outcome		P value
	Death (n = 5)	Survival (n = 23)	
Blood pH, mean ± SD	7.06 ± 0.27	7.26 ± 1.0	0.028*
Age group (year), n (%)			
< 15	0 (0.0)	3 (13.1)	0.370**
16-25	0 (0.0)	7 (30.4)	
26-35	2 (40.0)	6 (26.1)	
> 35	3 (60.0)	7 (30.4)	
Level of consciousness (Grady coma scale), n (%)			
I	0 (0.0)	16 (69.6)	< 0.001**
II	2 (40.0)	7 (30.4)	
III	3 (60.0)	0 (0.0)	
Elapsed time from poisoning to hospital admission (hour), n (%)			
≤ 4	0 (0.0)	10 (43.4)	

Treatments

All patients received sodium bicarbonate. Ethanol as antidote and folic acid were given to 18 patients (64.2%) and 16 patients (57.1%), respectively. Six patients (21.4%) underwent hemodialysis.

Outcomes

Over half of the patients (53.6%) fully recovered and were discharged without complications. Four patients (14.3%) developed total blindness who all of them were men. Four patients (14.3%) left the hospital against medical advice by self-discharge (they had no significant complication at the time of discharge). Five patients (17.9%) died; who compared to survived cases had significantly lower blood pH (P = 0.028), higher coma grade (P < 0.001) and more delayed presentation to hospital (P = 0.004). Age had no significant impact on mortality (Table 4).

DISCUSSION

In this paper, clinical findings (with a focus on neurologic effects) of a series of patients with methanol poisoning were presented and the effective factors on the patients' outcomes were analyzed. Epidemics and outbreaks of methanol poisoning occur every so often in Iran (3,7,8). They are mostly due to illegal production of alcoholic drinks. Nonetheless, if we look at the problem of methanol poisoning in our country from epidemiologic aspect, it may seem that it is not a major poisoning concern as it only constitutes a minor proportion of poisoning cases; but if we take its morbidity and mortality into account, it is potentially a health dilemma.

In this study, reduced consciousness and metabolic acidosis were the most common clinical effects. This is consistent with the findings of Gharaee et al, Davanzo et al and Paasma et al (7,9,10). Central nervous system depression is one of the very first signs of methanol poisoning (1,11). However, deep levels of reduced consciousness and ocular effects need more time to develop (1,11). Deep stupor was only seen in 10.7% of our patients which is comparatively lower than the rate of comatose patients in the studies done by Hovda et al (24%) and Davanzo et al (44.8%) (9,12). This can be due to the difference in poisoning severity of cases enrolled in the mentioned studies.

Over two-thirds of our patients had metabolic acidosis at presentation to hospital. Metabolic acidosis is one of the hallmarks of methanol poisoning. Once the methanol enters the blood stream and circulates through the liver, it is metabolized to formaldehyde and eventually to formic acid (11,13). This later substance is responsible for both metabolic acidosis and retinal and optic nerve damage (11,13). Blurred vision was present in nearly half of our patients. This was comparable to the findings by Hovda et al in Norway (12), though it was twice the rate of visual abnormalities reported by Kalkan et al in Turkey (14). We were able to treat three-fourths of the patients with visual reduction and only 14.2% of our patients eventually developed blindness. Davanzo et al, Paasma et al and Shadnia et al similarly reported total visual loss in about 7 to 12.2% of their patients (9,10,15).

The most effective antidote for methanol poisoning is fomezpizole (13,16). However, due to its high price in pharmaceutical market, it is not available in most poisoning treatment centers especially in developing countries. Hence, in such cases the ethanol with similar properties is given for methanol-poisoned patients. In addition, sodium bicarbonate can help to balance the blood pH of these patients. Hemodialysis is a necessary treatment for severe methanol toxicity (17), which refers to blood pH of lower than 7.3, visual abnormalities, renal failure or electrolyte imbalance unresponsive to conventional therapy and/or serum methanol concentration of over 50 mg/dL (5).

Methanol is highly toxic and causes high case fatality rate (18). In the present study, 17.9% of the patients died in the hospital. The hospital mortality rate of methanol poisoning has been reported to be 17.6 to 30% in different studies (8,10,12,15,19). In the current study, patients with delayed presentation to hospital, lower blood pH and deeper loss of consciousness were more likely to die. Paasma et al, Zakharov et al and Hovda et al similarly ascertained severe metabolic acidosis and reduced consciousness on admission

as the strongest predictors of poor outcome after methanol poisoning (8,12,19). Hence, early diagnosis and quick delivery of medical care to patients with a special attention to prompt normalization of pH level have essential roles in preventing serious complications and death.

Looking to this toxicologic problem from the public health aspect reveals that illegal production of alcoholic beverages and lack of awareness about detrimental effects of drinking methanol-containing products play the most important roles. Hence, it has been suggested that poison centers undertake the task of starting up informatory programs for public and triggering media alerts about illegally produced alcoholic beverages and methanol-containing liquids (20).

LIMITATIONS

The small number of cases presented in this study may limit the statistical inferences made. The blood methanol concentration of patients could not be measured in this study. In addition, researchers were not able to estimate the dose of methanol ingested by the patients.

CONCLUSION

Methanol poisoning causes major neurologic effects such as coma and blindness. It is also responsible for high mortality. Medical staff, especially medical toxicologists and emergency physicians should be trained about symptoms, diagnostic keys and early treatment of methanol poisoning.

Conflict of interest: None to be declared.

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