Prognostic Factors including clinical manifestation and Paraclinic finding in sever methanol toxicity

Seyed Ali Bahreini Moghaddam[1], Abdolkarim Pajoumand[2,3*]

[1]Executive management, Loghman-Hakim Hospital, ShahidBeheshti University of Medical Sciences, Tehran, Iran.
[2]Toxicological Research Center, Loghman-Hakim Hospital, Department of Clinical Toxicology, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[3]Poison Control Center, Loghman–Hakim Hospital, Shahid Beheshti University of Medical Sciences ,Tehran, Iran
*Corresponding Author: Dr_pajoumand@yahoo.com

Abstract: The aim of this study was to assess the clinical and laboratory factors in methanol poisoned patients to determine the prognosis of their toxicity. Methods: This survey was done as a prospective cross-sectional study in methanol-poisoned patients in Loghman-Hakim hospital poison center during 9 months from October 1999–June 2000 and also 42 patients by CT Methanol Toxicity finding in 2007. During this time 25 methanol-poisoned patients were admitted. Results: The mortality rate was 12 (48%). Amongst survivors, three (23%) of the patients developed blindness due to their poisoning and the other 10 (77%) fully recovered without any complication. The mortality rate in comatose patients was nine (90%) while in non-comatose patients it was three (20%) (P < 0.001). There was a significant difference in mean pH in the first arterial blood gas of patients who subsequently died (6.82±0.03) and survivors (7.15±0.06) (P < 0.001, M-W). The mean time interval between poisoning and ED presentation in deceased patients were (46 ±15.7) hours, in survived with sequelae were (16.7± 6.7) and in survived without sequelae were (10.3 ±7.2) hours (P<0.002, K-W). We found no significant difference between the survivors versus the patients who died regarding methanol. Conclusion: Simultaneous presence of ethanol and opium affected the outcome of the treatment for methanol intoxication favourably and unfavourably, respectively. In our study, poor prognosis was associated with pH< 7, coma on admission and >24 hours delay from intake to admission. It seems CT finding are important as Methanol concentration before any other Paraclinic findings and even clinical manifestations.
[Seyed Ali Bahreini Moghaddam, Abdolkarim Pajoumand. **Prognostic Factors including clinical manifestation and Paraclinic finding in sever methanol toxicity**. *Life Sci J* 2014;11(2s):11-14]. (ISSN:1097-8135). http://www.lifesciencesite.com. 3

Key words: fatal outcome; methanol; prognosis; toxicity

Introduction

Methanol is a toxic alcohol present in many solvents, antifreeze solutions, glass cleaner and windshield wiper fluid. Paint Remover and also may contaminated along with Home Ethanol production in some countries. Ingested methanol undergoes enzymatic oxidation to toxic formic acid, resulting in acidosis, neurotoxicity and death in severe poisoning. Massive methanol ingestion is still complicated by a high mortality rate. Patients who are admitted with delay have already developed a severe metabolic acidosis due to the biotransformation of methanol into toxic metabolites. Treatment relies on antidote administration (fomepizole or ethanol) to antagonize Methanol oxidation, folic acid to facilitate the catabolism of formic acid, correction of acidosis and dialysis to accelerate methanol elimination.(1) According to Iranian law, selling, buying and consumption of alcoholic beverages is a punishable crime. People who wish to drink alcohol use industrial or homemade ethanol that sometimes are a mixture consisting of methanol and ethanol. Both fear of punishment and delayed onset of symptomatic poisoning cause late presentation and is associated

with a high mortality rate. This occurs even though patient confidentiality is maintained. Rapid diagnosis and treatment are necessary to prevent death and to minimize the neurologic sequelae. The aim of this study was to assess the clinical and laboratory factors in methanol poisoned patients to determine the prognosis of their toxicity.

Materials, patients and methods

This was a prospective cross-sectional study which was carried at Loghman poison ward in Tehran, Iran. The Loghman toxicology unit serves a population excess of 12 million and normally sees 28 000 emergency ward presentations due to poisoning each year of which 12.5 thousand are admitted. This is the only tertiary hospital for poisoned patient in the capital city and is the largest in the nation. According to the best of our knowledge our inpatient complex seems to be the biggest clinical toxicology department in the world. The study period was from October 1999–June 2000. In that period of time all 113 patients who consumed alcohol and had poisoning examined and questionnaires were filled by physicians. Descriptive data were include age,

gender, time elapsed consumption, blood pH, level of consciousness, laboratory profile include ethanol and methanol level and presenting symptoms and physical examinations on date of admission. After taking 2 mL blood that contain sodium fluoride sample were analysed by a gas chromatograph method in order to detect methanol and ethanol (Varian 6000 USA, Pack column: Propack Q 1.5m× 5 mm, flame ionization detector, Carrier gas: nitrogen 99.99%, flow rate 1 mL/minute, analytical condition: injection temperature 160°C, oven temperature 200°C, detector temperature 210°C). Care was taken to select those who were methanol positive. Those who had just ethanol (71 cases) or no other alcohol levels (17 cases) were excluded. All cases reviewed were assigned to one of the following three categories based on their outcomes: (1) complete recovery, (2) blindness and other neurological morbidities, (3) death. Blindness was confirmed by an ophthalmologist. In another research which was done in our hospital and TRC by Dr.Hassanian et..al CT finding in sever Methanol intoxication (2,3). Treatment was given according to the available standard protocols, and in accordance with the Helsinki Declaration. Analyses were performed from blood samples already drawn for treatment purposes. Institutional review board or ethic committee approval was not required for this study. Coma was defined as Glasgow coma scale less than 7. Time interval between methanol ingestion and ED arrival time was traceable in approximately three-quarters of all patients. All data were analysed with SPSS software, version 12. All data were collected either as dichotomous variables (eg, outcome) or as, continuous (eg, blood pH, methanol levels). Statistical comparisons were carried out using Pearson chi-square to evaluate differences between dichotomous and nonordered categorical variables. Fisher's exact test of significance was used where contingency tables contained one or more cells with an expected cell count less than five and the Pearson chi-square P-value was 0.05 or less. The Kruskal–Wallis test was used to analyse significant difference within the three groups and the Mann–Whitney U-test to compare differences group by group in medians between categorical variables as appropriate.

Results

Analysis of data revealed a total 25 patients were included for methanol poisoning from October 1999–June 2000. Of these, 23 were male; their mean age was 38.5 years (range 16–75). Twelve (48%) patients died and the others were alive, whereas three of them (23%) were blind. Table 1 shows median value of serum analyses and delay from intake to admission in survivors without/with sequelae and

dead. Three cases of methanol poisoning had concomitant usage of opium which all of them died. Because of hemodynamic instability hemodialysis was performed just in 12 out of 25 patients. The mean serum pH was 7.00 ±0.22 for those patients who underwent dialysis (range 6.68–7.28) and 6.98±0.22 for the others (range 6.71–7.35) (P < 0.83). Three patients had detectable ethanol and methanol levels all survived, but death occurred in three other cases who had consumed opium. Respiratory arrest and coma on admission were robust markers of poor outcome (Table 2). Ninety Percent of all patients who had experienced coma died but 20% (3/15) of non-comatose patients passed away (P< 0.001). All four patients (16%) who had respiratory arrest on arrival time were died. Although we did not mention the correlation between pH and pCO2 on admission and the final outcome, the latter finding may point towards that the ability to hyperventilate as a prognostic factor. The most common findings at presentation were respectively: 60% blurred vision, 56% fixed and/or dilated pupil, 56% vomiting, 52% nausea and 40% coma. There was a patient who admitted with seizure that finally died. The objective was on early brain CT damaged separate from clinical manifestation   42 patients met inclusion criteria it showed 28 (66.7%) positive CT findings common features were bilateral hypodensity lesion in putamen and also low attenuation in subcortical while matter bilateral hemorrhagic necrosis in putamen and bilateral hypodensity in globus pallidus in regard with CT findings .(Table 3)

Discussion

The purpose of this study was to assess the clinical and laboratory factors in methanol-poisoned patients to determine the prognosis of their toxicity. We found a significant correlation between bad prognosis and coma upon admission, serum pH below 7, and more than 24 hours between intake of methanol and admission if no ethanol was coingested. These findings are in accordance with previous reports.(4) Also we found that there is close relation between mean serum pH and mean time elapsed since methanol consumption (P< 0.005 R = -0.6). The results show no correlation between methanol levels and prognosis; this may be due to its biotransformation into formaldehyde and formic acid under the influence of alcohol dehydrogenase. (5) It may also be due to the fact that most patients who died presented later. Our study shows that mean methanol level in our cases is lower (35 mg/dL versus 165, 60 and 196) than other studies.(4,6-8) One possible explanation for this discrepancy is that in untreated or delayed cases of methanol poisoning.

Table1. A median value of serum analyses and delay from intake to admission in the different group

	Group 1 Median (range)	Group 2 Median (range)	Group3 Median (range)	P-value	Stat. method
S-methanol (mg/dL)	40 (3–93)	12 (5–25)	34 (7–143)	NS	KW
S-methanol (mmol/L)	13.2 (1–30.8)	4 (1.7–10.3)	11.2 (2.3–47.3)		
pH	7.15 (6.68–7.35)		6.82 (6.69–6.95)	<0.001	MW
Time from intake to admission (hours)	10 (1–24)	17 (11–24)	46 (16–72)	<0.002	KW

Group 1: Survived without sequelae. Group 2: Survived with sequelae. Group 3: Dead. KW = Kruskall–Wallis, MW= Mann–Whitney, NS =non-significant.

Table 2. Comparison of important clinical features on admission in survivors and dead

Group	Survivors	Dead	P-value	Stat. method
Coma at admission	1 (10%)	9 (90%)	0.001	CS
No respiratory arrest on admission	13 (62%)	8 (38%)	<0.04	Fisher

CS= Pearson chi-square, Fisher= Fisher's exact test.

Table 3. Prognostic Factors including clinical manifestation and Para clinic finding in sever methanol toxicity

CT finding	Positive serum Methanol N(%)	Negative serum Methanol N(%)	Total N(%)
Positive CT finding	22(52.4)	6(14.3)	28(66.7%)
Negative CT finding	4(9.5)	10(23.8)	14(33.3%)

It is reasonable to suppose that eventually all of the methanol will be metabolized and the severity of methanol poisoning is reflected by the magnitude of metabolic acidosis,which is caused by formic acid accumulation.(9-11) Other studies have varying findings regarding this, which should come as no surprise. Toxicity comes from the toxic metabolite and not from methanol itself, hence the amount of methanol that was drunk, the time from intake to admission and concomitant ethanol intake would be a better theoretic prognostic element, although these are parameters not always known when the patient presents with a metabolic acidosis of unknown origin. That is why parameters/prognostic factors that can still be found while the patient presents in hospital is so important. (4-8-12) Our results also showed that all three cases who had ethanol blood level survived. This finding is in agreement with the other studies which showed that patients who ingested both methanol and ethanol were more likely to survive than those who ingested only methanol. (1, 8, 14) Concomitant opioids were found in three patients, whom all died. Also all of the patients who had respiratory arrest on arrival time passed away. This can be due to a lack of ability to compensate the metabolic acidosis by respiratory mechanisms, a feature already described by Hovda et al.6 Although the number of our cases was limited but we assume that methanol level is not a good predictor for prognosis in our patients and should not be used as an indication for establishing or cessation of hemodialysis. The severity of acidosis and the clinical presentation are better indicators of outcome.(4,8,14,15) According to existence of low methanol level in spite of severe metabolic acidosis in some of our cases it is logical if we suppose that hemodialysis should be continued until elimination of toxic metabolites and metabolic acidosis.(15-17) The mortality rate in our study was 48% while other studies revealed 18%,(6) 14.1%,(16) 16.7%,(17) 36%(18) and 3%.(21) To the best of our knowledge this is the highest mortality rate that has been published. The number of comatose patients and prolong time from intake to admission beside the illegality of alcohol and fear of punishment keep the patients from seeking help, and indirectly describe part of the high mortality.

Conclusion

In our study, poor outcome was associated with coma on admission, and metabolic acidosis on admission with pH below 7.00. Poor prognosis was also found when time from intake to admission was more than 24 hours. A positive S-ethanol on admission was associated with a good outcome while presences of opioids worsen it. Methanol concentration was not useful in our patients in predicting death. We recommend further research in a larger group based on correlation of methanol, formate, blood gas analysis and imaging finding. In conclusion, it seems CT finding are important as Methanol concentration before any other Paraclinic findings and even clinical manifestations.

CorrespondingAuthor:
Dr. Abdolkarim Pajoumand
Toxicological research center, Loghman Hakim Hospital ,Shahid Beheshti University of Medical Sciences ,Tehran, Iran and Poison Control Center, Loghman–Hakim Hospital, Shahid Beheshti University of Medical Sciences ,Tehran, Iran
E-mail:Dr_pajoumand@yahoo.com

References
1.   Barceloux B, Bond GR, Krenzelok EP, Cooper H, Vale JA. American Academy of Clinical Toxicology practice guidelines for the treatment of methanol poisoning. Journal of Toxicology Clinical Toxicology. 2002; 40: 415–46.
2.   Taheri MS, Moghaddam HH, Moharamzad Y, Dadgari S, Nahvi V. The value of brain CT findings in acute methanol toxicity. Eur J Radiol. 2010 Feb; 73:211-4.
3.   Paasma R, Hovda KE, Hassanian-Moghaddam H, Brahmi N, Afshari R, Sandvik L, Jacobsen D. Risk factors related to poor outcome after methanol poisoning and the relation between outcome and antidotes--a multicenter study. Clin Toxicol (Phila). 2012; 50: 823-31.
4.   Liu JL, Daya MR, Carrasquillo O, Kales SN. Prognostic factors in patients with methanol poisoning. Clinical Toxicology. 1998; 36: 175–81.
5.   Sejersted OM, Jacobsen D, Ovrebo S, Jansen H. Formate concentration in plasma from patients poisoned with methanol. Acta Medica Scandinavica. 1983; 213: 105–10.
6.   Nolla-Salas J, Nogue Xarau S, Marruecos Sant L, Palomar Martinez M, Martinez Perez. [Methanol and ethylene glycol poisoning. Study of 18 cases]. Medicina Clínica. 1995; 104: 121 25.
7.   Kerns W, Tomaszewski C, McMartin K, Ford M, Brent J. Formate kinetics in methanol poisoning. Journal of Toxicology. Clinical Toxicology. 2002;40: 137–43.
8.   Hovda KE, Hunderi OH, Tafjord AB, Dunlop O, Rundberg N, Jacobson D. Methanol outbreak in Norway 2002–2004: epidemiology, clinical features and prognostic signs. Journal of Internal Medicine. 2005; 258: 181–90.
9.   Mahieu P, Hassoun A, Lauwerys R. Predictors of methanol intoxication with unfavorable outcome. Human Toxicology. 1989; 8: 135–37.
10.   Martin-Amat G, McMartin KE, Hayreh SS, Hayreh SS, Tephly TR. Methanol poisoning: ocular toxicity produced by formate. Toxicology and Applied Pharmacology. 1978; 45: 201–205.
11.   Sharpe JA, Hostovsky M, Bilbao JM, Rewcastle NB. Methanol optic neuropathy: a histopathological study. Neurology. 1982; 32: 1093–100.
12.   Swartz RD, Millman RP, Billi JE, Bondar NP, Migdal SD, Simonian SK, Monforte JR, McDonald FD, Harness JK, Cole KL. Epidemic methanol poisoning: clinical and biochemical analysis of a recent episode. Medicine. 1981; 60: 373–82.
13.   Jacobsen D, McMartin KE. Methanol and ethylene glycol poisonings. Mechanism of toxicity, clinical course, diagnosis and treatment. Medical Toxicology. 1986; 1: 309–34.
14.   Jacobsen D, Jansen H, Wiik-Larsen E, Bredesen JE, Halvorsen S. Studies on methanol poisoning. Acta Medica Scandinavica. 1982; 212: 5–10.
15.   Osterloh JD, Pond SM, Grady S, Becker CE. Serum formate concentrations in methanol intoxication as a criteria for hemodialysis. Annals of Internal Medicine. 1986; 104: 200–203.
16.   Shahangian S, Ash KO. Formic and lactic acidosis in a fatal case of methanol intoxication. Clinical Chemistry. 1986; 32: 395–97.
17.   Fraser AD, MacNeil W. Gas chromatographic analysis of methyl formate and application in methanol poisoning cases. Journal of Analytical Toxicology. 1989; 13: 73–76.
18.   Kalkan S, Cevik AA, Cavdar C, Aygoren O, Akgun A, Ergun N, Tuncok Y. Acute methanol poisonings reported to the Drug and Poison Information Center in Izmir, Turkey. Veterinary and Human Toxicology. 2003; 45: 334–37.
19.   Meyer RJ, Beard ME, Ardagh MW, Henderson S. Methanol poisoning. The New Zealand Medical Journal. 2000; 113: 11–13.
20. Krishnamurthi MV, Natarajan AR, Shanmugasundaram K, Padmanabhan K, Nityanandan K. Acute methyl alcohol poisoning (a review of an outbreak of 89 cases). The Journal of the Association of Physicians of India. 1968; 16: 801–805.
21.   Chen WY, Jeng GY, Yen TS, Hsieh BS, Kuo TL, Fong JM. Studies on acute methanol intoxication. Taiwan yi xue hui za zhi. Journal of the Formosan Medical Association. 1978; 77: 97–102.

1/12/2014