İst Tıp Fak Derg 2012; 75:2
J Ist Faculty Med 2012; 75:2
www.itfdergisi.com

METHANOL POISONING IN THREE CASES: DIAGNOSIS AND TREATMENT IN EMERGENCY DEPARTMENT

ÜÇ OLGU İLE METANOL ZEHİRLENMESİ: ACİL SERVİSTE TANI VE TEDAVİ

Fatma Mutlu KUKUL GÜVEN*, Kenan Ahmet TÜRKDOĞAN*, Şevki Hakan EREN*, Hüseyin AYDIN, İlhan KORKMAZ*, Abuzer COŞKUN*****

ABSTRACT

Methanol is a very poisonous substance that is used as an industrial solvent and automotive antifreeze. Toxic dose is between 20-250 ml and causes neurological symptoms such as headache, cerebral edema and putamen necrosis within the first 12 to 14 hours. Central nervous system and visual cortex are the main areas which are damaged by methanol poisoning. Methyl alcohol is not toxic until its toxic metabolites turn into formic acid. Formic acid is especially responsible for the clinical findings. Serum half-life of methanol is 14 to 20 hours in mild and 24 to 30 hours in severe toxicity. Gastric lavage, fomepizole, ethanol and hemodialysis are used in the treatment. In this study, we aimed to review and discuss information from literature about the treatment and monitoring of methanol poisoning in three cases followed at emergency department.

Key words: Methanol poisoning, emergency, blurred vision, hemodialysis

ÖZET

Metanol endüstriyel bir çözücü ve otomotiv antifrizi olarak kullanılan çok zehirli bir maddedir. Toksik doz 20-250 ml. arasında olup 12-14 saat içinde baş ağrısı, beyin ödemi ve putamen nekrozu gibi nörolojik bulgular verir. Merkezi sinir sistemi ve görme yolu metanol zehirlenmesinde etkilenen ana bölgelerdir. Metil alkol toksik metabolitleri olan formaldehit ve formik aside dönüşünceye kadar toksik değildir. Klinik bulgulardan özellikle formik asit sorumludur. Metanolün hafif toksititeden sonra serum yarılanma ömrü 14-20 saat, şiddetli toksisiteden sonra 24-30 saattir. Tedavide gastrik lavaj, fomepizol, etanol ve hemodializ kullanılır. Bu çalışmada üç olgu ile acil serviste takip edilen metanol zehirlenmesinin takip ve tedavisinin gözden geçirilmesi amaçlanmıştır.

Anahtar Kelimeler: Methanol zehirlenmesi, acil, bulanık görme, hemodiyaliz

INTRODUCTION

Methanol is a colourless, odourless substance that is in liquid state in room temperature. Until 1930s it was also known as wood alcohol since it was produced from wood (1,2). Today, approximately 70% of the methanol produced worldwide is used in chemical synthesis(3). Ingestion of methanol instead of ethanol creates serious problems for alcohol abusers, although the harmful effects of methanol are known (4,5). The cases are mostly between the ages of 30-40 and a great majority -80-90%- of them are men (2). Acute methanol poisoning could be seen sporadically and epidemically and usually it results in death (6.7). With the suicidal idea of suicide in mind, chronic alcoholics may get poisoned by ingestion and consuming products containing methanol and alcoholic drinks which are illegally prepared and normally should not contain methanol. As a specific antidote treatment ethyl alcohol or fomepizole is used (8,9). If blood level of methanol is >50 mg/dl, treatment of acidosis with bicarbonate does not respond (pH<7.2), and in cases of ocular manifestations and renal failure, haemodialysis is recommended (8-10). If history of methanol ingestion is not exactly known, without wasting time with other examinations in diagnostic process, early diagnosis and right treatment could prevent mortality (7). In this study, we aimed to review and discuss the information from literature about the treatment and monitoring of methanol poisoning in emergency department.

CASE

Case 1. A male patient aged 22 admitted to our casualty department with complaints of blurred vision, nausea, and inability to maintain balance. It was learned that he had been found unconscious by his friends and had drunk 3-4 glasses of cologne (600-800ml) about 14 hours before the admission. In the casualty department, overall situation of the patient was normal, he was conscious, cooperative, oriented, IR:+/+ and his Glasgow Coma Scale (GCS) was 15 (Eyes: 4, Motor Response: 6, Verbal Response: 5). Vital signs were detected as; blood pressure (BP) 130/80 mmHg, pulse (P) 70/min, respiratory rate (RR) 22/min. Neurological examination of the patientwas natural except for hyperaemia on the optic disc. Other systemic findings were normal. ECG was normal and sinus rhythm rate was 72/min. With the diagnosis of methanol poisoning, he was taken into emergency department observation unit and treatment process was started. The following laboratory values were gained: arterial blood gases: pH: 7.21,

Date received/Dergiye geldiği tarih: 26.08.2011 - Dergiye kabul edildiği tarih: 13.11.2011

* Cumhuriyet Üniversitesi Tıp Fakültesi , Acil Tıp Anabilim Dalı
(İletişim kurulacak yazar: mutlukukul@gmail.com)
** Biyokimya Anabilim Dalı
***Numune Hastanesi, Acil Servis, Sivas

PCO2:31.2 mmHg, PO2:105.5 mmHg, HCO3:12.6 BE: 13.4 mmol/L, sO2 95.% Hemogram; WBC: 20500µL, Hgb: 16.4g/dl, Plt:341000µL, Glucose: 198mg/dl, BUN: 8mg/dl and creatinine: 1.1 mg/dl, AST:31U/L, ALT: 44 U/L. PA chest x-ray and brain tomography were assessed as normal. Due to acidosis (pH: 7.21) and ocular manifestations; oral ingestion of the patient was stopped and urgent dialysis was planned. As pH was < 7.3 and bicarbonate was < 20 meq/L (mmol/L), ethyl alcohol treatment was administered. Because the chronic alcohol ingestion history of the patient was unavailable, 43% oral ethyl alcohol solution was prepared for the patient and given as 1.8 ml/kg in bolus, 0.2 ml/kg/hour in maintenance, and 0.5 ml/kg/hour during dialysis. Arterial cannula was placed and arterial blood gases were monitored intermittently. After first dialysis, his blurred vision and the acidosis in arterial blood gases improved. Acidosis was not observed in the findings carried out every two hours until the 16th hour. In the blood analysis ordered at 16th hour, findings were; pH:7.28, pCO2: 22,4 mmHg, pO2: 89 mmHg, HCO3 10.4 mmol/L and BE15,2 mmol/L, and the patient was taken into dialysis without heparin for two hours. After 4 days, blood gases and lab findings were within normal ranges.

Case 2. A 60 year-old male patient who was referred to our department by another hospital with the pre-diagnosis of head trauma had the complaints of blurred vision, shortness of breath and dizziness. It was learned from the patient's relatives that he had hit his head on a wall. Along with his chronic alcohol history, it was learned that he had drunk 3 glasses of cologne (600 ml) about 48 hours before the admission. In his examination, he was conscious, cooperating, oriented, IR: +/+ , his GCS was 15 (Eyes: 4, Motor Response: 6, Oral Response: 5). BP: 180/110 mmHg, P: 85/min, RR: 24/min. In his right temporal region, a hematoma of 2x2 cm in size was detected. ECG was normal and sinus rate was 82/min. Fundus examination showed hyperaemia on the optic disc but other systemic examinations were normal. Laboratory investigations were as follows: arterial blood gases pH:7.25, PCO2:21.3 mmHg, PO2:109.5mmHg, HCO3: 9.4mmol/L, Glucose:149 mg/dl BUN: 14mg/dl, creatinine:1.3mg/dl, AST: 26U/L, ALT:33U/L, WBC:9400µL, Hgb:16.1 g/dl, PLT: 381000µL. Chest x-ray and brain tomography were assessed as normal. His history, physical examination findings and existence of metabolic acidosis in arterial blood suggested a final diagnosis of methanol poisoning and he was taken into observation unit. Urgent dialysis was planned due to ocular findings, arterial blood pH < 7.3, serum bicarbonate < 20 meq/L and ethyl alcohol treatment was started. As the patient had chronic alcohol ingestion, 43%. oral ethyl alcohol solution was administered 1.8 ml/kg in bolus, 0. 46 ml/kg for maintenance and 0.77 ml/kg/hour during the dialysis to the patient. He was taken into dialysis without heparin for once. He recovered from blurred vision and the hyperaemia on optic disc. After dialysis; recovery was detected in the monitoring of blood gases. As he showed clinical improvement, he was discharged from the hospital.

Case 3. A female patient aged-96 was brought to our department by an ambulance with the pre-diagnosis of CVD (cerebrovascular diseases). It was learned from her relatives that she did not wake up that morning and she had not had any complaints before. Her overall situation was bad, she was unconscious, IR: +/+, GCS 10, and she was taken into resuscitation room. On her examination in the casualty department her overall situation was bad and she was confused. She was uncooperative and disoriented. IR: +/+, GCS 8 (Eyes: 2, Motor Response: 3, Oral Response: 3). Vital signs were; BP: 80/35 mmHg, P: 42/min, RR: 12/min breath. As she went into arrest during stabilization process, she was intubated and CPR was introduced simultaneously. Due to lack of spontaneous respiration, she was connected to the mechanic ventilator. She responded to the CPR 20 minutes later. Her ECG after CPR was arrhythmic and tachycardic and she had V4-V6 T(-). Her GCS was 3 (Eyes: 1, Motor Response:1, Oral Response:1). Vital signs of the patient who had no spontaneous respiration after CPR were: BP: 110/ 75 mmHg, P: 125/min, RR: MV. In the blood samples taken after resuscitation, arterial blood gasses: pH: 7.29, PCO2: 29 mmHg, PO2: 98 mmHg, HCO3: 17.2 mmol/L, BUN: 24mg/dl, creatinine: 1.2 mg/dl, ALT: 51 U/L, AST: 71 U/L, WBC: 5200 µL, HB: 11.1 g/dl, PLT: 360000 µL. Chest x-ray showed bilateral hilar enlargement and pneumonic infiltration on the right lung lower lobe. There was cortical atrophy compatible with her age in the brain tomography.The causes of metabolic acidosis were pre-diagnosis of CVD, diabetic ketoacidosis, intoxication (salicylate, methanol etc..) and her history were re-questioned. Upon the evidence that her relatives had found an empty cologne bottle at home, it was considered that the patient could have drunk some cologne accidentally approximately 7 hours ago. Since she had the need for mechanic ventilator she was taken to the intensive care unit with the diagnosis of methanol poisoning. Because the arterial blood gases were pH<7.3, and serum bicarbonate <20 meq/L, she was started ethyl alcohol treatment. Since second blood gas was taken after resuscitation and pH value was 7,32 in the 30th minute after resuscitation, dialysis was not planned and she received supplementary treatment. Because the patient, whose oral ingestion was stopped in the intensive care unit, did have; history of chronic alcohol abuse, she was given ethyl alcohol treatment 1.8 ml/kg in bolus and 0.2 ml/kg/hour in maintenance. She was extubated after two days and discharged from the hospital on the 5th day.

Table 1. Arterial blood gases values

Arteriel blood gases value	pH	pCO2	pO2	HCO3	BE-ecf
FIRST CASE					
Arrival	7.21	31.2	105.5	12.6	-13.4
4th hours (after the first hemodialysis)	7.34	28.9	82.2	15.9	-10.0
8th hours	7.31	24.1	105.2	12.2	-14.3
16th hours	7.28	22.4	89	10.4	-15.2
18th hours (after second hemodialysis)	7.41	42.2	80.7	26.9	+ 2,0
36th hours	7.41	48.7	89	31.0	+ 2.0
48th hours	7.45	47.4	100.2	33.7	+ 9.6
SECOND CASE					
1st hour	7.25	21,3	109.5	9.4	-18.1

4th hours (after the first hemodialysis)	7.53	22.8	119.7	19.4	-3.4
10th hours	7.45	38.1	91	26.9	+3.6
24th hours	7.46	40.5	94	29.2	+5.1
36th hours	7.41	33.9	88	22.0	- 2.8
48th hours	7.43	38.7	89	26.4	+2.8
THIRD CASE					
post resuscitation 30th minutes	7.32	29	50	17.2	-7.9
4th hours	7.39	30	64.1	18	-7.3
10th hours	7.35	29	142	16	-8.8
24th hours	7.54	32	112	28.2	+6.2
36th hours	7.56	30	121	27	+5.0
48th hours	7.53	34	120	29.8	+6.0

DISCUSSION

In our country, laws and legislations which define the aspects of comestibles and goods and substances related to general health prohibit the use of methyl alcohol in alcoholic drinks and colognes and oblige the use of ethyl alcohol (2,12). Most of the methyl alcohol poisoning in our country are caused by illegally prepared and released alcoholic drinks containing methyl alcohol. Elmas et al. pointed out that 42. 5% of deaths of methyl alcohol poisoning in Turkey are due to alcoholic drinks and 19.2% due to cologne ingestion (12). Yaycı et al. explained in a series of 271 cases that 10.7% of the deaths were due to ingestion of alcoholic drinks or cologne and due to lack of adequate information of the products consumed -89.3 % of the products could not be identified (2,5) .

In our country, while 205 cases were reported between 1994 and 1998 in the study of İnanıcı et al. ,124 cases were reported between 1992 and 1997 in the study of Turla et al. (2,6,13). Stomach irrigation is advised in the first hour of methanol poisoning. Since methanol ingestion delays the stomach flush, aspiration with N/G is recommended. Oxygen inhalation, if necessary, beta-2 agonist and corticosteroid treatment; for eye contamination, washing for 15 minutes with water in room temperature; for exposure by way of skin washing with water and soap are recommended. Supplementary and symptomatic treatment is advised (9,10,14). Regression is achieved through amelioration of metabolic acidosis, by intravenous (IV) sodium bicarbonate (pH fixed at >7.3) (8). As a specific antidote treatment ethyl alcohol or fomepizole is used. Although it is stated that fomepizole has more specific effects and less adverse effects, there are no controlled studies that clinically prove the superiority of it (8-10,14). Indications for the use of ethyl alcohol (or fomepizole) in the treatment of methanol poisoning (8,9):

1. Plasma methanol concentration >20 mg/dl
2. History of methanol ingestion in toxic amounts and osmo gap >10 mOsm/kg H2O
3. Along with history or clinical evidence suggesting methanol poisoning, at least two of the criteria of arterial blood pH<7.3, serum bicarbonate < 20 meq/L (mmol/L), osmo gap > 10 mOsm/kg H2O.

If blood methanol level is >50 mg/dl, acidosis does not respond to bicarbonate treatment (pH<7.2), and in cases of ocular manifestations and renal failure, haemodialysis is recommended. Haemodialysis is stopped when methanol is reduced to the level below 20 mg/dl or metabolic acidosis shows regression (pH > 7.3) 8-10.14. It is recommended to go on with the treatment so that blood ethyl alcohol level is kept between 100-150 mg/dl or until blood methanol level is reduced to zero (3,10,15,16). Ethyl alcohol was used as the antidote in each three cases and haemodialysis was performed alongside. As blood methanol and blood ethanol levels could be investigated in our laboratory, treatment was completed according to clinical assessment and blood gases.

Lethal dose of methyl alcohol for people varies between 15 and 500 ml (9,15). There are reports of patients surviving with no organic damage to much higher methanol intakes (1). Among subjects who experienced seizures, coma, or an initial pH < 7, mortality was higher than 80%16. By contrast, in the absence of these findings, the mortality rate was less than 6%. In another series, morbidity was also high, and mortality occurred in up to 44% and 48% of the cases (10,17). Yaycı et al. argue that asymptomatic period after methyl alcohol ingestion is influential in the rise of death rates. They also explain that the patient keeps on having alcohol in the asymptomatic period so he/she has a higher dose of methanol (5).

Methanol, which is not toxic itself, shows its toxic effects via formaldehyde and formic acid which are its metabolites (1,5). When taken orally, it is quickly absorbed from the gastrointestinal system like ethyl alcohol (2). Despite the fact that it reaches to the level of peak concentration in plasma in 30-60 minutes, there is a period without symptoms after methanol ingestion varying between 40 minutes and 72 hours in which there are no complaints (18,19). This period is interpreted as methanol's slow process of metabolizing into formaldehyde (10). The differences in the emerging of the symptoms that lead to referral to the hospital (14 hours, 48 hours and 7 hours; respectively) are consistent with the literature. Consumption of ethyl alcohol along with methyl alcohol delays the symptoms (18,19). Compatible with the literature; it was detected in the second case which has a history of chronic alcohol ingestion, that asymptomatic period can last as long as 48 hours depending on the slow metabolizing of methanol into formaldehyde along with the ingestion of ethyl alcohol.

Methyl alcohol poisoning is usually limited to central nervous system, ocular and gastrointestinal system findings (2). Patients usually describe blurred or misty vision, double vision, or changes in color perception. There may be constricted visual field and, occasionally, total loss of vision. Characteristic visual dysfunctions include pupillary dilation and loss of pupillary reflex (19,20). Besides blurred vision, complaints of being uncomfortable with light, headache, nausea, vomiting, stomach ache, dyspnoea are the other signs that appear (2,21). In moderate poisonings, dizziness, lethargy and confusion are seen. Cerebral oedema and as a result of this, coma and convulsion are seen in serious poisonings (2,22,23). The first and second cases were referred to ED with blurred vision which is the most common symptom of methanol poisoning. In these cases, amount of the cologne ingestion, based on history, was over 400 ml and blurred vision described by the patient and fundus findings were compatible with the signs in the literature.

In some of the serious poisoning cases, Parkinson like extra-pyramidal signs and dementia develop. Necrosis is often seen in putamen and sub-cortical white-matter in radiological investigations. In some cases, this may appear in the form of hemorrhagic lesions (3). Some authors induce these haemorrhages to heparin usage during dialysis. In a series of methyl alcohol poisoning including 97 cases; Mittal et al. reported to have detected 85.7% haemorrhages and 7,1%

neuron degeneration in parietal cortex, 7.1% putamen lesions and spongious lesion in the optic chiasm (24). Moreover, in a study by Yaycı et al. 1.6% intracranial haemorrhage was reported (5). Dependent on intracranial haemorrhage, nuchal rigidity and other meningeal signs, cytotoxic oedema and hemorrhagic necrosis cases especially in putamen area are reported in literature (6,25). Despite serious methanol ingestion (400 ml and over), neither radiological cerebral oedema and other radiological signs nor convulsion was detected in any of the three cases. In the cases who survived serious, in a way that is similar to Parkinson's disease, rigidity, bradykinesia and extra-pyramidal system signs characterized by tremor are seen (22).

Other complications of serious methanol poisoning include transverse myelitis, cognitive disorder and pseudo bulbar palsy (2). Those were signs were not detected in any of the cases in the early period. Later however, neurological monitoring and questioning of history of methanol poisoning for possible neurological situations are necessary.

CONCLUSION

In conditions level of methanol can not be measured, arterial blood gases be determinet and history of chronic alcohol ingestion is questioned regardless of amount of information about the patient. Methanol toxication must be thought for any patient who does supply methanol ingestion history in the casualty department but who has the symptoms of blurred vision, metabolic acidosis in blood gases along with the detection of coma, convulsion and whose clinical tablean does not match with any other disease. Immediately initiation of dialysis would prevent serious results. We think that such an approach will save time in the diagnosis and treatment of methanol poisoning. Thus mortality rate could be reduced by early diagnosis and treatment, specially with the help of dialysis.Moreover, we also believe that the of treatment methods in casualty department will have a great benefit to reduce the rate of mortality in poisoned cases.

REFERENCES

1. Anderson IB. Methanol. In: Poisoning and Drug Overdose, Kent R. Olson (ed). 4th edition, The McGrawHill Companies, USA 260-261, 2004.
2. Barceloux GD, Bond GR, Krenzelok EP, Olson K, Watson W. American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Methanol Poisoning. Clin Toxicol 40:415-446, 2002.
3. Blanco M, Casado R, Vazquez F, Pumar JM. CT and MR imaging findings in methanol intocication. Am J Neuroradiol, 27:452-4, 2006.
4. Burkhart KK, Kulig KW. The other alcohols. Methanol, ethylene glycol, and isopropanol. Emerg Med Clin North Am 8:913-928,1990.
5. Dart RC, Goldfrank LR, Chyka PA, Lotzer D, Woolf AD, McNally J, Snodgrass WR, Olson KR, Scharman E, Geller RJ, Spyker D, Kraft M, Lipsy R.Combined evidence-based ing the dialysis however; putamenal haemorrhage may be seen in patients who were literature analysis and consensus guidelines for stocking of emergency antidotes in the United States. Ann Emerg Med 36:126-132,2000.
6. Eells JT, Makar AB, Noker PE, Tephly TR. Methanol Poisoning and Formate Oxidation in Nitrous Oxide Treated Rats. J Pharmacol Exp Ther 217:57-61,1981.
7. Elmas I,Tüzün B,Imrag C. Evaluation of deaths due to methyl alcohol intoxication with respect to forensic medicine. Istanbul Med. Faculty 59:64-69, 1996.
8. Hassanian-Moghaddam H, Pajoumand A, Dadgar SM, Shadnia Sh. Prognostic factors in methanol poisoning. Hum Exp Toxicol 26:583-586, 2007.
9. IPCS,Healthy and Safety Guide No. 105. Methanol; World Healthy Organization: Geneva, 105, 1997.
10. Kruse JR. Methanole poisoning. Intensive Care Med 18:391-397, 1992.
11. Liu JJ, Daya MR, Carrasquillo O, Kales SN.Prognostic factors in patients with methanol poisoning. J Toxicol Clin Toxicol, 36:175-181, 1998.
12. Liu ,JJ, Daya, MR, Mann, NC. Methanol-Related Deaths in Ontario. Clin Toxicol 37:69-73, 1999.
13. Mittal BV, Desai AP, Khade KR. Methyl alcohol poisoning an autopsy study of 28 cases. J Post Grad-Med 37:9-13, 997.
14. Naraqi S, Dethlefs RF, Slobodniuk RA, Sairere JS. An outbreak of acute methyl alcohol intoxication. Aust N Z J Med 9:65-8, 1979.
15. Nolla-Salas J, Nogué Xarau S, Marruecos Sant L, Palomar Martínez M, Martínez Pérez J. Methanol and ethylene glycol poisoning. Study of 18 cases. Med Clin (Barc) 104:121-125 1995.
16. Oliveras Ley C,Gali,G. Parkinsonien Syndrome after Methanol Intoxication. Eur Neurol; 22:405-409,1983.
17. Rley RJ, Ilson BE, Narins RG. Acute metabolic acid-base disorder.Crit Care Clin 5:699-724, 1987.
18. Scrimgeour, EM. Outbreak of Methanol and Isopropanol Poisoning in New Britain, Papua New Guinea. Med J Aust 2:36-38, 1980.
19. Server A, Hovda KE, Nakstad PH, Jacobsen D, Dullerud R, Haakonsen M. Conventional and diffusion-weighted MRI in the evaluation of methanol poisoning. Acta Neurol 44:691-5, 2003.
20. Sharma AN. Toxic alcohols. In: Goldfrank LR, Flomenbaum NE, Lewin NA, Weisman RS, Howland MA, Hoffman RS, eds.Goldfrank's Toxicologic Emergencies, 7th edition, USA, The McGraw-Hill Companies 980-990, 2002.
21. Suit PF, Estes ML. Methanol intoxication: Clinical features and differential diagnosis.Cleve Clin J Med 57:464-471, 1990.
22. Teo, SK, Lo KL,Tey BH. Mass methanol poisoning: A clinico- Biochemical Analysis of 10 Cases. Singap. Med J 37:485-487, 1996.
23. Turla A,Yaycı N, Koç S. Ölümle sonuçlanan metil alkol zehirlenmeleri. Adli Tıp Derg 15:37-40, 2001.
24. Yayci N, Ağritmiş H, Turla A, Koç S.Fatalities due to methyl alcohol intoxication in Turkey: an 8 year study. Forensic Sci Int 131:36-41, 2003.
25. Yaycı N, Inanıcı MA. Methyl Alcohol (methanol) Intoxication. T Clin J Foren Med 2:101-108, 2005.