Methanol Poisoning After Cologne Ingestion (Evaluation of 12 Cases)

Kolonya İçimi Sonrası Metanol Zehirlenmesi (12 Olgunun Değerlendirilmesi)

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ABSTRACT Objectives: Methanol poisoning by ingestion is a world-wide problem, and it is associated with high morbidity and mortality. Since methanol is cheap and easy to obtain, it is used in production of illegal alcoholic beverages in Turkey. For this study, we evaluated retrospectively 12 cases admitted to critical care unit of our hospital because of methanol intoxication after cologne ingestion between June 1997 and December 2006. **Material and Methods:** We collected the demographic data, clinical findings, and laboratory parameters after the study protocol was approved by the local human ethics committee. The relations between admission time, Glasgow coma scale, mechanical ventilation requirement, the findings of brain computorized tomography, liver enzymes, blood pH, blood pressure, and amount of ingestion and mortality were evaluated. **Results:** All cases were males and the range of ages were between 18-53 years. Gastric lavage and drainage were done in all cases by placement of a nasogastric tube. All cases required mechanical ventilation with the exception of 7 and 11. cases. Treatment of the cases were included using ethyl alcohol, sodium bicarbonate, folic acid, and hemodialysis. Negative correlation was found between mortality and Glasgow coma scale, blood pressure, and blood pH. Positive correlation was found between mortality and mechanical ventilation requirement and amount of ingestion ($p< 0.05$). While three cases had full recovery, one case survived with neurological sequel (case 3) and eight cases died. **Conclusions:** We concluded that the factors affecting the prognosis of the patients with methanol intoxication were level of consciousness, the presence of spontaneous respiration, depth of metabolic acidosis, amount of ingestion, and blood pressure at the admission time.

Key Words: Methanol, poisoning, mortality

ÖZET Amaç: Oral yolla metanol zehirlenmeleri dünya çapında bir problemdir ve yüksek morbidite ve mortaliteye neden olmaktadır. Metanol elde edilmesi kolay ve ucuz olduğundan, Türkiye'de alkollü içkilerin yasadışı olarak üretiminde kullanılmaktadır. Biz de bu çalışmada, Haziran 1997 - Aralık 2006 tarihleri arasında kolonya içimi sonrası metanol intoksikasyonu nedeniyle hastanemiz yoğun bakım ünitesinde takip ettiğimiz 12 olguyu retrospektif olarak değerlendirdik. **Gereç ve Yöntemler:** Yerel etik kurul onayı alındıktan sonra, olguların demografik verileri, klinik bulguları ve laboratuvar parametreleri kaydedildi. Hastaneye başvurma zamanı, Glasgow koma skalası, mekanik ventilasyon ihtiyacı, bilgisayarlı beyin tomografisi bulguları, karaciğer enzimleri, kan pH'sı, kan basıncı ve içilen metanol miktarı ile mortalite arasındaki ilişkiler değerlendirildi. **Bulgular:** Bütün olgular erkekti ve 18-53 yaşları arasında idi. Tüm olgulara bir nazogastrik tüp vasıtasıyla gastrik lavaj ve drenaj uygulandı. Yedinci ve onbirinci olgular dışındaki tüm hastalara mekanik ventilasyon uygulandı. Tüm olgulara, etil alkol, sodyum bikarbonat, folik asit ve hemodiyaliz tedavisi uygulandı. Mortalite ile glaskow koma skalası, kan basıncı ve kan pH'sı arasında negatif yönde korelasyon varken mekanik ventilasyon ihtiyacı ve alım miktarları arasında pozitif yönde korelasyon bulundu ($p< 0.05$). Üç olgu tamamen, bir olgu nörolojik sekelli iyileşirken, sekiz olgu öldü. **Sonuç:** Hastaneye başvurma anındaki bilinç düzeyinin, spontan solunumun varlığının, metabolik asidoz derinliğinin, alım miktarının ve kan basıncının metanol intoksikasyonlu hastaların prognozunu etkileyen faktörler olduğunu düşündük.

Anahtar Kelimeler: Metanol, zehirlenme, mortalite

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Methanol poisoning by ingestion is a world-wide problem, and in some regions it is associated with high morbidity and mortality.[1–3] Since methanol is cheap and easy to obtain, it is used in production of illegal alcoholic beverages in Turkey.[4]

Methanol is found in many cleaning materials, solvents, antifreeze, formaldehyde solution, contribution of fuel, shellac and cologne, and causes serious intoxication. It can be absorbed orally, transdermal and even by inhalational routes. Intoxication is characterized by profound metabolic acidosis, convulsion, unconsciousness and permanent neurological impairment.[5-7] The aim of this study was to evaluate the prognostic factors in 12 cases admitted to critical care unit of our hospital because of methanol intoxication after cologne ingestion.

MATERIAL AND METHODS

After the the study protocol was approved by the local human ethics committee, we evaluated retrospectively 12 cases that were accepted to critical care unit of our hospital because of methanol intoxication after cologne ingestion between June 1997 and December 2006. We collected the demographic data, clinical findings, and laboratory parameters including age, gender, history of alcoholism, amount of ingestion (70% methanol in solution), admission time to emergency unit, Glasgow coma scale (GCS) score, cooperation, light reflex, oculocephalic reflex, ciliospinal reflex, vision impairment, symptoms of gastro intestinal system (GIS), presence of spontaneous respiration (mechanical ventilation requirement: yes/no), blood pressure (BP), heart rate, fundoscopic examination, findings of brain computerized tomography (CT), liver enzymes, blood gases, duration of stay at ICU, and mortality (Table 1-2). Treatments of the cases were also recorded. Statistical analyses were performed Statistica 13.0. Software (Statsoft, Inc., Tulsa, AR, USA). The relations between admission time (≤ 24 hours), GCS (≥ 8), the presence of spontaneous respiratory (mechanical ventilation requirement: yes/no), brain CT (normal/abnormal), liver enzymes (normal/high), blood gases (pH ≥ 7), BP (≥ 90/50 mmHg), and amount of ingestion (≤ 50 ml) and mortality were evaluated with fisher's exact chi-square test. Phi coefficient was calculated to detect the relation between two qualitative variables.

RESULTS

All twelve patients were males and the range of ages were between 18-53 years. Intoxication occurred after cologne ingestion and intention was to be drunk in eleven case and to relieve the toothache in one case. There were correlation between mortality and GCS, mechanical ventilation requirement, blood gases, BP, and amount of ingestion ($p< 0.05$), whereas there was no correlation between mortality and admission time, brain CT, and liver enzymes ($p> 0.05$). Negative correlation was found between mortality and Glasgow coma scale, blood pressure, and blood pH. Positive correlation was found between mortality and mechanical ventilation requirement and amount of ingestion ($p< 0.05$). Dopamine was used for inotropic support for these cases with BP less than 90/50 mmHg (7 cases). Gastric lavage and drainage were done in all cases by placement of a nasogastric tube. All cases required mechanical ventilation with the excepti-

TABLE 1: Demographic data, amount of ingestion, and admission time of cases.

Cases	1	2	3	4	5	6	7	8	9	10	11	12
Age	18	35	21	41	44	53	27	51	48	21	25	42
Gender (M/F)	M	M	M	M	M	M	M	M	M	M	M	M
Alcoholism	-	+	-	-	+	+	+	+	+	-	+	+
Amount of ingestion (ml)	150	250	50	200	150	250	50	200	250	200	50	180
Admission time (hour)	36	48	24	16	24	72	48	40	15	48	13	13

+: yes, -: no, M: male, F:female

TABLE 2: Clinical findings and laboratory parameters of cases.

Cases	1	2	3	4	5	6	7	8	9	10	11	12
Conscious (GCS)	3	3	7	4	3	3	13	3	9	4	12	3
Cooperation	-	-	-	-	-	-	+	-	-	-	-	-
Light reflex	-	-	+	-	-	-	+	-	+	-	+	-
Oculocephalic reflex	-	-	+	-	-	-	+	-	+	-	+	-
Ciliospinal reflex	-	-	+	-	-	-	+	-	+	-	+	-
Vision impairment	+	+	+	+	+	+	-	+	+	+	+	+
Respiration when he came	-	-	+	-	-	-	+	-	+	+	+	-
Blood pressure (mmHg)	80/50	75/50	90/50	80/60	40/20	85/55	120/80	70/50	90/50	80/ 60	110/70	90/60
Heart rate (Beat/min)	100	80	88	80	130	92	90	84	60	60	100	120
Fundoscopy	PS	PS	PS	PS	PS	PS	N	PS	PS	PS	PS	PS
Computorise tomography	BE	BE	BE	BE/PN	BE	BE	N	BE	BE/PN	BE	N	BE
Symptoms of GIS	+	+	+	+	-	+	+	+	+	+	+	-
Elevation of liver enzyme	+	+	+	+	+	+	-	+	+	+	+	+
PH	6.62	6.88	7.02	6.66	6.70	6.94	7.29	6.76	7.22	6.80	7.37	6.91
Bicarbonate	5.2	6.5	10.2	9.1	5.3	6.6	13.8	8.0	13.1	8.2	14.8	2.2
Duration of stay at ICU	11 hour	48 hour	15 day	16 day	18 hour	4 day	5 day	40 hour	22 day	7 day	5 day	7 hour
Mortality	+	+	-	+	+	+	-	+	-	+	-	+

+: yes, -: no, ±: uncertain, PS: pupil stasis, N: normal, BE:brain edema, PN: putaminal necrosis.

on of cases 7 and 11.Treatment of the cases was performed using ethyl alcohol, sodium bicarbonate, folic acid, and hemo dialysis. Loading dose of ethyl alcohol 40% (3 ml/hour) was applied via gastric probe to all case. Following dose 0.5 ml/kg/hour was applied as infused via gastric probe. Everyday hemodialysis performed according to arterial pH and HCO_3 levels for all cases except 5 in whom hypotension encountered. Infusion dose of ethyl alcohol was maintained increasing at the same time during hemodialysis. Sodium bicarbonate was infused according to arterial pH and HCO_3 levels. Three cases had full recovery, one case survived with neurological sequel (case 3) and eight cases died.

DISCUSSION

The appearance of toxicity is mean 30 hours following methanol ingestion. However it can be changed 40 min.-72 hours. The earliest symptom of methanol intoxication is uneasiness of mind. Severe findings like metabolic acidosis, unconsciousness and convulsion occur late (6 –36 hours). Methanol causes inebriation but by itself in almost completely nontoxic. The methanol is metabolized by alcohol dehydrogenase to formaldehyde and then formic acid. The minimal lethal dose is 50 mL, whereas blindness may occur with as little as 10 mL ingestion. In methanol intoxication, responsible agents are formaldehyde and formic acid. The more methanol is metabolized, the higher the likelihood of end organ toxic effects.[5-7] For this reason, admission time to hospital and initial treatment time will effect to prognosis directly after methanol ingestion.[8-10] The half life of methanol is long and it is advantage for these intoxications.[7] In our study, there were no association between mortality rate and admission time to hospital, however, there was an association between mortality rate and the amount of methanol. It might be considered that the high mortality rate in cases admitted early was the reason of the high volume of ingested methanol.

Metabolic acidosis can be severe, and a pH below 7.0 has been found to be the strongest predictor of mortality. Patients with a pH below 7.0 have 20 times the mortality as compared with patients with pH greater than 7.0 .[11] Jacobsen et al.[12], emphasized that level of serum methanol was not important but grade of metabolic acidosis was important for prognosis. In the other study, Nolla Salas et al.[8], evaluated 18 cases. In this study, they

determined cases had been death that level of initial arterial pH and bicarbonate were lower. In our study we examined 12 cases and 3 cases who had the best initial arterial pH was recovered totally. In addition, case 1 recovered with sequelae. The others that had lower arterial pH, were exitus. For this reason direct relation observed profound of metabolic acidosis with prognosis. Generally high level of liver enzymes occurred in the moderate and severe intoxication.[7] GIS symptoms were appeared in all case that we presented. High level liver enzymes were determined in all cases except case 7 who had good prognosis. In this way GIS symptoms and high liver enzymes would not be indicator of mortality.

According to neurological findings after 12 cases were evaluated, 3, 7, 9, and 11. cases who had good prognosis, oculocephalic, silliospinal and light reflex were present at admission to the hospital. On the other hand, these reflexes were absent in other case that being exitus. Also according to GCS, consciousness was the best in, 3, 7, 9, and 11. cases. Consciousness grade and reflex condition in admission time could give an idea about prognosis of intoxication. In addition, the presence of spontaneous respiration and adequate blood pressure might be the denominators of the prognosis with methanol cases. Brain edema determined in the10 cases that were applied computerized tomography. Brain edema observed in all exitus cases also in 3 and 9. cases that recovered. Many researchers reported that brain edema occurred in methanol intoxication.[13-15] There was no correlation between brain edema and prognosis. Disturbance of vision is a presenting complaint in the majority of methanol intoxications and is one of the most specific clinical findings.[16-19] The lack of ocular findings on initial presentation is a positive prognostic sign.[20] Vision impairment was determined in all case except case 7 who had good prognosis. Mortality rate in our series is 66% due to methanol intoxication. Teo et al., examined 10 cases and reported mortality proportion as 10% .[21] In another study, 18 patients were examined that 16 of them with methanol intoxication and other 2 patients with ethyl glycol intoxication and in this study mortality proportion was 44%.[8] In our study, higher proportion of mortality might be due to late aplication to hospital . In all our cases, methanol intoxication developed because of cologne ingestion. When loss of consciousness was appeared, relatives of patient's supposed this situation as ingestion of ethyl alcohol excessively; this might be a reason of late admission.

Methanol is metabolized by alcohol dehydrogenase to formaldehyde and then by aldehyde dehydrogenase to formic acid rapidly. Folate is acted as co-factor and formic acid changed to CO_2 and H_2O. Methanol is not responsible for the toxicity, but formic acid and formaldehyde were responsible. For prevent to intoxication or reduce of methanol metabolization, formic acid must be metabolized rapidly. Ethyl alcohol and folic acid are used for this aim. Hemodialysis was very effective for elimination of metabolite.[7,21] Nolla Salas et al.[8], reported that 16 cases of methanol intoxication undergoing only by bicarbonate and ethanol therapy successfully. Also Chow et al.[22], reported 10 cases that were treated with only bicarbonate and ethanol therapy successfully. We applied ethanol, folic acid, sodium bicarbonate and hemodialysis to our cases.

We concluded that the factors affecting the prognosis of the cases with methanol intoxication treated with the same therapy, were the amount of ingestion, the depth of metabolic acidosis, the level of consciousness, the presence of spontaneous respiration, and blood pressure.

REFERENCES

1. Gossel TA, Bricker JD. Principles in management of the poisoned patients. Principles of Clinical Toxicology. 3rd ed. New York: Raven Press; 1984. p.65-8.
2. METHYL alcohol poisoning; an account of the 1951 Atlanta epidemic. J Med Assoc Ga. 1952;41(2):48-51.
3. Scrimgeour EM. Outbreak of methanol and isopropanol poisoning in New Britain, Papua New Guinea. Med J Aust 1980;2(1):36-8.
4. Yayci N, Ağritmiş H, Turla A, Koç S. Fatalities due to methyl alcohol intoxication in Turkey: an 8-year study. Forensic Sci Int 2003;131(1):36-41.
5. Baselt RC. Methanol. Disposition of Toxic Drugs and Chemicals in Man. 5th ed. Foster City, CA: Chemical Toxicology Institute; 2000. p.532-4.
6. Kinoshita H, Ijiri I, Ameno S, Tanaka N, Kubota T, Tsujinaka M, et al. Combined toxicity of methanol and formic acid: two cases of methanol poisoning. Int J Legal Med 1998;111(6):334-5.
7. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA; American Academy of Clinical Toxicology Ad Hoc Committee on the Treatment Guidelines for Methanol Poisoning. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol 2002;40(4):415-46.
8. 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) 1995;104(4):121-5.
9. Pamies RJ, Sugar D, Rives LA, Herold AH. Methanol intoxication. How to help patients who have been exposed to toxic solvents. Postgrad Med 1993;93(8):183-4, 189-91, 194.
10. Wu AH, Kelly T, McKay C, Ostheimer D, Forte E, Hill D. Definitive identification of an exceptionally high methanol concentration in an intoxication of a surviving infant: methanol metabolism by first-order elimination kinetics. J Forensic Sci 1995;40(2):315-20.
11. Meyer RJ, Beard ME, Ardagh MW, Henderson S. Methanol poisoning. N Z Med J 2000;113(1102):11-3.
12. Jacobsen D, Jansen H, Wiik-Larsen E, Bredesen JE, Halvorsen S. Studies on methanol poisoning. Acta Med Scand 1982;212(1-2):5-10.
13. Blanco M, Casado R, Vázquez F, Pumar JM. CT and MR imaging findings in methanol intoxication. AJNR Am J Neuroradiol 2006;27(2):452-4.
14. Kuteifan K, Oesterlé H, Tajahmady T, Gutbub AM, Laplatte G. Necrosis and haemorrhage of the putamen in methanol poisoning shown on MRI. Neuroradiology 1998;40(3):158-60.
15. Rubinstein D, Escott E, Kelly JP. Methanol intoxication with putaminal and white matter necrosis: MR and CT findings. AJNR Am J Neuroradiol 1995;16(7):1492-4.
16. Dethlefs R, Naraqi S. Ocular manifestations and complications of acute methyl alcohol intoxication. Med J Aust 1978;2(10):483-5.
17. Sejersted OM, Jacobsen D, Ovrebø S, Jansen H. Formate concentrations in plasma from patients poisoned with methanol. Acta Med Scand 1983;213(2):105-10.
18. McKellar MJ, Hidajat RR, Elder MJ. Acute ocular methanol toxicity: clinical and electrophysiological features. Aust N Z J Ophthalmol 1997;25(3):225-30.
19. Tarhan S, İlker SS, Kurt E, Yoldaş TK. [The lesions of basal ganglion in methanol poisoning: ct findings]. Turkiye Klinikleri J Ophthalmol 1998;7(1):35-7.
20. Benton CD Jr, Calhoun FP Jr. The ocular effects of methyl alcohol poisoning: report of a catastrophe involving three hundred and twenty persons. Trans Am Acad Ophthalmol Otolaryngol 1952;56(6):875-85.
21. Teo SK, Lo KL, Tey BH. Mass methanol poisoning: a clinico-biochemical analysis of 10 cases. Singapore Med J 1996;37(5):485-7.
22. Chow MT, Di Silvestro VA, Yung CY, Nawab ZM, Leehey DJ, Ing TS. Treatment of acute methanol intoxication with hemodialysis using an ethanol-enriched, bicarbonate-based dialysate. Am J Kidney Dis 1997;30(4):568-70.