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CASE REPORT

Methanol Intoxication and High D-Dimer Levels

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Abstract

Methanol is very similar to ethyl alcohol in terms of color, odor and consistency. Methanol intoxication is generally caused by oral intake of illegally produced fake drinks prepared by replacing ethanol with methanol. Abdominal pain, nausea, and vomiting,visual disturbances, headache, severe metabolic acidosis, vision loss, cardiovascular instability and death may develop in methanol intoxication. Severe metabolic acidosis is the most important cause of mortality. But a D-dimer elevation is not reported primarily due to methanol intoxication in the literatüre. In this case, the severe metabolic acidosis that develops will be pointed out by reminding the findings of methanol intoxication and the unexpected and persistent D-dimer elevation despite the normal clinical and laboratory status will be shared.

Key Words: Methanol intoxication, metabolic acidosis, D-dimer levels

Metanol Zehirlenmesi ve Yüksek D-Dimer Seviyeleri

Özet

Metanol, renk, koku ve kıvam açısından etil alkole çok benzer. Metanol intoksikasyonu genellikle etanolün metanol ile değiştirilmesiyle hazırlanan yasa dışı olarak üretilmiş sahte içeceklerin ağızdan alınmasından kaynaklanır. Karın ağrısı, bulantı ve kusma, baş ağrısı, görme bozuklukları, şiddetli metabolik asidoz, görme kaybı, kardiyovasküler instabilite ve ölüm metanol intoksikasyonunda gelişebilir. Şiddetli metabolik asidoz en önemli mortalite nedenidir. Ancak literatürde metanol intoksikasyonu sonucu olan bir D-dimer yüksekliği bildirilmemiştir. Metanol intoksikasyonuyla gelen bu vakada hem bulguları hatırlatılarak gelişen şiddetli metabolik asidoza dikkat çekilecek, hem de klinik ve laboratuar düzelmeye rağmen beklenmeyen D-dimer yüksekliği paylaşılacaktır.

Anahtar Kelimeler: Metanol intoksikasyonu, metabolic asidoz, D-dimer düzeyi

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Introduction

In December 2021, 84 people in Turkey died of poisoning due to fake alcohol (1). The substance that caused the poisoning of these people was methyl alcohol (methanol). It is very similar to ethyl alcohol in terms of color, odor and consistency. It is impossible to distinguish from ethyl alcohol with the naked eye or

smell. Methanol intoxication is generally caused by oral intake of illegally produced fake drinks prepared by replacing ethanol with methanol. Due to use in industry, methanol poisoning may also occur as a result of occupational accidents. Serum concentrations peak immediately after absorption and follow a zero-order elimination rate. Metabolism occurs mainly in the liver through serial oxidation via alcohol dehydrogenase and aldehyde dehydrogenase Alcohol dehydrogenase oxidizes methanol to formaldehyde, and aldehyde dehydrogenase subsequently oxidizes formaldehyde to formic acid. Methanol has a toxic effect through its metabolites (2). While visual disturbances, headache, abdominal pain, nausea, and vomiting may occur in the early period, severe metabolic acidosis, vision loss, cardiovascular instability and death may develop in the later process.

In this case, besides reminding the clinical and laboratory findings of methanol poisoning, unexpected and persistant D-dimer elevation despite clinical and laboratory improvement in a patient with methanol intoxication will be shared.

Case

On 19/01/2021, a 54 year old male patient was brought to Emergency Service of Medicine Faculty Education and Research Hospital of University Ordu with confusion, hypotension and respiratory failure. It was learned in the patient's history, that he did not have a systemic disease or drug use, that he drank alcohol 10 hours ago, he started to have a headache after a while, visual impairment and worsening in the later hours. His blood pressure was 70/40 mmHg, heart rate: 90/min, respiratory rate was 30/min, arterial oxygen saturation was 85%. On physical examination, his general condition was poor, and he was unconscious. The patient was monitored, and vascular access was established and hydration with 5% dextrose and physiological saline was started. Meanwhile, he was intubated due to superficial respiration. He was admitted to the intensive care unit (ICU).

In the emergency unit, pH: 6.97, HCO3: 9.4 mmol/L, PCO2: 36 mmHg, Base deficit: -29, Lactate: 7.2 mmol/L were found in the arterial blood gas(ABG). Glucose: 262 mg/dl, urea:10.3 mg/dl, creatinine:1.81 mg/dl, Na: 137 mmol/lt, K:5.8 mmol/lt, Ca: 8,4 mg/dl, Cl: 96,7 mmol/lt, ALT:88 U/L, AST:91 U/L, LDH: 376 U/L were found in biochemical analysis . Hemoglobin, hematocrit and thrombocyte counts were normal. Leukocytosis as 23500/mm3 was detected with 83.6% neutrophils, 11% lymphocytes, 4.8% monocytes, 0.2% eosinophils, 0.4% basophils. Peripheral smear was consistent with this count. In the urine analysis, pH was 6, density was 1015, ketone, protein, glucose, bilirubin, nitrite was negative, urobilinogen quantity was normal, and no leukocytes, crystals, or casts were detected. Serum osmolality was calculated as 292 mosmol/lt. Troponin and INR levels were normal. D-dimer was slightly elevated as 0.87 mg/dl. Since methanol measurement could not be performed in our hospital, the methanol level could not be detected. The ethanol level was found to be 163 mg/dl (range 0-10 mg/dl). In the emergency unit, 15 ampoules of bicarbonate infusion was given to the patient in the first hour. Due to the hypotensive course, norepinephrine was started at an infusion rate of 8 mcg/min. Meanwhile, cranial, thorax, abdominal tomography and pulmonary CT angiography were evaluated as normal. Bicarbonate infusion was continued in the intensive care unit, and blood pressure was stabilized, two hours hemodialysis was applied due to severe metabolic acidosis. A total of 30 ampoules of

bicarbonate were replaced in 24 hours by monitoring the bicarbonate level. Bicarbonate replacement and acute hemodialysis in the first 24 hours improved the fatal metabolic acidosis and he did not require repeat hemodialysis. In the follow-up of the patient, clinical and laboratory improvement was achieved within 48 hours. He regained consciousness, his spontaneous breathing improved, and he was extubated. The laboratory parameters of the patient in 48 hours are shown in the table (Table 1).

Table 1. Laboratory parameters in the first 48 hours in the Intensive Care Unit

	1. day				2. day
Parameters	firs 6 hours	second 6 hours	third 6 hours	fourth 6 hours	
PH	7,07	7,13	7,23	7,39	7,40
HCO_3 (mmHg)	11,9	13,1	16	19	24
PCO_2 (mmHg)	42	41	38	27	30
Laktat (mmol/L)	5,7	6,4	5,1	4,6	3,1
WBC (/$mm^{3)}$	23500			12600	8300
Glucose (mg/dl)	154	144	163	120	119
BUN (mg/dl)	10			19	18
Creatinine (mg/dl)	1,8			1,2	0,77
Na (mEq/l)	137			137	142
K^+ (mmol/lt)	5,8			3,5	3,4
ALT (IU/L)	88			38	42
Ethanol (mg/dl)	163		21		0
D-dimer (mg/dl)	0,87				0,60

The patient was transferred to inpatient service on the 3rd day of hospitalization. His general condition was good, he was cooperative and oriented, his vital signs were normal, and he had no complaints. Vital status was followed up and hydration was continued for 2 days. Discharge decision was made. While all tests were normal in the control blood tests taken before discharge, the D-dimer level was found to be high with 2.39 mg/dl. (Normal levels <0.5 mg/dl). The patient did not have any complaints. However, thorax CT angiography was performed, and it was found to be normal and pulmonary embolism was excluded. The patient's discharge was delayed, and anticoagulant treatment (oxapar 2x06 ml) was started. D-dimer level was followed up. On the 8th day of his hospitalization, his D-dimer level reached a peak value and then started to decrease. On the 10th day of hospitalization, the patient was discharged by giving 0.6 ml 1x1 of oxapar and outpatient follow-up was done. Fifteen days after discharge, D-dimer level was found to be 0.5 mg/dl and oxapar treatment was stopped. D-dimer values of the patient are shown in the table (Table 2).

Table 2. D-dimer levels

Date	D-dimer (mg/dl)
1. day (19/12/2021)	0,87
2. day	0,60
5. day	2,39
7. day	5,06
8. day	6,01
9. day	5,94
10. day	4,82
13/01/2022	2,69
25/01/2022	0,51

Discussion

Methanol is obtained by distillation from charcoal. It is a colorless, volatile and poisonous liquid. It is known that it was used for mummification for the first time in ancient Egypt (3). Due to its solvent effect, it is

industrially used especially in dry cleaning, automotive, fuel, etc., but the methanol level should not exceed 60 ppm in the air in the working environment. Since it is widely used in the sectors, it can be sold legally. Unfortunately, it is not possible to distinguish colorless and odorless methanol from ethyl alcohol when taken orally. For this reason, it can be used especially in the production of fake drink, since its cost is cheaper than ethyl alcohol. Even 8-10 ml of methanol taken from the body is toxic. Approximately 25-30 ml of methanol can lead to a poisoning picture that can cause permanent blindness, and ingestion of 1 ml/kg or 100 ml of methanol is fatal. When methanol is taken orally, it is absorbed very quickly from the gastric mucosa and reaches its peak plasma concentration in approximately 30-60 minutes (4). While clinical signs and symptoms related to methanol poisoning may begin during these periods, they may last up to 72 hours depending on the type of exposure, amount, and administration of antidote ethanol (5). Methanol itself is not toxic, but its metabolite, formic acid, has serious toxic effects on many tissues. Formic acid causes inhibition of cytochrome c oxidase in the electron transport chain, leading to cellular dysfunction and end-organ damage. Formic acid also inhibits oxidative phosphorylation, causing an increase in anaerobic metabolism. This causes an increase in lactate. This is another parameter that contributes to metabolic acidosis (6). Although the findings of poisoning are often specific ın the late phase of methanol poisoning, most of the early findings are unfortunately nonspecific. Gastrointestinal system findings such as nausea, vomiting and abdominal pain are prominent in the early period. After the latent period, blurred vision, double vision, photophobia, early or late blindness may occur accompanied by severe metabolic acidosis. The state of consciousness is variable according to the patient (7,8). D-dimer elevation is not mentioned in the theoretical information about methanol poisoning in the literature (9,10).

In this case, the anamnesis provides reliable evidence of methanol intoxication. All early and late toxic effects of methanol intoxication were observed in this patient. Patients who present within the first 12 to 24 hours following ingestion may appear normal, and this is described as the latent period. Symptoms associated with basal ganglia toxicity are not detectable early on due to mental status depression and the acuity of illness. Without treatment, patients may progress to coma, respiratory or circulatory failure, and death. In this case, the patient was quickly treated for metabolic acidosis and intubated before respiratory arrest. The most serious laboratory disorder known in methanol intoxication is metabolic acidosis, but a D-dimer elevation is not reported primarily due to methanol intoxication. It can be seen secondary to the hypotension, shock, multiple organ failure and disseminated intravascular coagulation. In such a situation, clinical and laboratory deterioration are observed together. However, in this case, it is noteworthy that the D-dimer level, which was slightly elevated at first, then decreased to normal levels, and increased again on the 5th day of hospitalization without any complaints. D-dimer levels returned to normal about 15 days after the discharge. This situation may have been caused by any chemical added to the fake drink other than methanol.

Conclusion

In most emergency departments, the plasma methanol level cannot be measured. The combination of the patient's suspected alcohol intake, clinical

presentation and severe metabolic acidosis is diagnostic. Suspicion in methanol intoxication is very important for diagnosis. Through this case, attention was drawn to methanol intoxication, and it was reminded that rapid intervention is life-saving. In addition, it was concluded that isolated D-dimer elevation could be observed despite clinical improvement in cases with methanol intoxication, therefore it should be the patient's follow-up after recovery in terms of D-dimer elevation.

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