

Accidental Transdermal Methanol Poisoning: Difficulties and Suggestions in Therapy: Case Report

Transdermal Metanol Zehirlenmesi: Tedavideki Zorluklar ve Öneriler

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ABSTRACT Methanol is a toxic substance that may cause metabolic acidosis, ophthalmic disturbances, permanent neurologic sequel and death if not treated. Methanol poisoning may occur as a result of ingestion, inhalation or dermal absorption of methanol containing spirits and/or commercially available solvents that are inexpensive and easily accessible. With transdermal absorption, methanol can reach very high blood levels. We present a case that transdermal methanol intoxication was treated in a lately admitted patient who was unintentionally exposed to methanol. The patient was treated for cellulitis and superficial thrombophlebitis in her leg with transdermal methanol application. She was referred to the hospital with nausea, vomiting and blurred vision. She was diagnosed as methanol intoxication. Even in late admitted cases treatment is possible. Transdermal methanol absorption should be kept in mind by the physicians.

Key Words: Methanol; administration, cutaneous

ÖZET Metanol metabolik asidoz, oftalmik bozukluklar, kalıcı nörolojik hasar ve ölüme yolaçabilen toksik bir maddedir. Metanol zehirlenmesi, metanol içeren ve piyasada oldukça ucuza bulunabilen sıvıların ağızdan alınması, inhalasyonu veya ciltten emilimi ile olabilir. Metanolün transdermal emilimi sonucu kan seviyeleri oldukça yüksek seviyelere ulaşabilir. Yazımızda istenmedik şekilde metanole maruz kalan ve transdermal metanol zehirlenmesi sebebiyle tedavi edilen bir hastayı sunmaktayız. Kadın hasta, bacağındaki sellülit ve yüzeysel tromboflebit için transdermal lokal metanol uygulanarak tedavi edilmeye çalışılmıştı. Hasta hastaneye bulantı, kusma ve görme bulanıklığı şikayetleri ile sevk edildi. Hastaya metanol zehirlenmesi tanısı kondu. Metanol zehirlenmesi sonrası geç gelen vakalarda da tedavi mümkündür. Metanolün transdermal emilimi ise konuyla ilgili klinisyenlerce akıldaki bulundurulmalıdır.

Anahtar Kelimeler: Metanol; ilaç uygulaması, kütanöz

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Methanol poisoning may occur as a result of ingestion, inhalation or dermal absorption of methanol containing spirits and/or commercially available solvents that are inexpensive and easily accessible. Nausea, vomiting, abdominal pain, visual disturbances and mental status changes are the symptoms of methanol poisoning that occurs after a latent period of 12 to 24 hours. Problems like metabolic acidosis, anion gap and permanent neurologic sequel commonly occur.

Methanol, using the ethanol metabolic pathway in the liver, is oxidized to formaldehyde by alcohol dehydrogenase and then to formic acid by

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aldehyde dehydrogenase. Formic acid is converted to CO₂ by a tetrahydrofolate-mediated reaction.¹

Formic acid is primarily responsible for most of the serious sequelae observed in methanol toxicity, including metabolic acidosis and ophthalmic toxicity. The reaction rate of the formation of formic acid is rather slow resulting to a latent period before the intoxication signs appear. This metabolite itself can be considered as an indicator for methanol poisoning in cases that approach lately, thus they have metabolized most of the methanol in their blood. Blood methanol levels might be minimal or might not even exist but the patient may suffer from all the severe consequences of methanol poisoning due to high blood formic acid concentration. The minimum toxic dose varies regarding to the differences in alcohol dehydrogenase activity, leading to different toxic metabolite conversion rates.² Nevertheless, 50% mortality rate was reported in patients with bicarbonate levels <10 mEq/L.³ The lethal dose has been reported to be 1 ml.kg⁻¹ with permanent visual disturbances occurring after exposure to as little as 0.1 ml.kg⁻¹.⁴

We present a case that transdermal methanol intoxication was treated in a lately admitted patient who was unintentionally exposed to methanol.

CASE REPORT

A 41-year-old female with a medical history of nausea, vomiting, and blurred vision presented to the emergency department of our hospital. Her medical record consisted of a deep venous thrombosis that was successfully treated 3 years ago. Four days before her arrival to the emergency unit, pain, edema, and erythema in her leg began and she took her former medications without consulting the doctor. The therapy included antibiotic administration and alcoholic dressing. The therapy continued for 3 days ending up with nausea vomiting, palpitation and blurred vision that forced her to apply to a medical institution, which directed her to our hospital.

In her physical examination upon arrival, the vital signs were as follows: temperature 36.1°C, heart rate (HR) 121 beats/min, respiratory rate (RR)

16 breaths/min and blood pressure (BP) 160/100 mmHg. There was a deep venous thrombosis in her right leg and a dilatation in both pupils. There was no pathology in the neurological examination and routine biochemical laboratory findings came out to be normal except the leukocyte count. Echocardiography was performed to find the origin of embolism and no pathological findings were obtained either. The presence of bilateral vision problem and the dilated pupils were thought to be the symptoms for sinus cavernous thrombosis. Magnetic resonance imaging (MRI) was taken which came out to be normal. Gradually respiratory problems and tachycardia developed. These symptoms led to blood gas examination and the results showed a severe acidosis with pH= 7.22, BE= -22.5 and pCO₂= 10.9 mmHg. Interestingly a light purple color was seen in a wide area on her leg at the point where the dressings were done.

The patient was then transferred to intensive care unit (ICU) for further examination. Despite the severe acidosis and the general conditions, the level of K of the patient was within the lower normal limits. The high anion gap and the normal K value indicated methanol intoxication but there was no such mention in the history of the patient. When the family was questioned about the possibility of ethanol-methanol use, they said that she was a religious Muslim and that she never ever consumed any kind of alcoholic beverage. The only possibility for the methanol exposure was the alcoholic dressing. With a careful repetition of the history it came out that the alcohol used for this purpose was a commercial solvent containing excessively high percentage (90%) of methanol that was definitely not suitable for medical use. 2000 mL of the solvent was applied to the right leg for 72 hours. This commercial solvent was purple in color which explained the coloring in the leg of the patient. The ophthalmologic findings were also in accordance with methanol intoxication. For the accurate diagnosis we needed to determine the blood methanol level; the test that showed 8.8 mg/dL implying that methanol was already metabolized. The therapy was immediately started before the test has resulted due to patient's critical

aspect. Metabolic acidosis was compensated with sodium bicarbonate. In order to achieve competitive inhibition of alcohol dehydrogenase we preferred to use fomepizole but it was not easy to reach it in the ICU therefore we used enteric administration of ethanol for this purpose. Folic acid was administered and also corticosteroids were used to decrease the risk of possible visual complications. Despite the fact that the patient applied late, hemodialysis or continuous venovenous hemodiafiltration (CVVHD) was not performed due to the rapid progress in clinical prognosis, decreasing of acidosis and the lack of any renal dysfunction. During the following 24 hours in the ICU the metabolic acidosis was normalized and the patient was stabilized. The patient was transferred to the ophthalmological unit following the stabilization of all the hemodynamic and metabolic parameters.

DISCUSSION

It's difficult to diagnose methanol especially in cases, which the administration route cannot be clarified by the history of the patient. On the other hand the blood methanol level determination is not a routine test in most of the biochemistry laboratories. As regards to these difficulties most of the reported cases include post mortem findings.⁴⁻⁸

This report has a target on highlighting the importance of diagnosis and management of methanol poisoning in a case that methanol was transdermally ingested and the patient was completely ignorant of its use. Our patient used a high methanol solvent-containing dressing to cure selulitis in her leg and skin penetration seriously affected her. It has been reported that the transdermal absorption rate of liquid methanol can reach 0.192 mg/cm²/min and this value can change depending to the exposure time.⁹ The total amount of the compound absorbed through skin is determined by two factors: The rate of absorption and the temporal length of the absorption phase.¹⁰

In studies performed in vivo using human subjects it has been reported that even brief skin contact with methanol can cause significant exposures. But some specific factors like skin thickness, hydra-

tion, temperature, and compound specific factors like polarity, lipophilicity and solubility can affect the uptake of the compound. On the other hand the rate of elimination of the specific compound that is absorbed depends on metabolism in the skin, liver etc. Factors like skin resistance, chemical bonding, can delay the maximum concentration in the body.¹¹ In our case it was extremely difficult to assume methanol intoxication since nothing was implied in the history of the patient. Therefore at least an awareness of the possibility of transdermal intoxication was essential.

Methanol determination is not one of the routine tests that are performed in the laboratories of our hospital. Therefore the diagnosis and the treatment of the patient for methanol poisoning was based on indirect indicators such as low pH, low serum bicarbonate concentration, and high anion gap.⁶ Methanol has already been metabolized to formic acid in lately admitted patients. Our treatment of methanol intoxication included bicarbonate to approve acidosis, folate to enhance formic acid oxidation and ethanol infusion to block the conversion of methanol to formic acid via alcohol dehydrogenase.

Fomepizol (4-methylpyrazole) is also suggested to be used since it has 8000 time higher affinity to alcohol dehydrogenase compared to ethanol and methanol and thus it prevents the toxicity of methanol.^{12,13} Although this was our preferable method of treatment it was not possible for us to find the drug immediately therefore we start the treatment using ethyl alcohol which competes with methyl alcohol for the alcohol metabolizing system. Administration of ethanol for the treatment of methanol intoxication is therefore common once alcohol dehydrogenase has a much higher affinity to ethanol than to methanol. Therefore ethanol inhibits the metabolism of methanol and reduces the rate of production of more toxic metabolites. Maintaining a moderately high blood-ethanol concentration about 100 mg/dL blocks the above-mentioned conversion.¹⁴ We preferred the protocol advising 43% ethyl alcohol administration.

Extracorporeal treatment modalities [hemodialysis, continuous hemofiltration, hemoperfusion, and the molecular absorbent recirculating system (MARS)] are indicated in case of severe toxicity.¹⁵

On the other hand hemodialysis succeeds for molecules those are kidney eliminated whereas the basic toxic molecule in the methanol intoxication cases is formic acid which is not eliminated via kidneys but it is converted to CO₂ by a tetrahydrofolate mediated reaction.⁷ Therefore although the method might be helpful for methanol elimination itself, in lately applied methanol poisoning cases that have primarily formic acid as in our case, hemodialysis is not essential.

Nevertheless the indications for hemodialysis including renal involvement and/or a peak of methanol level >50 mg/dL were not present in our patient. Therefore we did not use hemodialysis based also in the fact that a rapid normalization of the patient occurred.

We used folate treatment in order to decrease formic acid accumulation by pooling the reaction to the right decreasing thus the acidosis.²

Unintentional methanol intoxication is a lethal medical condition that should be kept in mind for diagnosis. An effective treatment may reduce the morbidity and mortality even in delayed cases.

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