ESETISMERTETÉS

CASE REPORT

Acute parkinsonism due to transdermal methanol intoxication: First report

Gozde BARAN[1], Ozlem GELİSİN[2], Gulsen Babacan YİLDİZ[3]

[1]Marmara University, Pendik Research and Training Hospital, Department of Neurology, Istanbul, Turkey
[2]Bezmialem Vakif University, Faculty of Medicine, Department of Neurology, Istanbul, Turkey
[3]Private Consultant, Istanbul, Turkey

PRINT | English | https://doi.org/10.18071/isz.76.0141 | www.elitmed.hu

Correspondent:
Gozde BARAN, MD,
Marmara University, Pendik Research and Training Hospital, Department of Neurology; Istanbul, Turkey.
Mailing Address: Fevzi Çakmak, Muhsin Yazıcıoğlu Cd No:10, 34899 Pendik/İstanbul.
Telephone: +905325994462,
Fax : +90 (216) 625 45 45
E-mail:
drgozdebaran@gmail.com
https://orcid.org/0000-0002-6369-7218

Érkezett:
2022. június 5.
Elfogadva:
2022. augusztus 2.

Introduction – Methanol is a colorless and highly toxic liquid similar to ethanol in odor and taste. Methanol intake can lead to severe metabolic acidosis, loss of vision, permanent neurological damage, and death.
Case report – We report a case of a 19-year-old female patient who had no known disease history. A large portion of her back was covered in spirits for back pain and kept on for 2 days. Cranial magnetic resonance imaging (MRI) on the 5th day showed hyperintense pathologic signal changes in the T2 sequence without contrast enhancement in the bilateral frontal cortical-subcortical regions and basal ganglia. Following neurological examination of the patient, she was found to have bradymimia, marked resting tremor, bradykinesia, and dystonia on the right upper and lower extremities. Our case is important because it is the only case where parkinsonism developed as a result of acute transdermal methanol intoxication.

Keywords: transdermal, methanol, intoxication, parkinsonism

Akut parkinsonizmus transdermalis metanolmérgezés következtében: Első beszámoló
Baran G, MD; Gelisin O, MD; Yildiz GB, MD

Bevezetés – A metanol színtelen és erősen mérgező folyadék, ami szagában és ízében az etanolhoz hasonló. A metanol bevitele súlyos metabolikus acidózishoz, látásvesztéshez, maradandó neurológiai károsodáshoz és halálhoz vezethet.
Esetismertetés – Egy 19 éves nőbeteg esetéről számolunk be, akinek anamnézisében nem szerepelt semmilyen betegség. A hátának nagy részét hátfájás miatt alkohollal borították be, amit 2 napig rajtatartottak. A koponya mágneses rezonanciás képalkotása (MRI) az 5. napon a T2 szekvenciában kontrasztfokozódás nélküli hiperintenzív kóros jelváltozást mutatott a kétoldali frontális corticalis-subcorticalis régiókban és a bazális ganglionokban. A beteg neurológiai vizsgálatát követően a jobb felső és alsó végtagokon bradymimia, kifejezett nyugalmi tremor, bradykinesia és dystonia volt kimutatható. Esetünk azért fontos, mert ez az egyetlen olyan beszámoló, ami akut transdermalis metanolmérgezés következtében kialakult parkinsonizmust ismertet.

Kulcsszavak: transdermalis, metanol, mérgezés, parkinsonizmus

Methanol is a colorless and highly toxic liquid similar to ethanol in odor and taste. It can be used commercially in varnish, lacquer, the textile industry, paints, and antifreeze fluids. Methanol is not noticed by users in counterfeit alcoholic beverages. Exposure may occur through oral intake, inhalation, or absorption through the skin[1]. Methanol intake can lead to severe metabolic acidosis, loss of vision, permanent neurological damage, and death. Computed tomography (CT) and magnetic resonance imaging (MRI) may show toxic effects due to methanol intake. Putaminal necrosis and subcortical white matter lesions are the most common findings[2]. Our case is interesting because it is the first in the literature to show that signs of parkinsonism developed as a result of transdermal methanol intoxication.

Case report

A 19-year-old female patient who had gone through normal developmental stages from birth and who had no known disease history was covered in spirit across a large area of her back for back pain. The spirits were kept on

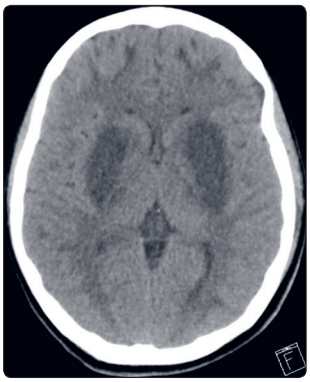

Figure 1. *On the second day of hospitalization, cranial CT showed hypodensity in the bilateral lentiform nucleus*

her back for 2 days. She was admitted to the emergency department with complaints of headache, nausea, vomiting, and she was lethargic. The patient's Glasgow coma score (GCS) was 11/15. The hemogram, biochemistry, and coagulation parameters were normal. Ammonia was detected as 114 μmol/L (normal range 18–87 μmol/L), D-dimer was 11.100 μg/L (normal range 0–583 μg/L), and fibrinogen was normal. Systemic metabolic acidosis with a high anion gap and high osmolar gap was detected in arterial blood gas. Blood acetyl salicylic acid and acetaminophen levels were normal. The blood methanol level could not be measured, but it was found that the spirit on the back was methanol. No pathology was detected following lumbar puncture examination of the patient. Cranial computed tomography (CT), thorax CT, pulmonary CT angiography, transthoracic echocardiography, and abdominal ultrasonography (USG) were normal. The patient's neurological status worsened and she was intubated and admitted to the intensive care unit. Hemodialysis was started, and ethyl alcohol was started as an antidote. Sodium bicarbonate treatment was given for metabolic acidosis. In addition, thiamine and folic acid were added to the treatment. On the second day of hospitalization, cranial CT showed diffuse symmetrical hypodense pathological density areas in the bilateral frontal lobe subcortical white matter and lentiform nuclei on both sides **(Figure 1).** Cranial MRI on the 5th day showed hyperintense pathologic signal changes in the T2 sequence without contrast enhancement in the bilateral frontal cortical-subcortical regions and basal ganglia **(Figure 2)**. Cranial MRI was performed at annual follow-ups. However, no change was observed in the MRI findings. The patient was discharged on the 30th day of her admission after the end of the intensive care and inpatient service follow-up. Upon discharge, her neurological examination results were normal, except for a significant resting tremor and postural tremor on the right side. Detailed eye examinations performed by ophthalmologist did not reveal any pathology. In the first year of outpatient examination, she had dysarthria, aprosodia, bradimimia, and prominent bradykinesia, as well as rigidity and dystonia in the right upper and lower extremities **(Video 1** can be seen on the homepage of Clinical Neuroscience: elitmed.hu). Levodopa treatment was started and levodopa dose was increased up to 750 mg/day but the patient did not benefit from the medication. No side effects were observed during levodopa treatment period. In the fourth year of follow-up, the patient is being followed closely without medication.

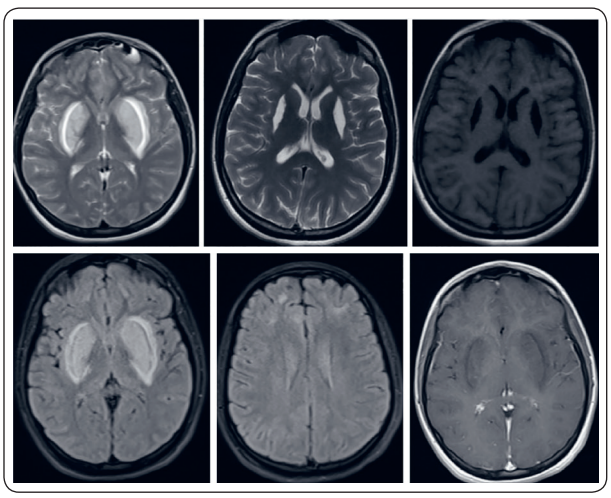

Figure 2. *Bilateral frontal cortical-subcortical pathological signal changes and lentiform fork signs were observed on cranial MRI taken on the 5th day of hospitalization*

Discussion

Methanol is used as a fuel additive and as a pioneer in the production of plastics, formaldehyde, acetic acid, and explosives. Exposure may occur by inhalation of methanol vapor, absorption of methanol-containing solutions from the skin, or oral intake. The metabolites of methanol are formaldehyde and formic acid and are more toxic than methanol[3]. Formic acid selectively inhibits the activity of mitochondrial cytochrome oxidase, leading to adenosine triphosphate (ATP) depletion and the death of retinal and optic nerve neurons[4]. Intoxication results in severe metabolic acidosis and severe neurological sequelae. Seizures, stupor, and coma can result from the consumption of high doses[5]. In the early stages of methanol intoxication, drowsiness, confusion, headache, nausea, abdominal pain, ataxia, and visual impairment may be observed, which is similar to the result of ethanol intoxication. After a latent period of 12–24 hours (the period in which methyl alcohol is metabolized to more toxic formaldehyde and formic acid), visual impairment secondary to late formic acid and lactate-induced optic nerve necrosis or demyelination may occur[5, 6]. The clinical manifestations of Parkinson's-like symptoms tend to occur immediately after the acute effects of methanol have improved and progress much faster than in Parkinson's disease. Methanol-induced parkinsonism develops due to high doses of or chronic exposure to methanol[7–9]. Cranial CT may show hypodensity in putamen; MRI shows bilateral putaminal necrosis, T2 hyperintense white matter lesions that may

Table 1. *Summary of cases reported in the literature due to transdermal methanol intoxication*

	Age	Sex	Complaints	GCS	Art. pH	Administered fluid	Reason for use	Exposure time	Results of imaging	Clinical course
Kahn et al.[17] (1979)	8 m	M	LOC	N/A	6,50	Methanol	Cough	2 times 12 hours each	N/A	Exitus
Soysal et al.[18] (2007)	51 y	F	LOC	3/15	7,10	Spirit	Headache	Short massage for 2-3 days	Normal CT	Exitus
Karaduman et[19] al. (2009)	47 y	F0	LOC, blurred vision	7/15	7,16	Spirit	Ankle injury	2 days	MRI: Bilateral putaminal necrosis	Vision loss
Iscan et al.[20] (2013)	54 y	F	LOC	6/15	N/A	Spirit	Pain in the legs	7 hours	CT: Symmetrical putaminal necrosis	Vision loss
Sahin et al.[21] (2013)	60 y	F	LOC	10/15	7,18	Spirit	Pain in the legs, OA	2 hours	Normal CT	Normal
Hizarci et al.[22] (2015)	57 y	M	Nausea, blurred vision	15/15	7,11	Spirit	Muscle pain	One and a half hours	Normal CT and MRI	Normal
Uca et al.[23] (2015)	68 y	M	LOC, blurred vision, weakness	11/15	7,18	Spirit	Knee pain	N/A	Normal CT and MRI	Vision loss
Dogan et al.[24] (2016)	59 y	M	Blurred vision, weakness	15/15	7,10	Spirit	Knee pain	10 hours	Normal CT and MRI	Normal
Bal et al.[25] (2016)	19m	F	Vomiting, seizure	6/15	6,89	Spirit	Soft tissue damage	3 days	CT: Edema and SAH	Exitus
Karaoglu et[28] al. (2017)	52 y	M	Vomiting, blurred vision	15/15	7,08	Spirit	Cough	4 hours	CT: Was not made	Normal
Vural (2019)[29]	34 y	F	Vomiting, LOC	13/15	7,10	Spirit	Knee and back pain	6 hours	N/A	Normal
Oguz et al.[30] (2019)	58 y	F	Vomiting, diplopia	15/15	7,19	Spirit	Knee pain	N/A	N/A	Normal

LOC: loss of consciousness, N/A: not available, OA: osteoarthritis, SAH: subarachnoid hemorrhage

show subcortical confluence, cerebellar involvement, diffuse cerebral edema, optic nerve necrosis, and cerebral and intraventricular hemorrhage[3, 10–12]. In addition, MRI may show a lentiform fork sign, which is a radiological description that must first be investigated for metabolic acidosis[13]. Ethanol and fomepizole may be used as antidotes for the treatment of methanol intoxication; ethanol is a competitor for dehydrogenase enzyme. It is known that the affinity of ethanol for the alcohol dehydrogenase enzyme is 10–20 times higher than of methanol. It is used to prevent the conversion of methanol to toxic metabolites. Fomepizole is an alcohol dehydrogenase inhibitor. This prevents the conversion of methanol into more toxic metabolites. Gastric lavage, sodium bicarbonate, folic acid, and hemodialysis are also used as treatments[3, 14–16].

In the literature, 12 cases of acute transdermal methanol intoxication have been reported. Cases occurred in people between 24–68-years-old. Nine of the cases developed due to the application of spirits for pain in various parts of the body. One of the cases was an 8-month-old boy, and an other was a 52-year-old man who had a cough and had alcohol applied to his chest. One case was admitted to the clinic for acidosis as a result of the application of spirits due to the development of redness and swelling at the site of intramuscular injection in a 19-month-old baby girl. Clinical and imaging findings varied according to the duration of exposure to methanol and the width of the site of administration. Six of these cases were discharged following a normal examination, after which three had bilateral optic atrophy and visual loss[17–25]. The other three cases resulted in death.

With COVID-19, the demand for alcohol-based hand rubs (ABHRs) has suddenly increased and many countries have expanded the laws to facilitate their production.

In addition to the increase in the production of ABHR commercially, the production of individual hand disinfectants has also become widespread. Of potential concern is where 'methylated spirits' is substituted for ethanol or isopropyl alcohol[26]. A tragic example is the case of poisoning in Iran after ingesting methanol in illegal alcoholic beverages to 'prevent' COVID-19, in which about 700 people died and more than 2,000 case became severely toxic[27]. Therefore, methylated spirits should not be used in ABHRs, not only because of the risk of toxicity from ingestion, but also from inhalation and skin exposure.

The transdermal methanol intoxication cases in the literature with three additional studies[28–30] can be found in **Table 1**.

Our case is important because it is the only case in which parkinsonism developed due to acute transdermal methanol intoxication.

Conclusion

In complementary and alternative medicine, plant extracts and liquids containing methanol can be used because they have anti-inflammatory and analgesic effects. However, in some countries, methanol can be sold for industrial use without government supervision. Because methanol has serious toxic and irreversible effects, its use must be governed by state control and subject to special permits.

CONFLICT OF INTEREST – The authors do not have any conflicts of interest to declare.

References

1. *Ahsan H, Akbar M, Hamee A.* Diffusion Weighted Image (DWI) findings in methanol ıntoxication. J Pak Med Assoc 2009;59(5):321-3.
2. *Rubinstein D, Escott E, Kelly JP.* Methanol intoxication with putaminal and white matter necrosis: MR and CT findings. AJNR Am J Neuroradiol 1995;16:1492-4.
3. *Blanco M, Casado R, Vazquez F, Pumar JM.* CT and MR imaging findings in methanol intoxication. AJNR Am J Neuroradiol 2006;27:452-4.
4. *Wallace KB, Eells JT, Madeira VM, Cortopassi G, Jones DP.* Mitochondria-mediated cell injury. Symposium overview. Fundam Appl Toxicol 1997;38(1):23-37. https://doi.org/10.1006/faat.1997.2320
5. *Fujita M, Tsuruta R, Wakatsuki J, Takeuchi H, Oda Y, Kawamura Y, et al.* Methanol intoxication: Differential diagnosis from anion gap-increased asidosis. Internal Medicine 2004;43:750-4. https://doi.org/ 10.2169/internalmedicine.43.750.
6. *Jacobsen D, McMartin KE.* Methanol and ethylene glycol poisonings. Mechanism of toxicity, clinical course, diagnosis and treatment. Med Toxicol 1986;1(5):309-34. https://doi.org/10. 1007/BF03259846.
7. *Reddy NJ, Sudini M, Lewis LD.* Delayed neurological sequelae from ethylene glycol, diethylene glycol and methanol poisonings. Clin Toxicol (Phila) 2010;48(10):967-73. https://doi.org/0. 3109/15563650.2010.532803.
8. *Finkelstein Y, Vardi J.* Progressive parkinsonism in a young experimental physicist following long-term exposure to methanol. Neurotoxicology 2002;23(4-5):521-5. https://doi.org/10.1016/s0161-813x(02)00033-5.
9. *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.
10. *Halavaara J, Valanne L, Setala K.* Neuroimaging supports the clinical diagnosis of methanol poisoning. Neuroradiology 2002;44:924-8. https://doi.org/10.1007/s00234-002-0855-2.
11. *Gaul HP, Wallace CJ, Auer RN, Fong TC.* MR findings in methanol intoxication. AJNR Am J Neuroradiol 1995;16:1783-6.
12. *Thirunavukkarasu S, Nair PP, Wadweka V*. Acute bilateral putaminal haemorrhagic necrosis in methanol poisoning. BMJ Case Rep 2013. https://doi.org/10.1136/bcr-2013-201026.
13. *Albin RL.* Basal ganglia neurotoxins. Neurol Clin 2000;18(3):665-80. https://doi.org/10.1016/s0733-8619(05)70217-6.
14. *Rietjens SJ, de Lange DW, Meulenbelt J.* Ethylene glycol or methanol intoxication: which antidote should be used, fomepizole or ethanol? Neth J Med 2014;72(2):73-9.
15. *Kraut JA, Kurtz I.* Toxic alcohol ingestions: clinical features, diagnosis, and management. Clin J Am Soc Nephrol 2008;3(1):208-25. https://doi.org/10.2215/CJN.03220807.
16. *Brent J.* Fomepizole for ethylene glycol and methanol poisoning. N Engl J Med 2009;360(21):2216-23. https://doi.org/ 10.1056/NEJMct0806112.
17. *Kahn A, Blum D.* Methyl alcohol poisoning in an 8-month-old boy: An unusual route of intoxication. The Journal of Pediatrics 1979; 94(5):841-3. https://doi.org/10.1016/s0022-3476(79)80176-6.
18. *Soysal D, Kabayegit OY, Yilmaz S, Tatar T, Ozatlı T, Yildiz B, Ugur O.* Transdermal methanol intoxication: a case report. Acta Anaesthesiol Scand 2007;51:779-80. https://doi.org/10.1111/j.1399-6576.2007.01332.x.
19. *Karaduman F, Asil T, Balci K, Temizoz O, Unlu E, Yilmaz A, Utku U.* Bilateral basal ganglionic lesions due to transdermal methanol intoxication. J Clin Neurosci 2009;16:1504-6. https://doi.org/10.1016/j.jocn.2009.01.017.
20. *İscan Y, Coskun C, Oner V, Turkcu FM, Tas M, Alakus MF.* Bilateral total optic atrophy due to transdermal methanol ıntoxication. Middle East African Journal of Ophthalmology 2013;20(1):92-4. https://doi.org/10.4103/0974-9233.106406.
21. *Sahin S, Solak S, Akyol O, Vatansever S, Ozyuvaci E.* Transdermal methyl alcohol intoxication cause of pain relief. West Indian Med J 2013;62(1):84-6.
22. *Hizarci B, Erdoğan C, Karaaslan P, Unlukaplan A, Oz H.* Transdermal methyl alcohol ıntoxication: A case report. Acta Derm Venereol 2015;95:740-1. https://doi.org/10.2340/00015555-2043
23. *Uca AU, Kozak HH, Altas M.* An undercovered health threat in turkey:transdermal methanol ıntoxication. Clinical Neuropharmacology 2015;38(2):52-4. https://doi.org/10.1097/WNF.0000000000000071.
24. *Dogan H, Karakus BY, Cabuk KS, Uzun O, Yenice H, Orucoglu A.* Transdermal spirit (methanol) poisoning: A case report. Iran Red Crescent Med J 2016;18(11):e23767. https://doi.org/10.5812/ircmj.23767.
25. *Bal ZS, Can FK, Anil AB, Bal A, Anil M, Gokalp G, Yavascan O, Aksu N.* A rare cause of metabolic acidosis fatal transdermal methanol ıntoxication in an ınfant. Pediatric Emergency Care 2015;32(8):532-3. https://doi.org/10.1097/PEC.0000000000000478.
26. *Dear K, Grayson L, Nixon R.* Potential methanol toxicity and the importance of using a standardised alcohol-based hand rub formulation in the era of COVID-19. Antimicrob Resist Infect Control. 2020;9:129. https://doi.org/10.1186/s13756-020-00788-5
27. *Soltaninejad K.* Methanol mass poisoning outbreak: a consequence of COVID-19 pandemic and misleading messages on social media. Int J Occup Environ Med 2020;11(3):148-50. https://doi.org/10.34172/ijoem.2020.1983
28. *Karaoglu U, Sarıhan A, Bulut M.* A rare case of transdermat methanol ıntoxication. J Emerg Med Case Rep 2017;8:52-4. https://doi.org/10.5152/jemcr.2016.1795.
29. *Vural S.* Transdermal methanol ıntoxication via folk medicine. Journal of Emergency Medicine Case Rep 2019;10(2):50-2.
30. *Oguz AB, Gunalp M, Polat O, Genc S, Gurler S.* Transdermal methanol ıntoxication. Arch Iran Med 2019;22(11):671-2.