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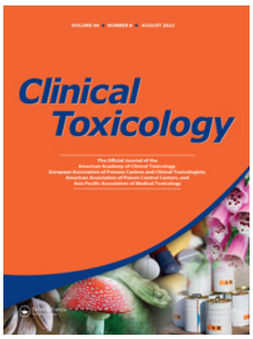

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ORCID

Khin Sam http://orcid.org/0000-0001-8029-2506
Andis Graudins http://orcid.org/0000-0002-0310-3983

References

[1] Agrawal VK, Bansal A, Kumar R, et al. Potassium permanganate toxicity: a rare case with difficult airway management and hepatic damage. Indian J Crit Care Med. 2014;18(12):819–821.
[2] Middleton SJ, Jacyna M, McClaren D, et al. Haemorrhagic pancreatitis-a cause of death in severe potassium permanganate poisoning. Postgrad Med J. 1990;66(778):657–658.
[3] Young RJ, Critchley JA, Young KK, et al. Fatal acute hepatorenal failure following potassium permanganate ingestion. Hum Exp Toxicol. 1996;15(3):259–261.
[4] Ong KL, Tan TH, Cheung WL. Potassium permanganate poisoning-a rare cause of fatal self poisoning. J Accid Emerg Med. 1997;14(1):43–45.
[5] Younan L, Eloubeidi M, Barada K. A rare cause of caustic gastric injury in a young man. Gastroenterology. 2013;145(1):60–260.

Khin Sam
Monash Clinical Toxicology Unit, Emergency Medical Service, Monash Health, Clayton, Australia
Monash Emergency Research Collaborative, Department of Medicine, School of Clinical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Dandenong, Australia
Emergency Department, Dandenong Hospital, Monash Health, Clayton, Australia
khin.sam@monashhealth.org

Andis Graudins
Monash Clinical Toxicology Unit, Emergency Medical Service, Monash Health, Clayton, Australia
Monash Emergency Research Collaborative, Department of Medicine, School of Clinical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Dandenong, Australia

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LETTERS TO THE EDITOR

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Lactic acidosis with elevated osmolal gap after ingestion of a lighter fluid containing dipropylene glycol monomethyl ether (DPGME), a case report

To the Editor,

A 58-year-old woman (178 cm in length, 88 kg in weight) with a medical history of hypertension, depression, sleep apnea, pulmonary embolism, heart failure and a previous suicide attempt with methanol, drank approximately 150 mL of a lighter fluid. She was found unresponsive by her husband and was last seen in a good condition four hours before hospital arrival. On arrival, she presented with coma (Glasgow Coma Scale score 3), hypotension (blood pressure 66/37 mm Hg) and a normal heart rate (65 beats/min). Other findings, including brain CT, liver and kidney values, were unremarkable. Laboratory examination showed a metabolic acidosis (pH 7.23, bicarbonate 15 mmol/L, pCO_2 4.9 kPa) with increased anion gap (23 mmol/L), increased lactate concentration (8.2 mmol/L) and elevated osmolal gap (22 mOsm/kg). Initial urine drug testing (Drug-Screen-Multi 12 V) was positive for paracetamol/acetaminophen, benzodiazepines and tricyclic antidepressants, but ingestion of large amounts was considered unlikely after inspection of remaining drugs. The electrocardiogram was normal. Laboratory analysis of blood plasma was negative for methanol, ethanol, acetone or other ketones (determined with gas chromatography (GC)), ethylene glycol, metformin (gas chromatographymass spectrometry (GC/MS)), salicylic acid, paracetamol (cobas immunoassay), excluding these chemicals as causes of the observed acidosis. Other specific substances were not further analyzed. Because of progressive respiratory insufficiency with a combined hypercapnia and metabolic acidosis the patient was intubated and transported to the intensive care unit for treatment and monitoring. Blood pressure was unresponsive to fluid resuscitation, but did respond to noradrenalin administration. The lactate concentration rose to 9.4 mmol per liter four hours after arrival despite treatment. The observed symptoms prompted further research into the exact contents of the lighter fluid. The consulted poison center stated that the lighter fluid in question consisted solely of dipropylene glycol monomethyl ether (DPGME). The lactate concentration steadily declined 12 h after admission and metabolic acidosis had fully resolved after 24 h (Figure 1). The patient awoke slowly, was detubated and discharged to a psychiatric hospital the following day.

DPGME is a glycol ether, produced as a mixture of four isomers, with industrial and cosmetic applications. In animals oral exposure to DPGME results in CNS and cardiac depression, atrial fibrillation, hypotension and/or respiratory arrest [1]. In humans exposures to mixtures containing DPGME have been described, with hypersalivation, hypoxia, stridor, bronchospasm, vomiting, drowsiness and seizures [2]. Large dose exposures to DPGME exclusively have not been

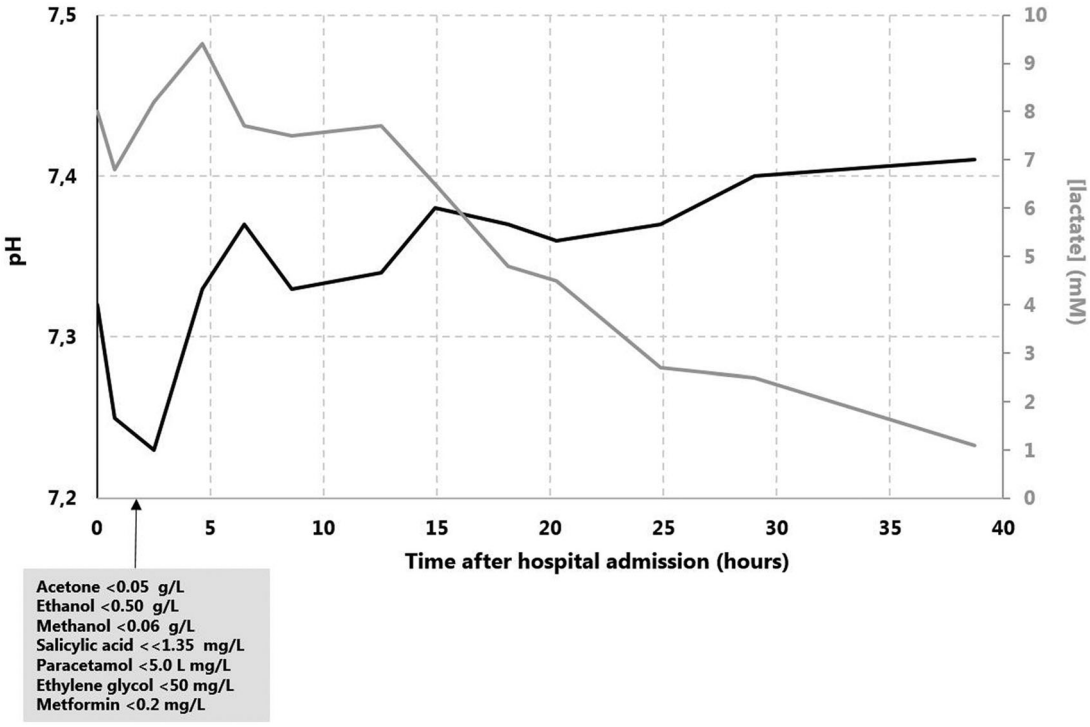

Figure 1. The course of the lactate plasma concentration (grey line) and the pH (black line) after hospital admission.

described before. Rat studies have shown that DPGME is metabolized to sulfate and glucuronide conjugates, which are renally cleared, and into mono- and dipropylene glycol, whether or not *via* the intermediate conversion to propylene glycol monomethyl ether (PGME) [3]. Mono- and dipropylene glycol can be converted into lactic acid [4], suggesting that the intake of DPGME can result in acid-base disturbances. In our patient, quantitative liquid chromatograpy-mass spectrometry (LC/MS) analysis confirmed the presence of dipropylene glycol and DPGME approximately 10 h after the presumed time of intake. Moreover, GC/MS analysis suggested the presence of propylene glycol (below the lower limit of quantitation). There is a possibility that (some of) the observed effects may be due to other substances as a broad tox screen of drugs of abuse and medicine has not been performed. However other drug intoxicating possibilities were carefully evaluated and selectively tested for. The combination of symptoms, together with the reliable anamnesis of exposure, strongly suggests that the symptoms were caused by exposure to DPGME.

To our knowledge, this is the first case description of a patient who ingested a large amount of the glycol DPGME, resulting in lactic acidosis with elevated osmolal gap.

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ORCID

Dylan W. de Lange http://orcid.org/0000-0002-0191-7270
Arjen Koppen http://orcid.org/0000-0002-1753-4637

References

[1] Shideman FE, Procita L. The pharmacology of the Mono methyl ethers of Mono-, di-, and tripropylene glycol in the dog with observations on the auricular fibrillation produced by these compounds. J Pharmacol Exp Ther. 1951;102(2):79–87.
[2] Panchal B, Eddleston M, Thomas SH, et al. 754 Exposures to reed diffusers reported to the United Kingdom national poisons information service 2010-2014. Clin Toxicol (Phila). 2016;54(4):333–338.
[3] Miller RR, Hermann EA, Calhoun LL, et al. Metabolism and disposition of dipropylene glycol monomethyl ether (DPGME) in male rats. Fundam Appl Toxicol. 1985;5(4):721–726.
[4] Cunningham CA, Ku K, Sue GR. Propylene glycol poisoning from excess whiskey ingestion: a case of high osmolal gap metabolic acidosis. J Investig Med High Impact Case Rep. 2015;3(3):2324709615603722.

Pepijn M. Langbroek
Department of Internal Medicine, Treant Zorggroep, Emmen, the Netherlands

Albert R. Dreijer
Department of Hospital Pharmacy, Treant Zorggroep, Emmen, the Netherlands

Dylan W. de Lange
Dutch Poisons Information Center (DPIC), University Medical Center Utrecht, Utrecht, The Netherlands
Intensive Care, University Medical Center Utrecht, Utrecht, The Netherlands

Rosalie D. Moorlag
Department of Hospital Pharmacy, Treant Zorggroep, Emmen, the Netherlands

Martijn Passier and Bram van Leer
Department of Critical Care, Treant Zorggroep, Emmen, the Netherlands

Arjen Koppen
Dutch Poisons Information Center (DPIC), University Medical Center Utrecht, Utrecht, The Netherlands
a.koppen@umcutrecht.nl

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LETTERS TO THE EDITOR

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Comment on "Efficacy of lipid emulsion therapy in treating cardiotoxicity from diphenhydramine ingestion: a review and analysis of case reports"

To the Editor,

I read with interest this thoughtful review and analysis of case reports entitled "Efficacy of lipid emulsion therapy in treating cardiotoxicity from diphenhydramine ingestion: a review and analysis of case reports" recently published in Clinical Toxicology [1]. Lipid emulsion is used to treat systemic toxicity caused by a toxic dose of local anaesthetics [2]. In addition, lipid emulsion is reported to ameliorate cardiovascular collapse induced by toxic doses of non-local anaesthetics, including diphenhydramine, which is an antihistamine (H1) with anticholinergic property [3]. I would like to share some comments regarding this study. Clemons et al. [1] described that mean arterial pressure (MAP) increased by 37 ± 17.5 mm Hg in the lipid emulsion group, whereas it decreased by 4.5 ± 11.5 mm Hg in patients who did not receive lipid emulsion treatment. In contrast, the changes in QRS duration and QTc interval were not significantly different between lipid emulsion and standard treatment groups [1]. This lipid emulsion-induced improvement in MAP may be owing to a significantly decreased MAP before lipid emulsion administration [1]. Before lipid emulsion or standard treatment (e.g., sodium bicarbonate) administration, MAP was significantly lower ($p = 0.0075$) in the lipid emulsion group (median ± interquartile range: 45.5 mm Hg [42.25–48.75], $N = 6$) than in the standard treatment group (87.5 mm Hg [68.5–113], $N = 10$), as analysed using the Mann–Whitney test [1]. Furthermore, the proportion of patients with pre-treatment MAP less than 65 mm Hg was significantly higher in the lipid emulsion group (6/6 = 100%) than in the standard treatment group (7/19 = 36.8%), as analysed using the Fisher's exact test ($p = 0.015$) [1]. However, pre-treatment QRS duration was not significantly ($p = 0.7546$) different between groups (146 ms [118–185], lipid emulsion group [$N = 6$] versus 143.5 ms [108.3–162], standard treatment group [$N = 8$]) [1]. In addition, pre-treatment QTc interval was comparable ($p = 0.9433$) between groups (573 ms [509–668], lipid emulsion group [$N = 5$] versus 588 ms [522–661], standard treatment [$N = 8$]) [1]. This significantly decreased MAP before lipid emulsion administration may be associated with the late treatment trial of lipid emulsion in cardiac toxicity caused by the toxic dose of diphenhydramine, which is unresponsive to supportive treatments, including charcoal, benzodiazepine, physostigmine, and sodium bicarbonate [4]. The non-significant differences in QRS duration and QTc interval change in both groups may be owing to a lack of simultaneous measurement of prolonged QRS duration and QTc interval with that of decreased MAP before lipid emulsion or standard treatment administration. A meta-analysis of lipid emulsion treatment of the toxicity caused by non-local anaesthetic drugs suggests that the quality of evidence is low to very low, and the effect is heterogenous [5]. Thus, systemic analysis of many case reports (positive or negative), animal studies, and observation studies involving propensity score matching are required to examine the effect of lipid emulsion resuscitation on diphenhydramine toxicity.

Disclosure statement

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References

[1] Clemons J, Jandu A, Stein B, et al. Efficacy of lipid emulsion therapy in treating cardiotoxicity from diphenhydramine ingestion: a review and analysis of case reports. Clin Toxicol. 2022;60(5):550–558.
[2] Ok SH, Hong JM, Lee SH, et al. Lipid emulsion for treating local anesthetic systemic toxicity. Int J Med Sci. 2018;15(7):713–722.
[3] Cao D, Heard K, Foran M, et al. Intravenous lipid emulsion in the emergency department: a systematic review of recent literature. J Emerg Med. 2015;48(3):387–397.
[4] Huynh DA, Abbas M, Dabaja A. Diphenhydramine toxicity [Internet]. Treasure Island (FL): StatPearls Publishing; [updated 2021 May 8; cited 2022 Jan]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557578/.
[5] Levine M, Hoffman RS, Lavergne V, et al. Systematic review of the effect of intravenous lipid emulsion therapy for non-local anesthetics toxicity. Clin Toxicol. 2016;54(3):194–221.