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CE - LETTER TO THE EDITOR

Toxic alcohol diagnosis and management: an emergency medicine review—comment

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To the Editor,

We read with great interest the valuable review of toxic alcohol diagnosis and management by Ng et al. [1]. We propose the possibility of disulfiram as an alternate therapy in resource-restricted settings, which has received scant research interest in the past. Fomepizole and ethanol are capable of blocking alcohol dehydrogenase (ADH), and are thus recognized as antidotes for methanol and ethylene glycol toxicity to prevent the generation of toxic acid metabolites. Ethanol as an antidote has several disadvantages, including intoxication, poorly predictable pharmacokinetics, and if intravenous, phlebitis and hyponatremia. Due to these disadvantages, despite the medication cost, therapy has rightly shifted from ethanol toward fomepizole as an effective antidote with a far superior safety profile. Fomepizole is not readily available in many countries, despite multiple manufacturers in several countries. It is currently on the World Health Organization model lists of essential medicines, but is listed as complementary instead of core. This designates medicines that are effective and safe, but often unaffordable. In many countries, ethanol remains the only available antidote. While ADH has been targeted by fomepizole and ethanol, the downstream enzyme aldehyde dehydrogenase (ALDH) has not received significant attention as a possible therapeutic target. Although downstream to ADH, the aldehyde substrate for ALDH may be preferable to the toxic acid metabolites in the case of toxic alcohols. Disulfiram blocks ALDH and is already in clinical use for the treatment of alcohol use disorder. Although it has been associated with dangerous ethanol-disulfiram reactions, it is generally considered safe. If ethanol is ingested after disulfiram, there is a buildup of acetaldehyde as an intermediate product [2]. Use of disulfiram after methanol or ethylene glycol may lead to the accumulation of formaldehyde or glycoaldehyde, respectively. These aldehydes are themselves potentially toxic, however, may have reduced toxicity when compared with the ultimate metabolites of an unblocked pathway (formic acid from methanol, and glycolic acid and oxalic acid from ethylene glycol). One in vitro and one animal study with unreliable results evaluated the effects of disulfiram on the accumulation of formaldehyde [3, 4]. Interestingly, they believed that disulfiram could not cause significant accumulation of formaldehyde. Moreover, some authors think that disulfiram may increase the toxicity of methanol [5]. So we believe there is time to reassess this therapy in further laboratory and animal studies, and potentially a clinical trial. In general, fomepizole is the ideal antidote, and the focus should be on widespread availability and adoption of fomepizole. We raise the interesting possibility of studying disulfiram as an adjunct therapy to ethanol in settings that lack fomepizole.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Statement of human and animal rights This is a letter to the editor that did not involve the care of humans or animals.

Informed consent There is no requirement for informed consent with this letter to the editor.

References

1. Ng PCY, Long BJ, Davis WT, Sessions DJ, Koyfman A (2018) Toxic alcohol diagnosis and management: an emergency medicine review. Intern Emerg Med 13(3):375–383

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2. Mutschler J, Grosshans M, Soyka M, Rösner S (2016) Current findings and mechanisms of action of disulfiram in the treatment of alcohol dependence. Pharmacopsychiatry 49(4):137–141
3. Koivusalo M (1959) Effect of disulfiram (tetraethylthiuramdisulphide) on the metabolism of methanol in rat liver homogenates. Acta Physiol Scand 31(45):271–277
4. Koivusalo M (1956) Effect of disulfiram (tetraethylthiuram disulphide) on the elimination rate of methanol; studies with rabbits. Ann Med Exp Biol Fenn 34(2):163–169
5. Ap Gilger, Am Potts, Lv Johnson (1952) Studies on the visual toxicity of methanol. II. The effect of parenterally administered substances on the systemic toxicity of methyl alcohol. Am J Ophthalmol 35(52):113–126