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Acute Reversal of Severe Disulfiram-Ethanol Reaction using Fomepizole

Case Report

John Cambron*, Michael A. Miller and Christus Spohn Shoreline
Emergency Department, Corpus Christi, USA

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***Corresponding author:** John Cambron D.O, Emergency Department, Corpus Christi, TX 78404, USA

Abstract

Medications that inhibit aldehyde dehydrogenase when co-administered with ethanol produce an accumulation of acetaldehyde. Disulfiram-alcohol reactions can be severe and include life threatening arterial hypotension and refractory shock. This shock state can be resistant to aggressive intravenous fluid resuscitation and vasopressor administration. Fomepizole, an alcohol dehydrogenase inhibitor has been discussed as a safe and rapidly effective treatment for these severe reactions. This case report describes a middle-aged male who while heavily intoxicated ingested an unknown amount of disulfiram. Aggressive intravenous fluid resuscitation and vasopressor support were unsuccessful in treating his hemodynamic compromise and thus fomepizole was given with drastic improvement in the patient's status in short time. This case report is important to medical literature because it demonstrates that the early use of fomepizole may negate the use of inotropes/vasopressors; invasive procedures and ICU admission in patients with severe disulfiram-ethanol reactions.

Introduction

For more than half a century disulfiram has been thought of as a relatively safe therapy in alcohol use disorder[1-4]. Alcohol dehydrogenase metabolizes ethanol to acetaldehyde. Acetaldehyde, in high concentrations, acts as a potent vasodilator and is responsible for the unpleasant side effects of disulfiram-ethanol reactions[fig 1]. If disulfiram is taken in conjunction with ethanol the alcohol induced acetaldehyde may accumulate to blood levels 5 to 10 times higher than those observed during metabolism of alcohol alone[1-3]. Ingesting alcohol in even small amounts, in the presence of disulfiram results in severe symptomatology that includes flushing, nausea, copious vomiting, respiratory distress, palpitations and tachycardia [1-4]. Taking disulfiram while heavily intoxicated may result in complete cardiovascular collapse through widespread vasodilation. This can be life threatening [5,6]. Fomepizole competitively inhibits alcohol dehydrogenase and acts as an antidote to ethanol poisoning by halting the production of acetaldehyde [6-8]. Fomepizole functions as a competitive inhibitor of alcohol dehydrogenase and is approved for treatment of ethylene glycol and methanol toxicities [9] (Figure 1). In this case report we present fomepizole as a safe, efficient and 1st line medication in the treatment of severe disulfiram-ethanol reactions.

Case Description/Summary

A 35-year-old male presented to our emergency with a chief complaint of severe nausea/vomiting and altered mental status. His medical history included alcohol use disorder for more than 10 years. He had recently obtained an unknown amount of disulfiram from an online source and had been taking it without prescription or supervision.

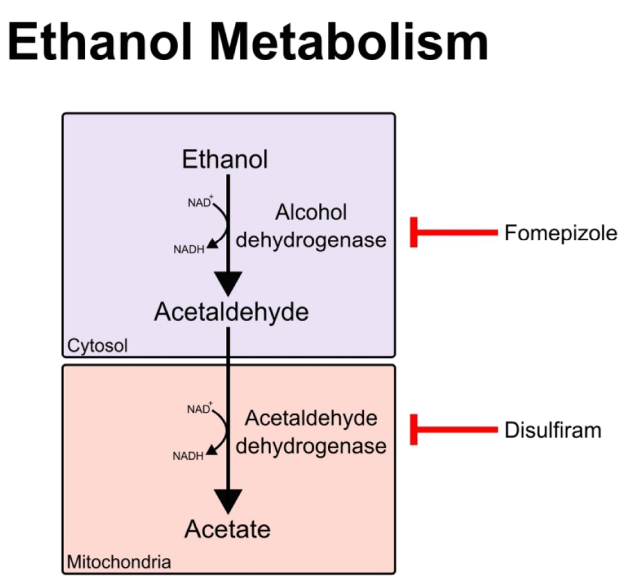

Figure 1: Ethanol metabolism.

He reportedly had been drinking alcohol heavily earlier in the evening then ingested an unknown amount of disulfiram. Patient begin experiencing vomiting, diarrhea, diffuse skin flushing and altered mental status which led to family calling emergency medical services (EMS).

Patients presenting vital signs demonstrated tachycardic heart rate of 150, hypotension with blood pressure of 60/40 and normal oxygen saturation on room air. On physical exam he was actively vomiting, experiencing loose stools and his neurologic status was significant for GCS of 8 as he was only opening his eyes to painful stimuli, localizing to pain and was nonverbal upon presentation. He was noted to have diffuse erythema on integumentary exam.

The patient was placed in our resuscitation bay and he received 3 L boluses of lactated ringer's intravenously. He remained hypotensive after receiving these boluses and was given0.4mg naloxone and fomepizole 1g (15mg/kg) were administered intravenously. This occurred 30 minutes into his ER visit. It should be noted that he received the naloxone approximately 20 minutes prior to the fomepizole with no observed clinical improvement occurring post naloxone administration.

Concomitant to fomepizole administration, laboratory values had returned. These values revealed an ethanol level of 167 mg/dl; a leukocytosis with white blood cell count of 35.2; and acute kidney injury with creatinine level of 1.8 mg/dl. Urine Drug Screen was negative for all testable values including opiates and central nervous system depressants.Thirty minutes post fomepizole administration the blood pressure had improved to 98/48 and tachycardia improved to heart rate of 110. At two hours post fomepizole administration the patient was alert and oriented to self, place and time, was cooperative with exam and answering questions appropriately. All vital signs were within normal limits and the patient was admitted to a medical/surgical floor. He was discharged 24 hours later. His repeat laboratory values demonstrated resolution of previous abnormalities and he remained asymptomatic during his hospital stay.

Discussion

This case describes the use of fomepizole as an important early intervention in the treatment of disulfiram-ethanol reactions. This patient was hemodynamically unstable and on the verge of cardiovascular collapse despite supportive measures. After the administration of fomepizole, he experienced a rapid reversal of hemodynamic instability as well as symptoms. There have been few descriptions of disulfiram intoxications leading to severe disulfiram-ethanol reactions treated with fomepizole. Verite reported a similar case in 2005, Sande in 2012, and Schicchi in 2019 [10,11]. Acetaldehyde accumulates in the presence of disulfiram when alcohol is consumed and leads to the development of disulfiram-ethanol reactions. Fomepizole prevents the accumulation of acetaldehyde by blocking its production.

In most patients with disulfiram-ethanol reactions, symptoms are mild to moderate and supportive care is sufficient. A small category of patients, such as the one mentioned in our case, may progress to severe toxicity. Our clinical observations, in addition to those case reports mentioned in literature, have led us to conclude that there is a role for early administration of fomepizole in these patients.

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