Ethanol Ingestion in Two Infants Under 2 Months Old: A Previously Unreported Cause of ALTE

abstract

The differential diagnosis for the infant presenting with an apparent life-threatening event (ALTE) is broad. Toxic ingestions are a relatively uncommon cause of an ALTE, although several over-the-counter, prescription, and illicit drugs have been implicated. We present 2 cases of ethanol intoxication in infants as a previously unreported cause of an ALTE. Additionally, serial ethanol levels for these patients offer novel insight into the pharmacokinetics of ethanol metabolism in infants. Ethanol ingestion may be an underrecognized cause of an ALTE and should be considered if the history or physical examination is suggestive. Pediatrics 2013;131:e604–e607

AUTHORS: Taylor McCormick, MD, Michael Levine, MD, Oma Knox, MD, and Ilene Claudius, MD

Department of Emergency Medicine, Los Angeles County and University of Southern California, Los Angeles, California

KEY WORDS apparent life-threatening event, ALTE, ethanol, alcohol, intoxication, poisoning, ingestion, toxic ingestion, toxicology, emergency medicine, infant

ABBREVIATIONS

ALTE—apparent life-threatening event
DCFS—Department of Children and Family Services
ED—emergency department

Dr McCormick collected data, drafted the initial manuscript, reviewed and revised subsequent drafts, and approved the final manuscript as submitted; Dr Levine analyzed the ethanol pharmacokinetic data, created the ethanol elimination figure, drafted the kinetics portion of the discussion section, reviewed and revised the manuscript, and approved the final manuscript as submitted; Dr Knox participated in data compilation, drafted the initial abstract, and approved the final manuscript as submitted; and Dr Claudius conceptualized the report, critically reviewed and revised the manuscript through its many drafts, and approved the final manuscript as submitted.

doi:10.1542/peds.2012-1652

Accepted for publication Aug 17, 2012

Address correspondence to Taylor McCormick, MD, LAC+USC Department of Emergency Medicine, 1200 N State St, Ste 1011, Los Angeles, CA 90033. E-mail: taylormccormick@gmail.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2013 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.
An apparent life-threatening event (ALTE) is defined as an episode that is frightening to the observer and characterized by some combination of apnea, color change, change in muscle tone, and choking or gagging. The potential causes of an ALTE range widely from a minor choking episode to potential causes of an ALTE presenting with an ALTE.4–7 Toxic ingestion is a recognized, but uncommon, cause of an ALTE. Case reports and small studies have implicated opioids, phenothiazines, benzodiazepines, barbiturates, cocaine, cough and cold preparations, and colic medications as potential causes of an ALTE.8–11 However, there are no previously published cases of ethanol intoxication as the cause of an ALTE. Although toxicology screens are often recommended in the evaluation of a patient presenting with an ALTE, most standard toxicology screens do not include ethanol and would have been of little use in the cases described here. Failure to identify ethanol as the cause of an ALTE leads to unnecessary diagnostic evaluation and, more importantly, could have significant consequences for the future health and safety of the child. We also present the pharmacokinetics and clinical course of ethanol intoxication in infants, which thus far have been poorly described.

In our inner city, academic, pediatric emergency department (ED) with an annual census of 22,186, an ethanol level was sent 6 times between July 2010 and November 2011 for patients <15 months old. We identified 3 patients with a detectable ethanol level. One case involved an unintentional witch hazel ingestion in an asymptomatic 25-day-old with a serum ethanol level of 97 mg/dL. Two patients presented with an ALTE and the cases are described here.

PATIENT PRESENTATIONS

Case 1: Ethanol Concentration of 278 mg/dL

A 2-month-old, 3.8-kg full-term male infant was brought in via ambulance for ALTE at home. His mother reported the infant had been fussy early in the evening, and she called 911 after noticing apnea, labored respirations, and limpness without color change while he was sleeping. Paramedics reported the infant was unresponsive on their arrival but had a partial improvement in mental status after an intramuscular injection of naloxone 0.5 mg. In addition, the paramedics expressed concern about the condition of the home and the erratic demeanor of the family on their arrival, but they were unable to provide specifics. According to the mother, the infant had been a term delivery at 3.2 kg with an unremarkable prenatal and past medical history and with normal development. He had been formula-fed without exposures to tobacco or drugs and resided with his 21-year-old mother, uncles, and paternal grand-mother. The father, who was involved, had a history of mental illness and substance abuse, and the couple had 2 additional children who were reported to be visiting family in Sacramento. The patient arrived in the ED at a temperature of 98.0°F, heart rate of 131 beats per minute, blood pressure of 79/39 mm Hg, respiratory rate of 30 breaths per minute, and oxygen saturation of 100% on room air. He initially appeared well and was vigorous with an unremarkable physical examination; however, he fell asleep when not stimulated. Blood glucose was 111 mg/dL. Based on the paramedics’ concerns about the home and the child’s response to naloxone, a toxicological workup revealed a serum ethanol concentration of 278 mg/dL, as measured with an enzymatic test. Other laboratory test results were white blood cells $18 \times 10^{3}/mm^{3}$, hemoglobin 10.1 g/dL, hematocrit 29.1%, sodium 142 mEq/L, potassium 5 mEq/L, chloride 108 mmol/L, bicarbonate 19 mmol/L, serum urea nitrogen 5 mg/dL, creatinine 0.23 mg/dL, glucose 108 mg/dL, salicylates <2 mg/dL, acetaminophen <5 µg/mL, and lactate 5.2 mmol/L. Urine toxicology screen for opiates, cocaine, amphetamines, barbiturates, and benzodiazepines was negative. Although the possibility of a narcotic ingestion cannot be completely excluded based on the urine toxicology screen, it is most likely that the painful injection, not the naloxone itself, awoke the patient. The Department of Children and Family Services (DCFS) was notified, and the child was admitted to the PICU for ethanol intoxication and failure to thrive (weight <5% with 12 g/d gain). He remained stable as his serum ethanol level approached zero over the next 12 hours. He was discharged to foster care 8 days later with normal neurologic function.

Case 2: Ethanol Concentration of 405 mg/dL

An 8-week-old full-term male infant was brought in via ambulance for ALTE at home. The babysitter witnessed 30 minutes of abnormal respirations with periods of apnea and gasping, depressed level of consciousness, and minimal response to vigorous stimulation. The child’s history was significant for suspected in utero cocaine and phencyclidine exposure, but he had been healthy and exclusively formula-fed since birth, with no additional tobacco or drug exposure. He resided with the father exclusively, although the mother had monitored visitation rights, and his development had been normal. On arrival to the ED, vital signs included temperature of 96.6°F, heart rate of 168
beats per minute, blood pressure of 101/71 mm Hg, respiratory rate of 48 breaths per minute, oxygen saturation of 98% on room air, and weight of 5.6 kg (65%). The infant had normal color and respirations but a weak cry and floppy muscle tone alternating with right-sided facial twitching and upper extremity movements concerning for seizure. He was not visually tracking and did not respond to intravenous line placement, and the emergency physician noted the smell of alcohol. His blood glucose was 168 mg/dL and his serum ethanol concentration was 405 mg/dL. This level was initially measured via an enzymatic approach but was confirmed via gas chromatography–flame ionization detection. Other laboratory test results were white blood cells $11.3 \times 10^3/mm^3$, hemoglobin 10.1 g/dL, hematocrit 28.3%, sodium 140 mEq/L, potassium 4.5 mEq/L, chloride 106 mmol/L, bicarbonate 18 mmol/L, serum urea nitrogen 7 mg/dL, creatinine 0.17 mg/dL, glucose 159 mg/dL, salicylates <2 mg/dL, acetaminophen <5 µg/mL, and lactate 5.7 mmol/L. When approached regarding the ethanol level, the father stated that he “accidentally” mixed the baby’s formula with gin instead of water. The DCFS was notified and the patient was admitted to the PICU, where he was intubated because of concern for apnea. The patient had a prolonged hospital course secondary to respiratory complications. After 2 normal electroencephalograms and a thorough neurology consult, the twitching movements were ultimately deemed not to represent seizure activity. He was eventually discharged to foster care in stable condition with outpatient occupational therapy for risk of developmental delay.

**DISCUSSION**

The differential diagnosis for the infant with an ALTE or neurologic abnormalities is broad, and toxic ingestions remain an uncommon cause. However, we identified 2 infants presenting with an ALTE secondary to ethanol intoxication in a several-month period. This suggests that ethanol ingestion may be an underrecognized cause of these symptoms, because of a lack of recognition on the part of the practitioner or because of hesitation to publish information regarding recognized cases. Ethanol levels would not be advised as part of a standard ALTE or altered mental status workup; however, the possibility should be considered and pursued if the history or physical examination is supportive.

Ethanol intoxication in infants produces similar clinical effects as seen in adults: central nervous system and respiratory depression. However, 2 important distinctions are known. First, because of poor glycogen stores in infants and the ability of ethanol to inhibit gluconeogenesis, hypoglycemia is relatively common in pediatric ethanol ingestions,
although both infants described here maintained normal blood glucose concentrations.\textsuperscript{15,14} Second, infants appear to metabolize ethanol faster than adults.\textsuperscript{15} It is likely that this accelerated metabolism is the result of different elimination kinetics.

In adults, ethanol is primarily metabolized by alcohol dehydrogenase to acetaldehyde, which is subsequently converted to acetate by acetaldehyde dehydrogenase. Because alcohol dehydrogenase is a saturable enzyme, ethanol metabolism follows Michaelis-Menten kinetics, with first-order elimination at low concentrations and zero-order elimination at a rate of \(\sim 20\) mg/dL/h at concentrations exceeding \(\sim 20\) mg/dL.\textsuperscript{16} There is some suggestion that the infant liver has 10-fold less alcohol dehydrogenase and an equal or greater amount of catalase compared with adult livers.\textsuperscript{17} Therefore, ethanol metabolism may follow first-order elimination in infants at higher concentrations than observed in adults. Serial ethanol levels were available for both of the infants described here. Based on these 2 patients, it appears that ethanol follows Michaelis-Menten kinetics, with a change from first-order elimination to zero-order elimination at \(\sim 225\) mg/dL (Fig 1). Both cases resulted in DCFS involvement. While reporting of suspected child abuse should commence based on clinical suspicion, final legal judgment may require some level of certainty of the validity of the test. Previously, high lactate (\(\geq 14\) mmol/L) or high lactate dehydrogenase (\(\geq 682\) IU/L) levels have been shown to cause false elevations of ethanol concentrations from 17 to 138 mg/dL when measured by enzymatic assays but not by gas chromatography.\textsuperscript{18} Our 2 infants had levels well above this range; however, in patients with lower levels and no contributory history, confirmation by gas chromatography or measurement of the lactate and lactate dehydrogenase might be helpful in confirming child abuse or neglect.

These patients both presented with ALTEs without a history of ingestion. Although toxicology screening is probably unnecessary in the evaluation of all patients presenting with an ALTE, maltreatment should always be considered in the differential diagnosis. In cases where there is concern for maltreatment, toxic ethanol ingestion should be considered, and appropriate diagnostic testing should be obtained. The correct diagnosis of this rare but serious ingestion as a cause of an ALTE has the potential to improve patient outcomes.

\textbf{ACKNOWLEDGMENT}

We thank Dale Bikin, PharmD (Department of Pharmacy, Banner Good Samaritan Medical Center, Phoenix, AZ), for his assistance in the kinetic calculations.

\textbf{REFERENCES}

Ethanol Ingestion in Two Infants Under 2 Months Old: A Previously Unreported Cause of ALTE

Taylor McCormick, Michael Levine, Oma Knox and Ilene Claudius

Pediatrics 2013;131;e604; originally published online January 14, 2013;
DOI: 10.1542/peds.2012-1652

Updated Information & Services
including high resolution figures, can be found at:
/content/131/2/e604.full.html

References
This article cites 16 articles, 7 of which can be accessed free at:
/content/131/2/e604.full.html#ref-list-1

Citations
This article has been cited by 3 HighWire-hosted articles:
/content/131/2/e604.full.html#related-urls

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Fetus/Newborn Infant
/cgi/collection/fetus:newborn_infant_sub
Pharmacology
/cgi/collection/pharmacology_sub
Toxicology
/cgi/collection/toxicology_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml
Ethanol Ingestion in Two Infants Under 2 Months Old: A Previously Unreported Cause of ALTE
Taylor McCormick, Michael Levine, Oma Knox and Ilene Claudius
Pediatrics 2013;131;e604; originally published online January 14, 2013;
DOI: 10.1542/peds.2012-1652

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/131/2/e604.full.html