Severe Poisoning After Accidental Pediatric Ingestion of Glycol Ethers

Abstract

Human glycol ether poisonings are sparsely reported in the medical literature. We describe a healthy 22-month-old boy who accidentally drank up to 330 mL of brake fluid containing a 75% bleed of various glycol ethers (5%–50% polyethylene glycol monomethyl ether, 15%–40% triethylene glycol monoethyl ether, 1%–30% triethylene glycol monomethyl ether, 1%–25% triethylene glycol monobutyl ether, 1%–20% polyethylene glycol, monobutyl ether, 1%–20% triethylene glycol, and <10% of other glycol ethers). Within 4 hours, he became somnolent and developed a persistent metabolic acidosis. Thirty minutes later, he received 1 dose of fomepizole. Neither progression nor improvement in clinical or metabolic status was noted after the fomepizole. He received hemodialysis for 3 hours ~8 hours after ingestion, and his symptoms resolved resulting in an uneventfully recovery.

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Abbreviation

IV—intravenous

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The 2 most common nonethanol alcohol exposures reported to poison control centers are methanol and ethylene glycol. These alcohols cause severe metabolic acidosis, and the utility of alcohol dehydrogenase blockers and hemodialysis are well documented in adults and children. Glycol ethers are less commonly encountered nonethanol alcohols, and although deliberate ingestions by adults have caused mental status depression, hypotension, and metabolic acidosis, significant toxicity after pediatric exposures are very rare. Furthermore, the effectiveness of alcohol dehydrogenase blockers is unclear. We describe an accidental pediatric ingestion of Valuecraft Brake Fluid, which contains a 75% blend of various glycol ethers (5%–50% polyethylene glycol monomethyl ether, 15%–40% triethylene glycol monoethyl ether, 1%–30% triethylene glycol monomethyl ether, 1%–25% triethylene glycol monobutyl ether, 1%–20% polyethylene glycol, monobutyl ether, 1%–20% triethylene glycol, and <10% of other glycol ethers), that rapidly developed a metabolic acidosis and mental status depression, who received fomepizole and a course of hemodialysis.

**CASE REPORT**

A healthy 22-month-old boy was transported by ambulance to a children’s hospital with a chief complaint of altered mental status 1 hour after the father witnessed him drinking from an orange juice container found in the garage. Earlier that day, the father filled the 360-mL orange juice container with an unknown amount of Valuecraft Brake Fluid for Drum and Disc Brakes. By the time the father stopped him, <30 mL was remaining. The father immediately called the regional poison center for assistance. While on the phone, the patient was outside with other children, and he was noted to be stumbling and fell onto the grass from standing position. He initially cried but became more sleepy and difficult to arouse over the next 20 to 30 minutes. The patient was transported to a children’s hospital. En route, he was reported to have depressed mental status and hypoventilation requiring bag mask ventilation.

**Emergency Department Course**

Upon arrival to the emergency department, 1 hour after ingestion, the patient was crying with stimulation, but very sleepy. His heart rate was 173 beats per minute, respiratory rate was 36 breaths per minute, temperature 37.4°C, blood pressure was 96/58 mm Hg, and oxygen saturation of 90% to 93% on room air. His head was normocephalic, with a small hematoma to left frontal scalp. Pupils were equal, round, and reactive to light, conjugate gaze without nystagmus, and opening his eyes spontaneously. His neck was placed in a c-collar, and no abnormalities were noted to palpation. He had normal respirations with clear examination and a normal cardiac examination. His abdomen was soft, nontender, nondistended, and without hepatosplenomegaly. Extremities were warm, well perfused, and without deformities or swelling noted. He was somnolent on examination but arousable to external stimulus and intermittently crying. He would withdraw and localize to pain, moving all extremities equally, and had normal reflexes and tone to his extremities.

Laboratory tests were ordered upon arrival and were remarkable for a metabolic acidosis with an anion gap of 18 (Table 1) and normal renal function, normal serum transaminase, and a hemoglobin level of 12.6 g/dL. Acetaminophen, salicylate, and serum ethanol concentrations were undetectable. Urine toxicology screen was negative for cocaine, methadone, opioids, benzodiazepines, barbiturates, amphetamines, cannabinoids, and phencyclidine. A computed tomography scan of the brain was performed and revealed a normal brain and skull, without evidence of trauma. Cervical spine radiographs were also normal.

The patient was observed in the emergency department and received a 20 mL/kg normal saline intravenous (IV) bolus. Four hours after ingestion, he became more somnolent, difficult to arouse, with minimal response to external stimuli and no gag reflex. Laboratory tests were repeated (Table 1) and revealed a worsening anion gap metabolic acidosis, mild renal insufficiency, normal lactate, and an osmolar gap of 29. Serum concentrations of various alcohols were sent at that time, and the patient was then intubated by using rocuronium, atropen, and etomidate for inability to protect his airway and worsening acidosis. A right femoral central venous line was placed. The local regional poison center was consulted and recommended starting fomepizole and hemodialysis. The patient was given 15 mg/kg fomepizole IV 4.5 hours after ingestion, and he was admitted to the PICU.

**PICU Course**

The patient remained intubated upon arrival to the PICU. A right radial arterial line was placed. Six hours after ingestion, his blood pressure decreased to 74/22 mm Hg despite 60 mL/kg of normal saline. Dopamine infusion was started and titrated to 10 µg/kg per minute to maintain normal blood pressures. He also received 2 mEq/kg of sodium bicarbonate IV bolus for persistent acidosis without improvement. Laboratory testing at this time revealed an anion gap metabolic acidosis and a respiratory acidosis (Table 1), stable renal function, normal serum transaminase, and a hemoglobin level of 10.5 g/dL without evidence for hemolysis.
Later that night, 8 hours after ingestion, the patient received hemodialysis for 3 hours. Dialysis bath consisted of 3 mEq/L potassium, 35 mEq/L bicarbonate, and 140 mEq/L sodium. Follow-up laboratory results revealed resolution of the acidosis, a fall in serum urea nitrogen, creatinine, and osmolality (Table 1). The dopamine infusion was quickly weaned off shortly after dialysis; he was extubated the following day and discharged from the hospital on day 3 in normal health. Serum concentrations (measured on samples from presentation) of isopropanol, methanol, and ethylene glycol were undetectable, and serum propylene glycol was 9 mg/dL.

**DISCUSSION**

Our patient rapidly developed mental status depression and persistent metabolic acidosis after a witnessed ingestion of brake fluid. The material safety data sheet of the product revealed the main ingredients as a 75% blend of various glycol ethers as previously mentioned. The patient was given 1 dose of fomepizole 4.5 hours after ingestion, and he continued to have a persistent metabolic acidosis 8 hours after ingestion (Table 1). He then received a course of hemodialysis and recovered without complications. In this case, specific glycol ether serum concentrations were unavailable, especially with the various percentages present in multiple types of glycol ethers. Thus, it is impossible to determine the specific concentrations of glycol ethers in the exposure. However, it was a witnessed ingestion of a known product, there were no evidence of detectable concentrations of other nonethanol alcohols, and the patient developed symptoms and laboratory abnormalities consistent with previous reports of glycol ether ingestions in adults. Furthermore, the detectable propylene glycol level of 9 mg/dL is low and would not account for the osmolar gap (1 mmol/L) or clinical symptoms.

Case series suggest that pediatric ingestion of ethylene glycol monobutyl ether, a common glycol ether, does not commonly cause severe toxicity. The reported lack of symptoms may have been reflective of small exposures or products of varying concentrations. In addition, there was no laboratory confirmation in this series. The authors of 1 previous report described a 16-month-old girl who ingested an unknown amount of a cleaning solution containing 10% to 30% 2-butoxyethanol and developed mental status depression and a moderate metabolic acidosis (serum bicarbonate 13 mmol/L, anion gap 19) within 2 hours of ingestion. As with our patient, the rapid onset of symptoms suggests that the parent compound is responsible for the initial altered mental status. Further decline in clinical status and worsening metabolic acidosis could have been due to metabolites. Although pediatric toxicity is rare, there have been several reports of significant toxicity after intentional adult ingestions of glycol ethers by adults. They report various adverse effects, including altered mental status, metabolic acidosis, hemolysis, and renal insufficiency.

The metabolism of glycol ethers has been described in animal models, and these models suggest the metabolite is responsible for at least some of the toxic effects, such as hemolysis. It is well known that alcohol dehydrogenase inhibition prevents metabolism of methanol and ethylene glycol to toxic metabolites. The role for alcohol dehydrogenase inhibition for glycol ether ingestions remains unclear. It has been reported that patients who ingest glycol ethers have recovered uneventfully after treatment with either an ethanol infusion or fomepizole. At least 1 case report reveals progression of acidosis after fomepizole; however, the patient was hypotensive and had significantly elevated serum lactate concentrations. The authors of other reports describe patients only improving with hemodialysis. In the previously mentioned pediatric report, the patient received fomepizole soon after her ingestion, and her symptoms resolved within 2 hours of administration. Our patient had a metabolic acidosis before the administration of fomepizole, which persisted despite the fomepizole. The difference in response may be due to dose of glycol ether ingested (ie, higher volume and/or concentration), differences in

| TABLE 1 Time Frame of Significant Laboratory Values During Clinical Course |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Hours Post Ingestion     | Blood Gas                | Sodium (mmol/L)          | Chloride (mmol/L)        | Bicarbonate (mmol/L)     | Glucose (mg/dL)          | Anion Gap (mmol/L)       | Serum Osmolality (mOsm/kg) | Osmolar Gap (mg/dL) |
| 1                        | 7.35/35/115/8/8 (arterial) | 139                      | 104                      | 17                       | 86                      | 18                      | NA                       | NA                       | 0.25                     |
| 4                        | 7.11/71/116/15/14 (arterial) | 143                      | 107                      | 15                       | 87                      | 21                      | 327                      | 28                       | 0.51                     |
| 4.5                      | Intubation, Fomepizole 15 mg/kg IV × 1 |
| 8                        | 7.13/43/66/15/14 (venous)   | 149                      | 115                      | 14                       | 94                      | 20                      | 320                      | 12                       | 0.35                     |
| 8                        | Hemodialysis × 3 h         |
| 11                       | 7.44/41/119/27/2.5 (arterial) | 141                      | 107                      | 25                       | 125                     | 9                       | 286                      | −4                       | 0.19                     |

NA, not applicable.
the metabolism of 2-butoxyethanol as opposed to the other glycol ethers in the product our child ingested (prolonged metabolism), or differences in timing (ie, our patient already had an acidosis, which may have been indicative that the toxic metabolites had already been formed). However, it is also possible that fomepizole is not effective for glycol ether poisonings and that the previously published report may have been the course of poisoning after a smaller exposure. Overall, there is limited data on the use of fomepizole in pediatric patients, and although the literature suggests it is efficacious in methanol and ethylene glycol poisonings, there is no clear evidence it is effective for other alcohols. POISINDEX currently recommends fomepizole or ethanol for treatment of significant glycol ether poisoning. Because most pediatric ingestions of glycol ethers are accidental and small in amount, and do not develop clinical sequelae, very few cases will require treatment. However, our case reveals that large ingestions of glycol ethers can have rapid and severe effects. The decision to use an alcohol dehydrogenase blocker or hemodialysis should be made in conjunction with the timing of the ingestion and the significance or persistence of clinical and metabolic effects. If an alcohol dehydrogenase blocker is given, close observation for further deterioration is warranted because hemodialysis may still be indicated.

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