

Childhood Methanol Ingestion Treated With Fomepizole and Hemodialysis

Mandy J. Brown, MD; Michael W. Shannon, MD, MPH; Alan Woolf, MD, MPH; and Edward W. Boyer, MD, PhD

ABSTRACT. Fomepizole (4-methylpyrazole; Antizol) is used increasingly in the treatment of methanol toxicity in adults. Little experience exists with this drug in the pediatric population, however. We present a case of methanol poisoning in a child in whom the use of fomepizole averted intravenous ethanol infusion and the attendant side effects of this therapy. *Pediatrics* 2001;108(4). URL: <http://www.pediatrics.org/cgi/content/full/108/4/e77>; 4-methylpyrazole, fomepizole, Antizol, methanol, pediatric.

ABBREVIATION. ADH, alcohol dehydrogenase.

Methanol may produce severe morbidity and mortality if undetected or treated improperly. In 1999, more than 970 methanol exposures were reported to poison centers in the United States, with 363 exposures occurring in the pediatric population.¹ Formerly, treatment for methanol poisoning required intravenous ethanol infusion, hemodialysis, or both. Fomepizole (4-methylpyrazole, Antizol) was approved recently by the Food and Drug Administration as an antidote for methanol poisoning in adults.² In 1 case series of patients who were poisoned with methanol, fomepizole eliminated the need for ethanol therapy, although many still required hemodialysis.² Although clinical experience with fomepizole has been expanding, its use in children remains uncommon and is limited to cases of ethylene glycol toxicity.³⁻⁶ We report a case of methanol poisoning in a child who was treated with fomepizole. Fomepizole obviated the need for intravenous ethanol infusion, prevented metabolic acidosis as well as neurotoxicity, and produced no discernible adverse effects.

CASE REPORT

A 5-year-old male ingested an unknown amount of windshield washer fluid (40% solution of methanol) that was stored improperly in a sports drink bottle. He was brought to a local emergency department within 60 minutes of the ingestion. Initial vital signs were as follows: temperature, 37°C; pulse, 101 beats per minute; blood pressure, 101/59 mm Hg; respiratory rate, 22 breaths per minute. He weighed 24.5 kg. Physical examination was normal with no signs of intoxication or ophthalmologic abnormality.

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Initial laboratory evaluation revealed a normal complete blood count. Serum chemistries were as follows: sodium, 134 mEq/L; potassium, 3.7 mEq/L; chloride, 110 mEq/L; bicarbonate, 23 mEq/dL; blood urea nitrogen, 12 mg/dL; creatinine, 0.5 mg/dL; and glucose, 136 mg/dL. Anion gap was 4.7 mEq/dL. The serum osmolality was 320 mOsm/kg H₂O; the calculated serum osmolality was 284 mOsm/kg H₂O, yielding an osmolal gap of 36 mOsm/kg H₂O. Plasma aspirin, acetaminophen, and ethanol were negative. Serum methanol concentration measured by gas chromatography was 35 g/dL.

Transfer to a tertiary care center was arranged. On arrival to the referral intensive care unit, he complained of intermittent abdominal pain, was slightly confused, and was tachypneic. An arterial blood gas was as follows: pH, 7.43; Pco₂, 36 mm Hg; Po₂, 137 mm Hg. Serum bicarbonate was 20. Eight hours after the ingestion, the child received a 15 mg/kg intravenous loading dose of fomepizole. A repeat serum methanol concentration was 29 mg/dL. Fourteen hours after the ingestion, the serum methanol concentration was 28 mg/dL, so hemodialysis was started. Serum methanol concentrations are plotted against time in Fig 1.

Informed consent was obtained, and hemodialysis was performed for 4 hours. A postdialysis methanol concentration was 0 mg/dL. Fomepizole therapy was discontinued. The child was discharged the following day, with no visual abnormalities or other evidence of methanol toxicity.

DISCUSSION

Methanol is found in deicing solutions, windshield washer fluid, solvents, chafing dish heat sources, and other commercial products. Pure methanol is odorless and colorless. After ingestion, methanol is absorbed rapidly from the gastrointestinal tract. The presence of methanol in blood produces the osmolal gap.⁷ Nontoxic itself, hepatic alcohol dehydrogenase (ADH) oxidizes >95% of methanol to formaldehyde then formic acid; the remainder is eliminated via the lungs and kidneys.⁸ Acidosis is due primarily to the presence of formic acid.⁹ Because of the poor affinity of methanol for ADH, clinical manifestations of toxicity may be delayed up to 24 hours after ingestion.⁸ Serum methanol concentrations of >20 mg/dL can be expected to generate ocular injury and metabolic acidosis.¹⁰

The diagnosis of methanol poisoning is supported by a history of ingestion as well as the clinical findings of mental status alteration, metabolic acidosis, and visual disturbances.⁸ The diagnosis is established, however, by the measurement of serum methanol concentration or by an estimate of the toxin's concentration extrapolated from the osmolal gap.^{8,11} Antidotal therapy is reserved for serum methanol concentrations estimated or measured to be >20 mg/dL. In these cases, ethanol, preferably a 10% solution, is administered as a 600 mg/kg intravenous bolus followed by continuous infusion. The goal of

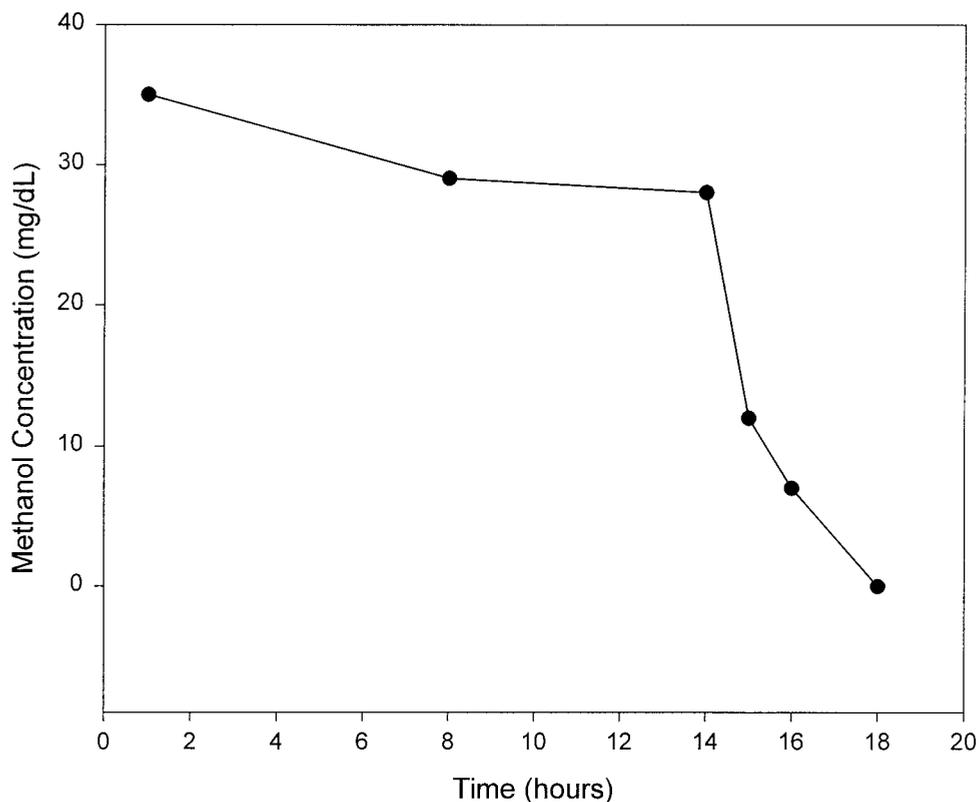


Fig 1. Methanol concentration over time.

therapy is to achieve a minimum blood ethanol concentration of 100 mg/dL; at this level, ethanol is a competitive substrate of ADH and thus prevents the metabolism of methanol. Hemodialysis, in conjunction with antidotal therapy, is indicated for patients with methanol levels of >25 mg/dL, metabolic acidosis, or stable, elevated serum methanol concentrations in the setting of fomepizole administration.^{2,10} Pediatric experience with the management of methanol intoxication is limited.¹²⁻¹⁵

Fomepizole, a competitive inhibitor of ADH, was approved recently as an antidote for methanol intoxication in adults.² Like many pharmaceuticals, fomepizole is not approved for use in children. Independent of patient age, fomepizole potentially offers a significant advantage in that it eliminates the need for intravenous ethanol therapy with its attendant problems. In children, the hyperosmolarity of an ethanol solution (1713 mOsm/L) often requires central venous access.¹⁶ Adverse effects of ethanol in young children include obtundation, hypoglycemia, and hypothermia.¹⁷ Ethanol is difficult for clinicians to use: oral absorption is erratic, and intravenous solutions are rarely stocked in hospital pharmacies.¹⁸ Maintaining a serum ethanol concentration of 100 mg/dL is a difficult task that requires frequent monitoring. An ethanol infusion itself may produce frank intoxication as a result of individual variations in metabolism and response to ethanol. In contrast, fomepizole does not cause hypoglycemia and has no sedating side effects.² Also, fomepizole is administered as an intravenous infusion every 12 hours except during hemodialysis when the interval is increased to every 4 hours. Serum fomepizole concen-

trations do not require monitoring. Consequently, fomepizole has greater ease of administration compared with ethanol and is potentially safer as well.^{2,19,20}

Methanol poisoning in the pediatric population is rare, with reports of intoxication limited to infants.^{12-15,21} Methanol intoxication in other pediatric age groups is described less frequently. Current recommendations advocate blocking ADH and enhancing elimination.^{10,12,13,15} Although peritoneal dialysis, formerly used, is no longer considered a viable treatment option, reports of hemodialysis for methanol intoxication in the pediatric population are infrequent.¹⁰

This case also demonstrates the toxicokinetics of methanol under a variety of conditions (Fig 1). In the absence of therapy, the serum concentration of methanol decreased from 35 mg/dL to 29 mg/dL over a 6-hour period, during which the patient became symptomatic. The administration of fomepizole blocked methanol metabolism, leading to stable serum methanol concentrations over an 8-hour period. Hemodialysis eliminated methanol from the serum with a single 4-hour session. Hemodialysis remains a critical intervention for patients with elevated methanol concentrations, even in the setting of fomepizole therapy. As long as ADH remains blocked, methanol is not oxidized to formic acid. With little metabolism or elimination outside of the liver, serum methanol concentrations may remain stable in the setting of fomepizole therapy. Although fomepizole prevents the formation of toxic metabolites, dialysis is still required for elimination of methanol. This feature is

distinct from ethylene glycol intoxication, where fomepizole may eliminate the need for dialysis.⁵

As pediatric experience with fomepizole grows, the drug is being shown to be safe and effective. For children, it offers the added benefits of eliminating ethanol administration with its attendant side effects. This case supports previous observations that fomepizole therapy in conjunction with hemodialysis represents a safe and effective treatment for methanol ingestion.

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