Formate Concentrations in a Case of Methanol Ingestion

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An eight-month-old infant ingested at least 3.5 g of methanol when he accidentally received 5 mL of amoxicillin suspended in 70% methanol. The serum methanol concentration 8 h later was 9.7 mmol/L (310 mg/L) and the formate concentration 23 mmol/L (1.0 g/L). At 18 h after the ingestion, total CO₂ had decreased to 6.8 mmol/L. Throughout the second day, 21–32 h after the ingestion, the methanol concentration was 2.8–3.4 mmol/L (90–110 mg/L) and that of formate was 31–33 mmol/L (1.4–1.5 g/L). On the third day, 46 h after the ingestion, methanol was not detected and the formate concentration had declined to 16 mmol/L (720 mg/L). The patient was treated with activated charcoal 7 h after the ingestion and with ethanol, administered both orally and intravenously, 21 h after the ingestion. No abnormalities of the infant’s eyes were noted upon ophthalmological examination approximately 55 h after the incident.

Methanol poisoning syndrome in humans and monkeys has been attributed to the generation of formate, a product of methanol metabolism (1–4). The two major physiological effects of formate are metabolic acidosis and optical disk edema, leading in severe cases to blindness and death (1, 5, 6). Two cases of methanol poisoning in humans have been reported in which formate concentrations were determined (1) with an enzymatic fluorescence method (3).

In this report, we present a case of methanol poisoning in which an improved enzymatic method was used in the analysis for formate (7). Formate concentrations remained at 22 to 24 times the upper limit of our adult reference interval for 21–32 h after the ingestion. However, an ophthalmological examination approximately 55 h after the ingestion revealed no optical neuropathy. Formate had declined to 11 times the upper reference limit 46 h after the ingestion.

Materials and Methods

Electrolytes were measured by use of ion-selective electrodes, in either an Astra 8 or an Astra 4 analyzer (Beckman Instruments, Inc., Brea, CA 92621).

Methanol and ethanol were measured in a gas chromatograph equipped with a hydrogen flame detector (Model 2700 Moduline; Varian Associates, Inc., Walnut Creek, CA 94598), and with a Varian Model 282 linear recorder. The column was 5% Carbowax 20M on 60/80 mesh Carbopack B (Supelco, Inc., Bellefonte, PA 16823). The 180 × 0.6 cm (o.d.) column was made of non-silanized glass. The carrier gas was nitrogen at a flow rate of 20 mL/min. Temperature conditions were: injector, 160 °C; column, 70 °C; detector, 160 °C. The internal standard for methanol and ethanol was n-propanol.

Formate was determined by an enzymatic fluorescence method (2, 3) with certain modifications (7), including the use of the patient’s serum or plasma as the blank and as the matrix for the construction of a patient-specific formate calibration curve (method of internal standard addition). Plasma was from blood collected in 7-mL tubes containing sodium fluoride-potassium oxalate as anticoagulant. The fluorometer was an Amino SPF-125 (Travenol Laboratories, Inc., Silver Spring, MD 20910). Formate dehydrogenase and β-NAD⁺ were from Sigma Chemical Company, St. Louis, MO 63176. Resazurin was from Pfaltz and Bauer, Inc., Stamford, CT 06902. All other reagents, of the highest grade available, were from commercial sources.

Our reference range for total CO₂ in this age group is 18–26 mmol/L. Analysis of 29 specimens from apparently healthy adult subjects yielded a reference range of 0.2–1.4 mmol/L (7–63 mg/L) for plasma formate (7).

Case History and Results

An eight-month-old boy was accidentally given amoxicillin suspended in methanol/water (70/30 by vol) rather than in water. He received two 5-mL oral doses, 6 h apart, but he spat out most of the second dose. When the error was discovered shortly after the second dose, he was taken to a community hospital emergency room, and was treated with activated charcoal; this was about 7 h after the first ingestion. Serum or plasma specimens were analyzed for electrolytes, methanol, and formate. Except for total CO₂, all other electrolyte concentrations were within reference limits. Figure 1 shows the changes in total CO₂, methanol, and formate concentrations with time. Total CO₂ concentration declined to 6.8 mmol/L (reference range, 18–26 mmol/L) 18 h after the first ingestion, reflecting a severe metabolic acidosis. The highest methanol concentration, 9.7 mmol/L (310 mg/L), was observed in the first specimen received for methanol determination, 8 h after the first dose.

After 21 h, the patient was started with ethanol treatment (200 mL of a 50 mL/L solution orally, followed by 24 mL/h intravenously). At this time, the methanol concentration has decreased to 3.4 mmol/L (110 mg/L) but the formate concentration was at its highest, 33 mmol/L (1.5 g/L), 24 times the upper reference limit (Figure 1).

An ophthalmological examination before the infant was discharged on the evening of the third day, approximately 55 h after ingestion of the first dose, revealed no abnormalities.

Discussion

The laboratory data in this case illustrate the following metabolic inter-relationships:

• Methanol is rapidly absorbed and metabolized to formate. Only 8 h after the first dose, the formate/methanol molar ratio was 2.4 (Figure 1), which increased to 10–12 by 21–32 h after the first dose.

• Methanol peaked before (or at) 8 h after the ingestion; formate peaked at 21–26 h, and it had an apparent half-life of approximately 20 h (Figure 1). Metabolism of formate to CO₂ is therefore the rate-limiting step in the overall metabolism of methanol.

• Molar quantities of total CO₂ and formate are in general inversely related. However, the decrease in total CO₂ concentration caused by formate acidosis is not rapid; at 7 h
Despite the increase in formate to 22–24 times the adult upper reference limit by 21–32 h after the ingestion, no abnormalities of the infant's eyes were noted at approximately 55 h. Apparently, in this case, formate concentration needs to persist longer and/or at higher concentrations before any permanent optical neuropathy ensues.

This work was supported by Associated University Pathologists Fellowship in Clinical Chemistry at the University of Utah (to S.S.) and in part by R. J. Reynolds Industries, Inc. We thank those of the staff of the Clinical Toxicology Laboratory and the Center for Human Toxicology at the University of Utah who were involved with this work. We thank Dr. K. Owen Ash for editorial assistance.

References