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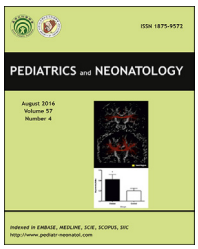

CASE REPORT

Use of Fomepizole in Pediatric Methanol Exposure: The First Case Report in Taiwan and a Literature Review

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Methanol poisoning is rare in the pediatric population, but a delay in diagnosis and intervention may cause severe morbidity and mortality. The current therapy for methanol poisoning is ethanol or fomepizole, which acts as a competitive inhibitor of hepatic alcohol dehydrogenase to inhibit the production of toxic metabolites derived from the oxidation of methanol. However, clinical experience in pediatric methanol poisoning is limited, and the safety profiles of the antidotes have not been established in children, especially in Asian populations. This is the first case to describe the use of fomepizole in a child with methanol exposure in Taiwan.

1. Introduction

Methanol is commonly used in antifreezes, solvents, and many other products. Methanol itself is not toxic, but it is oxidized by hepatic alcohol dehydrogenase to formaldehyde and then oxidized to formic acid, which is responsible

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for metabolic acidosis and retinal toxicity.[1] Even small amounts of methanol ingestion may be fatal in children without timely treatment.[2] The traditional antidote is ethanol, a competitive inhibitor of alcohol dehydrogenase, to inhibit the metabolism of methanol. Fomepizole (4-methylpyrazole), a more potent competitive inhibitor of alcohol dehydrogenase, has been recommended as a superior antidote due to higher efficacy and less adverse effects than ethanol.[1] However, clinical experience of fomepizole use in children is limited,[3] and no cases have been reported in Asian populations. Herein, we report a case of pediatric methanol exposure with successful treatment of fomepizole.

2. Case Report

A 1-year, 5-month-old boy swallowed an unknown amount of alcohol paste (content = 80% methanol), which was a type of fuel of a chafing dish. He was sent to the emergency department 50 minutes after ingestion. Initial vital signs were stable. His consciousness was alert, but his activity was mildly to moderately decreased. His body weight was 10 kg. Physical and neurological examinations were normal. A blood gas analysis was as follows: pH, 7.176; PCO_2, 49.9 mmHg; PO_2, 104.4 mmHg; and bicarbonate, 18 mmol/L. Biochemical analyses of plasma revealed the following: sodium, 138 mmol/L; potassium, 4.4 mmol/L; chloride, 108 mmol/L; lactate, 2.1 mmol/L; blood urea nitrogen, 6.7 mmol/L; creatinine, 23.0 μmol/L; and glucose, 4.8 mmol/L. Anion gap was 12 mEq/L. The measured serum osmolality was 294 mOsm/kg, and the calculated serum osmolarity was 288 mOsm/kg, yielding an osmolal gap of 6 mOsm/kg. Serum concentrations of methanol and ethanol were measured, but the data could not be obtained immediately.

Initially, we performed nasogastric irrigation and fed the patient 45 cc of Shaoxing wine (content = 17% ethanol), and then we initiated fomepizole therapy. He received a 15 mg/kg loading dose of fomepizole and was then admitted to the pediatric intensive care unit.

Five hours after the loading dose, arterial pH level was 7.354, and serum bicarbonate level was 21 mmol/L. We continued to give him a 10 mg/kg maintenance dose of fomepizole every 12 hours, and we also administrated intravenous sodium bicarbonate to correct acidemia. Measurement of arterial blood gas, electrolytes, blood urea nitrogen, creatinine, glucose, and serum methanol concentration was followed up every 6 hours. Arterial pH and serum bicarbonate levels over time are shown in Figure 1. No visual deficits were found by the ophthalmologist on the 2nd day. After treatment, vital signs were stable, and no additional acidemia was noted, thus we discontinued fomepizole. He was transferred to the general pediatric ward on the 4th day and discharged on the 5th day. We obtained the following reports on the 9th day: serum concentration of methanol <0.1 mg/dL and ethanol <5 mg/dL on arrival to the emergency department and subsequent follow-up, respectively. No signs of methanol intoxication, no visual deficits, and no adverse effects of fomepizole were found at the outpatient department on the 10th day.

3. Discussion

Methanol is absorbed rapidly by the gastrointestinal tract and reaches peak concentration within 30–60 minutes.[4] The typical signs and symptoms of methanol poisoning include visual dysfunction, nausea, vomiting, abdominal pain, and central nervous system depression, with a latent period of 12–24 hours for methanol to oxidize to toxic metabolites.[2,4] Therefore, the antidotes should be administrated as soon as possible prior to formate formation, and early treatment may prevent fatalities and the need for hemodialysis.[2,5] Serum methanol concentration is unavailable immediately; moreover, clinical symptoms, visual impairment, and mortality correlate closely to the degree of metabolic acidosis rather than to serum methanol concentrations.[4] The indications of ethanol or fomepizole therapy are listed in Table 1 according to the guidelines of the American Academy of Clinical Toxicology.[4] Here, we report the first pediatric case of methanol exposure to be treated successfully with fomepizole in Taiwan.

Interestingly, the laboratory data of our patient were not typical of those found in patients with methanol poisoning, including high anion gap metabolic acidosis with high osmolal gap. Osmolal gap is an important biomarker in methanol poisoning, but its wide normal range makes it insensitive to small concentrations of methanol.[6] The reference range of osmolal gap is from 0 mOsm/kg to

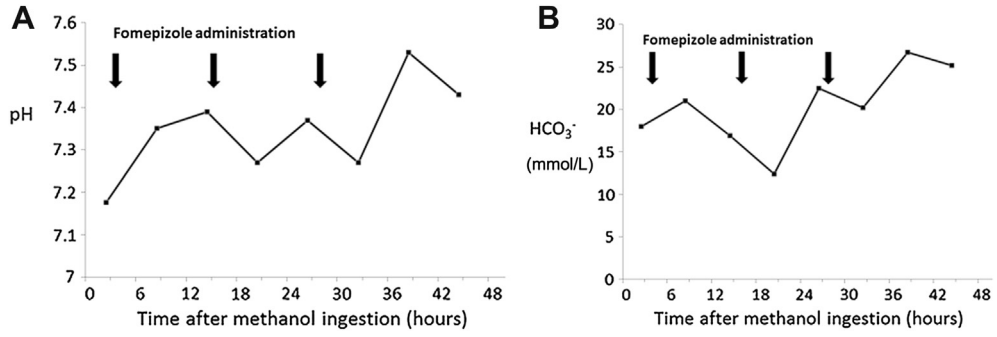

Figure 1 (A) Level of arterial pH over time after methanol ingestion. (B) Level of serum bicarbonate over time after methanol ingestion.