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Acute ethylene glycol poisoning after intentional ingestion

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Abstract

Background: We describe a case of acute ethylene glycol poisoning following ingestion of antifreeze agent in which serum ethylene glycol and anion gap were serially measured.

Patients: A 66-year old man was hospitalized after intentional ingestion of automotive antifreeze. Upon admission, vital signs, mental status, and neurological functions were normal. Initial laboratory tests revealed no serum ethanol, normal serum electrolytes, and no osmolal gap, but slightly elevated serum lactate, and a high anion gap.

Interventions: The patient was admitted to the Intensive Care Unit (ICU) 3 hours after ingestion. Intravenous infusion of 10% ethanol was started without delay and continued for 48 hours. A single course of haemodialysis was performed shortly after admission. After 3 days, the patient was discharged from the hospital on his own request.

Measurements and results: Toxicological analysis of blood was positive for ethylene glycol. Gas chromatographic measurements of serial serum specimens revealed a maximum ethylene glycol concentration of 1644 mg/l and an exponential decline with a half-life of $t_{1/2}$ = 31 hours.

Conclusion: Ethylene glycol has a slow elimination rate and a long half-life after infusion of ethanol maintaining the blood level between 1.0-1.5 ‰. The patient was dialyzed because of a metabolic acidosis and a beginning renal failure. The glycol concentration and the anion gap acidosis were effectively diminished.

1. Introduction

Ethylene glycol ingestion may cause serious poisonings due to the high toxicity. Intentional ingestion of ethylene glycol is frequently related to suicide attempts or as a substitute for ethanol. Some intoxications were reported in adults [1-6]. Additionally, unintentional poisonings may occur, particulary by children [7-9]. It is readily absorbed from the gastro-intestinal tract, and the maximum blood concentration is reached within 2-4 hours [10]. Ethylene glycol itself has a low toxicity but is metabolized by the alcohol dehydrogenase to glycoaldehyd, and further hepatic enzymes to glycolic acid, glyoxylic acid which is finally metabolized to oxalic acid. The rate limiting step in the metabolism of ethylene glycol is the conversion to glycolic acid which accumulates in the blood causing severe acidosis with a high anion gap. Oxalate is precipitated as calcium salt in the renal tubules leading to acute renal failure [11]. The onset of symptoms is usually delayed, suggesting a time lag in which ethylene glycol is converted to metabolites. Ethylene glycol toxicity generally begins with an initial stage of central nervous system (CNS) depression and coma [12, 13]. Depending on the doses and the begin of an effective treatment regimen, neurological signs are observed from 1 to 12 hours after ingestion, cardiorespiratory symptoms with elevations in heart rate and blood pressure after 12-24 hours and renal failure in the third clinical phase after 24 to 72 hours [14]. Systemic hypocalcemia due to oxalate chelation can cause arrhythmias, tetany, and seizures.

Recommended management includes basic supportive care, infusion of sodium bicarbonate to correct acidosis and inhibit precipitation of calcium oxalate. The traditional mainstay for antidotal treatment is ethanol, but there have been no prospective studies. The goal is a serum ethanol concentration between 1 to 1.5 ‰ to saturation the binding sites of alcohol dehydrogenase. Fomepizole was introduced as a safer and more effective antidote than ethanol, and

can be used in a non-critcal patient setting. Fomepizole has few adverse effects and should be preferred over ethanol. However, it is more expensive and frequently not available in time.

Persistent metabolic acidosis, elevated serum creatinine concentration, or renal failure are new indications for haemodialysis [15, 16].

We present a case of ethylene glycol ingestion to illustrate the beneficial effect of prompt therapy in a potentially lethal poisoning. The report is accompanied by the most important clinical and toxicokinetic features of the poisoning.

2. Case report

A 66-year-old man weighing 80 kg was admitted to the intensive care unit (ICU) 3 hours after intentional ingestion of approximately 100 ml of antifreeze. Apart from transient dizziness, no symptoms were reported. The patient had no relevant medical history. Upon admission, he was fully alert, without neurological deficit, physical examination including vital signs was unremarkable.

Laboratory parameters: The most striking laboratory findings are represented in Table 1. Serum osmolality, calcium, and urea were in the normal range. On admission, the ethylene glycol concentration in plasma was 1644 mg/l.

Table 1. Laboratory findings in a patient with ethylene glycol poisoning

	pH	Base deficit mmol/l	Anion gap mmol/l	Osmolar gap mosmol/kg	Serum creatinine µmol/l	Leukocyte count Gpt/l
patient	7.26	11	24	0	137	17.9
normal	7.40	0	11-18	0	55-100	5-10

Interventions: Intravenous infusion of 10% ethanol was initiated immediately, the dose was adjusted to reach a blood ethanol concentration of 1‰, and maintenance infusion was continued for 48 hours. Because of the very high plasma concentration of ethylene glycol, a single course of haemodialysis was started 2 hours later. To assure sufficient fluid intake, electrolyte solutions were infused intravenously. The patient's physical and neurological condition remained stable, acid-base-homeostasis, serum creatinine and leukocyte count returned to normal. On day 4, against medical advice, the patient demanded to be discharged immediately, and left the hospital on his own request.

3. Procedures

Reagents and analytical setup: All chemicals used were of analytical reagent grade. Ethylene glycol was purchased from Merck (Darmstadt, Germany).

In the ICU the samples of blood and urine were taken and submitted to the laboratory for toxicological analysis where they were stored at –20°C before being analysed. All samples were screened by gas chromatography/mass spectrometry (GC/MS). Quantitative analysis was done likewise by a GC method with flame ionisation detection [17]. The plasma standards were calibrated between 200 – 2500 mg/l ethylene glycol. The calibration curve was linear in this range and the limit of detection was 10 mg/l.

4. Results and discussion

The concentrations measured are represented in Figure 1. One-compartment pharmacokinetic model was used for elimination. The plasma concentration declined over the next days with a half-life of $t_{1/2}$=31 hours following a first-order kinetics.

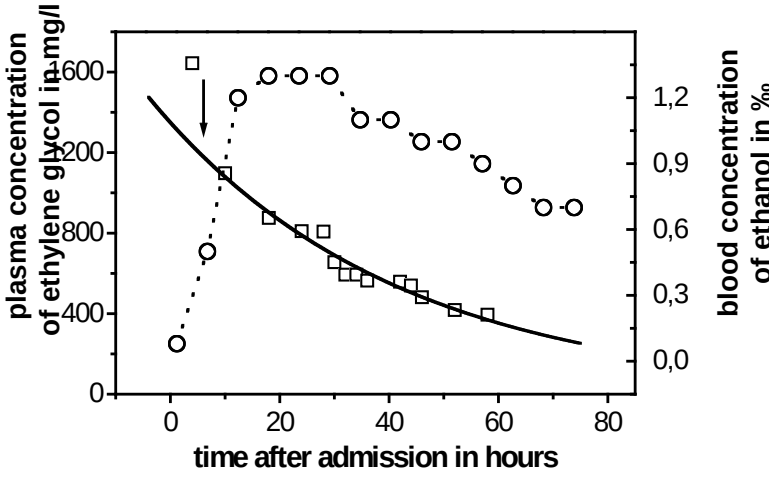

Figure 1. Course of plasma ethylene glycol concentration (□) after antifreeze poisoning and blood ethanol concentration (○) during treatment. Plasma half-life was $t_{1/2}$ = 31 hours using one-compartment model and a first order kinetic in the presence of ethanol. The duration of intravenous ethanol infusion was 48 hours. The arrow indicates the begin of a single course of haemodialysis two hours after admission which, at 60 hours, decreased the ethylene glycol concentration by 33 %.

The single course of haemodialysis decreased the ethylene glycol concentration by 33 %. The standard treatment of ethylene glycol intoxications is based on a limited number of observations and includes inhibition of alcohol dehydrogenase with ethanol or fomepizole. The META trial study group describes the toxicokinetics of ethylene glycol in poisoned patients who received fomepizole as antidote. They found the half-life to be about 19 hours in patients with normal renal function, while being significantly longer in patients with a serum creatinine concentration of 130 µmol/l or above [18, 19]. Other patients with normal serum creatinine concentration were found to have an ethylene-glycol elimination half-life of 11-18 hours during ethanol therapy [16]. In our case, initial serum creatinine was 137 µmol/l, and the elimination half-life was markedly prolonged. This confirms that elevated serum creatinine predicts slower ethylene glycol elimination.

Haemodialysis efficiently eliminates ethylene glycol and its toxic metabolites, and reduces the acid-base disturbance. Haemodialysis is typically recommended in cases of severe metabolic acidosis with arterial pH < 7.25, serum creatinine concentration > 265 µmol/l and the onset of acute renal failure or deteriorating vital signs [20]. Serum ethylene glycol concentrations above 35 mgl/l have been considered a symptom-independent indication for haemodialysis, although some controversies still remain [21].

5. Conclusion

In cases of alcohol poisoning, ethanol or fomepizole are effective inhibitors of alcohol dehydrogenase and, if applied without delay, would prevent generation of toxic metabolites. Haemodialysis effectively eliminates ethylene glycol and is recommened for cases with very high ethylene glycol plasma concentrations or incipient renal failure, or for severe metabolic acidosis.

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