

Rapid diagnosis of ethylene glycol poisoning by urine microscopy

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Rapid Diagnosis of Ethylene Glycol Poisoning by Urine Microscopy

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Male, 57
Final Diagnosis: Ethylene glycol poisoning
Symptoms: Unconsciousness and high anion gap
Medication: Bicarbonate • electrolyte correction • intravenous ethyl alcohol infusion • hemodialysis
Clinical Procedure: icrosopy of calcium oxalate monohydrate crystals
Specialty: Nephrology • Intensive Care Unit • Biochemistry and Immunology

Objective: Challenging differential diagnosis

Background: Ethylene glycol poisoning remains an important presentation to Emergency Departments. Quick diagnosis and treatment are essential to prevent renal failure and life-threatening complications.

Case Report: In this case report, we present a patient who was admitted unconscious to the hospital. Ethylene glycol poisoning was immediately suspected, because the patient had previously been hospitalized with similar symptoms after intake of antifreeze coolant.

A urine sample was sent for microscopy and showed multiple calcium oxalate monohydrate (COM) crystals, which supported the clinical suspicion of ethylene glycol poisoning. The patient was treated with continuous intravenous ethyl alcohol infusion and hemodialysis. Two days after admission, the patient was awake and in clinical recovery.

Conclusions: Demonstration of COM crystals using microscopy of a urine sample adds valuable information supporting the clinical suspicion of ethylene glycol poisoning, and may serve as an easy, quick, and cheap method that can be performed in any emergency setting.

MeSH Keywords: Acute Kidney Injury • Calcium Oxalate • Ethylene Glycol • Poisoning

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/908569>

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Background

Ethylene glycol is a common ingredient in many household products such as household cleaners, cosmetics, and antifreeze coolant [1, 2]. In the United States there are nearly 6000 yearly cases of ethylene glycol poisoning reported to poison control centers, with most cases of accidental poisoning occurring in children [3, 4]. Ethylene glycol poisoning is associated with risk of severe morbidity and it continues to occur in many countries around the world [3]. Several deaths have been described occurring 11–18 h after intake of ethylene glycol [2], and early diagnosis and treatment are therefore essential.

Ethylene glycol is metabolized in the liver by alcohol dehydrogenase to glycol aldehyde and then oxidized to glycolic acid, which is then metabolized to glyoxylic acid and finally to oxalic acid. Oxalic acid binds with calcium to form calcium oxalate monohydrate (COM) crystals, which may deposit and cause tissue damage, especially in the kidneys [5].

When COM crystals accumulate in renal tubules, they can lead to cell necrosis and serious renal failure [6]. The treatment for ethylene glycol poisoning is often commenced based on clinical suspicion because diagnostic testing, such as measuring the ethylene glycol concentration in blood, is not available in emergency settings [3,7]. The suspicion of ethylene glycol poisoning is often supported by indirect findings in blood samples, such as an increased serum osmolal gap and severe unexplained anion gap metabolic acidosis [1].

Guidelines recommended quickly testing for ethylene glycol poisoning within 4 h and initiation of treatment within 6 h after intoxication, which is a challenge in clinical settings [4]. Ideally, the validated biochemical diagnostics test would be preferred to measuring the ethylene glycol concentration in blood, but such a method is not available in most hospitals [3,7]. A feasible and quick diagnostic approach is therefore needed in most Emergency Departments.

Case Report

A 57-year-old man was brought unconscious to our Emergency Department.

The patient was known to abuse alcohol and to have alcohol dementia and arterial hypertension. Earlier that day, he was described by relatives as fully conscious but became increasingly confused before becoming unresponsive for no known reason. Noteworthy, the patient was previously hospitalized with a similar picture after intake of antifreeze coolant, and at that time, ethylene glycol poisoning was suspected and later confirmed by the patient.

On arrival, the patient had Glasgow coma scale 3/15; he was cyanotic and hypothermic (temperature 34.7°C), had Kussmaul breathing with frequency 28 breaths per min, blood pressure was 150/90 mmHg, and heart rate was fluctuating at 75–150 beats per min. ECG showed atrial fibrillation with frequency of 92 beats per min, and no other ECG abnormalities were described. The neurological examination revealed rigid limbs, and pupils with absent light reflex.

Computed tomography of the cerebrum and chest X-ray was performed and findings were unremarkable. Initial laboratory tests (Table 1) showed hyperkalemia (K^+ =5.1 mmol/L), high anion gap (anion gap 34.7mEq/L) and elevated lactic acid (lactic acid >30 mmol/L). An arterial blood gas test suggested high anion gap metabolic acidosis (pH 7.07, HCO_3^- 6.4 mmol/L).

Bladder catheterization showed clear urine and urine drug screening was positive for benzodiazepines. The patient was immediately intubated and transmitted to the Intensive Care Unit (ICU). Treatment with bicarbonate and electrolyte correction was initiated, and, due to the suspicion of ethylene glycol poisoning, the patient received continuously intravenous ethyl alcohol infusion [7,8]. Due to the high level of lactic acid, the suspicion of sepsis could not be ruled out and treatment with intravenous antibiotics (Meropenem and Metronidazole) was initiated. Within 6 h after arrival, the first signs of renal failure were observed by increasing creatinine values from 90 to 138 μ mol/L, decreasing urine production, and hyperkalemia. Furthermore, a worsening of acidosis (pH 6.90) and increased anion gap (35.5 mEq/L) was observed, and hemodialysis was therefore initiated. The patient developed hypotension and increased heart rate, which were treated according the local guidelines in the ICU. A new urine sample was sent for examination of urine sediment by means of light microscopy and showed multiple COM crystals, supporting the diagnosis of ethylene glycol poisoning. The morphologic features of the COM crystals are presented in Figure 1 and are indicated by arrows.

Two days after admission, the patient was in clinical recovery. The patient was extubated, hemodialysis and ethyl alcohol infusion were discontinued, and the patient had regained acceptable urine production under furosemide stimulation. Blood analyses showed normalized creatinine and calcium, the acidosis was corrected, lactate was decreasing, and the patient was transferred from the ICU to the medical ward. The patient was later discharged to home in stable condition.

Discussion

Ethylene glycol poisoning remains an important presentation in Emergency Departments; quick diagnosis and treatment are necessary to prevent serious harm [9,10]. The limited access to

Table 1. Patient's blood test, blood gas, and drug test at arrival in the Emergency Department.

Blood test at arrival		Normal range
WBC	15.6	4.00–10.80×10 ⁹ /L
Hemoglobin	9.5	8.0–11 mmol/L
Creatinine	90	60–105 μmol/L
Urea	4.0	3.5–8.1 mmol/L
Na	140	137–145 mmol/L
K ⁺	5.1	3.5–4.4 mmol/L
Cl ⁻	104	98–07 mEq/L
Calcium	2.67	2.15–2.51 mmol/L
Glucose	6.1	6.0–8.0 nmol/L
CRP	0.7	<6 mg/L
Ethanol	<3	0/00 mmol/L
Anion gap ([Na ⁺] + [K ⁺]) – ([Cl ⁻] + [HCO ⁻ 3])	34.7	7–15 mEq/L
Calculated osmolarity 2×[Na ⁺] + [Glucose] + [Urea]=	290.1	278–305 mOsm/kg
Blood gas investigation		Normal range
pH	7.07	7.35–7.45
pCO ₂	1.02	4.7–6.4 kPa
pO ₂	19.4	11.1–14.4 kPa
HCO ₃ ⁻	6.4	22.0–26.0 mmol/L
Base excess	–29	–2.0–2.0 mmol/L
Lactic acid	>30	0.3–2.0 mmol/L
Urine toxicology screen		
Benzodiazepines	Positive	
Amphetamines	Negative	
Methamphetamines	Negative	
Barbiturates	Negative	
Marijuana	Negative	
Cocaine	Negative	
Phencyclidine (PCP)	Negative	
Methadone	Negative	
Opioids	Negative	

directly diagnostic method often leaves clinicians with undiagnosed patients; the several differential diagnoses may challenge the clinicians to initiate relevant treatment and presents the dilemma of whether to treat on a presumptive basis. Several quantitative tests for the diagnosis are described in the literature, but they all have limitations. Mc Quade et al. describes gas chromatography as the criterion standard for measuring ethylene glycol in blood, but this is a specialized technique only offered by some centralized laboratories and only available in a few hospitals [3]. Furthermore, the value of this test to guide acute diagnostics is limited because obtaining the results often

takes 24–48 h. Sankaralingam et al. presented an enzymatic spectrophotometric assay for measuring ethylene glycol, but this method is not available in most hospitals [4]. As indirect tests, osmolar gap, anion gap, lactic acidosis, and hypocalcemia are used, but these analyses can only support the clinical suspicion of ethylene glycol poisoning, and none of these can serve as a definitive diagnostic test [1,11]. Microscopic visualization of COM crystals in the urine is not definitive, but it adds valuable information to support the diagnosis and thus facilitates early targeted treatment.



Figure 1. Microscopic demonstration of calcium oxalate monohydrate crystals in a urine sample.

In our case, ethylene glycol poisoning was immediately suspected because the patient had a history of ethylene glycol poisoning, and the initial diagnostic tests supported this by showing an increased serum osmolal gap and a high anion gap metabolic acidosis. The patient was treated with intravenous ethyl alcohol infusion and antibiotics as sepsis was the primary condition or as a concomitant complication that could not be ruled out.

Retrospectively, the high lactic acid could be explained by the use of an ABL analyzer (ABL800 FLEX gas analyzer, Radiometer®, Denmark), which cannot always differentiate between lactate and glycolate (an ethylene glycol metabolite) [12–14].

The clinical presentation of ethylene glycol intoxication is described by 3 phases initiated by neurological findings involving slurred speech, somnolence and coma, followed by an increased anion gap metabolic acidosis. Afterwards cardiopulmonary findings as Kussmaul's respiratory, tachycardia, and hypertension followed by hypotension and progressive renal injury [3]. In the literature, case reports describe similar subjects as ours, with unresponsive condition and metabolic acidosis [10,15]. At onset of these symptoms, the patient might already be critically affected and successful treatment may be problematic. We could not measure ethylene glycol blood concentration because no hospital laboratories in Denmark provide this test on a routine basis, and if transported to laboratories in either Sweden or Germany, the response time would be at least 24 to 36 h, providing no value in relation to guidance of rapid diagnosis.

To support the diagnosis of ethylene glycol poisoning, we demonstrated the presence of multiple COM crystals using urine microscopy. However, this was unfortunately first done 5 h after the admission when the first signs of kidney failure were evident. If the urine microscopy had been performed at admission, it could have added valuable information to support the diagnosis and thus facilitate earlier targeted treatment with hemodialysis. One must bear in mind, however, that microscopic identification of COM crystals in urine only serves as a tool supporting the diagnosis of ethylene glycol poisoning, as there are sources of error. Thus, COM crystals may be mistaken for hippuric acid crystals, and COM crystals might also be found naturally in some plant tissues, potentially causing false-positive results [3].

In our case, we demonstrated that the use of urine microscopy is a quick and easy investigation that may add valuable information to support the diagnosis of ethylene glycol poisoning. It is available in most hospitals and can be useful in such cases. More frequent and timely correct use of this method could add important information to support the diagnosis of ethylene glycol poisoning and thus allow early initiation of treatment.

Because demonstration of COM crystals using urine microscopy can aid in the diagnosis of ethylene glycol poisoning, we will advocate for a more widespread use of this feasible, quick, and cheap method in clinical settings.

Conclusions

Microscopy of the urine to visualize COM crystals is a simple, quick, cheap, and easy method that adds valuable information to support the diagnosis of ethylene glycol poisoning, thus facilitating early initiation of the correct treatment.

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Conflict of interest

None.

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