

CONCOMITANT INGESTION OF ETHYLENE GLYCOL AND ETHANOL: A DIAGNOSIS TRAP?

Otilia-Elena Frasinariu^{1,2}, Aniela Rugina^{1,2}, Cristina Jitareanu², Radu Russu², Nicolai Nistor^{1,2}, Violeta Streanga^{1,2}

¹Pediatric Department, "Gr. T. Popa" University of Medicine and Pharmacy, Iasi

²"Sf. Maria" Emergency Clinical Hospital for Children, Iasi

ABSTRACT

Ethylene glycol is one of the most toxic alcohols; it may be accidentally or intentionally consumed as a substitute for ethanol or related to suicidal attempts. Ingestion of ethylene glycol causes a severe metabolic acidosis with increased anion and osmotic gap due to its toxic metabolites, leading to a clinical picture of central nervous system depression, cardiovascular and renal impairment. A 16-year-old boy was admitted with clinical and biological signs of ethylene glycol poisoning after simultaneous ingestion of antifreeze and ethanol. The patient had mild anion gap metabolic acidosis only at the debut, rapidly corrected with one dose of sodium bicarbonate; further evaluation did not reveal acidosis, even if the subsequent evolution included acute renal failure requiring hemodialysis. Due to the absence of a positive history and of a persistent metabolic acidosis, the diagnosis of ethylene glycol poisoning was delayed until it was confirmed by serum toxicological test. Conclusions: concomitant ingestion of ethanol may mask the symptoms of ethylene glycol poisoning; the absence of persistent metabolic acidosis does not rule out the diagnosis.

Keywords: ethylene glycol, metabolic acidosis, acute renal failure, hemodialysis, poisoning

INTRODUCTION

Ethylene glycol (EG) is a toxic, colorless, odorless alcohol, found in antifreeze, brake fluid and as a stabilizer in foam agents and solvents. Due to its sweetness, children are tempted to consume it in large quantities, leading to accidental poisoning (1).

Ethylene glycol is mostly metabolized by hepatic alcohol dehydrogenase (ADH). The main toxic metabolites are glycolic acid, contributing to a significant acidosis, and oxalic acid that binds to calcium, leading to calcium oxalate crystals formation. Deposition of crystals in various organs explains multisystem damage. The precipitation of calcium oxalate in kidney may result in tubular epithelial necrosis, associated with decreased glomerular filtration and renal failure (2).

CASE REPORT

We present the case of a 16-year-old teenager admitted in a tertiary hospital for headache, abdominal pain and vomiting. Symptoms started 48 hours before admission, after ingestion of approximately

1500 ml of wine and beer. His first medical examination revealed: confusion and balance disorders. Biological tests showed significant metabolic acidosis (bicarbonate level = 10 mEq/l), with increased anion gap (22), azotemia (urea = 0.78 g/l, creatinine = 1.8 mg/dl), oliguria with microscopic hematuria and negative result of breathalyzer test. Sodium bicarbonate and intravenous fluids were given. Six hours later, increasing levels of blood urea and creatinine and severe oliguria required the transfer to Acute Care Unit at our hospital.

On admission, the patient was in a severe general condition, presenting confusion with short periods of hallucinations, abdominal pain, diarrhea, oliguria (0.17 ml/kg/h) and hematuria. The biological exams highlighted neutrophilic leukocytosis, azotemia (blood urea = 56 mg/dl, creatinine = 3.54 mg/dl), increased uric acid levels (8.8 mg/dl), pH=7.33, sodium bicarbonate 18.8 mmol/l with pseudonormal anion gap (18) and mild hyponatremia (Na^{2+} = 133 mEq/l). The osmolar gap could not be calculated because we could not measure osmolality. Urinalysis revealed hematuria, proteinuria, leucocyturia, fre-

Corresponding author:

Violeta Streanga, "Gr. T. Popa" University of Medicine and Pharmacy, 16 Universitatii Street, Iasi, Romania

E-mail: streangavioleta@yahoo.com

quent calcium oxalate crystals and negative toxicological test. The diagnosis was acute renal failure due to septic or toxic interstitial nephritis; treatment started with sodium bicarbonate and antibiotics. The patient's family denied EG ingestion.

One day after admission, the patient was still confused, creatinine level increased (up to 6.49 mg/dl), oliguria became severe, with creatinine clearance = 20.49 ml/min/1.73m², and blood pressure raised (up to 165/95 mmHg), so hemodialysis was started. 48 hours later, the serum toxicological test result confirmed EG poisoning. When the patient became conscious and cooperative, he told us he had bought antifreeze, which was afterwards poured into wine by his friends.

Seven hemodialysis sessions were conducted, associated with antibiotics, antihypertensive medication, supportive treatment, leading to favorable outcome: the renal function and blood pressure normalized (Fig.1). The patient was discharged after 14 days in good general condition, with minimum hematuria and proteinuria. One month later, biological picture was normal.

DISCUSSIONS

EG poisoning occurs most often in children through the ingestion of antifreeze. EG is rapidly absorbed in the gastrointestinal tract, with a plasmatic peak within 1-4 hours. Lethal dose is 1 to 1.4 ml/kg of pure ethylene glycol. Serum levels of ethylene glycol > 20 mg/dl were associated with 98% mortality in untreated patients (3).

Usually, the clinical picture of ethylene glycol poisoning comprises of three stages. During the first 12 hours after ingestion, patients present confusion, hallucinations, euphoria, seizures, central nervous system depression and general signs of intoxication such as: nausea, vomiting, diarrhea. In the following 12-24 hours, cardiovascular and respiratory signs are noticed: dyspnea, tachycardia, cyanosis, hypertension, arrhythmia, due to accumulation of organic acids through ethylene glycol metabolism. The final stage, which occurs after 24-48 hours, is characterized by oliguria, acute tubular necrosis, hematuria, proteinuria and acute renal failure (4). Severe cases of poisoning can present delayed neurological deficits (1-2 weeks), such as

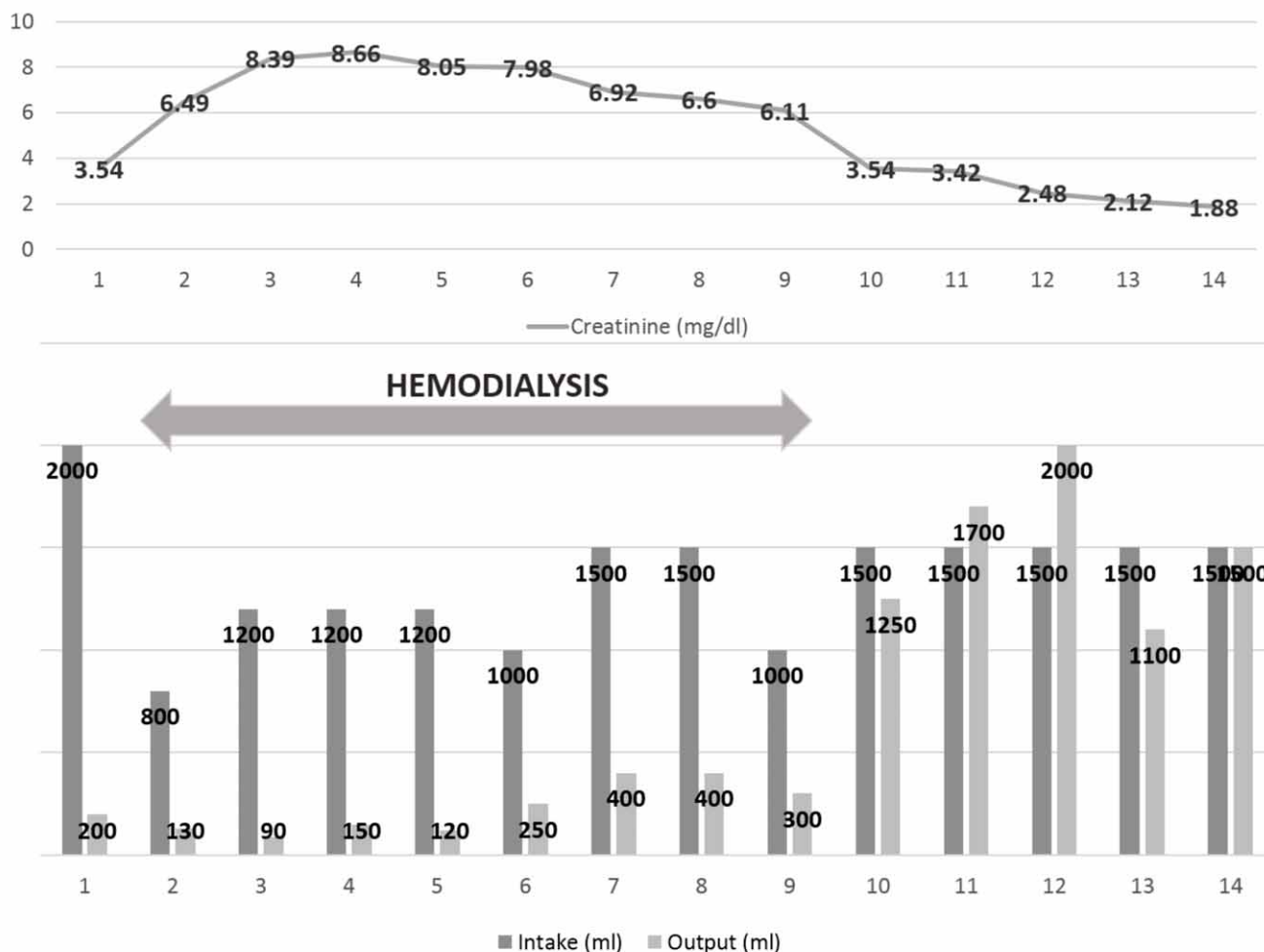


FIGURE 1. Dynamic changes of intake, urine output and serum creatinine

cranial nerve neuropathy, facial paralysis, loss of motor acquisitions, visual impairment. However, in the long run, late onset of renal or neurological impairment was not recorded (5).

The diagnosis can sometimes be difficult in the absence of a positive anamnesis. Many of the signs and symptoms of ethylene glycol poisoning are nonspecific and common to other intoxications. The diagnosis is established by toxicological test results. Measuring the blood EG concentration by chromatographic method is laborious and often inaccessible in many hospitals (6). The presence of severe acidosis with a large osmolar gap and/or increased anion gap supports a diagnosis of EG poisoning (7). Urinalysis may reveal the presence of calcium oxalate crystals, although these may not be present until the late stages (2). Severe poisoning and death have been reported in clinical trials in the absence of calcium oxalate crystals and anionic gap. Other metabolic abnormalities that may be present are hypocalcemia and hyperkalemia.

Treatment of ethylene glycol poisoning include general supportive care (correction of acid-base and electrolyte disturbances, intravenous fluids, providing ventilatory support), use of antidotes and hemodialysis (8). Due to rapid absorption in the digestive tract, gastric decontamination efficacy is limited. Sodium bicarbonate is recommended to correct metabolic acidosis. The antidotes for ethylene glycol poisoning are represented by inhibitors of alcohol dehydrogenase: ethanol or fomepizole. Ethanol is a competitive substrate for alcohol dehydrogenase and fomepizole is an enzyme inhibitor (9). Early administration of antidote may prevent kidney failure, being most effective before the formation of significant toxic metabolites. Hemodialysis is considered a key element in severe ethylene glycol poisoning. Hemodialysis removes ethylene glycol and its toxic metabolites, corrects anion gap, and reduces the antidote administration period and the length of hospitalization (8).

Treatment of EG poisoning should be initiated from the first suspicion, to avoid severe complications. In the long run, the renal prognosis is correlated with tubulointerstitial damage caused by nephrocalcinosis (2), in some cases requiring chronic dialysis or kidney transplantation.

In the case we presented, the absence of persistent metabolic acidosis and anion gap had delayed the diagnosis until it was confirmed by toxicological test. The concomitant ingestion of ethanol had increased the half-life of EG, due to its role as competitive substrate for ADH, whose affinity for ethanol is greater than for EG; thus, the metabolism of EG and the accumulation of toxic organic acids were delayed, explaining the lack of metabolic acidosis.

Similar cases were described by the medical literature, caused by concurrent ingestion of EG and ethanol (10, 11), EG and methanol (12), suggesting that the lack of metabolic acidosis and anion gap does not exclude the diagnosis of EG poisoning.

Because the patient had altered consciousness and no positive history was available to us, oral administration of antidote was delayed; however, no intravenous administration of antidote (ethanol or fomepizole) was available in our hospital. Despite the rapid deterioration following admission, the evolution was still favorable, due to hemodialysis, which improved renal function and corrected metabolic imbalances.

CONCLUSIONS

The absence of persistent metabolic acidosis does not rule out the diagnosis of EG poisoning. Concomitant intake of alcohol might act as a diagnostic trap. A previously healthy patient admitted with acute neurological and renal dysfunction should be investigated for EG poisoning, even if there is no history of ingestion and no metabolic acidosis. Hemodialysis is highly efficient in treatment of severe poisoning with ethylene glycol.

REFERENCES

1. Fujita T., Nakamura N., Hitomi H., Okumura K. Risk of sweet 'ethylene glycol' consumption. *Intern Med.* 2013; 52(3):409.
2. Monet C., Richard E., Missonnier S., Rebouissoux L., Llanas B., Harambat J. Secondary hyperoxaluria and nephrocalcinosis due to ethylene glycol poisoning. *Arch Pediatr.* 2013; 20(8):863-866.
3. Cox R.D., Phillips W.J. Ethylene glycol toxicity. *Mil Med* 2004; 169: 660-663.
4. Warrell D., Cox T.M., Firth J.D., Benz E.J. Oxford Textbook of Medicine, Oxford University Press, 2004.
5. Ting S.M., Ching I., Nair H., Langman G., Suresh V., Temple R.M. Early and late presentations of ethylene glycol poisoning. *Am J Kidney Dis.* 2009; 53(6):1091-1097.
6. Velez L.I., Gracia R., Neerman M.F. Ethylene glycol poisoning: current diagnostic and management issues. *J Emerg Nurs* 2007; 33: 342-345.
7. Glaser D.S. Utility of the serum osmol gap in the diagnosis of methanol or ethylene glycol ingestion. *Ann Emerg Med.* 1996; 27(3):343-346.
8. Barceloux D.G., Krenzelok E.P., Olson K., Watson W. American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Ethylene Glycol poisoning. Ad hoc Committee. *J Toxicol Clin Toxicol.* 1999; 37:538-542.
9. Rietjens S.J., de Lange D.W., Meulenbelt J. Ethylene glycol or methanol intoxication: which antidote should be used, fomepizole or ethanol? *Neth J Med.* 2014; 72(2):73-79.
10. Head J.M. Ethylene glycol ingestion masked by concomitant ethanol intoxication. *BMJ Case Rep.* 2012; 2012: doi: 10.1136/bcr.12.2011.5326
11. Krenová M., Pelclová D. Course of intoxications due to concurrent ethylene glycol and ethanol ingestion. *Przegl Lek.* 2005; 62(6):508-10.
12. Haviv Y.S., Rubinger D., Zamir E., Safadi R. Pseudo-normal osmolal and anion gaps following simultaneous ethanol and methanol ingestion. *Am J Nephrol.* 1998; 18(5):436-8.