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Delayed fomepizole initiation after massive ethylene glycol ingestion: a case report of survival with dialysis support

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Abstract. *Ethylene glycol poisoning is a rare but life-threatening intoxication. Early diagnosis is often difficult, as the initial presentation resembles ethanol intoxication, while later stages are characterized by severe high–anion gap metabolic acidosis. Diagnostic challenges are compounded by the fact that glycolic acid, a toxic metabolite of ethylene glycol, may be falsely detected as lactate by blood gas analyzers.*

We report a 25-year-old man who ingested 500 mL of automobile antifreeze along with 10 fluoxetine tablets in a suicide attempt. He presented with dizziness, abdominal pain, agitation, and rapidly progressed to coma (Glasgow Coma Scale score 6). Laboratory tests showed severe metabolic acidosis (pH 7.09, HCO_3^- 3.2 mEq/L, anion gap 22.5 mEq/L), osmotic gap 83 mOsm/L, hyperlactatemia, hyperglycemia, mild hypocalcemia, and urinary calcium oxalate crystals. Immediate management included intravenous bicarbonate and calcium gluconate. Continuous hemofiltration was started shortly after admission to the intensive care unit, followed by conventional hemodialysis the next day. Since fomepizole was not available, ethanol was administered via nasogastric tube as an alternative antidote until fomepizole could be procured more than 20 hours after admission. Despite delayed antidotal therapy, the patient's metabolic status improved and he was extubated on day 5. However, he developed acute kidney injury with persistent anuria, requiring ongoing dialysis. On day 8, he was transferred to his home country for continuation of renal replacement therapy.

This case demonstrates the importance of early recognition of ethylene glycol poisoning through the combined assessment of anion and osmotic gaps. When fomepizole is not immediately available, ethanol remains a reliable substitute to delay toxic metabolism. Prompt initiation of supportive therapy and dialysis is crucial for survival, even in cases with delayed presentation and massive ingestion.

Keywords: *ethylene glycol, poisoning, acute kidney injury, anion gap, antidote therapy.*

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Відстрочене введення фомепізолу після масивного вживання етиленгліколю: випадок виживання за умови діалізної підтримки

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Резюме. Отруєння етиленгліколем є рідкісним, але загрозливим для життя станом. Рання діагностика часто утруднена, оскільки початкова клінічна картина подібна до інтоксикації етанолом, тоді як на пізніших стадіях розвивається тяжкий метаболічний ацидоз з високим аніонним розривом. Додаткові труднощі діагностики зумовлені тим, що гліколева кислота, токсичний метаболіт етиленгліколю, може хибно визначатися газоаналізаторами як лактат.

Ця робота описує клінічний випадок 25-річного чоловіка, який із суїцидальною метою прийняв 500 мл автомобільного антифризу разом з 10 таблетками флуоксетину. Пацієнт поступив зі скаргами на запаморочення, абдомінальний біль, збудження і швидко перейшов у кому (6 балів за шкалою Глазго). Лабораторні дослідження виявили тяжкий метаболічний ацидоз (pH 7,09; HCO_3^- 3,2 ммоль/л; аніонний розрив 22,5 ммоль/л), осмотичний розрив 83 мОсм/л, гіперлактатемію, гіперглікемію, легку гіпокальціємію та кристали оксалату кальцію в сечі. Невідкладна терапія включала внутрішньовенне введення бікарбонату натрію та глюконату кальцію. Після госпіталізації до відділення інтенсивної терапії було розпочато безперервну гемодіафільтрацію, а наступного дня проведено конвенційний гемодіаліз. Оскільки фомепізол був недоступний, через назогастральний зонд вводився етанол як альтернативний антидот до моменту отримання фомепізолу, що відбулося більш ніж через 20 годин після госпіталізації. Попри затримку специфічної терапії, відзначалося метаболічне покращення, і на 5-ту добу пацієнта екстубували. Проте розвинулося гостре пошкодження нирок із стійкою анурією, що потребувало подальшого діалізу. На 8-му добу пацієнта транспортували до його рідної країни для продовження ниркової замісної терапії.

Цей випадок підкреслює важливість ранньої діагностики отруєння етиленгліколем шляхом поєднаної оцінки аніонного та осмотичного розривів. У разі відсутності фомепізолу, етанол залишається надійною альтернативою для уповільнення токсичного метаболізму. Своєчасний початок діалізу та терапії супроводу має вирішальне значення для виживання навіть у разі масивного отруєння та відстроченому зверненні.

Ключові слова: етиленгліколь, отруєння, гостре ураження нирок, аніонний розрив, антидотна терапія.

Introduction. Ethylene glycol poisoning, despite being quite common in the USA (more common than methanol) [1], is not particularly well known in our country, since this is the first case of this poisoning, which was even accompanied by acute kidney injury (AKI). This is obvious since in our country, alcoholic beverages are cheap and freely available, so there is easy access to everyone. It is a special poisoning, which if not suspected by the doctor can be fatal for the patient. This is because initially, the poison, while increasing the osmotic gap, the symptoms it causes are to those of intoxication by ethyl alcohol, while then, after its metabolism, severe metabolic acidosis with an increased anion gap is observed. Another peculiarity, which complicates the problem, is that the determination of lactate in blood gas machines measures glycolic acid (a metabolite of ethylene glycol) as lactate, which incorrectly establishes the diagnosis of lactic acidosis. All of this delays the diagnosis, so that time is given for ethylene glycol to be metabolized and its metabolites to now exert their toxic effects. Therapeutically, the administration of antidotes, such as ethyl alcohol or fomepizole (they have a greater affinity for alcohol dehydrogenase and therefore do not allow the metabolism of ethylene glycol), and the application of hemodialysis (but also hemofiltration) are the measures applied to treat these patients. This is probably the first patient in the Greek literature with ethylene glycol poisoning who developed AKI.

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Case description. A 25-year-old man was admitted to the emergency department (ED) with dizziness, abdominal discomfort and pain, agitation and gait disturbances. On admission, his arterial pressure was 130/90 mmHg, arterial pulses 88/min, and he had 20 breaths/min with SpO_2 99%. He denied taking anything prohibited (drink or drug), despite being repeatedly and persistently asked. Intravenous fluids were administered (0.9% NaCl solution), a dimenhydrinate tablet for his dizziness, and a 2.5 mg diazepam tablet because he continued to be agitated. After 45 minutes, he expressed a desire to leave the hospital, being agitated, aggressive, and extremely nervous. A psychiatrist was called and administered 0.5 ml of haloperidol

(100 mg/ml) and 2.5 mg of biperidine intravenously (5 mg). At that time, he confessed to his relative that he had taken auto antifreeze for suicidal purposes.

Later (at 09:00), he was in a semi-comatose state, with an inability to react to intense painful stimuli. He had intense bilateral miosis in both pupils; the pupils did not react to light, and his tendon reflexes were abolished. He was administered 1 amp of flumazenil (0.5 mg/5 ml), and initially, he seemed to recover. However, despite its re-administration, he did not recover from his comatose state. Clinically, he had intense tachypnea, so blood gases were taken. Severe metabolic acidosis was detected (pH 7.09, O_3^- 3.2 mEq/L, $PaCO_2$ 9.9 mmHg, PaO_2 147.6 mmHg), with an increased anion gap (22.5 mEq/L), hyperkalemia (K^+ 7.4 mEq/L), and hyperchloremia (CI^- 113 mEq/L), at which time a nephrologist of our clinic was called. It was suspected that he had taken ethylene glycol (because he had an osmotic gap of 83 mOsm/L), at which time he confessed that he had indeed taken the antifreeze with the intention of committing suicide. Objectively, the patient did not initially have an alcoholic breath. However, after 12:00 o'clock on the same day, he developed such breath. From the rest of history, the patient was a known psychiatric case.

After about an hour, a blood sample was taken again for gases and lactate determination (since the acidosis was of an increased anion gap), where it was increased (>15 mmol/L), while hyperglycemia (glucose 242 mg/dl in gases and 157 gm/dl in serum) and hyperlactatemia were detected. In this second gas sample, the patient's condition worsened (pH 6.93, HCO_3^- undetermined, $PaCO_2$ <5 mmHg, PaO_2 146 mmHg). A Foley catheter was placed in his bladder, and 1400 ml of urine, yellow cabbage in color (they gave the feeling that they were phosphorescent), was immediately released.

Another characteristic of ethylene glycol poisoning is the rhabdomyolysis it causes, which was detected in this patient from his first blood tests. The remaining serum tests of the patient from his admission to his discharge are shown in Table 1.

Table 1

Hematological and biochemical results of the patient

Day	1st	2nd	3rd	4th	7th	10th
Hb (gr/dl)	15.1	11	9.1	9.1	10.5	10.8
Ht (%)	45.9	32.3	27	24.6	30.2	32.1
Glucose (mg/dl)	101	100	86	84	93	75
Urea (mg/dl)	19	25	44	90	94	129
Creatinine (mg/dl)	1.6	2.5	4.7	5,5	7	5.7
Sodium (mEq/L)	151	141	147	139	141	136
Potassium (mEq/L)	4.5	3.2	3.2	4.1	3.4	4.0
Calcium (mg/dl)	7.8	7.1	6.7	8.7	8.5	8.9
Phosphate (mg/dl)	2.0	3.8	2.8	3.2	4.5	4.6
SGOT (IU/L)	36	50	43	49	67	35
SGPT (IU/L)	26	26	26	12	41	10
CPK (IU/L)	941	857	606	2233	1159	124
LDH (IU/L)	256	277	227	456	616	395
Alk. Phosphate (IU/L)	72	58	54	77	79	80
Proteins (gr/L)	6.5	5.1	5.0	5.1	6.8	6.4
Albumin (gr/L)	3.6	3.2	3.2	3.7	4.0	4.0
CRP (mg/L)	0.1	6.3	7.3	6.9	7.8	4.3
Magnesium (mg/dl)		1.7	1.9			

Abbreviations: CRP, C-reactive protein; CPK, creatine phosphokinase; Hb, hemoglobin; Hct, hematocrit; LDH, lactate dehydrogenase; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase.

Because the patient had an increased anion gap (the fact that it was 22.5 mEq/L indicates that some time had passed since he intake of ethylene glycol, sufficient for it to be absorbed and metabolized into glycolic acid), continuous monitoring of the serum osmotic pressure was performed with an osmometer as well as its determination with the well-known equation (osmotic pressure = 1.86 x Na^+ + Glucose/18 + Urea/6) (Table 2).

Table 2

Changes in the osmotic gap during patient hospitalization (with an osmometer and the equation mentioned above)

	Sample (time)	Osmotic pressure (osmometer) (mOsm/L)	Osmotic pressure (determined) (mOsm/L)	Osmotic gap
Day 1st	11:00	370	287	83
	16:30	366	305	61
Day 2nd	08:00	332	293	39
	12:30	312	278	24
	16:30	294	288	6

In the ED, he received 300 mEq $NaHCO_3$ (almost continuously in rapid infusion), 1 amp of calcium gluconate, and a solution of dextrose 5% with complex vitamin B.

The patient, who was in a coma, was admitted to the Intensive Care Unit (ICU), where he was intubated and placed on mechanical ventilation. Continuous hemofiltration was started, which was completed in 24 hours. Urine taken 14 hours after his arrival at the ED and while he was hospitalized in the ICU, was tested and the characteristic "trial envelope" crystals of ethylene glycol poisoning were found (Fig. 1). The urinalysis performed at the same time showed pH 5, specific gravity 1009, albumin 150 mg/dl, glucose 50 mg/dl, nitrite negative (red blood cells and pus cells increased).

Fig. 1. Arrows indicate types of calcium oxalate crystals (two dihydrate octahedral [envelope-like] crystals are shown with red arrows, and two monohydrate dumbbell- or cigarette-shaped crystals are shown with black arrows)

While he was in the ICU, fomepizole was requested from the poison control center (which was 700 kilometers away in Athens), so whiskey was administered as an antidote, at a dose of 50 ml/hour, through a nasogastric tube (he received a total of approximately 1200 ml).

Throughout the night, he was hemodynamically stable and slightly excitable despite the sedation he was receiving. In the ICU from his admission until 07:00 the next day (over a period of 19 hours), he had a urine output of 865 ml. The next (3rd) 24 hours, he was anuric (95 ml/24 hours). The next morning, with the help of a portable ventilator, he was transferred to our renal unit. He underwent a 4-hour conventional hemodialysis session with bicarbonates (polysulfone filter [surface area 1.8 m^2], with blood flow rate of 180 ml/min, dialysate flow 500 ml/ml, and 1000 IU of unfractionated heparin at the beginning [loading dose] and then then 400 IU/hour [the heparin dose was reduced because he had hemorrhagic urine], due to the hyperkalemia he had and to remove the ethylene glycol. During the session, he was hemodynamically stable, with mild tachycardia and normal ventilation, and he was administered 7 amps of 10 ml calcium gluconate (10%) intravenously (knowing that it increases the risk of calcium oxalate precipitation). However, due to the fear of worsening hypocalcemia from the bicarbonate of dialysate, it was chosen to be given [2].

The fomepizole that arrived the day after his admission (noon), while the patient was still urinating, was administered after the end of the dialysis session, that is, approximately 22 hours after his admission. Until fomepizole, which is the absolute antidote to this poisoning (it has the best affinity for alcohol dehydrogenase), arrived, we administered whiskey (which was used in the past, before the introduction of fomepizole in this treatment), because ethyl alcohol also has a better affinity for alcohol dehydrogenase, which means that it delays the metabolism of fomepizole.

Since it was not possible to determine the blood levels of ethylene glycol, an attempt was made to estimate them from the osmotic gap. When the latter was normal, then we would be sure that there was no unmetabolized ethylene glycol in the blood. Table 3 shows the changes in HCO_3^- and the anion gap.

Table 3

Changes in blood bicarbonate (HCO_3^-) and anion gap during the first three days of hospitalization

Time	HCO_3^- (mEq/L)	Anion gap (mEq/L)
Day 1		
10:10	3.2	22.5
11:34	8.9	36.4
12:02	5.7	40.4
13:28	6.7	37.6
15:12	8.6	37.0
17:11	9.0	35.3
19:16	10.6	30.3
23:16	12.2	24,3
Day 2		
00:37	13.1	24.4
06:16	14.1	24.0
07:26	18.2	17.7
12:25	20.6	14.0
16:37	24.7	13.2
Day 3		
07:41	22.6	12.8
11:46	21.9	11.3

The patient was detubated two days after stopping ethyl alcohol and fomepizole (5th day of hospitalization) and continued to be on a dialysis program with conventional hemodialysis, due to anuria and non-recovery of the AKI, hospitalized in a ward of the internal medical clinic. After detubation and when he was able to communicate with the environment, he confirmed that he had received at 10:00 the previous night 500 ml of antifreeze solution for auto radiators, which he had procured himself for suicidal purposes.

This case is very rare and particularly important, since: a) the patient took 500 ml of auto antifreeze with the intention of committing suicide, a huge dose, compared to the very small one that is toxic, b) he was late in arriving at the hospital and the final diagnosis was delayed for a few hours, so that the patient could be put on the right treatment, c) fomepizole (it was approved for use in ethylene glycol poisoning by the FDA in 1997) was not immediately available in our hospital and instead a fixed hourly dose of ethyl alcohol (whiskey) was administered and d) dialysis was applied (hemofiltration at the beginning because there was no dialysate provided in the ICU and conventional hemodialysis afterwards, because it was possible to transfer the patient with a portable ventilator to the dialysis unit). All of this happened so that the patient ultimately survived, although the difficulties encountered were many.

Discussion. Ethylene glycol (molecular weight, MW=62 g/mol) is a colorless and odorless solution, sweet in taste. After absorption, it is metabolized in the liver by alcohol dehydrogenase to glycolaldehyde, which is rapidly metabolized to glycolic acid (at this level, its metabolism can be slowed down by ethyl alcohol or fomepizole). Glycolic acid precipitates as a calcium salt in the renal tubules, but in other tissues, leading to AKI, which is oliguric or anuric [3]. Approximately 20% of ethylene glycol is excreted unchanged in the urine.

Ethylene glycol poisoning is responsible for 3% of poisoning deaths in the USA [4] and causes gastric ir-

ritation within 30 minutes to 12 hours of ingestion and central nervous system (CNS) depression, dysarthria, hypertonia, agitation, altered mental status (common clinical signs like those of ethyl alcohol ingestion), and coma, as our patient had. After 12-24 hours of ingestion, tachycardia, hypertension, and congestive heart failure are observed from the cardiovascular system, and adult respiratory distress syndrome from the lungs [5, 6]. In 24-72 hours after taking poison, it appears from the kidneys dull pain or sensitivity in the renal areas and AKI, with the well-known crystals in the urine and oliguria [7]. Calcium oxalate crystals, in addition to being found in the urine, are deposited in the kidneys, brain, lungs and myocardium.

Even small amounts can cause falsely elevated plasma lactate levels (up to 10-20 mmol/L) when measured on standard gas analyzers [8]. It is important for physicians to be aware of this problem, as this can lead to misdiagnoses and delayed initiation of appropriate treatment. In particular, the glycolate (toxic metabolite of ethylene glycol) molecule has an almost identical structure to that of lactate (glycolate=CH_2OH-COO^- and lactate CH_3CHOH-COO^-). Thus, the reagents that detect lactate in gas analyzers and rely on lactate oxidase (spectrometric method) do not distinguish glycolic acid (as well as glyoxylate, which is a toxic ethylene glycol metabolite) and count it as lactate, thus yielding increased values [9, 10, 11], as was the case in our patient (we have a GemPrimer3000 analyzer). In contrast, analyzers that rely on amperometric methods or gas chromatography and lactate dehydrogenase do not identify glycolate as lactate [12]. Our patient ultimately developed hyperlactatemia (>15 mmol/L), with an anion gap of 22.5 mEq/L, which could not be explained by hypotension, convulsions, or medication. Of course, a small amount of lactate is produced during the conversion of glycolaldehyde to glycolate from pyruvate.

Metabolic acidosis with an increased anion gap i.e. a metabolic acidosis due to an unmeasured anion such as lactate, ketones, etc. (96% due to glycolic acid) [13] and an increased osmotic gap (which is the difference between the measured osmotic pressure from the calculated osmotic pressure by the known equation) are characteristics of ethylene glycol poisoning (in case of bigger difference of 10 mmHg there is high anion gap metabolic acidosis, due to methanol or ethyne glycol). Serum osmolality increases a few hours after poison ingestion, but later decreases as ethylene glycol is metabolized, increasing the anion gap (due to an increase of glycolate). That is, as ethylene glycol is metabolized, the osmotic gap decreases (since the amount of the responsible molecule decreases) and the anion gap increases (since the metabolism of ethylene glycol produces an unmeasurable anion, the glycolate).

Glucose disturbances are relatively rare in ethylene glycol poisoning. However, hyperglycemia has been reported in animal poisoning [14], as well as in humans [15, 16], which we also found in our patient. This may be due to transient pancreatitis caused by the poison, which reduces insulin levels [15, 17] or to insulin resistance in the presence of AKI [18]. Neither of these explanations explains hyperglycemia in our patient, since he had neither pancreatitis nor AKI when he had hyperglycemia.

Hypocalcemia (responsible for arrhythmias, tetany and convulsions) occurs after the metabolism of ethylene glycol to glycolate and is due to the precipitation of calcium glycolate in the kidneys and other tissues [4]. Our patient's calcium levels were not particularly low, perhaps because he was initially given increased amounts, but we did find calcium oxalate crystals in the urine.

Rhabdomyolysis associated with ethylene glycol ingestion was also observed in this patient (it is the most common cause of rhabdomyolysis from toxic substances) [19]. Therapeutically, in our case, and as long as there was diuresis, alkalinization of the urine was performed. The possible mechanism of rhabdomyolysis from ethylene glycol, among others, is vasoconstriction (the release of calcium from the smooth endoplasmic reticulum is promoted, which leads to vasoconstriction and irreversible muscle injury) [20, 21]. Others also consider that osmotic diuresis and the subsequent dehydration are responsible for rhabdomyolysis [20]. Of course, in our case, the AKI was probably due to ethylene glycol toxicity and not due to rhabdomyolysis, since it developed very early, but also because creatine phosphokinase levels were not particularly elevated throughout his hospitalization.

It is essential that ethylene glycol poisoning be diagnosed quickly. Measuring blood levels, although helpful in diagnosis, is not necessary. This is done by gas chromatography, which is not available in many hospitals, usually takes days to give results, and is expensive [22]. Although calcium oxalate crystals in the urine are important in diagnosing ethylene glycol poisoning, some have not found them in all their patients [22].

The goals of treatment of ethylene glycol poisoning are to reduce the load of it (by emesis and use of activated charcoal, although these measures are minimally effective, since the poison is absorbed very quickly from the gastrointestinal tract) [23], to correct acidosis (with bicarbonates and hemodialysis), to inhibit the precipitation of calcium oxalate (by bicarbonates), which precipitates rapidly as calcium monohydrate or dihydrate, to inhibit the metabolism of ethylene glycol (by ethyl alcohol or fomepizole), and to remove ethylene glycol and its metabolites from the body (by hemodialysis or hemofiltration) [6]. Intubation is necessary, even to protect the patient when he is in a coma (as was our patient, who had a Glasgow score of 6).

In past, as we mentioned ethyl alcohol was administered (intravenously, orally by nasogastric tube), in any suspected ethylene glycol poisoning, because the affinity of alcohol dehydrogenase for ethyl alcohol is greater than that for ethylene glycol. The recommended dose of ethyl alcohol is 0.6 g as a loading dose, followed

by a maintenance dose such that the blood ethyl alcohol levels are maintained between 100 and 200 mg/dl. Ethyl alcohol levels of 100 mg/dl prolong its half-life by 5 times, i.e. increase it to 15-20 hours [7, 24]. Ethyl alcohol administration should be continued until blood ethylene glycol levels are <20 mg/dl and the patient is asymptomatic with normal arterial pH [7]. The disadvantages of ethyl alcohol are that it is associated with CNS depression, gastritis, hepatotoxicity, and possible hypoglycemia. We discontinued administration when the patient's arterial pH returned to normal, while the osmotic gap and lactate levels became normal (serum lactate 1.8 mmol/L, osmotic gap 6 mOsm/L).

Indications for treatment with fomepizole include proven elevated blood ethylene glycol concentration (>20 mg/dl), a history of recent intake with an osmotic gap >20 mOsm/L, arterial blood pH <7.3, and urinary calcium oxalate crystals (our patient had a history of intake, an increased osmotic gap [83 mOsm/L], pH 7.109 and 6.93, and urinary calcium oxalate crystals). Both ethyl alcohol and fomepizole provide time for ethylene glycol to be excreted in the urine. This means that they are of no value in anuric patients (when hemodialysis or hemofiltration is not being applied).

Conventional hemodialysis is important in the treatment of ethylene glycol poisoning (removing 60% of it from the blood through the dialyzer) [25, 26], especially in patients with metabolic acidosis and AKI, as is hemofiltration [27, 28]. It also removes ethylene glycol metabolites (glycolic acid, which removes 5 times more) from the blood and corrects the metabolic acidosis [29]. Glycolic acid is the main metabolite of ethylene glycol and is responsible for the increased anion gap [4]. Current guidelines recommend that the patient undergo dialysis if the blood ethylene glycol level is >50 mg/dl and when there is severe metabolic acidosis and AKI (as our patient had). Persistence of the osmotic gap >10 mOsm/L is also an indication for dialysis. This should be performed with bicarbonate in dialysate until the blood ethylene glycol level goes <20 mg/dl [30]. The benefit of dialysis is a faster discharge from the hospital and a reduction in the cost of treatment, not a better patient outcome. Today, the trend is not to use dialysis in ethylene glycol poisoning when renal function is normal, acidosis is not resistant to other treatments, and the patient improves with fomepizole and other supportive measures [31].

The knowledge that the absence of an osmotic gap means the disappearance of ethylene glycol, while the decrease in lactate, as determined by gas analyzers, means the disappearance of ethylene glycol metabolites, provides certainty that there is no need for further administration of fomepizole or ethyl alcohol and that there is no reason to continue hemodialysis [8].

In the treatment of ethylene glycol poisoning, good hydration of the patient (1 L of 0.9% NaCl every hour for 4 hours) and the administration of bicarbonates are also helpful, which are basically indicated in patients with blood pH<7.3 [32], which was done in our patient, since in the first two days he was positive in terms of his fluid balance by 3,500 ml per day. The $NaHCO_3$ administered in the ED (300 mEq) and thereafter, aimed at correcting the acidosis, increasing the excretion of glycolic acid from the kidneys, and preventing the precipitation of calcium oxalate in the tissues [13]. For the latter two, a urine pH >7.0 is required.

Because pyridoxine and thiamine are cofactors in the metabolism of ethylene glycol (they help metabolize ethylene glycol into less toxic metabolites such as α-hydroxy-keto-adipic acid), some, like us, administer them intravenously in ethylene glycol poisoning [17], as does folic acid.

In the USA, approximately 5,500-6,000 cases of ethylene glycol poisoning are reported each year, with a fatal outcome of around 20-23 [1, 33, 34], depending on the amount of alcohol consumed and the time between ingestion and initiation of treatment [35]. The mortality rate of ethylene glycol poisoning varies from 1-22% [3, 17]. In the early stages, it is due to cardiorespiratory failure (24-48 hours) and is then attributed to respiratory infections and various CNS lesions [36]. Higher mortality is observed in patients with severe metabolic acidosis (pH<7.1) or in those who started treatment after 10 hours of taking the poison (our patient survived despite receiving 500 ml of poison and starting treatment approximately 22 hours after taking it). The lethal dose is 1.4-1.5 ml/kgBW (the minimum lethal dose is 100 ml), although death has been reported with lower doses and survival with higher doses [5, 6]. A 500 ml dose taken by a 50-year-old man was fatal [28], while another case of a 60-year-old man with a body weight of 65 kg and ingestion of 500 ml of antifreeze survived [37].

Most renal injuries are reversible, and recovery of renal function to normal may occur even after weeks [26] or months (even in the presence of anuria) [38]. However, some have found persistence of renal injuries and the need for chronic renal replacement therapy [8, 22].

A major limitation of this report is the inability to measure serum ethylene glycol concentrations, a challenge that likely applies to most hospitals worldwide. This could pose a significant problem if there were no indirect diagnostic methods available. In practice, the presence of a markedly increased osmotic gap strongly suggests methanol or ethylene glycol intoxication, except in patients who present very late, when the alcohol has already been fully metabolized. In such cases, however, the therapeutic approach remains the same. Another limitation is that the patient was transferred to a neighboring country, which prevented long-term follow-up of renal function. Since recovery of kidney function can occur even after several weeks, we were unable to document whether kidney failure eventually resolved or required chronic dialysis.

Conclusions. It is concluded that the presence of an osmometer is essential for the diagnosis of ethylene glycol toxicity, the use of ethyl alcohol (when fomepi-

zole is not available) is reliable in the treatment of ethylene glycol toxicity, and any type of dialysis (conventional hemodialysis, hemofiltration) when applied in a timely manner contributes to the best outcome of such patients. We managed to save the patient's life, while he received a huge amount of ethylene glycol and appeared at the hospital quite late. However, he remained on hemodialysis (as far as we know) because after leaving the hospital, he returned to his country.

Ethics statement. The study was followed in accordance with ethical standards of the responsible committee on human experimentation (Scientific Council of General Hospital of Komotini), approval number (3/2021), and with the Helsinki Declaration of 1975, as revised in 2013. Written consent was obtained from the patient after first being informed of the publication.

Conflicts of interest statement. The authors are employed by the Renal Unit «Dimokrition». The institution had no role in the study design, data collection, analysis, interpretation, or publication decision. The authors declare no commercial or financial conflicts of interest. They had full access to all the data and took responsibility for the integrity of the data and accuracy of the data analysis. The results in this paper have not been published previously in whole or in part.

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Data availability statement. The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions.

Konstantinos S. Mavromatidis: analyzed and interpreted the data, drafted and revised the manuscript, and approved the final version.

Irini M. Kalogiannidou: collected the data, revised the manuscript, conducted literature searches, and provided critical input to the study.

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