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Complete Recovery after Repeated Suicidal Ethylene Glycol Ingestion

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Abstract: We report here on a patient who attempted suicide four times by ingesting a lethal dose of antifreeze. Reversibility of renal damage due to ethylene glycol (EG) ingestion is not complete in all patients, and its predictor factors are not well understood. A 30-year-old man suffering from a depressive disorder repeatedly attempted suicide between 2002 and 2005. In December 2002 the patient was admitted in a coma. EG intoxication was confirmed (serum EG level 1.025 g/l) and intensive therapy was started (sodium bicarbonate, ethanol, haemodialysis). After treatment he recovered. In February 2003 this patient again drank EG (serum EG level 0.257 g/l). On admission he had no symptoms of intoxication and received only ethanol i.v. Only mild metabolic acidosis (pH = 7.365) developed. In May 2003 the patient arrived at the hospital six hours after ingestion of 500 ml of EG (serum EG level 0.282 g/l). Metabolic acidosis (pH = 7.176) and signs of nephrotoxicity (serum creatinine 168 micromol/l) had developed, for which he received intensive therapy. In May 2005 the patient was found comatose on the street. Laboratory monitoring on admission showed severe metabolic acidosis (pH = 6.899) and a serum EG level of 2.877 g/l. Intensive therapy was performed again. This case report describes for the first time the repeated ingestion of a large amount of EG by a single patient and documents the improvement of renal functions. These findings support the opinion of full recovery in patients with intensive treatment and no history of kidney damage.

Introduction

EG has been recognized as a poison for nearly 70 years [1] and remains available today mostly in antifreeze solutions also in the Czech Republic [2, 3, 4]. The lethal dose is estimated at 1–1.5 ml/kg of body weight, or approximately 100 ml for an adult [5]. EG itself produces only mild intoxication, similar to that produced by ethanol. However, organic acids and aldehydes produced by the hepatic metabolism of EG are highly toxic. The first step of this metabolic pathway is catalysed by enzyme alcohol dehydrogenase in the liver [6]. Thus, inhibitors of alcohol dehydrogenase (ethanol or fomepizole) prevent the biotransformation of EG to toxic metabolites. Organic acids (glycolic, oxalic) cause the metabolic acidosis observed in EG poisoning. The clinical course can be quite variable and includes neurological, cardiopulmonary and renal stages. The first stage is the neurological stage (from 0.5 to 12 hours after EG ingestion). Early effects may include slurred speech, nausea, vomiting, somnolence, sopor and coma. In the second phase, the cardiopulmonary stage (from 12 to 36 hours after EG intake), commonly reported signs include tachycardia, hypertension, and severe metabolic acidosis with compensatory tachypnoea, Kussmaul's respiration and congestive heart failure. The final phase of EG poisoning, the renal stage (from 24 to 72 hours after EG ingestion), is the result of acute renal injury and is characterised by renal tubular necrosis, haematuria, proteinuria, flank pain, oliguria, anuria and renal failure [7,8]. Serum creatinine level (normal range 44–110 micromol/l) and serum

urea level (normal range 2.0–8.0 mmol/l) are commonly used factors for monitoring nephrotoxicity. Death usually occurs due to cardiopulmonary failure [9].

Prompt diagnosis and initiation of treatment, including ethanol or fomepizole therapy and haemodialysis, is necessary to ameliorate the effects of EG ingestion [5, 10, 11]. The indications for treatment with an antidote are [5]: documented plasma EG concentration > 0.200 g/l or documented recent (hours) history of ingesting toxic amounts of EG and osmol gap > 10 mosm/l or strong suspicion of EG poisoning and at least two of the following criteria (arterial pH < 7.300, serum bicarbonate < 20 mEq/l, osmol gap > 10 mosm/l, urinary oxalate crystals present). The reversibility of renal function impairment after ingestion of lethal doses with intensive treatment is usually good; however, the predictor parameters of early recovery of kidney damage are not completely elucidated. In some patients plasma creatinine may not return to normal for months [12].

We describe a patient who ingested four massive doses of antifreeze between 2002 and 2005 in suicide attempts and recovered without consequences.

Case report

A 30-year-old homeless man attempted suicide four times in the years 2002–2005 by ingesting various amount of antifreeze solution containing EG. He had been treated intensively for a severe depressive bipolar affective disorder with a combination of several antidepressants (citalopram, risperidon, nitrazepam, clonazepam, trazodon), and had no history of kidney disease. We report courses of his four intoxications; the data are presented in Table 1.

Table 1 – Summary information and biological findings of the patient

Date of intoxication	December 2002	February 2003	May 2003	May 2005	Reference range
Reported dose (ml)	?	1000	500	500–700	
Time interval (hours)	?	12	6	?	
Length of hospital stay (days)	24	2	3	7	
Maximal serum ethylene glycol level (g/l)	1.025	0.257	0.282	2.877	
Maximal urine ethylene glycol level (g/l)	3.765	6.490	2.389	11.460	
Metabolic acidosis (minimal pH)	6.854	7.365	7.176	6.899	7.360–7.450
Maximal osmolality (mOsm/l)	301	320	315	367	285–295
Maximal serum creatinine level (micromol/l)	388	59	168	301	44–110
Maximal serum urea level (mmol/l)	28.00	1.40	6.74	8.17	2.00–8.00

Abbreviations: ? – unknown; Time interval – time interval between ingestion and hospitalisation

In December 2002 the patient was found outwith, algid and unconscious, with rattling breath and a score of 3 on the Glasgow Coma Scale. He received Anexate (flumazenil) and Intrenon (naloxon) but no improvement was noted; then he was intubated and monitored at the department of anaesthesiology and resuscitation. On admission he was in coma, had peripheral cyanosis, miosis and an irregular pulse (90 bpm). Serum creatinine, urea and liver enzymes were in the normal range with the exception of a twofold increase in alanine aminotransferase (1.45 microkat/l), but severe metabolic acidosis (lactate 20 mmol/l) and hyperosmolality developed. Intoxication with EG was suspected from this clinical course, and therapy with sodium bicarbonate, ethanol i.v. and haemodialysis was started. Laboratory analysis confirmed EG and propylene glycol in serum and urine. During the next days the patient developed ARDS, acute cardiovascular and renal failure, and coagulation impairment with bleeding from the airways and left ear. The patient was anuric (6–10 ml of urine/24 hours) for three days; however, starting from day 4, with diuretic therapy, his diuresis slowly normalised. With the intensive symptomatic treatment the patient recovered: his serum urea and creatinine normalised within three weeks, and he was transferred to the psychiatric department twenty-eight days after ingestion.

In February 2003 during an afternoon walk (he was still hospitalised at the psychiatric department) the patient again drank EG (according to the patient, 1000 ml) and two beers, after which he vomited twice. On admission to the department of intensive medicine twelve hours after ingestion he had no symptoms of intoxication, with normal electrolyte serum concentrations findings. He received ethanol i.v. Only mild metabolic acidosis developed during the next two days when he returned to the psychiatric department. Laboratory analysis showed lower serum and urine EG levels than would normally be expected after a dose of 1000 ml. We suppose that the ingested dose was substantially lower and that the concomitant ethanol intake positively influenced the clinical course.

In May 2003 the patient arrived at the hospital six hours after he ingested about 500 ml of EG. No clinical symptoms of intoxication were present. However, metabolic acidosis was found, and serum creatinine and serum osmolality were mildly elevated. He received sodium bicarbonate, ethanol i.v. and underwent one course of haemodialysis, after which his serum EG decreased to 0.125 g/l. After three days he was transferred to the psychiatric department.

In May 2005 this man was discharged from the psychiatric department, but later the same day he was found comatose on the street. Gastric lavage was performed and activated charcoal was administered. Laboratory monitoring on admission to the department of intensive care showed severe metabolic acidosis, elevated serum creatinine levels and osmolality. Therapy (sodium bicarbonate and ethanol i.v.) was performed upon suspicion of EG ingestion. Toxicological analysis confirmed an extremely high serum EG level. The patient admitted to the consumption of about 500–750 ml of EG. Haemodialysis was started, during the

course of which the patient improved. His diuresis was normal. Only serum creatinine and urea levels increased to a maximum on the sixth day of hospitalisation, but both normalized before discharge on day twenty-two.

The patient refused next hospitalization at the psychiatric department. According to our knowledge he was not interested in further follow up.

Discussion

In the Czech republic 249 patients were hospitalized due to EG poisoning during 2000–2004 according to the Institute of the Health Information and Statistics of the Czech Republic. The number of EG intoxication is increasing in many countries. In 1997, the American Association of Poison Control Centres Toxic Exposure Surveillance System registered 4867 exposures to EG. There were 21 fatalities among the reported cases [13]. In 2003 this association recorded 5 081 reports of EG ingestion, 16 of which related to fatalities [14]. Stompór et al [15] as well as Sydor et al. [16] from Poland presented an analysis of EG acute intoxication treatment results in two groups of 36 and 15 patients. In both studies the mortality rate was about 50%. The main reason of the high mortality was long time interval between poisoning and administration to hospital (antidotal treatment).

Four articles [17, 18, 19, 20] also demonstrate the negative impact of information concerning toxicity in mass media. After detailed information about dangers of EG intoxication in newspapers and in TV following lethal adult cases of accidental EG poisoning was given, a large epidemic of suicidal EG intoxication usually occurred.

The presented case report is unique for several reasons. It demonstrates that EG in antifreeze remains quite a common and available agent for suicide attempts in the Czech Republic. According to our knowledge of the literature, this is the only case report that describes the repeated ingestion of lethal doses of EG by a single patient.

Over the course of the years described, the patient developed severe symptoms and was adequately treated. He always met the criteria for the use of the antidote ethanol, i.e. serum EG level higher than 0.200 g/l (or suspicion on the ingestion of a toxic EG dose) and metabolic acidosis ($pH < 7.300$) [5]. Another antidote fomepizole is not available in the Czech Republic. On three occasions the patient received haemodialysis, which is indicated in cases of severe metabolic acidosis ($pH < 7.300$), renal failure and elevated serum EG level > 0.500 g/l [5]. Twice this patient developed life-threatening symptoms of intoxication. Undoubtedly, the clinical course was mostly positively influenced by the rapid administration of appropriate therapy. In addition to that, during the second EG ingestion in February 2003 the outcome may have been improved by the concomitant ingestion of alcohol, and thus haemodialysis was not necessary. It was described already in 1984, that ethanol can prevent metabolic acidosis [21]. Ammar [22] and

Davis [23] reported about patients who consumed ethanol (serum ethanol level 4 and 1.2 ‰) and large amount of EG (serum EG level 8.9 g/l) concurrently and survived. This was undoubtedly due to the patient achieving "therapeutic levels" of ethanol together with the EG ingestion.

A renal biopsy was not performed in our patient, because the laboratory markers of nephrotoxicity (serum creatinine and urea level) improved to a normal range prior to each discharge from the hospital.

Conclusion

EG in antifreeze remains quite a common and available agent for suicide attempts. To our knowledge, this is the only case report that describes the repeated ingestion of lethal doses of EG by a single patient. It documents the complete early recovery of renal function in a patient with rapid intensive treatment and no history of kidney disease.

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