Submitted: 08 March, 2024 Accepted: 27 June, 2024 Published: 08 December, 2024 DOI:10.22514/sv.2024.164

Open Access
Signa Vitae

CASE REPORT

Successful extracorporeal cardiopulmonary resuscitation in a refractory out-of-hospital cardiac arrest after ethylene glycol poisoning

Peter Sklienka[1,2,3,*], Jan Neiser[1,2], Juraj Rodina[1], Filip Burša[1,2,3], Jan Máca[1,2,3], Michal Frelich[1,2], Tomáš Jonszta[4]

[1]Department of Anesthesiology and Intensive Care Medicine, University Hospital Ostrava, 70800 Ostrava, Czech Republic
[2]Department of Anesthesiology and Intensive Care Medicine, University of Ostrava, 70300 Ostrava, Czech Republic
[3]Institute of Physiology and Pathophysiology, Department of Intensive Care Medicine and Forensic Studies, Faculty of Medicine, University of Ostrava, 70300 Ostrava, Czech Republic
[4]Department of Radiology, University Hospital Ostrava, 70800 Ostrava, Czech Republic

***Correspondence**
peter.sklienka@fno.cz
(Peter Sklienka)

Abstract

Here, we report the first case of successful extracorporeal cardiopulmonary resuscitation (eCPR) in a patient with an out-of-hospital cardiac arrest following the ingestion of a lethal dose of ethylene glycol (EG). A 49-year-old man was found unconscious for an unknown period of time after suspected ethylene glycol ingestion. Upon arrival of the Emergency Medical Service (EMS), the patient was found to have a Glasgow Coma Score of 3, bilateral non-reactive mydriasis, and hypoventilation. Despite the urgent orotracheal intubation, the patient developed cardiac arrest immediately thereafter. After 8 minutes of conventional CPR, the regional ECMO (extracorporeal membrane oxygenation) center was contacted. The patient was transferred under mechanical CPR to an ECMO center where veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was initiated 59 minutes after the cardiac arrest. Laboratory tests confirmed EG intoxication with a plasmatic EG level of 1474 mg/L, greatly exceeding reported lethal values. A left stellate ganglion blockade was performed because of refractory ventricular fibrillation, and the return of spontaneous circulation was achieved 149 minutes after the cardiac arrest. As a result of direct organ toxicity, the patient developed anuric acute kidney injury and multifocal brain lesions revealed by nuclear magnetic resonance imaging. In addition to the VA-ECMO, the therapeutic protocol included hemodialysis, intravenous ethanol and fomepizole. This multimodal treatment eventually led to the patient's survival with near complete recovery.

Keywords

Ethylene glycol; Out-of-hospital cardiac arrest; Extracorporeal cardiopulmonary resuscitation

1. Introduction

Ethylene glycol (EG) is a liquid alcohol substance used as an antifreeze and industrial solvent. Due to its wide availability, ethanol-like effects, and sweet smell and taste, EG represents a common cause of intoxication, both accidental and intentional. The mortality rate after EG intoxication ranges between 1 and 22%, depending on the amount of ingested alcohol and the period between the ingestion and the initiation of therapy [1]. The mechanism of EG toxicity is determined by its metabolites (glycolic acid and oxalic acid) leading to the development of metabolic acidosis, and by chelation of oxalic acid to calcium oxalate, which may lead to direct nephrotoxicity and neurotoxicity. Severe metabolic acidosis is the leading cause of cardiopulmonary failure after EG poisoning. Life-threatening hemodynamic poisoning presentations include rapid progression to cardiogenic shock, high-degree atrioventricular block, ventricular tachycardia, or cardiac arrest from ventricular fibrillation or asystole [2].

Here, we report a case of EG poisoning leading to out-of-hospital cardiac arrest with prolonged cardiopulmonary resuscitation immediately followed by extracorporeal cardiopulmonary resuscitation (eCPR). Multimodal treatment included hemodialysis, intravenous ethanol and fomepizole. This complex treatment led to the patient's survival with near complete recovery despite the plasmatic levels of EG highly exceeding the elsewhere reported lethal doses and the prolonged period until the return of spontaneous circulation.

2. Case report

A 49-year-old man with a medical history of depression and chronic ethanol abuse was found unconscious but breathing spontaneously at home (Day 1). Next to him, an empty 750 mL bottle of antifreeze containing 50% ethylene glycol was found. At the time of ambulance arrival, he was found to have a Glasgow Coma Score of 3, bilateral mydriasis (non-reactive 4 mm pupils), hypoventilation with oxygen peripheral saturation of

82%, sinus heart rate of 80 bpm, and blood pressure of 100/70 mmHg. The patient was immediately orotracheally intubated but subsequently developed ventricular fibrillation. Advanced cardiopulmonary resuscitation according to the current European Resuscitation Council Guidelines 2021 was initiated, and a short-lasting return of spontaneous circulation was achieved; however, ventricular fibrillation reappeared within a minute. This necessitated continuation of CPR with mechanical external chest compression (using a continual mechanical chest compression system Lund University Cardiopulmonary Assist System—LUCAS). An ECMO center was contacted after 8 minutes of unsuccessful CPR. The patient was admitted under continuous CPR to the Emergency Room 39 minutes after the cardiac arrest (Day 0). The initial rhythm was described as ventricular fibrillation with no effective myocardial mechanic activity on echocardiography. VA-ECMO in the femoral-femoral configuration was immediately initiated (cannulated under ultrasound guidance), without interrupting the CPR. Initial blood samples for laboratory and toxicology were obtained from the arterial cannula. Effective VA-ECMO support (Cardiohelp, Maquet—Getinge; initial blood flow 4.5 L/min, sweep gas flow 3 L/min with oxygen fraction of 1.0) was initiated 20 minutes after the arrival to the Emergency Room. The total duration from the cardiac arrest to the initiation of VA-ECMO was 59 minutes. Ventricular fibrillation persisted even after the initiation of ECMO support, and echocardiography (ECHO) confirmed no effective myocardial contractions. The initial acid-base status demonstrated severe metabolic acidosis outside the analyzer range—pH <6.8, base excess >20, lactate >20 mmol/L. Boluses of 4.2% sodium bicarbonate were applied repeatedly to neutralize the acidosis. Native computed tomography (CT) revealed no acute brain pathology; however, bilateral pulmonary aspiration and bilateral rib fractures were found. Ventricular fibrillation persisted despite the ECMO support and gradual correction of the acid-base status. Ultrasound-navigated blockade of the left stellate ganglion was, therefore, performed, followed by the intravenous application of 5 mg of esmolol. Sinus rhythm and effective myocardial contractions verified by echocardiography reappeared 149 minutes after the onset of the cardiac arrest. The toxicology laboratory (Shimadzu gas chromatograph mass spectrometer GCMS QP2010 SE, Shimadzu, Kyoto, Japan) confirmed blood levels of EG of 1474 mg/L and glycolic acid (GA) of 1186 mg/L. Multimodal therapy for EG intoxication was initiated, including continuous hemodialysis connected to the ECMO circuit (the patient was anuric from the start), intravenous application of ethanol targeted to the ethanol serum level of 2 g/L, and intravenous fomepizole at a dose of 15 mg/kg body weight. The patient remained anuric, but subsequent blood laboratory tests verified the effective elimination of both EG and GA (Table 1).

Subsequently, ECMO settings were titrated against the ECHO parameters, with a proven gradual improvement in the myocardial function and a gradual reduction of norepinephrine. On Day 4, the patient was successfully disconnected from ECMO support. No complications related to the VA-ECMO support were reported during the VA-ECMO treatment. Nuclear magnetic resonance imaging (MRI) performed on Day 5 revealed bilateral hyperintensities within the basal ganglia, the arteria cerebri media basin, and the central part of pons Varoli (Fig. 1). Sedation was discontinued on Day 5, with gradual improvement in the clinical neurological functions and the electroencephalogram record. On Day 13, the patient was conscious and cooperative and then extubated. The patient remained anuric throughout the treatment at our department, but kidney functions also fully recovered eventually. Ninety days after the intoxication, the patient was discharged from the hospital, under psychiatric treatment, with only a minimal cognitive deficit (Cerebral Performation Score of 2) but fully self-sufficient and without other organ dysfunctions.

3. Discussion

Ethylene glycol is a substance responsible for 727 reported intoxications and 11 deaths in the USA in 2021. A lethal ingested dose of ethylene glycol is estimated to be in the range of 1.000–1.600 mg/kg body weight [3]. Because the toxicity is determined by metabolites of EG, clinical manifestations and outcomes also depend on the time between EG ingestion and treatment initiation.

In our patient, the exact dose and time of ingestion were unknown. The initial measured serum levels of EG and GA were 1474 mg/L and 1186 mg/L, respectively. These levels are comparable to ethylene glycol serum levels of 590–3900 mg/L reported in ten lethal cases from the United States database from 2021 and are higher than postmortem blood levels from twenty-one patients who died from EG intoxication (median 870 g/L) [3, 4].

Ethylene glycol is not toxic *per se*, but life-threatening toxicity results from highly toxic EG metabolites—glycolaldehyde, glycolic acid, glyoxylic acid and calcium oxalate, causing severe metabolic acidosis and direct organ toxicity [5]. The concentration of plasma glycolate and associated acid-base disorders predict complications and unfavorable outcomes [6]. Cardiovascular toxicity is determined mainly by metabolic acidosis; the kidney and the central nervous system are most affected by direct toxicity. Cardiovascular toxicity in severe intoxication is characterized by cardiogenic shock, dysrhythmias, and, finally, cardiac arrest from ventricular fibrillation or asystole. The incidence of oliguric acute kidney injury (AKI) in victims of EG poisoning varies between 30 and 70%. Pathophysiology is determined by the formation of oxalate crystals in the renal parenchyma and urine [6]. Moreover, calcium oxalate crystal deposits in the walls of intracranial blood vessels and inflammatory cellular infiltration surrounding blood vessels cause diffuse cerebral edema and hypodensities in the basal ganglia, thalami, midbrain, and pons Varoli, which typically develop 2–3 days after intoxication [7, 8]. In our patient, refractory cardiac arrest, severe acidemia with non-measurable pH (<6.8), and anuric acute kidney injury were present on admission, and a brain MRI performed five days later revealed EG-related injury to the central nervous system. The multimodal therapeutic approach, therefore, aimed at restoring adequate circulation by VA-ECMO and minimizing organ toxicity.

Extracorporeal cardiopulmonary resuscitation is defined as VA-ECMO cannulation during refractory cardiac arrest (re-

TABLE 1. Ethylene glycol and glycolic acid serum levels.

Time from admission to ER (h)	T_0	T_{ECMO}	16	28	40	52
Ethylene glycol (mg/L)	1474	NE	553	356	225	143
Glycolic acid (mg/L)	1186	NE	191	3	0	0
Ethanol (g/L)	0	NE	1.8	2.4	2.5	0.6
Lactate (mmol/L)	>30.0	>30.0	12.7	8.3	3.8	3.2
Base excess (mmol/L)	<−30.0	−24.6	−9.5	−7.4	−4.9	−4.5
pH	<6.80	6.95	7.38	7.32	7.35	7.38

T_0: time of admission to the emergency department; T_{ECMO}: time of ECMO (extracorporeal membrane oxygenation) arterial cannula insertion; ER: emergency room; NE: not evaluated.

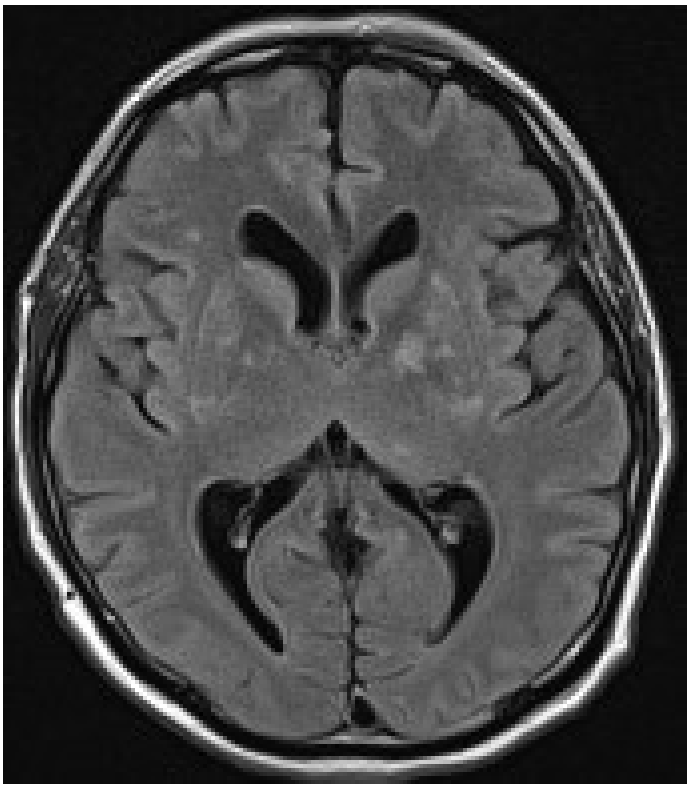

FIGURE 1. Nuclear magnetic resonance imaging performed on Day 5. Bilateral hyperintensities within the basal ganglia, the arteria cerebri media basin, and the central part of pons Varoli are apparent.

fractory cardiac arrest is defined as the absence of the return of spontaneous circulation despite the provision of appropriate CPR for 15 to 30 minutes) [9]. As far as patients with EG intoxication are concerned, successful eCPR was previously reported only in a single patient who was, however, already admitted to the intensive care unit at the time of the onset of the cardiac arrest [10]. Among intoxicated patients in refractory cardiac arrest reported in the literature (15 case series papers, 158 patients in total; 96.5% of those patients suffered from intra-hospital cardiac arrest, IHCA), the mortality rate was 32.3% (51/158). The neurological outcome was usually favorable in surviving patients [11]. On the other hand, 100% mortality was reported in victims of intoxication with out-of-hospital cardiac arrest (OHCA) (nine patients) [12]. The likelihood of good neurological outcomes decreases rapidly during both conventional and extracorporeal CPR, with the low-flow duration being the most critical determinant of the outcome, showing an almost linear relationship: after 15–20 minutes of conventional cardiopulmonary resuscitation, the probability of survival with good neurological function drops as low as to approximately 2% [9]. In our patient, cardiac arrest occurred in an out-of-hospital setting in a remote area. According to our regional protocol, the ECMO center was activated early (within 10 minutes after the cardiac arrest onset). The patient was admitted under continual CPR to the Emergency Room after 39 minutes, and the VA-ECMO was initiated 59 minutes after the cardiac arrest onset. However, even under ECMO treatment, refractory ventricular fibrillation was still present. Ultrasound-guided navigated blockade of the left stellate ganglion using a local anesthetic and intravenous beta-blocker application was performed to reverse the malignant ventricular dysrhythmia by suppression of the "adrenergic storm" [13]. This approach was followed by the restoration of the sinus rhythm and by the return of effective cardiac

mechanical activity. Summing up the time of conventional CPR and extracorporeal CPR, the period without effective myocardial contraction lasted for 149 minutes in total. Alongside the circulatory support by VA-ECMO, a complex therapeutic approach included hemodialysis, intravenous ethanol and fomepizole. EG and its metabolites have a small molecular size, high water solubility, absence of protein binding, and a low distribution volume. These characteristics lead to high hemodialysis clearance (similar to that of urea). According to the current recommendations, dialysis is recommended (i) in all patients presenting with coma, seizures or kidney impairment; (ii) in patients with EG concentration >620 mg/L (>10 mmol/L) in situations when no antidote was administered; (iii) suggested in patients with EG plasma concentration >1240 mg/L and (iv) recommended at concentrations of >3100 mg/L if antidotes are given. Antidotes for EG comprise ethanol and fomepizol, both of which block the enzyme alcohol dehydrogenase (ADH) [6]. ADH blocking inhibits the degradation of EG to glycolaldehyde and its toxic metabolite formation. EG can then be effectively removed from plasma without the formation of toxic metabolites. We used hemodialysis and antidotes to prevent the further formation of toxic metabolites, which led to a rapid decrease in plasma EG and glycolic acid concentrations. This multimodal treatment eventually led to the patient's survival with near complete recovery despite prolonged cardiac arrest and apparent direct organ toxicity (acute kidney injury and pathological findings on brain MRI). Ninety days after the intoxication, mild cognitive impairment (Cerebral Performance Score of 2) was the only disability present.

In patients who suffer from refractory cardiac arrest, extracorporeal life support might represent a life-saving therapy. According to the current knowledge, VA-ECMO should be strongly considered in all patients with acute poisoning who have developed cardiac arrest [14]. Despite the previously reported unfavorable outcomes in intoxicated patients suffering from out-of-hospital cardiac arrest, this report might serve as an encouraging case for further development of the eCPR program. Creating local protocols for rescue services and institutions where the method is not available that would facilitate timely ECMO center consultations can be crucial for the survival of victims of intoxication who suffer from out-of-hospital cardiac arrest.

4. Conclusions

VA-ECMO application represents a life-saving intervention for patients suffering from refractory out-of-hospital cardiac arrest caused by ingestion of lethal doses of ethylene glycol. According to current recommendations, subsequent treatment includes the application of antidotes (fomepizole and/or ethanol) and hemodialysis to minimize the toxicity caused by ethylene glycol metabolites. Near-complete recovery can be achieved despite the prolonged out-of-hospital cardiac arrest, acute kidney injury, and multifocal damage to the brain. Creating local protocols for early referral and transport to the local ECMO center might further improve the survival of victims of intoxication who develop out-of-hospital cardiac arrest.

AVAILABILITY OF DATA AND MATERIALS

Data are available on request from the corresponding author.

AUTHOR CONTRIBUTIONS

JR, FB, MF and TJ—collected and analyzed the data. JN, JM and PS—wrote the manucript. All authors contributed to the editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Ethics Committee of the University Hospital Ostrava waived the need to approve this study because of its retrospective nature (Opinion of the Ethics Committee on Clinical Trial Reference Number 137/2024). Informed consent for data analysis and publication also waived by the Ethics Committee of the University Hospital Ostrava because of its anonymous nature.

ACKNOWLEDGMENT

Thanks to University Hospital Ostrava, 70800 Ostrava, Czech Republic.

FUNDING

This research was supported by MH CZ-DRO (FNOs/2024).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for ethylene glycol. U.S. Department of Health and Human Services, Public Health Services: Atlanta. 2010.

[2] Brogan TV, Lequier L, Lorusso R, MacLaren G, Peek G. Extracorporeal life support: the ELSO red book. 5th edn. Extracorporeal Life Support Organization: Ann Arbor, Michigan, United States. 2017.

[3] Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Rivers LJ, Feldman R, *et al*. 2021 annual report of the National Poison Data System© (NPDS) from America's Poison Centers: 39th annual report. Clinical Toxicology. 2022; 12: 1381–1643.

[4] Viinamäki J, Sajantila A, Ojanperä I. Ethylene glycol and metabolite concentrations in fatal ethylene glycol poisonings. Journal of Analytical Toxicology. 2015; 6: 481–485.

[5] Latus J, Kimmel M, Alscher MD, Braun N. Ethylene glycol poisoning: a rare but life-threatening cause of metabolic acidosis—a single-centre experience. Clinical Kidney Journal. 2012; 2: 120–123.

[6] Ghannoum M, Gosselin S, Hoffman RS, Lavergne V, Mégarbane B, Hassanian-Moghaddam H, *et al*. Extracorporeal treatment for ethylene glycol poisoning: systematic review and recommendations from the EXTRIP workgroup. Critical Care. 2023; 27: 56.

[7] Malhotra A, Mongelluzzo G, Wu X, Durand D, Kalra VB, LeSar B, *et al*. Ethylene glycol toxicity: MRI brain findings. Clinical Neuroradiology. 2017; 27: 109–113.

[8] Owen EB, Calhoun AW, McDonald MJ. Reversibility of severe cerebral

magnetic resonance imaging changes associated with ethylene glycol toxicity. Journal of Pediatric Intensive Care. 2017; 6: 214–220.

[9] Wengenmayer T, Tigges E, Staudacher DL. Extracorporeal cardiopulmonary resuscitation in 2023. Intensive Care Medicine Experimental. 2023; 11: 74.

[10] Rosen R, Robbins-Juarez S, Stevens J. Ethylene glycol intoxication requiring ECMO support. Case Reports in Critical Care. 2021; 2021: 5545351.

[11] Ng M, Wong ZY, Ponampalam R. Extracorporeal cardio-pulmonary resuscitation in poisoning: a scoping review article. Resuscitation Plus. 2023; 13: 100367.

[12] Rousse N, Robin E, Juthier F. Extracorporeal life support in out-of-hospital refractory cardiac arrest. Artificial Organs. 2016; 40: 904–909.

[13] Savastano S, Schwartz PJ. Blocking nerves and saving lives: left stellate ganglion block for electrical storms. Heart Rhythm. 2023; 20: 1039–1047.

[14] Upchurch C, Blumenberg A, Brodie D, MacLaren G, Zakhary B, Hendrickson RG. Extracorporeal membrane oxygenation use in poisoning: a narrative review with clinical recommendations. Clinical Toxicology. 2021; 59: 877–887.

How to cite this article: Peter Sklienka, Jan Neiser, Juraj Rodina, Filip Burša, Jan Máca, Michal Frelich, *et al*. Successful extracorporeal cardiopulmonary resuscitation in a refractory out-of-hospital cardiac arrest after ethylene glycol poisoning. Signa Vitae. 2024; 20(12): 131-135. doi: 10.22514/sv.2024.164.