Antifreeze poisoning: A case report

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Abstract. The current study reported the case of a 35-year-old male that presented with antifreeze poisoning. The clinical manifestations, laboratory investigations and treatments were analyzed, and the obtained results were compared with those in previous reports. Subsequent to consuming antifreeze, the patient mainly presented nausea and agitation, without disturbance of consciousness. Laboratory investigations indicated severe metabolic acidosis, renal dysfunction and hyperkalemia. The patient underwent hemodialysis and his condition was significantly improved on the day of admission. Renal function gradually deteriorated, but was eventually improved due to treatment, including hemodialysis, mannitol for catharsis, furosemide for diuresis, Xuebijing for the removal of blood stasis and detoxication, and reduced glutathione for the protection of major organs. The patient was discharged 1 month after hospital admission. In conclusion, the significance and clinical manifestations of antifreeze poisoning should be identified in clinical practice, and active hemodialysis should be provided. The aim of the current study was to summarize the clinical manifestations and treatments of patients with antifreeze poisoning, and to advance the recognition of antifreeze poisoning.

Case report

A 35-year-old male purposely consumed automobile antifreeze solution (~200 ml) in February 2013. The patient presented with nausea and with significant vomiting, facial blushing and agitation at the primary stage; however, the patient did not inform his family members regarding the incident. After ~19 h, the patient was found by family members in a state of severe agitation and immediately presented to the First Affiliated Hospital of Bengbu Medical College (Bengbu, China). Informed consent was obtained from the patient. In the Outpatient Department, the patient was subjected to gastric lavage and transferred to the Department of Emergency Internal Medicine following consultation and diagnosis of antifreeze poisoning. The symptoms the patient presented with upon admission included nausea, vomiting, facial blushing, severe agitation and shortness of breath. The patient did not experience symptoms of fever, disturbance of consciousness, coughing, palpitation, chest tightness, precordial discomfort or hematemesis, while normal emiction and defecation were reported. The patient was fasted during hospitalization. Physical examination obtained 20 h after antifreeze consumption recorded a temperature of 36.7˚C, heart rate of 115 bpm, respiratory rate of 35 breaths/min, and blood pressure of 154/87 mmHg. The patient was conscious with respiratory rapidity, and was cooperative during the physical examination. Routine check-ups concluded that the systemic skin and mucosa of the patient were not yellow in color, the skull was not malformed, and the bilateral pupils were round with the same diameter of ~3 mm; however, the pupillary light reflex was slightly slow. In addition, the patient's lips were not cyanotic and his neck was soft without resistance (with regard to meningeal stimulation of neck stiffness). Upon auscultation, coarse respiratory sounds were reported in the two lungs, without significant dry or moist rales heard. Furthermore, the cardiac rhythm was regular and pathological murmurs were not observed. The abdomen was soft with no tenderness, while the bilateral kidney regions showed weakly positive percussion pains and the tendon jerk reflex was hyperreactive. Results of other examinations were unremarkable.

Laboratory investigations were also performed upon hospital admission. A blood routine test performed ~20 h after consumption of antifreeze observed the following: White blood cells, 29.82×10^9/l (normal range: 4-10×10^9/l); neutrophils, 84.9% (normal range: 43-70%); red blood cells, 6.02×10^{12}/l (normal range: 4.0-5.7×10^{12}/l); hemoglobin level, 187 g/l (normal range: 130-172 g/l); and platelet level, 270 g/l. In addition, an electrolyte test at admission indicated the following: K^+ level, 5.75 mmol/l (normal range: 3.5-5.3 mmol/l); Ca^{2+} level, 2.62 mmol/l (normal range: 2.03-2.54 mmol/l); total CO_2 (TCO_2), 7.3 mmol/l (normal range: 22-29 mmol/l); anion gap, 25.7 mmol/l (normal range: 8-16mmol/l); creatine kinase (CK), 257 U/l (normal range: 55-170 U/l); CK-MB, 35 U/l (normal range: 0-25 U/l); creatinine (Cr), 171 μmol/l (normal range: 33-133 μmol/l.); and blood urea nitrogen (BUN),

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Table I. Dose, route of administration and treatment duration of the therapies received by the patient.

Therapy	Dose	Administration route	Therapy duration
Mannitol	125 ml	Intravenous drip infusion	16 days
Furosemide	20 mg	Intravenous injection	7 days
Xuebijing	40 ml	Intravenous drip infusion	14 days
Reduced glutathione	1.8 g	Intravenous drip infusion	17 days

5.75 mmol/l (normal range: 2.3-8.2mmol/L). Furthermore, emergency blood gas analysis (BGA) was also performed ~21 h after antifreeze consumption, and the results were as follows: pH, 6.85; CO_2 partial pressure (PCO_2), 23 mmHg; O_2 partial pressure (PO_2), 76 mmHg; Na^+, 129 mmol/l; K^+, 6.7 mmol/l; HCO_3^-, 4.0 mmol/l; base excess (BE), 29.7 mmol/l; and lactate, 14.6 mmol/l. The liver function and electrolyte tests were reexamined after ~8 h from the initial tests (i.e. 28 h from antifreeze consumption), and the results indicated the following: Cr, 213 μmol/l; BUN, 8.35 mmol/l; K^+, 4.76 mmol/l; TCO_2, 10.7 mmol/l; and AG, 19.3 mmol/l. An electrocardiogram performed at admission indicated sinus tachycardia and frequent ventricular premature beats.

Based on the aforementioned findings, the patient was diagnosed with acute antifreeze (ethylene glycol) poisoning, acute kidney failure, and with an electrolyte disorder (hyperkalemia, due to the elevated levels of K^+).

Upon arrival at the hospital, the patient was given ~10 l of clean water for gastric lavage, after which the patient was immediately admitted to our department. The patient was fasted and monitored using an electrocardiogram device. Various treatments were administered, including oxygen inhalation, mannitol (Sichuan Kelun Pharmaceutical Co,. Ltd, Sichuan, China) for catharsis, furosemide (Shanghai Hefeng Pharmaceutical Co,.Ltd, Shanghai, China) for diuresis, Xuebijing (Tianjin Hongri Pharmaceutical Co,.Ltd., Tianjin, China) for removal of blood stasis and detoxication, reduced glutathione (Chongqing Yaoyou Pharmaceutical Co,.Ltd., Chongqing, China) for the protection of major organs (Table I). Nutritional supports and other therapies for maintenance of the water-electrolyte balance specific to the patient's requirements were also given, including a compound amino acid injection (150 ml; Cisen Pharmaceutical Co., Ltd., Jining, China) and propylene ammonia acyl glutamine injection (1 00 ml; Harbin Medisan Pharmaceutical Co., Ltd., Harbin, China), intravenously guttae once daily; a 5% glucose injection (250 ml; Anhui Fengyuan Pharmaceutical Co., Ltd., Bengbu, China); a vitamin B6 injection (4 ml; Fangming Pharmaceutical Group, Heze, China), intravenously guttae, once daily; a 0.9% Sodium chloride injection (500 ml) and a fructose booster injection (25 g; Hai Nan Huang Long Pharmaceutical Co., Ltd., Haikou, China), intravenously guttae once a day. On the day of hospital admission (21 h after antifreeze consumption), an emergency BGA was performed (results shown in Table II), after which 5% sodium bicarbonate (250 ml; Shandong Qidu Pharmaceutical Co,. Ltd., Zibo, China)was administered. After 3 h, BGA reexamination revealed improvement in various BGA indices, including PCO_2 (decreased), PO_2 (increased), K^+ (decreased), HCO_3^- (increased) and BE (increased). Approximately 42 h after antifreeze consumption, the BGA was normal.

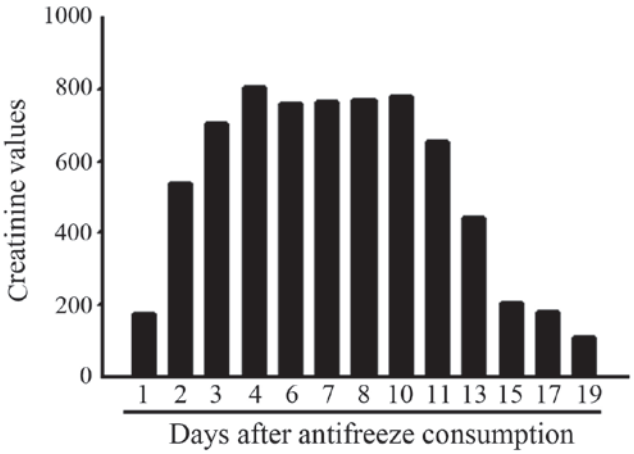

Figure 1. Alterations in creatinine levels according to the days after antifreeze consumption (patient was admitted within day 1, at ~20 h after consumption).

The initial emergency kidney function test upon hospital admission showed a Cr level of 171 μmol/l, and thus the patient underwent hemodialysis six times since admission (once per day between days 1 and 6 of admission). At 7 days after antifreeze consumption, the frequency of hemodialysis was altered to once per 2 days. Regarding the 24-h urine volume, the patient presented oliguria on hospital admission until day 3 after antifreeze poisoning, at which point the volume was ~300 ml (normal range: 1,000-2,000 ml). On day 4, the urine volume increased to 500 ml, and then gradually increased further from day 5. In addition, the corresponding changes in creatinine levels as determined by the kidney function test are shown in Fig. 1. As mentioned earlier, the emergency test upon hospital admission showed a Cr level of 171 μmol/l, and the renal damages was aggravated between days 4 and 6 after antifreeze consumption (with the creatinine level peaking at 804 μmol/l on day 4; Fig. 1). Reexamination of creatinine levels showed a gradual decrease from day 13 and dropping to normal levels on day 19 after antifreeze poisoning.

Regarding changes in the electrolyte levels, hyperkalemia appeared with slightly elevated blood calcium on day 1, which decreased from day 2 onwards. On day 7, blood potassium, sodium and chloride levels were reduced due to several hemodialysis sessions. On day 17 after antifreeze poisoning, the patient experienced fever, with a highest body temperature of 39˚C. Chest computed tomography performed in February 2013 indicated a large patchy opacity on the right inferior lung and a small amount of pleural effusion in the

Table II. Alterations in major BGA indices.

Time after antifreeze consumption	pH	PCO_2 (mmHg)	PO_2 (mmHg)	Na^+ (mmol/l)	K^+ (mmol/l)	HCO_3^- (mmol/l)	BE (mmol/l)	Lac (mmol/l)
21 h	6.85	23	76	129	6.7	4.0	-29.7	14.6
24 h[a]	7.24	12	188	137	4.5	5.1	-22.3	>15
42 h	7.29	31	140	132	4.2	14.9	-11.7	1.0
Normal range	7.35-7.45	35-48	83-108	135-145	3.5-5.0	21-28	(-3)-(+3)	0.5-1.6

[a]At 24 h after antifreeze consumption, the BGA indices were reexamined subsequent to the initial hemodialysis. BGA, blood gas analysis; PCO_2, CO_2 partial pressure; PO_2, O_2 partial pressure; BE, base excess; Lac, lactate.

right thoracic cavity associated with mediastinal lymphadenopathy. As a result, cefotiam (2.0 g; Harbin Pharmaceutical Group Co.,Ltd., Harbin, China) and levofloxacin (0.6 g; Yangtze River Pharmaceutical Co,.Ltd., Taizhou, China) were administered for anti-infection treatment. The patient was supplementally diagnosed with pulmonary infection due to the long-term bed rest and poor human resistance contributing to the infection. The infection was under control in March 2013, and the patient was discharged with all normal indices (including creatinine, BGA and blood routine test values) approximately 1 month after antifreeze poisoning. During a 4-month follow-up period (March to July 2013), the patients received a renal function test once per month, and did not present any relapse.

Discussion

Common antifreeze components include ethylene glycol, rust inhibitor, fungicide, pH value regulator and pour point depressant. Ethylene glycol is a colorless, sweet and low-toxicity fluid, however its metabolites are highly toxic (1,2). The adult lethal dose is 80-100 ml if antifreeze solution is consumed orally. Ethylene glycol (which has a high water solubility) is absorbed by the gastrointestinal tract, and quickly spreads to the blood and interstitial fluid. It is metabolized by ethanol dehydratase into glycolaldehyde in the liver, and then by aldehyde dehydrogenase into glycolic acid, which is later oxygenized by glycolate oxidase into glyoxylic acid. The major end product is oxalic acid (1), while other products include formic acid and hippuric acid. Due to the formation of a large amount of organic acids, metabolic acidosis and hyperkalemia occur. In addition, the combination of oxalic acid with calcium leads to hypocalcemia, and the deposition of calcium oxalate crystals in renal tubules results in renal injury, and even acute renal failure (2,3). If not timely treated, severely poisoned patients succumb due to severe hyperkalemia or metabolic acidosis at the early stage, while certain individuals may succumb after several days due to acute renal failure or central nervous system exhaustion (3,4).

Acute toxicity of ethylene glycol mainly targets the central nervous system, lungs, kidney and liver (5,6), and is generally divided into three stages. At the first stage, central nervous system symptoms primarily occur within 0.5-12 h after ethylene glycol consumption, and the manifestations include intoxicated appearance and excitation, followed by coma, loss of deep and superficial reflexes, convulsion, myosis, disappearance of light reflex, bradypnea, deep breathing and acidosis. At the second stage, the cardiac and pulmonary symptoms become significant, and the patient presents respiratory rapidity, tachycardia, mild hypertension and cyanosis. In severe cases, pulmonary edema, heart and lung enlargement, and congestive heart/circulatory failure also appear. At the third stage of the poisoning, the patient present different degrees of renal failure, and if the patient survives the acute stage, symptoms of renal damage occur within 2-3 days, including proteinuria, hematuria, oliguria and anuria.

At present, there are numerous reports regarding the rescues and treatments of antifreeze poisoning, with the majority of cases caused by accidental intake (7). In the present case, the patient consumed the antifreeze with the intention of self-poisoning, at a dosage (200 ml) that was far higher than the lethal dose of 80-100 ml. Although the patient consumed a very high dose of antifreeze, no intellectual impairments were reported, apart from symptoms of nausea and agitation on hospital admission, which is inconsistent with numerous previous clinical reports (1,8). However, the metabolic acidosis and significant renal damage observed in the current patient are consistent with the manifestations of large-dose antifreeze poisoning observed in clinical settings.

Ethanol and 4-methylpyrazole are clinical antidotes for antifreeze poisoning. Ethanol is quickly oxygenized *in vivo* and competes with ethylene glycol for liver alcohol dehydrogenase, which is essential for glycol oxidation, and inhibits the production of more toxic oxygenic glycol metabolites. As a result, ethylene glycol is urinated in its primary form (1-3). An input of ethanol at 0.7 g per liter of blood can inhibit most of the ethylene glycol metabolism *in vivo* (6). In addition, 4-methylpyrazole is an antidote that has been recently approved by the Food and Drug Administration for use in ethylene glycol poisoning. Compared with ethanol, its pharmacokinetic behavior is clearer, and the dosage is more easily controlled. Furthermore, 4-methylpyrazole does not require blood concentration monitoring, and results in reduced adverse drug events during its clinical use compared with ethanol, since it does not cause central nervous system inhibition. Patients receiving 4-methylpyrazole do not normally require observation in an intensive care unit, with the exception of patients in unstable disease conditions (1-3). According to a previous study (1), 4-methylpyrazole can be replaced with intravenous drip of 10% ethanol, with

similar results observed in certain Chinese studies (2,9). However, 4-methylpyrazole is expensive and has not been approved for use in China to date. Therefore, the patient of the present study was treated mainly by correction of acidosis, hemodialysis, protection of major organs, as well as by other symptomatic and supportive treatments. Early and active correction of metabolic acidosis along with early and repeated hemodialysis are vital for treatment success. Early hemodialysis assists in the elimination of ethylene glycol and its toxic metabolites, as well as of other toxic ingredients of antifreeze; thus, the metabolic acidosis, hyperkalemia and hypocalcemia, which are irresponsive to drug treatments, can be quickly treated. Furthermore, hemodialysis stabilizes the body environment, reduces complications of the heart, lungs and brain, and prevents acute renal failure (1,2,9).

In conclusion, the present study reported the case of a 35-year-old male who had consumed high-dose antifreeze and was admitted to the hospital at a late stage, at ~19 h after antifreeze consumption. Timely and repeated hemodialysis, the correction of acidosis and the protection of major organs were thus found to be effective treatments for antifreeze poisoning patients. For the prevention and treatment of acute renal failure, hemodialysis was the main factor for the successful treatment of the current patient.

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