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Acetonitrile Poisoning for Suicidal Purposes Treated with Hydroxycobalamin and Disulfiram-Case Report

Joanna Rzodkiewicz[1*], Ilona Dębkowska[1], Dorota Zalewska[1], Mirosław Pryzmont[1], Dorota Klimaszyk[2], Mariola Tałałaj[1], Piotr Jakubów[1]

[1]Clinic of Anesthesiology and Intensive Care of Children and Adolescents with the Postoperative and Pain Management, University Children's Clinical Hospital in Bialystok, Poland

[2]Department of Toxicology, City Hospital in Poznan, Poland

***Corresponding author**: Joanna Rzodkiewicz, Clinic of Anesthesiology and Intensive Care of Children and Adolescents with the Postoperative and Pain Management, University Children's Clinical Hospital in Bialystok, Poland

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Abstract

Acetonitrile (methyl cyanide) is an organic solvent mainly used in laboratories and chemical industries. It is very rare poison used to commit suicide. It can be absorbed through the skin, orally or by inhalation. Toxicity of acetonitrile is caused by releasing cyanide and formaldehyde in delayed hepatic metabolism. Cyanide transforms aerobic metabolism into anaerobic metabolism, which by product is lactic acid. Symptoms of acute cyanide poisoning are headache, nausea, anxiety, confusion, drowsiness, tachycardia and tachypnoea. There are known several cyanide antidotes: the Cyanide Antidote Kit, 4-dimethylaminophenol, dicobalt edetate and hydroxycobalamin. This is the first case of acetonitrile poisoning reported in Poland, which was successfully treated with hydroxycobalamin and disulfiram. A 16-year-old boy poisoned himself with acetonitrile for suicidal purposes. Neurological and cardiovascular symptoms appeared after 10 hours after ingestion. The laboratory analysis showed severe metabolic acidosis with base deficiency and high concentration of lacid acid. He was admitted to Intensive Care Unit in serious condition and started treated with hydroxycobalamin (5g i.v.). After first dose he responded quickly, by regaining consciousness and normalizing lactic acid. On days 2, 3 and 4 lacid acid was increasing again and consciousness were observed and he required further doses of hydroxycobalamin. In search of other therapeutic methods, disulfiram was added to treatment on day 4. The metabolism is probably based on the inhibition of cytochrome P450 which transform acetonitrile to cyanide. After adding disulfiram to treatment the boy was completely cured.

Keywords: Acetonitrile; Cyanide; Hydroxycobalamin; Disulfiram; Antidote.

Introduction

Acetonitrile (ACN) is a colourless liquid, high-polarity organic solvent used in laboratories and chemical industries [1-4]. Acetonitrile could be absorbed through many ways by dermal absorption, inhalation or through gastrointestinal tract and metabolized to cyanide [4,5]. This is the first case of acetyl nitrile poisoning reported in Poland, which was successfully treated with hydroxycobalamin and disulfiram.

Case Presentation

A 16-year-old boy was admitted in the evening to the Emergency Department (ED) after consuming the solvent acetonitrile in a suicide attempt. He brought with him a brown bottle with the name

of the substance- Acetonitrile. The boy said that he had consumed about 50 ml of the substance dissolved in icetea. Additionally, he admitted to drinking alcohol earlier. Physical examination revealed a reddened throat, developed fatty tissue, his body weight was 125 kg. Laboratory tests at admission were red blood cell 4,19 10^6/ul (normal range 4,50-5,50), white blood cells 9,93 10^3/ul (normal range 4,20-9,10), thrombocytes 333 10^3/ul (normal range 140-450). potassium 4,13 mmol/L (normal range 3,50-5,10), sodium 142 mmol/L (normal range 135-146), chloride 106 mmol/L (normal range 96-107), serum creatinine 0,89 mg/dl (normal range 0,57-0,87), aspartame aminotransferase 37 U/l (normal range < 39), alanine aminotransferase 69 U/l (normal range <37), gamma-glut amyl transferase 46 IU/l (normal range 9-40), lipase 25 IU/l (normal range 13-60, prothrombin time 11,5 (normal range 10,4-14), index normalized ratio 1,04 (normal range 0,8-1,3), blood gas: pH 7,393 (normal range 7,350-7,450), pCO2 36,4 mmHg (normal range 35,0-45,0), pO2 75,4 mmHg (normal range 80-100), standard bicarbonate 21,7 mmol/L (normal range 21-28), base excess -2,6 mmol/L (normal -2,5-2,5), ethanol level 0,65‰. Urine drug screen and blood toxicology screen were negative. He was admitted to the pediatric clinic for observation. During the stay he was vomiting. Early in the morning, which was 9-10 hours after ingestion, the first symptoms appeared: confusion, weakness and sweating on the face, increased heart rate 100/min, rapid breathing, while oxygen saturation was 97%. The blood gas showed pH 7,223 (normal range 7,350- 7,450), pCO2 16,7 mmHg (normal range 35,0-45,0), pO2 129,2 mmHg (normal range 80-100), standard bicarbonate 6,8 mmol/L (normal range 21-28), base excess -18,3 mmol/L (normal -2,5- 2,5), ethanol level was 0,00‰. The patient in a very serious condition with acute cardiorespiratory failure, was transferred to the Intensive Care Unit (ICU), where in pharmacological preparation with propofol and rocuronium he was urgently intubated and mechanical ventilation was started. Simultaneously he was receiving a 15-minute infusion of hydroxocobalamin (5g i.v.) – preparation called Cyanokit®. The skin of the body intensely became pink and the urine turned red that was an effect after the administration of hydroxocobalamin. In the ICU the first laboratory analysis showed severe metabolic acidosis with base deficiency pH 6,869 (normal range 7,350-7,450), pCO2 33,8 mmHg (normal range 35,0-45,0), pO2 345,4 mmHg (normal range 80-100), standard bicarbonate 6,0 mmol/L (normal range 21-28), base excess -27,1 mmol/L (normal -2,5-2,5) and very high concentration of lactic acid in the serum 7,34 mmol/l (normal range 0,50-2,20). He was also treated with catecholamine and sodium bicarbonate. After few hours the patient clinical condition was better, control blood gas was pH 7,362 (normal range 7,350-7,450), pCO2 32,2 mmHg (normal range 35,0-45,0), pO2 289,3 mmHg (normal range 80-100), standard bicarbonate 17,9 mmol/L (normal range 21-28), base excess -6,4 mmol/L (normal -2,5-2,5) and lactate level normalized it was 1,1 mmol/l (normal range 0,50-2,20).

The patient regained consciousness and was disconnected from the respirator and extubated on the second day of stay in ICU. However after 24 hours after first dose of the antidote admittion, the level of lactic acid increased and consciousness disorders reappeared. The treatment with hydroxocobalamin was repeated during next days which brought temporary improvement in laboratory tests and patient condition, but for a shorter period of time. After fourth dose of hydroxycobalamin, we did not wait for the re-accumulation of lactic acid. Subsequent doses were depended on the assessment of the patient's state of consciousness. At the same time, we started looking for other treatment methods, therefore, on the day 4 of stay in the ICU, disulfiram was added to the treatment [6]. It was administered for next 5 days. The lactate level increased and normalized immediately and no disturbances of consciousness were observed (Figure 1). Psychiatric consultation was performed and on the 11th day of stay in ICU he was transferred to the psychiatry department where he received psychiatric support.

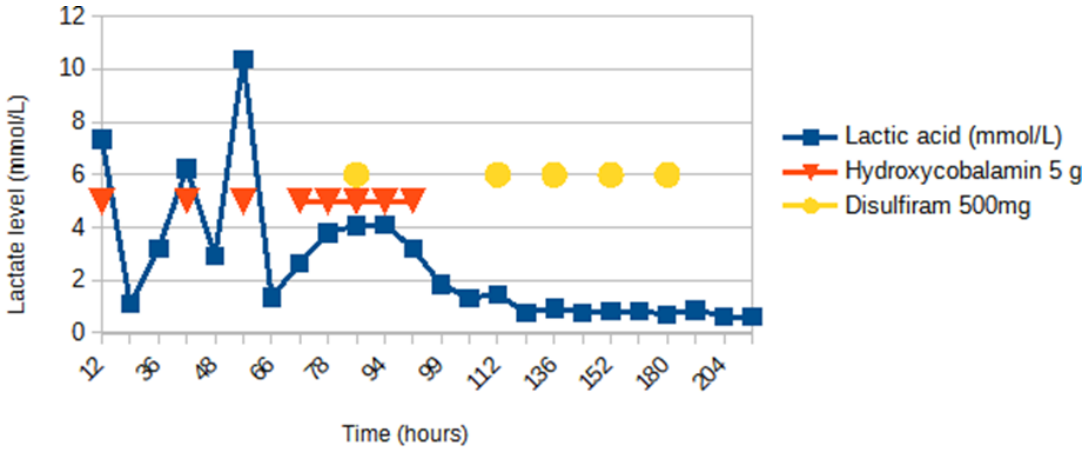

Figure. Lactate concentration during the time after ingestion of acetonitrile and after receiving antidotes (hydroxycbalamin, disulfiram).

Discussion

The discussed case draws attention to the use of acetonitrile as an unusual poisoning agent for suicide purposes. Acetonitrile, was used as a cosmetic product like nail polish remover since March 2000 [7], currently it is only used in the chemical industry and laboratories as a solvent. It is important to know that the toxic effect of acetonitrile is delayed due to its metabolism to cyanide and formaldehyde [6]. There are few reported cases of oral acetonitrile ingestion [1,5,6,8,9,10-17]. Toxicity of cyanide is caused by inactivating mitochondrial cytochrome P450 oxidase in liver cells [18]. Therefore, this process is prolonged and the first symptoms of anoxia appear after 3-12 hours [3]. Cyanide inhibits cytochrome oxidase, which blocks cellular respiration. Cyanide transforms aerobic metabolism into anaerobic metabolism, which toxic by-product is lactic acid [18,19]. The organs that are particularly dependent of oxygen supply are the heart, brain, liver. The symptoms that accompany cyanide poisoning are primarily neurological and cardio logical. Early symptoms of acute poisoning are headache, nausea, anxiety, dizziness, confusion, drowsiness, tachycardia, palpitations and tachypnoea. In case of moderate and severe poisoning the neurological, respiratory and cardiovascular symptoms may occur like loss of consciousness, convulsions, vomiting, hypotension, deep lactic acidosis, coma, arrhythmias with circulatory and respiratory arrest [3]. There are several cyanide antidotes: the Cyanide Antidote Kit (CAK amyl nitrite, sodium nitrite and sodium thiosulfate), 4-dimethylaminophenol (4-DMAP), dicobalt edetate and hydroxycobalamin (Cyanokit®) [20]. In this case we used hydroxycobalamin (Cyanokit®), which is precursor of vitamin B12 that convert cyanide to cyanocobalamin in chelatation mechanism which is excreted in urine [18,20]. Dosing recommendations of hydroxycobalamin for adult persons in Europe is 5g (maximum total infusion dosage 15g) [18]. In the summary of product characteristics the maximum total dose is 10 g for adults, and 140 mg/kg in children up to a maximum of 10 g [21]. Another antidote that blocks the metabolism of acetonitrile to cyanides is disulfiram. Mechanism of disulfiram may be based on inhibiting cytochrome P450 which contributes to block the reaction of converting acetonitrile to cyanide [6,22]. The use of disulfiram with additional ethanol ingestion is contraindicated [6,23,24].

The boy's symptoms anxiety, confusion, sweating, tachycardia, tachypnea which showed after several hours after ingestion acetonitrile could be the result of anoxia caused by cyanide poisoning. In this case there was a rapid and complete return to normal hemodynamic functions and consciousness and normalizing lactic acid after the administration of the hydroxycobalamin. However, the metabolism of acetonitrile to cyanides continued, the level of lactic acid increased and disturbances of consciousness repeated so it was necessary to administer further doses of the antidote. The total dosage of hydroxycobalamin was 40g which encouraged us to find and use another antidote disulfiram [6]. Disulfiram was stared on day 4 after ingestion alcohol and acetonitrile, when the ethanol level in the blood was zero. Disulfiran therapy was continued for 5 more days. No disturbances of consciousness or increased lactic acid levels were observed in the following days. Using disulfiram to therapy completely cured the boy. This is the first case of acetonitrile poisoning reported in Poland, which was successfully treated with hydroxycobalamin and disulfiram.

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