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Severe ethylene glycol poisoning of 56 years old woman – case report

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Abstract

Backgrounds: Ethylene glycol poisoning is one of the heaviest poisonings in the toxicological practice of. Ethylene glycol is quickly absorbed from the digestive tract. Its toxicity is the result of combining few different mechanisms. Metabolites of decomposition, especially glycolic acid, are responsible for appearance of metabolic acidosis. Precipitated crystals of calcium oxalate additionally impair the function of organs such as kidneys, central nervous system (CNS) and circulatory system. Worldwide, from 2013 to 2018 about 30% of ethylene glycol poisoning cases end in death.

Case report: We present the case of 56 years old woman, who was admitted to Toxicology Department because of ethylene glycol poisoning. We could observe presence of metabolic acidosis, respiratory insufficiency and organ damage. The patient has been treated pharmacologically and has been given specific antidote. Due to the ethylene glycol intoxication, metabolic acidosis and increasing parameters of kidney failure the patient also underwent hemodialysis.

Conclusions: In pathogenesis of ethylene glycol poisoning toxic metabolits are crucial. The diagnosis of ethylene glycol is often a very hard task. In the clinical aspect it is based on the interview, a set of syndromes and biochemical tests and targeted toxicological tests. This kind

of poisoning occur the most often among patients addicted to alcohol. It may lead to multi-organ damage or even death. It is very important to react quickly and implement pharmacotherapy and hemodialysis. The other essential aspect is to improve the level of knowledge of students and doctors about symptoms, diagnostics and proper proceeding with a patient poisoned with ethylene glycol. According to statistics and knowing how often the alcohol poisoning happens it is necessary to have knowledge in this field, be fluent in management and choosing methods of treatment in such cases.

Key words: poisoning; ethyleneglycol; toxicology

Introduction

Ethylene glycol was first synthesized in 1859 by Charles- Adolphe Wurtz and first widely produced as an engine coolant during World War II, when its precursor ethylene oxide became readily available. Today its primary use remains as an engine coolant (antifreeze) in car radiators.[1] Ethylene glycol can be consumed accidentally and unintentionally by children and animals because of its sweet taste, odorlessness and colourlessness. It is often referred to a “sweet killer” due to its physicochemical properties. Moreover it does not irritate the oral mucosa while it is ingested which may also be conducive to accidential intoxication.[2] In the case of adults such poisoning concerns patients with cognitive impairment. Nevertheless referring to toxicological practice we know that predominantly it happens in the course of alcoholic addiction, intentional glycol intake or as an suicide attempt. According to the National Agency for Solving Alcohol Problems in Poland there are approximately 800 000 people who are addicted to alcohol.[3] Worldwide, according to World Health Organisation (WHO) – 3,3 million deaths every year result from harmful use of alcohol, this represent 5,3% of all deaths.[4] It is worth emphasizing that this is one of the heaviest poisonings in the practise of toxicology.

Case report

We present 56 years old woman who was admitted to Toxicology Department. According to report of her family we know that the patient has been consuming alcohol for a few days before the incident and on the day of admission to hospital she was found unconscious at home. Due to unclear information from the anamnesis she has undergone neurological examination. She had also computer tomography (CT) done, which has not shown any visible damage of central nervous system (CNS). According to neurological examination we know that she was unconscious (GCS-3) with narrow pupils and weak reaction for light. The diagnostic work-up led to a diagnosis of metabolic acidosis due to severe ethylene glycol intoxication. In laboratory tests it turned out that not only ethylene glycol (190mg/dl) but also benzodiazepines (745,13ng/ml) were present. (Fig 1) Her general condition in the moment of entering the emergency department was very severe, with very low respiratory efficiency. Due to bad clinical condition and obtained laboratory results the patient has been intubated and ventilotherapy was initiated. After several hours of respiratory therapy she was extubated.

LABORATORY PARAMETERS	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Ethylene glycol [ng/ml]	190; 38,5	33,73	0	-	-	-	-
Benzodiazepines [mg/dl]	745,13	-	-	-	-	-	-
Creatinine[mg/dl]	1,26	2,6	4,05	4,43	2,59	2,52	1,79
eGFR [ml/min/1,73^2)	47,7	19,9	11,6	10,4	20	20,7	31,2
pH	6,847 ; 7,166 ; 7,213	7,262 ; 7,294	7,341	-	-	-	-
BE(B) [mmol/l]	-30,2 ; -13,1 ; -11,3	-4,9 ; -6,7	-1,5	-	-	-	-
K (Potassium) [mmol/l]	6,9 ;3,8	4,5	3,8	-	3,3	-	4,0
Glucose [mg/dl]	330,1	-	-	171	-	-	-

Fig 1. Laboratory parameters at the time of admission to the hospital and during further hospitalization.

During further hospitalization there were observed features of acute kidney injury (Creatinine: 4,43mg/dl; eGFR: 10,4ml/min/1,73m^2). (Fig 1) The intensive pharmacotherapy was carried out, including antidotal treatment with use of ethanol. Because of intoxication, acidosis and electrolyte disturbances the patient underwent two hemodialysis treatments - eight- hour hemodialysis during the first and five- hour hemodialysis during the fourth day of hospitalization. The pharmacotherapy was continued reaching improvement of the patient's general condition and normalization of laboratory parameters. After few days of hospitalization the patient was showing resignation thoughts, therefore she was consulted psychiatrically. After the toxicology proceeding was done – she was transported to psychiatric hospital in order to re-evaluate the mental state and continue the hospitalization.

Discussion

Alcohols are generally quickly absorbed after ingestion. The symptoms of glycol poisoning include gastric symptoms such as abdominal pain, nausea and vomiting. Moreover we can observe Kussmaul breathing, disorders of cardiovascular system such as dysrythmia and hypotension. There can occur also electrolyte abnormalities, acute kidney injuryand consciousness disturbances which can even lead to coma. These symptoms are a consequence of combining few different mechanisms of ethylene glycol metabolism which takes place in liver and kidney with the participation of alcohol dehydrogenase (ADH), aldehyde dehydrogenase (ALDH), lactate dehydrogenase (LDH) and proceeds as shown in Fig 3. Ethylene glycol itself is non-toxic but its metabolic byproducts are toxic – acids have no rapid natural metabolic pathway of elimination and therefore they accumulate. Main toxic metabolic products accumulating in the body are glycoaldehyde, glycolic acid, precipitating calcium oxalate crystals and oxalic acid. Aldehydes inhibit central nervous system respiration, glucose metabolism, oxidative phosphorylation and serotonin metabolism.[5] The oxalic acid metabolite is responsible for the renal damage and acidosis due to formation of complex with calcium to precipitate as calcium oxalate monohydrate crystals in the renal tubules.[1] Occasionally oxalic acid can participate in the formation of hypocalcaemia following precipitation as calcium oxalate and in consequence lead to prolongation of the QT interval on the electrocardiogram and ventricular dysrhythmias. End- organ manifestations can be various depending on the time after which the patient has been admitted to the hospital and diagnosed properly. Among other complications after ethylene glycol ingestion we can distinguish

cerebral edema, neurological manifestations, increased intracranial pressure with papilledema and abduscens palsy, parkinsonism, vision disorder and deafness.

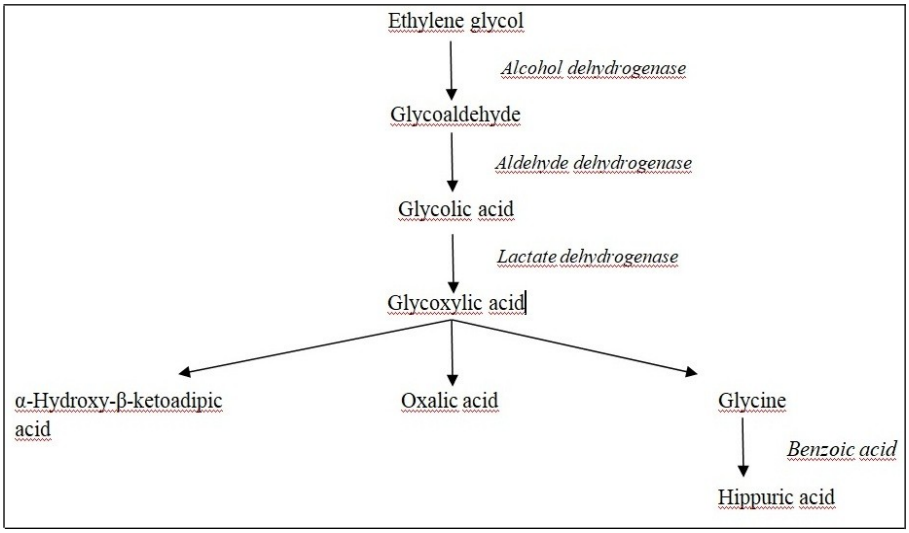

Fig 2. Pathways of ethylene glycol metabolism.

This kind of poisoning should be strongly suspected in the presence of coma associated with metabolic acidosis and large anion gap, urinalysis demonstrating calcium oxalate crystalluria. [6] Traditionally ethylene glycol concentration greater than 25 mg/dL has been considered toxic, but the evidence supporting this as a threshold is often questioned.[1] Biochemical tests are also often disturbed, especially gasometry parameters such as decreased pH level and decreased partial concentration of CO_2. In course of ethylene glycol intoxication the impaired renal function is also manifested by abnormal levels of creatinine and eGFR. The most essential part of the detoxification procedure of poisoned patients is to maintain basic life functions and to use specific antidotes in order to stop the progress of ethylene glycol metabolism. The most important is blockade of ADH. Due to the competitive inhibition ethanol and ethylene glycol compete with each other for the binding site of enzyme. After implementing ethanol treatment – ADH activity on ethylene glycol is diminished and ethanol begins to be metabolized. Ethanol has less toxic metabolites and greater affinity to ADH than ethylene glycol. However it is extremely important to keep the ethanol concentration at an appropriate level. In some cases ADH blockade may itself serve as definitive therapy.[1] The traditional method of inhibition ADH is implementing ethanol or Fomepizole. In the case of conscious patients ethanol can be administred orally as 40% solution, whereas in unconscious patients it has to be administered as 10% solution through a central venous catheter and titrated to maintain ethanol level about 1,0-1,5g/l. Maintaining adequate ethanol levels is difficult in everyday practice; therefore, frequent testing and infusion adjustments are

mandatory.[7] Another inhibitor is Fomepizole which exists only in intravenous form. It is worth emphasizing that Fomepizole is also a competitive antagonist of ADH that has many advantages over ethanol.[1] First of all concentrations do not need to be monitored as with an ethanol infusion. Intensive care unit monitoring is also not required because of fewer adverse effects and not causing inebriation. It has distinct advantage over others because it is easy to titrate and does not cause central nervous system, depression, hypoglycemia, etc.[8]

Quick implementation of proceedings is very important here - we can avoid or diminish many negative effects of toxic alcohol activity. However, in some cases there can occur distant complications due to the intoxication, such as kidney damage and renal failure. The definitive therapy for symptomatic patients poisoned by toxic alcohols is hemodialysis, which has been also done in our patient. It is crucial to start hemodialysis as soon as possible in the case of patients with metabolic acidosis. It helps to speed up purification of blood from ethylene glycole and its toxic metabolites and corrects the acid- base disorder.[1] Hemodialysis should be carried out until complete elimination of ethylene glycol and compensating for metabolic disorders, as in the presented case. It can take up to even 2-3 weeks to continue the treatment until normal kidney function returns. Too late diagnosis of poisoning may lead to death. Our patient was admitted to the toxicology department with previously mentioned symptoms which are characteristic for ethylene glycol poisoning. The patient has been treated pharmacologically and has been given specific antidote. Due to the ethylene glycol intoxication, metabolic acidosis and increasing parameters of kidney failure the patient also underwent hemodialysis. According to our patient's results we know that she has been intoxicated not only with ethylene glycol but also with benzodiazepines. Benzodiazepine (BDZ) overdose symptoms include ataxia, impaired balance, slurred speech and CNS depression. However combining those two substances can me particularly dangerous. Symptoms of ethylene glycol poisoning observed in our patient could be intensified by the toxic effect of benzodiazepines because BZD augment alcohol effect synergistically.[5] It is worth emphasizing that an acute BZD overdose can result in significant respiratory and central nervous system depression and it is even more dangerous if used in combination with other drugs or alcohol.[9,10] Our patient has been diagnosed quickly and properly. Thanks to effective treatment applied the patient survived and and distant complications were avoided.

Conclusions

The ethylene glycol intoxication is one of the most serious cases in toxicological practice due to very high percent of mortality reaching 30%.[11] It often occurs among patients addicted to alcohol. It may lead to multi- organ damage. In the clinical aspect the early diagnosis and adequate therapy can meaningfully reduce the mortality caused by ethylene glycol poisoning. It is based on the interview, a set of syndromes and biochemical tests and targeted toxicological tests. It is crucial to do supportive measures to combat shock and respiratory distress as well as to rectify the metabolic acidosis. Next important aspect is to improve the level of knowledge of students and doctors in terms of dealing with the patient poisoned by ethanol glycol. According to statistics and knowing how often the alcohol poisoning happens it is necessary to have knowledge in this field, be fluent in management and methods of treatment in such cases.

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