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Disulfiram-alcohol reaction in 49 year old patient

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Abstract

Alcoholism is a disease in which person lose control over the amount of consumed alcohol. The problem of alcohol abuse in Poland concerns about 9% of the population. One of the treatment methods is disulfiram therapy, which is associated with the risk of disulfiram-alcohol reaction. Due to many negative reports of side effects and questionable efficacy, this drug is nowadays rare used.
We present a case of a patient who had a disulfiram reaction due to alcohol consumption during disulfiram therapy.

Key words: alcoholism, disulfiram, DER

Introduction

Alcoholism is a disease in which person lose control over the amount of consumed alcohol.
It is estimated that in Poland the problem of alcoholism and harmful drinkers affects approximately 3.3 million people, which is approximately 9% of the population. Only

about 150 000 addicts undergo alcohol treatment. The most important treatment method is to maintain abstinence, which is attempted to achieve through various forms: psychotherapy, support groups or pharmacotherapy. Disulfiram is nowadays rarely used [3].
Effect of disulfiram on the body was for the first time observed in the 1930s. At that time, the workers of the vulcanization industry who were exposed to this substance felt ill shortly after drinking alcohol. This symptoms included flushing, nausea, dizziness, headache and hypotension. In the later years, a number of these symptoms were called the disulfiram reaction [4]. For medical purposes, disulfiram was first used at the turn of 1940/1950 and was the first drug registered by the FDA (Food and Drug Administration) in USA for the treatment of alcoholism [5].
We present a case of a patient who had a disulfiram reaction due to alcohol consumption during disulfiram therapy.

Case report

A 49 year old man, who had been addicted to alcohol for many years, was admitted to the Clinical Toxicology and Cardiology Department due to progressive weakness, tachycardia, anxiety, dyspnoea, hotness, headache and palpitations. The interview showed that two weeks earlier, the patient had implanted a subcutaneous prolonged release tablet. In the past, the patient several times went on a rehab treatment, but quickly resigned and returned to addiction. Patient admitted to drinking alcohol on that day. The exact amount of drunk alcohol was unknown. He was in logical contact, circulatory and respiratory effective. In the examination hypertension (150/105 mmHg), tachycardia (HR=100/min), visible reddening of the upper half of the body were found. Laboratory tests revealed a concentration of ethanol- 3.24 g/l and indicators of liver damage (AST- 99 U/l, ALT 87 U/l). Basing on the history, clinical picture and laboratory tests, disulfiram reaction was diagnosed. During hospitalization iron preparation, vitamin C and multi electrolyte fluids were used to compensate electrolyte disturbances. After three days of hospitalization, the patient was signed off the hospital in a general good condition with the recommendation of attendance a rehabilitation treatment in a closed unit.

Discussion

Disulfiram works by blocking one of the routes of alcohol metabolism. After ingestion, ethanol is converted to acetaldehyde by alcohol dehydrogenase. The toxic aldehyde is then converted to less harmful acetic acid by the action of aldehyde dehydrogenase. This last transformation is blocked by disulfiram [6]. The scheme of action of the drug is shown in Figure 1. As a result, the concentration of acetaldehyde increases, which affects the central nervous system, inhibiting β-hydroxylase of dopamine and affecting the serotoninergic conduction. This

mechanism is responsible for symptoms from nervous system such as convulsions of psychosis. The high concentration of acetaldehyde also contributes to degranulation of mast cells and the release of histamine responsible for the heat and redness of the skin [7]. Possible effects of disulfiram reaction are shown in Table 1 [5]. The disulfiram-alcohol reaction usually starts 10 to 30 minutes after alcohol consumption and its intensity is proportional to the amount of alcohol consumed and the concentration of the disulfiram in the blood. Slight symptoms may appear at concentration of 0.05 g/l ethanol in the blood and a serious 1.25-1.5 g/l [5].

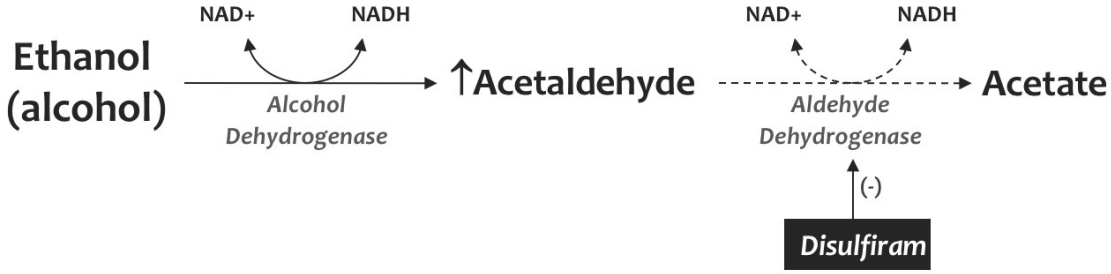

Figure 1. Disulfiram interaction in metabolism of alcohol.

Body Part Affected	Moderate symptoms	Severe symptoms
Body skin	Sweating Warmth and flushing, particularly on upper chest and face	None
Respiratory system	Hyperventilation Respiratory difficulty/dyspnea	Respiratory depression
Head, neck, throat	Acetaldehyde breath odor Blurred vision Head and neck throbbing Thirst	None
Stomach, digestive system	Nausea/vomiting	None
Chest, heart, circulatory system	Chest pain/palpitations Hypotension Tachycardia	Cardiovascular collapse Arrhythmia Myocardial infarction (in individuals with preexisting coronary artery disease) Acute congestive heart failure (in individuals with preexisting myocardial dysfunction)
Brain/nervous system	Vertigo Syncope Marked uneasiness Confusion	Seizures
Other	Weakness	Death

Table 1. Possible effects of disulfiram reaction

First clinical trials with disulfiram showed excellent results in most cases. However, nowadays some mistakes are pointed to these researches. They concern lack of control group or the absence of a blank test, which reduces the value of these experiments. In addition, initially, when disulfiram began to be used, the doses were significantly higher (1000 mg- 3000 mg) than at present (250 mg- 500 mg). It resulted in more reports of toxicity, psychosis episodes and even death caused by disulfiram reaction that time [8-10].

The accumulation of toxic metabolites of ethanol results in life-threatening symptoms. So, the treatment of disulfiram is based on the fear of patient against adverse symptoms after drinking alcohol. This mechanism is supposed to be responsible for maintaining abstinence. Providing organism even the least alcohol dose may cause unpleasant symptoms that can even lead to death [3]. However, it often happens that a large group of addicted patients discontinues disulfiram treatment before planned drinking, while others try low doses of alcohol to test their severity and whether a disulfiram reaction will occur at all. These are one of the main reasons for aborting treatment and abstinence [11]. In addition, it is believed that 25% to 75% of patients who are in the course of disulfiram therapy consume alcohol [12].

In Poland two forms of disulfiram are registered to use: oral tablets, and prolonged release tablets for subcutaneous implantation. Disulfiram implants are a highly-chosen method of alcoholism treatment and are used in specific cases. A questionnaire survey carried out by the State Agency for Prevention of Alcohol Related Problems [13] shows that disulfiram in oral form is used in almost 30% of cases and the form of implants in just over 7% of all medications available in treatment of alcoholism in Poland. As it is shown above, subcutaneous form is used quite rarely, which may be associated with low efficacy of this therapy [3]. Bergstrom et al. [14] claim that classical implantation of disulfiram does not provide enough level of medicine in the blood that would ensure the occurrence of disulfiram-alcohol reaction. In addition, according to Wilson's study [15] there are no clear differences in the frequency and manner of drinking among patients who were implanted with 800 mg, 1200 mg or 1600 mg of disulfiram. However, it has been proven that doses of over 1000 mg significantly increase the risk of local complications (abscesses).

In the presented case, patient had a concentration of alcohol in blood at level of 3.24 g/l. Due to lack of standards for monitoring the concentration of disulfiram in the blood, the level of the drug at the time of alcohol consumption can not be clearly determined. The patient presented typical symptoms of disulfiram syndrome. Fortunately, the symptoms did not pose a direct threat to life and due to performed treatment, symptoms resolved and patient's condition stabilized.

Indications for disulfiram-alcohol reaction among alcohol addicts are following: 500-

1000 mg of vitamin C and 40-100 mg of iron i.v. This procedure immediately interrupts the action of aldehyde dehydrogenase and the symptoms associated with excessive level of acetaldehyde [16].

It must be noted that disulfiram should not be assigned as monotherapy of alcoholism. It may be an addition in psychosocial therapy to reduce desire of drinking (as a negative stimulus), in a group of patients who are determined to maintain abstinence, agree to take medications and have no contraindications to its use. It is also believed that in order to reduce number of complications, patients should be accurately qualified for treatment, eg. by eliminating people with seizures, suicidal attempts of cardiovascular disease [11].

In conclusion, disulfiram therapy is not an alternative, but one of the elements of comprehensive treatment of an addict. Numerous reports of side effects and of questionable effectiveness, result in the increasingly rare use of disulfiram and displacement by newer drugs with fewer side effects. Disulfiram therapy may be considered and used in a well-defined group of patients including indications (i.e. motivation and strong will), contraindications, monitoring of sobriety and regularity in taking medicine.

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