Disulfiram-induced seizures with convulsions in a young male patient: 
A case study

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ABSTRACT

Disulfiram is the aversive therapeutic agent which has been used to treat alcohol dependence more than 50 years. It causes the complications like neurological toxicity, postural hypotension, circulatory collapse, mental confusion, etc. The aim of our study was to report a rare case of disulfiram-induced seizures in a patient of alcohol dependence syndrome. This case study is about a 35-year-old male patient who had one episode of seizures during treatment with disulfiram.

Key words: Alcohol dependence syndrome, disulfiram, seizures

INTRODUCTION

Disulfiram is an aldehyde dehydrogenase inhibitor which is useful in maintaining abstinence from alcohol in patients of alcohol dependence syndrome. It inhibits the enzyme called aldehyde dehydrogenase, probably after conversion into the active metabolite. In addition to the physical symptoms associated with the concomitant use of alcohol, disulfiram may lead to adverse drug reactions when used alone, which are flushing, throbbing headache, perspiration, etc. Disulfiram has been used as an aversion technique in chronic alcoholics who have been motivated and sincerely desire to leave the habit. According to de Melo and Lopes, if patient has a family history of psychosis, disulfiram-induced psychosis is more likely due to genetic background. There are very few case reports regarding disulfiram-induced seizures. However, because of its adverse drug reactions and its dangerous effects with alcohol, it has to be prescribed with caution and always monitored by medical supervision.

CASE REPORT

A 35-year-old male patient dependent on alcohol for 10 years is currently abstinent from alcohol since 20 days. He was detoxified in the hospital for alcohol dependence and was instituted with disulfiram 250 mg twice daily for initial 5 days then once daily for 10 days. While patient was in home, he was completely abstinent from alcohol as confirmed by his mother and also investigation of serum gamma-glutamyl transferase levels were also 15 IU/L suggestive of no recent intake of alcohol. Patient’s mother reported that the patient had one episode of loss of consciousness with the movement of limbs suggestive of generalized tonic-clonic seizures. There was no past history or family history or childhood history of seizures. No abnormalities were found on physical examination and neurological examination. Computed
tomography scan of the brain revealed no abnormality and electroencephalography (EEG) revealed generalized spike wave activity during photic stimulation. Disulfiram was discontinued, then there was no further history of seizures for 1-month. Investigations such as complete blood count, urea, creatinine, serum electrolytes-sodium, potassium, chloride, hepatic transaminases, blood sugar, urinanalysis, thyroid function, and uric acid levels were all within normal limits ruling out other causes of seizures.

**DISCUSSION**

Disulfiram (tetraethylthiuram disulfide) is a quaternary ammonium compound, it has been used for more than 50 years as an aversion therapeutic agent in the treatment of alcohol dependence.[3] Disulfiram acts as a deterrent agent against drinking alcohol. It is used to manage the impulsive drive to drink in patients with alcohol dependence, and it is recognized for its physical and psychological effects. Other significant action of disulfiram is its inhibition of dopamine-β-hydroxylase causing an increase in the concentration of the dopamine in the mesolimbic system. In addition to the physical symptoms associated with concomitant use of alcohol, disulfiram may lead to adverse reactions when used alone, including psychosis. However, it is estimated that 25–75% of patients under disulfiram treatment have concomitant alcohol consumption, and produces sensitivity to alcohol, leading to an unpleasant reaction called ethanol-disulfiram reaction (aldehyde syndrome), caused by the accumulation of acetaldehyde through the inhibition of the enzyme acetaldehyde dehydrogenase with histamine release.[1] Our patient has got the seizures with convulsions during disulfiram therapy. On EEG patient showed photoparoxysmal response with spike wave activity but no other epileptic form discharges; however, patient did not have any history of past or family history of epilepsy. Disulfiram causing seizures are very rare but reported.

Basal ganglia are one of the major targets of disulfiram neurotoxicity which may involve carbon disulfide (CS₂) metabolite. The most important toxic metabolites are diethyldithiocarbamate (DDC) and its metabolite CS₂. DDC chelates copper, thus impairing the activity of dopamine beta-hydroxylase, an enzyme that catalyzes the metabolism of dopamine to norepinephrine. In this way, DDC causes depletion of presynaptic norepinephrine and accumulation of dopamine, so increasing the levels of dopamine and reducing those of norepinephrine in the mesolimbic region.[4] Disulfiram and DDC increase the release of glutamate from striato-cortical synaptic vesicles, both in vitro and in rats, suggesting yet another possible mechanism for DDC-mediated neuronal damage.[5] Acute exposure to CS₂ causes rapid onset of headache, confusion, nausea, hallucinations, delirium, seizures, coma, and potentially death.[4]

Many case studies on disulfiram have been reported, and only one study reported disulfiram causing seizures with convulsions. Michael A Peszke reported a case of seizures with convulsions in a patient on disulfiram therapy, who was abstinent from alcohol over a period of 6 months. Then seizures occurred in a context of clinical delirium over a 5–6 weeks period of time.[6] Liddon and Satran, in a study of 52 patients described to have disulfiram psychosis, actually only five were, in fact, psychotic and the others had toxic delirium but not seizures and convulsions.[6]

**CONCLUSION**

Apart from disulfiram alcoholic reaction, evidences suggest that disulfiram when used alone can cause various effects and adverse effects including seizures, which are rare but needs to be considered. This would open up areas for further research on mechanisms by which disulfiram causes seizures with convulsions and about prevention.

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**Conflicts of interest**

There are no conflicts of interest.

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