OJPAS
Open Journal of Psychiatry & Allied Scienes (2015)
6: 143-5.doi: 10.5958/2394-2061.2015.00013.0

CASE

Catatonia induced by disulfiram

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Abstract

Catatonia is a clinical syndrome with varieties of psychomotor abnormalities of retardation and excitement. It can occur both in psychiatric and medical conditions. The aetiology of catatonia has not been fully described. Many researchers suggest that catatonia can occur due to deficiency of cortical gamma-aminobutyric acid (GABA) which is an inhibitory neurotransmitter. Disulfiram is an agent that is being used in the treatment of alcohol dependence by its aversive effect. It has been seen that disulfiram is one of the causes of catatonia. This paper aimed to report a case of catatonia induced by disulfiram with no past history of any psychiatric or medical illness.

Goswami HK, Bhuyan D, Talukdar B. Catatonia induced by disulfiram. Open J Psychiatry Allied Sci. 2015;6:143-5. *doi: 10.5958/2394-2061.2015.00013.0*

Keywords: Alcoholism. gamma-Aminobutyric Acid. Benzodiazepines.Motivation.Adverse Drug Reaction.

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Received on 25 October 2014.Revised on 19 December 2014.Accepted on 23 December 2014.

Catatonia is a clinical syndrome with varieties of psychomotor abnormalities of retardation and excitement. It can occur both in psychiatric and medical conditions. It is mostly characterised by mutism, stupor, refusal to eat or drink, posturing, and excitement or hypokinesia.[1]

The aetiology of catatonia has not been fully described. Many researchers suggest that catatonia can occur due to deficiency of cortical gamma-aminobutyric acid (GABA) which is an inhibitory neurotransmitter.[2] This is the reason why benzodiazepine is used in catatonia, as it increases the GABA level. Another suggested mechanism is the hyperactivity of glutamate, which is an excitatory neurotransmitter.[3]

Disulfiram has been used in the treatment of alcohol dependence for more than 40 years. It is tetra-ethylthirumdisulfide, which is a creamy white, almost odourless bitter crystalline powder.[4] It is given in a dosage of 250 mg per day with a maximum dosage of 500 mg per day.[5] Disulfiram may cause the accumulation of acetaldehyde metabolised from alcohol in toxic amounts, by inhibiting the acetaldehyde dehydrogenase enzyme. It also acts on the dopaminergic system; diethyldi-thiocarbamate, the breakdown product of disulfiram, blocks the dopamine β-hydroxylase enzyme and inhibits the conversion of dopamine into noradrenaline, and may cause neuropsychiatric side effects such as delirium, paranoid conditions, lack of concentration, memory impairment, depression, ataxia, and dysarthria.[6] Here, we are presenting a case of catatonia induced by disulfiram.

The case

A 54 years old male from Sivsagar district of Assam, who was a known case of alcohol dependence with a history of treatment on several occasions in the past presented to us with symptoms of alcohol withdrawal in the month of November 2013. He was hospitalised and detoxified with tablet oxazepam 60 mg which is gradually tapered over a period of ten days along with injection thiamine 100 mg, tablet ursodeoxycholic acid 300 mg, and intravenous (IV) fluid with glucose infusion. On examination, there was no evidence of jaundice and neuropathy. His liver function test (aspartate amino-transferase [AST]: 187 IU/L, alanine aminotransferase [ALT]: 103 IU/L, gamma glutamyltransferase [GGT]: 105 IU/L), ultrasonography of abdomen, and renal function test reports were within normal limits. Patient was assessed and was found to be motivated, and was willing to take tablet disulfiram when options were given. If the individual is given motivational intervention to cease consuming alcohol, the chances of accepting to stop the drinking habit are more likely.[7] Subsequently, tablet disulfiram 250 mg was started in once daily dose after obtaining proper consent and patient was discharged after two days of initation of antabuse therapy. After ten days, patient was brought to us with the history of not talking to anyone, withdrawn behaviour, and decrease oral intake.

Table: The Naranjo adverse drug reaction (ADR) probability scale; To assess the adverse drug reaction, please answer the following questionnaire and give the pertinent score

		Yes	No	Do not know	Score
1	Are there previous *conclusive* reports on this reaction?	+1	0	0	+1
2	Did the adverse event occur after the suspected drug was administered?	+2	-1	0	+2
3	Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered?	+1	0	0	+1
4	Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	+2
5	Are there alternative causes (other than the drug) that could have on their own caused the reaction?	-1	+2	0	+2
6	Did the reaction reappear when a placebo was given?	-1	+1	0	0
7	Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9	Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?	+1	0	0	+1
10	Was the adverse event confirmed by any objective evidence?	+1	0	0	0
				Total	9

His general examination and systemic examination revealed no abnormality. However, mental state examination (MSE) revealed mutism, waxy flexibility, and posturing. Liver function test, renal function test, serum electrolytes, ultrasonography of whole abdomen, and computed tomography (CT) scan brain reports were within normal limits. On further enquiry, patient's wife reported that he was prescribed with tablet disulfiram earlier by a local psychiatrist two years back. At that time also, he had similar kind of symptoms following initiation of the therapy for which they had contacted the psychiatrist over phone who asked them to stop tablet disulfiram and to bring the patient to his clinic. But, they did not visit that psychiatrist after that as following stoppage of the tablet the symptoms improved within three days. She lamented that she had forgotten to mention this incident when she was asked for any past history of side effect while on any antabuse and anticraving therapy prior to initiation of tablet disulfiram. The Naranjo adverse drug reaction (ADR) probability scale was applied to assess the adverse drug reaction and score was found to be nine (Table), and it signifies that disulfiram is the causal factor for catatonia. So, patient was diagnosed as a case of catatonia induced by disulfiram. Tablet disulfiram was stopped, and he was prescribed injection lorazepam slow IV thrice daily and intravenous fluid, and his vitals were monitored regularly. Four days after treatment, his catatonic signs were reduced and he started to take orally. He was discharged on tablet amisulpiride 100 mg once daily and tablet baclofen 60 mg in two divided doses. Later, on two subsequent follow ups, there was no catatonic sign and patient was found to be on abstinence.

The Naranjo adverse drug reaction (ADR) probability scale:The Naranjo criteria classify the probability that an adverse event is related to drug therapy based on a list of weighted questions, which examine factors such as the temporal association of drug administration and event occurrence, alternative causes for the event, drug levels, dose–response relationships, and previous patient experience with the medication. The ADR is assigned to a probability category from the total score as follows: definite if the overall score isnine or greater, probable for a score of five to eight, possible for one to four, and doubtful if the score is zero. The Naranjo criteria do not take into account drug-drug interactions. Drugs are evaluated individually for causality, and points deducted if another factor may have resulted in the adverse event, thereby weakening the causal association.

Discussion

This paper reported a case of catatonia induced by disulfiram. In this case, the patient was alcohol dependent and after detoxification with tablet oxazepam he was started with tablet disulfiram for deaddiction. Ten days after disulfiram therapy, he developed catatonia. There are many hypotheses which explain that disulfiram is one of the causes of catatonia.

In a study of Balaban*et al*.,[8] patient on alcohol dependence after treatment with disulfiram developed symptoms which first affected the cognitive functions, then paranoid symptoms emerged, and 36 hours after the clinical manifestation, the patient was in catatonia. There are many studies where itching and puffiness are mentioned after disulfiram therapy.[9]

In a study of Laplane*et al*.,[10] they reported three cases of disulfiram induced Parkinsonism and frontal lobe-like syndrome. Symptoms developed either after an acute high dose of disulfiram (one case) or after several

days to weeks of disulfiram treatment (two cases), and persisted over several years in two patients. In our case, patient presented with waxy flexibility, posturing, and mutism ten days after disulfiram therapy, and dose of disulfiram was 250 mg once daily dose. In their study, they also found bilateral lesions of the lentiform nuclei on CT scan brain report. These observations suggest that basal ganglia are one of the major targets of disulfiram neurotoxicity. The mechanisms of the lesions of basal ganglia may involve carbon disulfide toxicity.[10] However, in our case CT scan brain finding was normal.

Maccari*et al*.[11] reported a study on eight abstinent cases where direct disulfiram-induced toxicity on the central nervous system was observed in whom a disulfiram-ethanol reaction had been excluded. They mentioned that risk is increased when: 1) excessive amounts of the drug are ingested; 2) the patient is already suffering from a major psychiatric illness; 3) the patient has anatomical brain lesions.

Weddington*et al*.[12] conducted a study where they found disulfiram encephalopathy as a cause of the catatonia syndrome. In our case, there was no such finding and patient developed catatonia on 250 mg disulfiram once daily dose.

Since disulfiram plays an important role in alcohol deaddiction in present day, it's long term usage demand safety profile by close monitoring and awareness between physicians while treating cases of alcohol dependence.

Source of support: Nil. **Declaration of interest**: None.

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