Short Communication

Disulfiram Induced Mania — A Case Report

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Disulfiram has been most widely used in patients suffering from alcohol dependence. When taken along with alcohol it can cause various side effects like flushing, drowsiness, rashes, hyperventilation, palpitations etc. Mania due to Disulfiram is an uncommon side effect and there are only a few reports of it. We hereby report a case of the development of Mania in an individual with alcohol dependence following 2 months of treatment with a therapeutic dose of Disulfiram. Before the onset of mania, the patient was abstinent from alcohol for about 2 months, which made substance-induced mania unlikely. The possible mechanism for this is the dopamine hypothesis which suggests that Disulfiram inhibits dopamine-Beta-hydroxylase which is responsible for the conversion of dopamine to Nor-adrenaline and increases the dopamine level which is responsible for psychotic and mania symptoms. This possibility of Disulfiram induced mania should be assessed whenever clinicians encounter patients with dual diagnosis, as this might change the management as such.

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Disulfiram which is also known as tetraethylthiuram disulfide is commonly used for patients suffering from alcohol dependence for de-addiction treatment for the past 50 years. Disulfiram inhibits aldehyde dehydrogenase which affects the metabolism of alcohol and increases the level of acetaldehyde in the blood. There are many adverse reactions reported due to Disulfiram which include dermatological, hepatological, neurological and psychiatric conditions like psychoses, confusion, delirium, loss of memory, mania. Among the psychiatric side effects, psychosis is more common than any other condition[1].

There is a known dopamine hypothesis that suggests that Disulfiram inhibits the dopamine-Beta-hydroxylase which converts dopamine to Nor-adrenaline and increases the dopamine level which is responsible for psychotic and manic symptoms[2]. By reviewing the relevant literature, we came across a few case reports about psychotic and mood disorders caused by Disulfiram. However, the prevalence of Disulfiram induced mania as such is unknown and rare. In a review, after a study of 52 patients, it was reported that 4 out of 52 patients reported mania or hypomania symptoms on Disulfiram[3]. Murthy *et al*, 1997 followed up 51 patients with alcohol abuse for 4 weeks receiving 250 mg of Disulfiram twice daily and found out that Mood disorder developed in 6 patients. The authors also found out that the mood symptoms resolved shortly after discontinuation of Disulfiram[4]. In one of the case reports authors have suggested the possibility of manic episodes as a consequence of Disulfiram ethanol reaction[5].

In this case report, we describe the presentation of 39 yrs old male who developed mania without any psychotic symptoms after administration of a therapeutic dose of Disulfiram. Informed consent was obtained from the patient.

Case Report

A 39-year-old married male, educated up to BA 1st year, auto driver cum fruit seller, Buddhist by religion, living in a joint family, belongs to a low socio-economic status, resident of Wardha.

He presented with an illness duration of 12 years, with precipitating factor of financial stress, a predisposing factor of mental illness in the family, illness was insidious in onset, continuous and fluctuating in course with alcohol use in the form of craving, tolerance, withdrawal, use despite harm, the usual amount being 500ml- 1L in a day of the country made liquor, the last intake of alcohol was 2 months back.

His history suggested 1 episode of sadness of mood, irritability, death wishes with an aborted suicide attempt under the influence of alcohol 1 year

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back. From the last 6 days patient presented with a new set of complaints with abrupt onset and continuous course characterized by irritability, big talks, over talkativeness, smiling to self, aggressive behaviour, sleep disturbance.

The patient was taking treatment for de-addiction from a private psychiatrist for 2 months. For 2 months patients received tab. Sodium valproate 200mg HS, tab. Disulfiram 250mg OD initially then gradually over 15 days increased to 500mg in divided doses, tab. Olanzapine 5mg HS (poor compliance for olanzapine due to increased sedation). 2 days prior to admission in our psychiatry ward patient went to a private psychiatrist and received tab. Escitalopram 10mg in combination with Clonazepam. He consumed half tablet for 2 days only. There was no history of any other substance abuse. No history of any other medical co morbidities.

Family history was suggestive of Alcohol dependence in father and psychosis in elder sister. Personal history was suggestive of well adjusted pre-morbid personality. Physical and systemic examination was unremarkable; his haematological and biochemical indices were found within normal limits. MSE revealed uncooperativeness, aggressive behaviour, increased psychomotor activity, increased rate, amount, volume of speech, decreased reaction time, irritable affect, ideas of grandiosity, attention and concentration- arousable and ill sustained, insight being 2/5.

The patient was hospitalized and the possibility of Mania induced by Disulfiram (F30.8) was kept. All the medications patient received from outside were stopped including Disulfiram. Young Mania Rating Scale (YMRS) was applied on the day of admission and the score was 26 (moderate mania).

Tablet Sodium Valproate was started at 500mg twice a day and along with this patient was kept on Inj. Haloperidol 10mg and Inj. Promethazine 50mg IM BD for the initial 2 days in view of his irritable behavior. After that Tablet Quetiapine 50mg BD was added and Tab. Sodium Valproate continued at 1gm/day. The patient gradually improved within 4 days after stopping Disulfiram.

No evidence of alcohol withdrawal was seen (CIWA-Ar at baseline), so detoxification was not done and patient was put on thiamine supplementation. No signs and symptoms of disulfiram-ethanol reaction were observed during hospitalization. The patient was discharged within 7 days and before discharge Young Mania Rating Scale (YMRS) was again applied and the score came to be 5 (Normal) and On further follow-up after 15 days patient was asymptomatic and abstinent to alcohol.

Discussion

Our patient was a young male who developed manic features without any psychotic symptoms who was on continuous treatment with Disulfiram while completely abstinent on alcohol for 2 months.

Because of the 2 months alcohol abstinent period, we attribute it is not due to Disulfiram-alcohol reaction but due to Disulfiram itself. The initial recommended dosage of Disulfiram usually is 500 mg per day for the first 1 or 2 weeks, which should be followed by a maintenance dosage of 250 mg per day[6]. The development of Disulfiram related mania or psychosis is usually seen on either therapeutic or higher than recommended dosages[1,6,7]. Our patient developed mania symptoms with the dose of 500 mg per day of Disulfiram. Rapid response to the mood stabilizer and low dose Quetiapine after discontinuation of Disulfiram (within 3-4 days of stopping) also suggests that the manic episode was secondary to Disulfiram use.

Naranjo Adverse Drug Reaction probability scale was applied to the patient. This scale explains the probability of an adverse event that is related to drug therapy and is based on a list of ten questions[8,9]. In this patient, the total score was 7. Hence, Disulfiram can be considered as the probable cause of mania in our patient.

A study reported irritability (1.9%) and over talkativeness (3.8%) as psychiatric side effects which our patient has[5,10]. In one similar case report of 40yrs old male developed mania on the maintenance dose of Disulfiram and improved after stopping the drug[11]. As per the literature review of 52 patients, the development of mania symptoms was seen only in 4 patients on Disulfiram which also suggests that the development of only mania symptoms is less as compared to mania with psychotic symptoms or psychosis[3]. The risk factors for the development of Disulfiram related psychiatric symptoms include a past history or family history of psychiatry illness which our patient has[12].

What is unique in this case is that patient developed mania without any psychotic symptoms and there were only a few case reports on developing only manic symptoms due to Disulfiram use.

Finally, we would like to recapitulate that Disulfiram induced mania is a rare entity and due to these reports, a clinician must not restrict themselves to prescribe Disulfiram, where it is otherwise required and should recognize the risk factor before prescribing.

Declaration of patient consent :

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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