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CASE REPORT

Mania as a Result of Using Disulfiram at the Prescribed Amount During the Fifth Month of Maintenance Therapy: A Case Report

Ali İnaltekin[1], **İbrahim Yağcı**[2]

[1]Department of Psychiatry, Oltu State Hospital, Erzurum, Turkey
[2]Department of Psychiatry, Harakani State Hospital, Kars, Turkey

ORCID IDs of the authors: A.İ. 0000-0003-0933-0308, İ.Y. 0000-0003-0755-2695.

Main Points

- This case is the first instance of a new-onset manic episode accompanied by psychotic symptoms in an alcoholic patient following a 5-month treatment with disulfiram.
- The manic episode occurred at the recommended dose as a result of long-term maintenance treatment.
- The manic episode occurred without dose change.

Abstract

Disulfiram is a medication that raises blood acetaldehyde levels by inhibiting aldehyde dehydrogenase. It has been reported that taking disulfiram can cause psychosis or mania. There are only a few case reports about mania in the literature. We introduce this case of disulfiram-induced mania without dose adjustment, whereas continuing maintenance alcohol addiction treatment with disulfiram at the prescribed amount in a patient with no psychiatric history. Mr KA, a 57-year old patient with a history of 25 years of alcohol consumption, had stopped drinking 5 months ago and had been taking disulfiram (500 mg/day) for 5 months. During treatment, he was admitted to the outpatient clinic with complaints of decreased need for sleep, increased speech, and psychomotor activity, in particular for 4 – 5 days. During the psychiatric examination, it was discovered that the rate of speech had increased, that flight of ideas was present, and that the affect was cheerful and nervous. There was an increase in self-esteem and grandiose delusion. The examination revealed psychomotor agitation. The patient was admitted to the hospital for examination, follow-up, and treatment. Mania was observed. Treatment with valproate 1000 mg/day and risperidone 4 mg/day was planned. The patient showed no psychotic or manic symptoms while continuing outpatient clinic controls. Rare complications, such as manic episodes, might occur even in patients receiving the prescribed amount and long-term disulfiram treatment.

Keywords: Alcohol, alcohol dependence, dependence, drug side effects, mania

Corresponding Author:
İbrahim Yağcı,
E-mail:
ibrahimyagci53@hotmail.com

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Introduction

Disulfiram was the first drug to be administered in the treatment of alcohol addiction, and it is still used today. Disulfiram, which is involved in the breakdown of alcohol, inhibits the dehydrogenase enzyme and causes acetaldehyde accumulation (Gaval-Cruz & Weinshenker, 2009). This accumulation has a deterrent effect on alcohol consumption, assisting patients in reducing its consumption (Gaval-Cruz & Weinshenker, 2009). There are numerous hepatological, dermatological, neurological, and psychiatric side effects associated with disulfiram (Christensen et al., 1984; Mohapatra et al., 2015; Tartara et al., 2013). Confusion, forgetfulness, and psychosis are psychiatric side effects (Mohapatra & Rath, 2017; Murthy & Praveenlal 1988). Disulfiram's main metabolite, diethyldithiocarbamate, inhibits dopamine-betahydroxylase, an enzyme that catalyzes dopamine metabolism (Ashok et al., 2017). This inhibition has been linked to psychosis and mania. Furthermore, as far as we

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can reveal from the literature, there are only a few cases of manic episodes following disulfiram use (Ceylan et al., 2007; Li & Shen 2008; Lin et al., 2020; Masali et al., 2009). In this article, we introduce a 57-year-old male patient who developed manic episodes upon taking disulfiram and had no psychiatric history.

Case Presentation

KA is a married, working, 57-year-old male patient who was brought to the psychiatric outpatient clinic by his wife and children. The interview with the patient and his family revealed that he had less need for sleep in the last 4 – 5 days, that he started talking more than usual, and that his psychomotor activity had increased. The patient claims that "he administers the president and ministers, he can call them and get them to do whatever he wants."

The patient, who had been drinking for 25 years, had a history of three standard units of alcohol consumed 5 days a week. The patient began taking 500 mg/day disulfiram (Antabus tablet) with a doctor's prescription 5 months before hospitalization in order to quit drinking, as agreed upon by his wife. The patient stated that he had not consumed alcohol in the previous 5 months and that he was still taking disulfiram at a dose of 500 mg per day. This data was also confirmed by the patient's wife.

During the psychiatric examination, it was discovered that the rate of speech increased, there was a flight of ideas, and the affect was cheerful, but he was nervous at intervals with unstable characteristics. There was an increase in self-esteem and grandiose delusion. Furthermore, psychomotor agitation was observed during the examination, and he reported that his sleep was reduced but vigorous. The Young Mania Rating Scale was used, and the patient received 40 points. The patient was thought to be experiencing a manic episode.

The patient's disulfiram treatment was discontinued upon admission to the psychiatric service. The patient's physical and neurological examinations, as well as blood tests, revealed no pathology. The patient had no family history of affective disorders. There were no signs of alcohol withdrawal or a disulfiram – alcohol reaction. The magnetic resonance imaging of the brain was normal. The urine substance screening test came back negative. To control the symptoms of manic episodes, valproate 500 mg/day and risperidone 2 mg/day were prescribed. The drug doses were increased, with valproate being increased to 1000 mg/day and risperidone being increased to 4 mg/day. There were no drug side effects observed. The Young Mania Rating Scale was re-applied and scored as 10 points on the fifth day of hospitalization. The patient's outpatient treatment was continued with good social support, and he was called for outpatient control at regular intervals. The patient's symptoms of manic attack improved significantly after 2 weeks of valproate and risperidone treatment, and no abnormal mood or psychotic symptoms were observed in his subsequent follow-up. Written informed consent of the patient was obtained for publishing a scientific article.

Discussion and Conclusion

It has been reported that a dose of 250 mg for disulfiram used in the treatment of alcohol addiction is rational and that if the patient consumes alcohol and there is no disulfiram – alcohol reaction, the dose can be increased to 500 mg (Fuller & Gordis, 2004). As far as we know, this is the first instance of a new-onset manic episode accompanied by psychotic symptoms in an alcoholic patient following a 5-month treatment with disulfiram with the recommended dose and without dose change. In our case, unlike in other case reports, the manic episodes occurred at the recommended dose as a result of long-term maintenance treatment. In the case report presented by Ceylan et al., the manic episode developed as a result of the use of disulfiram at a dose up to 1500 mg higher than the recommended dose. In a scenario similar to this one, the dose of disulfiram was increased to 1500 mg, and delirium and subsequent manic episodes were reported (Li & Shen, 2008). In another report, a 2-month treatment with 200 mg of disulfiram at a lower dose than suggested resulted in manic episodes (Li & Shen, 2008). Manic episodes developed after a month of use with 500 mg in a case report from our country (Maşalı et al., 2009).

Even though the average age of onset for bipolar disorder ranges from 20 to 30 years, it is more common in the early 20s (Pini et al., 1995), but our patient was 57. A number of studies have looked into bipolar rates based on sociodemographic factors, and there is evidence that they are more common in low-income, unemployed, and unmarried people, though the results are inconsistent, as is family history in general (Mortensen et al., 2003; Tsuchiya et al., 2003). Our patient was married with a steady job and income. As a result, our patient lacked risk factors for bipolar disorder.

Dopamine-betahydroxylase inhibition is the mechanism of action of disulfiram, which may cause manic episodes and psychosis. An excessively rapid increase in dose or an increase above the suggested total dose, impaired liver function, concurrent use of dopaminergic drugs, or misuse of psychoactive substances are all risk factors for the development of psychotic symptoms associated with disulfiram (Mackie & Clark, 1994, Mohapatra & Rath, 2017). Our patient was taking disulfiram at the prescribed amount; no dose adjustments were made. The patient did not consume any drugs or psychoactive substances other than disulfiram, and his liver function tests were normal. These findings support the link between disulfiram use and the onset of manic symptoms in our patient.

Disulfiram was immediately discontinued in this patient, and valproate and risperidone were started to treat the manic episode. Because the discontinuation of one treatment and the initiation of another treatment occur concurrently, it is unclear whether healing is associated with treatment discontinuation or initiation. On the other hand, this manic episode could be the first episode of bipolar disorder that is unrelated to the use of disulfiram. However, considering the age of onset and risk factors as epidemiological features of bipolar disorder, the probability of developing a manic episode as a result of disulfiram increases.

In this case report, we describe a case of manic episode caused by disulfiram at the prescribed amount and after long-term use. Even though disulfiram-induced manic episodes have been reported in the literature, no late-onset manic episode has been reported for as long as ours. As the first case, we assume that our case will contribute to the literature. This case highlights the significance of this uncommon complication, even in patients receiving the prescribed amount and long-term disulfiram therapy.

Informed Consent: Written informed consent of the patient was obtained for publishing a scientific article.

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