

Case Series

Practice of Covert Administration of Unprescribed Disulfiram in Madhya Pradesh — A Case Series of Disulfiram-induced Psychosis

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Abstract

Background : Disulfiram, an alcohol-aversive agent, is known for its role in alcohol addiction treatment. However, its unsupervised use poses significant risks, including the development of psychosis.

Case Reports : This case report presents five patients from different tertiary care centers in Madhya Pradesh, India, who developed psychosis as a result of covert administration of unprescribed disulfiram. After discontinuing disulfiram, the patients were treated with antipsychotic medications, resulting in symptom resolution. This article emphasizes the legal and ethical concerns associated with unauthorized medication administration and highlights the need for public awareness, improved access to addiction treatment, and stricter regulations to prevent the unsupervised use of disulfiram.

Conclusion : Healthcare professionals should remain vigilant regarding such adverse effects and closely monitor patients receiving disulfiram.

Key words : Disulfiram, Induced Psychosis, Dopamine, Alcohol, Covert Administration.

Disulfiram, an Alcohol-aversive agent, functions by inhibiting the Acetaldehyde Dehydrogenase (ADH) enzyme, thereby leading to the accumulation of acetaldehyde, which elicits unpleasant physiological reactions upon alcohol consumption (Fig 1). Disulfiram has various documented side effects including gastrointestinal disturbances, hepatic complications, dermatological reactions and neurological manifestations¹⁻⁴. Psychosis following Disulfiram administration has been also reported in some cases Worldwide⁵⁻⁶. However, limited literature is available on disulfiram-induced psychosis, emphasizing the rarity of this adverse event. While disulfiram-induced psychosis is a rare occurrence, this case series highlights the development of psychosis in individuals who were covertly administered unprescribed disulfiram. We present a case series of five patients from different Tertiary Care Centres in Madhya Pradesh who developed psychosis as a result of the covert administration of disulfiram.

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Received on : 06/08/2023

Accepted on : 28/11/2023

Editor's Comment :

- Disulfiram-induced psychosis, caused by unauthorized self-medication, underscores the risks of unsupervised treatment and the need for professional involvement in addiction care.
- Addressing this issue requires public health campaigns, better access to formal treatment services, and stricter regulations on disulfiram dispensing, along with increased awareness among healthcare professionals to monitor patients closely for adverse effects.

CASE SERIES

Case 1 :

A 38-year-old married Hindu male brought to the psychiatric emergency with main complaints of disturbed sleep, suspiciousness and aggressive-violent behavior for two days. He developed a suspicion that someone was trying to harm him and was conspiring against his family. Furthermore, he would accuse others discussing him with malicious intent. These symptoms gradually worsened over the next few days, leading to increased agitation and behavioral disturbances. There was no significant history of any associated medical illness. There was no history of major psychiatric illness in past and family. On substance history, patient was found to be user of alcohol for 3 years but not at dependency level. He was on abstinence for 1-month due restricted accessibility to liquor during COVID lockdown. Patient's general and systemic examination were normal. He was fully conscious and well oriented to time and place. On bed side formal mental status examination findings were anxious and scanning behavior, increased psychomotor activity, difficult rapport establishment, Paranoid and referential delusions, and auditory

How to cite this article : Practice of Covert Administration of Unprescribed Disulfiram in Madhya Pradesh — A Case Series of Disulfiram-Induced Psychosis. Pathak U, Singh AK, Mishra R³, Shukla S. *J Indian Med Assoc* 2025; **123(3)**: 69-72.

hallucinations. Comprehensive psychiatric evaluation did not revealed any underlying primary psychotic disorder. No sign or symptoms suggestive of alcohol withdrawal and disulfiram-alcohol reactions were noted. His necessary routine investigations were within normal limits. Urine analysis was found negative for recent use of alcohol or other substance metabolites. The findings of EEG, MRI-brain and CSF examinations were within normal limits.

Later, Patient's wife disclosed that she had been secretly administering disulfiram tablets to him for the past 5 days as an attempt to help her husband maintain his alcohol abstinence, fearing that he would not willingly seek treatment. She admitted to obtaining the medication from pharmacy without a prescription. The disulfiram was discontinued immediately. Patient was initially managed with intramuscular haloperidol (5mg) and promethazine (25mg) and then tablet olanzapine 5mg at bedtime was started. Patient's psychotic symptoms started resolving within 2 days of discontinuation of disulfiram and completely vanished in 5-7 days. After the discharge patient was followed up for next 2 months and there was no recurrence of any psychotic symptom. Probable diagnosis disulfiram induced psychosis was made.

Case 2 :

A 26-year-old unmarried Hindu male, unemployed, came to the Outpatient Department of psychiatry with main complaints of disturbed sleep, hearing of unusual voices and fearfulness for 3-4 days. He began hearing unusual voices that were derogatory and abusive comments towards him. These voices were persistent, occurring throughout the day and caused him significant fear and distress. The patient denied any history of psychiatric symptoms or psychosis in the past and family. There was no significant medical or surgical comorbidity. Patient was user of alcohol for 2 years. He tried to stop alcohol many times and remained in abstinence for more than 2 months but relapsed every time. His last intake was 45 days before. Patient's mother revealed that she was admixing tablet disulfiram 250 mg/day in patient's food for past 5 days without his knowledge which she had bought from chemist without prescription on recommendation from relatives. Patient's consciousness and orientation were intact. No Significant abnormality was detected on clinical examination. Mental status examination findings were anxious affect and auditory hallucinations. He was admitted in the psychiatric ward and comprehensive psychiatric evaluation was conducted, ruling out any underlying primary psychotic disorder. The findings of routine laboratory blood investigations were within normal limits. Urine analysis was found negative for recent use of alcohol or other substance metabolites. EEG, MRI-brain, and CSF examinations were normal.

Disulfiram was stopped and olanzapine 5mg at bedtime was started. Patient recovered over the subsequent 4-5 days. He was discharged and advised to come in follow up in 10 days. In follow up patient's mental state was found

normal, olanzapine stopped and his probable diagnosis disulfiram induced psychosis was made. No recurrence of psychosis was noted in next follow ups for 3 months.

Case 3 :

A 36-year-old married Muslim male, unemployed, referred to the Tertiary Care Center with main complaints of disturbed sleep, self-muttering and suspiciousness for 3 days. He began muttering to himself, often engaging in prolonged conversations without any apparent external stimuli. He also displayed suspiciousness, believing that people were watching him and plotting against him. Family history and past history of psychiatric illness were insignificant. There was no significant medical or surgical comorbidity. Patient had chronic remitting and relapsing history of alcohol use disorder for 12 years. He was on abstinence for 1 month due to religious region during *Ramdaan* period. Physical examination, including neurological assessment, was unremarkable. He was conscious and oriented to time, place and person. Mental status examination revealed auditory hallucinations consisting of derogatory voices and persecutory delusion. Laboratory investigations, including complete blood count, electrolytes, liver function tests, and toxicology screen, were within normal limits. CT Brain and EEG showed no significant abnormalities.

Anamnesis obtained from his wife revealed that the patient had given up alcohol 40 days earlier and for 5 days had been on a tablet which they had bought on their own. The tablet was disulfiram 250mg. Wife was mixing a tablet per day in food of patient without awareness of patient. Considering the temporal connection between the consumption of disulfiram and the psychosis onset and ruling out other organic causes, a probable diagnosis of disulfiram-induced psychosis was established. Disulfiram was immediately stopped, and the patient was started on olanzapine 5mg bedtime. Within the following 2-3 days, his psychotic symptoms gradually diminished, leading to resolution. Olanzapine was stopped after 10 days and patient was followed up for 2 months. There was no re-emergence of psychotic symptoms.

Case 4 :

A 36-year-old male without any past history of neurological and psychiatric illness referred by medical specialist to psychiatry OPD with complaint of self-muttering, unprovoked aggression, suspiciousness against neighbours along with violent behavior for 3 days. There was history of opioid use for 2 years, however his last intake of opioid was 25 days ago due to unavailability of illicit opioid. On examination, there were no sign of withdrawal. On mental status examination, patient was oriented to time, place, person and referential thinking and auditory hallucinations was elicited. All routine investigations and Urinary drug screen were within normal limits. On further enquiry, it was revealed that the patients' wife had initiated medication surreptitiously (Disulfiram

1000mg/day for the last 5 days) for the treatment of substance use on advice of a local pharmacist. Provisional diagnosis of disulfiram induced psychosis was made. Patient was managed with injectable haloperidol for aggression and violent behaviors when required. Patient fully improved over 3 days after stopping disulfiram and subsequently discharged. He has been maintaining well on subsequent 6 months follow ups.

Case 5 :

A 30-year-old married but separated male, brought by family members with acute-onset fearfulness and self-muttering for 4 days. He had history of Alcohol and opioid dependence for the last 5 years. The patient was maintaining complete abstinence from substances for 3 months as he was kept in a deaddiction facility for 4 months. There was no history of any neuropsychiatric illness. About 3 days prior to the emergence of psychosis, he had started craving for alcohol after attending a social gathering. Hence, family members consulted a local non-registered medical practitioner who advised them to mix the tablet into his food and tea. (disulfiram 250 mg thrice daily). 3 days after disulfiram use, patient developed psychotic features. On physical examination, the patient was conscious and well-oriented without any significant neurological deficit. MSE findings were increased psychomotor activity, dysphoric affect, elementary auditory hallucinations and half-formed delusion of persecution. Blood and urine investigations were within normal limits. After admission in psychiatry unit, disulfiram was stopped and patient was with diazepam 5 mg twice daily and 2 mg risperidone for 5 days, which lead to full resolution of psychosis within the hospital stay. Patient was followed up for next 6 months and there was no emergence of psychosis again. Psychotropics were then gradually discontinued.

In all five cases, the treatment plan also included appropriate pharmacological and non-pharmacological management of alcohol use disorder.

DISCUSSION

Disulfiram is a medication used to support individuals with alcohol addiction by inducing unpleasant effects when alcohol is consumed. However, its availability without a prescription has led to its misuse as a self-administered treatment option for individuals seeking to quit alcohol. In India, Disulfiram, is commonly referred to as “Sharab Chhudane Ki Dawa” (the medicine to wean off alcohol). This case series reported five patients of psychosis induced by the covert use of disulfiram, purchased from a pharmacy without prescription from expert specialist doctor. These patients had a prior history of alcohol abuse. The symptoms in all cases emerged after consumption of disulfiram tablets. Delirium due to disulfiram-ethanol

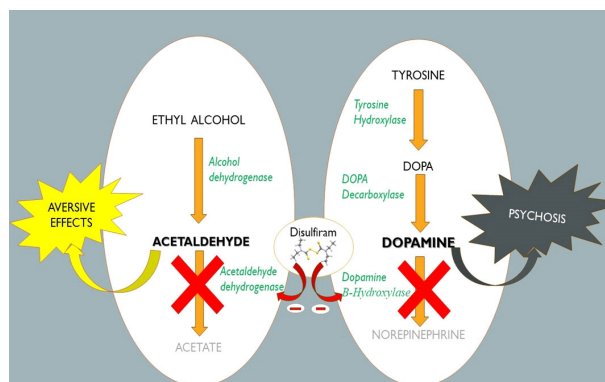


Fig 1 — Mechanism of Disulfiram Producing Aversive Effects and Psychosis

interaction and encephalopathy manifestations induced by disulfiram have been reported in some studies^{7,8}. Since patients from our case series had not drunk alcohol while they were being administered disulfiram, the possibility of disulfiram-reaction due to interaction with alcohol was eliminated. Similarly, the patients were in abstinence for at least one month and urine tests did not reveal any findings related to illicit substance. The symptoms of withdrawal usually occur within 6-8 hours after the last drink, reach the peak by 24-72 hours and usually last 1 week. Therefore, the alcohol intoxication or withdrawal would not be the most probable diagnosis. All the patients were fully conscious, attentive and well oriented to time, place and person during presentation and the common laboratory investigations related to delirium were within normal limit. Hence, diagnosis of delirium was not considered. EEG, CT- Brain and CSF analysis findings were normal which ruled out common organic causes of induced psychosis. Lack of past or family psychiatric history, temporal relationship of onset of symptoms with disulfiram consumption and finally, rapid resolution of symptoms after discontinuation of disulfiram were more suggestive of disulfiram induced psychosis rather than a primary psychiatric disorder.

The exact mechanisms underlying disulfiram-induced psychosis are not fully understood. Disulfiram's influence on neuro-transmitter systems, particularly dopamine, has been proposed as a potential contributing factor. The breakdown product of disulfiram, Diethyldithiocarbamate is an inhibitor of *dopamine-beta-hydroxylase* (DBH) enzyme which converts dopamine into noradrenalin. Inhibition of DBH enzyme by disulfiram metabolite may cause increase in dopamine levels⁹, and may induce psychotic effects. However, further research is necessary to elucidate the precise pathophysiology (Fig 1).

The important issue in these five cases was the over-the-counter sale of non-prescription medications and covert administration by family members without knowledge of patient. The popularity of disulfiram as “*Sharab Chhudane Ki Dawa*” can be attributed to several factors. Firstly, the

societal stigma associated with alcohol addiction often deters individuals from seeking professional help. Lack of awareness about available treatment options and limited access to addiction specialists and rehabilitation centres also contribute to this phenomenon. Furthermore, the relative affordability and easy availability of disulfiram from local pharmacies make it an accessible choice for those attempting to quit alcohol.

This case series raise significant legal and ethical concerns. Family members' actions of obtaining and administering disulfiram without proper authorization or supervision constitute a breach of medical ethics. It is crucial to educate patients and their families about the importance of seeking professional medical advice and avoiding self-medication practices. In cases where a patient lacks capacity to give informed consent, it is essential to follow established legal protocols to ensure the patient's well-being and autonomy are protected.

CONCLUSION

Disulfiram-induced psychosis resulting from unauthorized and unsupervised administration of medication highlights the potential risks associated with self-medication and the importance of involving healthcare professionals in treatment decisions. Addressing this issue requires a multi-faceted approach. Public health awareness campaigns must be launched to educate the general population about the risks associated with self-administration of disulfiram. Additionally, improving access to formal addiction treatment services and implementing stricter regulations on the dispensing of disulfiram can discourage its misuse. Collaborative efforts between healthcare professionals, policymakers, and the community are crucial to curbing this practice and providing comprehensive support to individuals struggling with alcohol addiction. It is essential for healthcare professionals also to be aware of such adverse effects and closely monitor patients receiving disulfiram.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.

In the form, the patients have given their consent for their clinical information to be reported to the journal. The patient understands that their name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Funding : None

Conflict of Interest : None

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