

Disulfiram Induced Psychosis in Patients Seeking Over the Counter Treatment

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ABSTRACT

Disulfiram is a deterrent in the management of alcohol use associated with neuropsychiatric manifestations, of which psychosis is common. The postulated mechanism is being its metabolite diethyldithiocarbamate being an inhibitor of dopamine beta-hydroxylase (DBH), an enzyme that catalyses the metabolism of dopamine (DA) to norepinephrine (NE) which results in an increase of DA concentrations in mesolimbic system resulting in psychosis. Other mechanisms are also postulated, like direct CNS toxicity, free radical damage. Here, are the two cases that were dependent to opioid given disulfiram surreptitiously land up with psychosis.

Key words: Substance use disorders, Disulfiram, Psychosis, over the counter medicine

BACKGROUND

Disulfiram functions as a deterrent in the treatment of alcohol dependence by discouraging individuals from consuming alcohol but is associated with various neuropsychiatric symptoms such as confusion, loss of memory, affective symptoms and frank psychosis.¹ Disulfiram's major metabolite diethyldithiocarbamate is an inhibitor of dopamine beta-hydroxylase

(DBH), an enzyme that catalyses the metabolism of dopamine (DA) to norepinephrine (NE). By inhibiting this metabolic pathway from DA to NE in the central nervous system, disulfiram results in an increase of DA concentrations in mesolimbic system resulting in psychosis.^{2,3,4} Patients with alcohol dependence who experienced psychosis during disulfiram treatment were observed to have low levels of amine and monoamine oxidase, indicating a potential blockade of DBH. We present two cases here highlighting psychosis associated with disulfiram given to the patients surreptitiously who were dependent on opioid rather than alcohol.

CASE 1

A 38 year male, with history of opioid dependence for the last 5 years (last intake was one week back) presented with fearfulness, suspiciousness, easy irritability, muttering to self, decreased sleep from 2-3 days. Haematogram, biochemical indices, urine drug screening, NCCT head came out to be normal (Table 1). On mental status examination, fearfulness, delusion of persecution and auditory hallucinations were elicited although his orientation was intact. On further exploration, it was revealed that he was administered disulfiram surreptitiously, after procuring it from local medical shop as a drug for

getting rid of opioid use. He developed the above mention symptoms within 2 days of administration of 250 mg of Disulfiram/day for two days. He was admitted at tertiary care centre and was started on tablet haloperidol 0.5 mg thrice a day along with management of opioid withdrawal with

clonidine and benzodiapine. His symptoms improved over a period of one week and the medications were tapered down. Motivational and relapse prevention therapies were given and he has been maintaining well, devoid of any psychotic symptoms.

Table 1: Routine Investigation

| Investigation | Case 1 | Case 2 |
|-----------------------|-----------------------|----------------------|
| Haemoglobin | 11.2 | 12.9 |
| Total leucocyte count | 10.0 | 9.8 |
| Kidner function test | Within normal limits | Within normal limits |
| Liver function test | Within normal limits | Within normal limits |
| MRI brain (p+C) | Normal study | Normal study |
| Urinary drug screen | Positive for morphine | Normal study |

CASE 2

A 45-year-old male without any past history of neurological illness came to psychiatry OPD with complaint of irrelevant talks, difficulty in sleep, irritability and unprovoked aggression along with suspiciousness against neighbours from 4 days. Patient has been using alcohol in dependence pattern from last 15 years however his last intake of alcohol 1 month prior to start of the above-mentioned symptoms. On clinical examination, no sign or symptoms of alcohol withdrawal was noted. On mental status examination, patient was oriented to time, place, person and paranoid ideations was elicited. All routine investigations including GGT, LFT, KFT,

USG abdomen, Urinary drug screen was within normal limits (Table 1). Upon further investigation of the patient's medical history, it was revealed that the individual had initiated medications for the treatment of alcohol dependence, including Disulfiram 1000mg/day for the last 7 days, prescribed by a local pharmacist. Provisional diagnosis of disulfiram induced psychosis was kept. Patient was managed conservatively by maintaining hydration and vitals and giving lorazepam injection when required. Patient improved significantly over next 1 week and subsequently discharged. He has been maintaining well since then and is on frequent follow ups.

TABLE 2: THE NARANJO ADVERSE DRUG REACTION PROBABILITY SCALE SCORES

| QUESTIONNAIRE | CASE 1 SCORE | CASE2 SCORE |
|---|--------------|-------------|
| ARE THERE PREVIOUS CONCLUSIVE REPORTS ON THIS REACTION? | +1 | +1 |
| DID THE ADVERSE EVENTS APPEAR AFTER THE SUSPECTED DRUG WAS GIVEN? | +2 | +2 |
| DID THE ADVERSE REACTION IMPROVE WHEN THE DRUG WAS DISCONTINUED OR A SPECIFIC ANTAGONIST WAS GIVEN? | +1 | +1 |
| DID THE ADVERSE REACTION APPEAR WHEN THE DRUG WAS READMINISTERED? | 0 | 0 |
| ARE THERE ALTERNATIVE CAUSES THAT COULD HAVE CAUSED THE REACTION? | +2 | +2 |
| DID THE REACTION REAPPEAR WHEN A PLACEBO WAS GIVEN? | +1 | +1 |
| WAS THE DRUG DETECTED IN ANY BODY FLUID IN TOXIC CONCENTRATIONS? | 0 | 0 |
| WAS THE REACTION MORE SEVERE WHEN THE DOSE WAS INCREASED, OR LESS SEVERE WHEN THE DOSE WAS DECREASED? | 0 | 0 |
| DID THE PATIENT HAVE A SIMILAR REACTION TO THE SAME OR SIMILAR DRUGS IN ANY PREVIOUS EXPOSURE? | 0 | 0 |
| WAS THE ADVERSE EVENT CONFIRMED BY ANY OBJECTIVE EVIDENCE? | 0 | 0 |
| | TOTAL 7 | TOTAL 6 |

DISCUSSION

The Naranjo adverse drug reaction probability scale was applied in both cases and score of 6, 7 was obtained (table2) which fairly hinted towards possibility of

disulfiram as offending agent.⁵ Several theories have been proposed to explain the pathophysiology of disulfiram-induced psychosis, with the most prevalent suggesting that the major metabolites of

Disulfiram, namely carbon disulfide and diethyldithiocarbamate (DDC), are linked to adverse effects. Specifically, DDC has the potential to inhibit dopamine- β -hydroxylase, resulting in an elevation of dopamine concentration in the mesolimbic system. This process aligns with the "dopamine hypothesis" associated with schizophrenia, potentially inducing psychosis.^{6,7} Disulfiram is often mistaken as wonder drug by chemist and other medical professionals for treating substance addiction. Many a times aggrieved family members of substance users out of desperation seek over the counter or covert treatment from multiple sources. In our two cases, use of disulfiram was not under supervision of trained professionals, and users were not warned about potential side effects. Patients frequently experience side effects that are initially misinterpreted as other medical conditions, only to later realize they are manifestations of disulfiram-induced effects among the differential diagnoses. The non-prescription availability of disulfiram for combating various substance addictions, beyond alcohol misuse, has surged in tandem with the increasing prevalence of diverse addictions. Unfortunately, many healthcare providers and pharmacy personnel remain uninformed about the indications, contraindications, and side effect profiles of disulfiram. Consequently, it is often prescribed over the counter without proper consent or comprehensive explanation of potential side effects and necessary precautions. This lax approach may lead to severe consequences, such as untreated disulfiram reactions, which can prove fatal. Additionally, instances of disulfiram-induced psychosis are not uncommon. There is a pressing need for increased awareness regarding disulfiram usage, side effects, and dosing among medical professionals. Implementing stricter

mandatory provisions for supervised disulfiram dispensing is essential to ensure patient safety and prevent adverse outcomes.

Declaration by Authors

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REFERENCES

1. Murthy KK. Psychosis during disulfiram therapy for alcoholism. *J Indian Med Assoc.* 1997 Mar;95(3):80-1. PMID: 9212576.
2. Murphy DL, Goodwin FK, Brodie HK, Bunney WE., Jr L-dopa, dopamine, and hypomania. *Am J Psychiatry.* 1973; 130:79–82. doi: 10.1176/ajp.130.1.79.
3. Quail M, Karelse RH. Disulfiram psychosis. A case report. *S Afr Med J.* 1980 Apr 5;57(14):551-2. PMID: 7368025.
4. Rex HH, Møller-Madsen S. Psykose efter indtagelse af overdosis disulfiram (Antabus) [Psychosis due to an overdose of disulfiram (Antabus)]. *Ugeskr Laeger.* 1986 Jun 30;148(27):1679-80. Danish. PMID: 3750452.
5. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981; 30:239–45. [PubMed]
6. Mohapatra S, Sahoo MR, Rath N. Disulfiram-induced neuropathy: a case report. *Gen Hosp Psychiatry.* 2015 Jan-Feb;37(1):97.e5-6. doi: 10.1016/j.genhosppsych. 2014.09.015. Epub 2014 Oct 7. PMID: 25445071
7. Rossiter SK. Psychosis with disulfiram prescribed under probation order. *BMJ.* 1992 Sep 26;305(6856):763. doi: 10.1136/bmj.305.6856.763. PMID: 1422334; PMCID: PMC1883409.

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