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Case Study

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DISULFIRAM INDUCED PSYCHOSIS

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ABSTRACT

Disulfiram is a drug of choice in alcohol dependence. It has been used for more than 65 years. Disulfiram produces its action by altering the normal metabolism of alcohol. There are various adverse drug reactions (ADR) associated with disulfiram use. Among which, psychosis is a major one. The mechanism of ADR is the inhibition of Dopamine Beta Hydroxylase (DBH). Patients receiving disulfiram must be sensitized regarding the possible ADR.

KEYWORDS: Disulfiram, Alcohol dependence, DBH, Psychosis.

INTRODUCTION

Disulfiram is a drug used to treat alcohol dependence. It is available as an oral preparation. Tablets are usually given once daily at doses ranging from 250mg to 500mg. Most common adverse effects are metallic taste, sleepiness, tiredness and headache. While, serious ADR include peripheral neuropathy, optic neuritis, psychosis and hepatotoxicity.[1] This case report on psychosis induced by disulfiram warrants special attention towards this serious and preventable ADR.

CASE REPORT

A 41 year old gentleman presented to general medicine department with agitation and complaints of decreased sleep for 2 days after an episode of binge drinking. He was on treatment with disulfiram 250 mg since one month, for alcohol deaddiction. He had no past history of psychiatric illnesses, other significant illnesses, or history of abuse of substances other than alcohol.

The patient's initial management consisted of tablet melatonin 3mg and tablet quetiapine 25 mg. His investigations showed reversed Albumin/ Globulin ratio with a mild elevation in SGOT and ALP levels, reduced platelet counts, hyponatremia and anemia. The patient was admitted and psychiatry consultation was sought. The patient was diagnosed with psychosis, and was advised injection haloperidol 2.5 mg twice daily intravenously as well as injection lorazepam 2 mg intravenously at bedtime if sleep deprived or agitated. During the hospital stay, he was managed with antipsychotics, sedatives, injection thiamine, gastroprotective and other supportive measures. Disulfiram was suspected to be the cause of psychosis and was withdrawn.

DISCUSSION

Disulfiram inhibits the alcohol dehydrogenase (ALDH1A1) by competing with nicotinamide adenine dinucleotide (NAD) at the cysteine residue in the active site of the enzyme. Alcohol dehydrogenase is an enzyme involved in the oxidative pathway of alcohol metabolism, which converts acetaldehyde to acetate.[2] There are various adverse effects associated with the disulfiram use. Among them psychosis is one of the major ADR. The mechanism of psychosis might be due to inhibition of dopamine beta hydroxylase (DBH) enzyme. This enzyme catalyses the metabolism of dopamine into norepinephrine. Inhibition of DBH increases dopamine level.[2]

Disulfiram can develop psychosis based on the frequency and duration of treatment. Disulfiram should be used cautiously in patients with previous history or family history of psychosis as this can precipitate psychosis in such patients.[3] An inherent low DBH activity could be a cause for vulnerability to psychosis with disulfiram when no clues are obtained from history.[2]

Among all ADR caused by disulfiram, reported globally to Uppsala Monitoring Centre (UMC), Sweden, through the WHO program for International drug monitoring, around 10 percent are cases of psychiatric disorders.[1] This case of Disulfiram Induced Psychosis (WHO-UMC ID: IN-IPC-300696860) was reported by the ADR monitoring Centre of this institution.

In this case the patient was on minimum effective therapeutic dose of 250 mg disulfiram. On evaluation at our AMC, the causality was assessed as 'probable' using the WHO- UMC causality assessment scale, the type of

ADR was evaluated according to Rawlins – Thompson Classification, and found to be type C. Seriousness assessed by WHO criteria, was 'hospitalization-initial' with a level 4 severity in modified Hartwig's scale. The outcome of the reaction according to WHO criteria was "recovering". Upon assessment of preventability, this reaction was not a preventable one, since there were no indications of vulnerability to psychosis in this patient and because the causal drug was given at the minimum effective therapeutic dose.

Before administering disulfiram, detailed history of the patient should be noted. Careful monitoring is required for patients who are on disulfiram treatment. Timely management with antipsychotic medications and cessation of disulfiram usage helps to improve the outcome.

CONCLUSION

This case demonstrates the occurrence of psychosis following the administration of minimum therapeutic doses of disulfiram in a patient with no previous indications of vulnerability towards mental illness. It warrants towards the need for clinicians to be cautious towards occurrence of psychosis while starting disulfiram, even when the patients gives no history of mental illness.

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Conflicts of interest

There are no conflicts of interest.

Abbreviations

ADR: Adverse Drug Reaction
ALDH1A1: Alcohol Dehydrogenase
AMC: ADR Monitoring Centre
DBH: Dopamine Beta Hydroxylase
NAD: Nicotinamide Adenine Dinucleotide
UMC: Uppsala Monitoring Centre
WHO: World Health Organisation

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