Disulfiram for Alcohol Use Disorder

Q. What is disulfiram?

A. Disulfiram, which is more commonly known by the brand name Antabuse, is a deterrent drug that may serve as an adjunctive therapy to treat alcohol use disorder (AUD). It has been used in the United States since 1948 and is typically prescribed in pill form to be taken once daily. When taken as prescribed, it will create an unpleasant effect in a patient who consumes even a small amount of alcohol. This reaction typically occurs within 10 to 20 minutes after ingestion of alcohol and includes the following deterrent effects: flushing of the face, headache, nausea, vomiting, chest pain, weakness, blurred vision, mental confusion, sweating, choking, breathing difficulty, and anxiety (Nace & Isbell, 1991). These effects typically last 30 to 60 minutes and the severity of the reaction is proportional to the dosage of disulfiram and the amount of alcohol ingested. It may produce a reaction up to two weeks following the last dose. As the drug is used to produce this reaction, it is only prescribed after withdrawal symptoms have subsided, when alcohol has cleared the patient's body.

Q. What are the potential mechanisms of action underlying disulfiram?

A. There are two potential mechanisms of action underlying the use of disulfiram: chemical and psychological. Chemically, the drug is unlike other medications used for the treatment of AUD as it does not affect brain receptors. Instead, it works by altering how the body breaks down and expels alcohol. The typical metabolism process begins by converting alcohol into acetaldehyde. This is the intermediate substance that causes the effects associated with hangovers. Typically, the body further breaks down acetaldehyde to reduce these effects. However, the chemical properties of disulfiram allow it to block this breakdown process (Gallant, 1994). When alcohol is consumed and a patient is on disulfiram, serum acetaldehyde levels are raised above their normal limits to produce the unpleasant effects.

At the psychological level, the threat of a reaction from drinking while on disulfiram may lead to aversion from alcohol consumption and thus encourage abstinence. Patients are educated and made fully aware of the risks of the alcohol-disulfiram reaction and instructed to avoid alcohol and alcohol containing substances of any type, including mouth-wash and cough syrups. Disulfiram may be a particularly helpful adjunct during early recovery and the abstinence phase of detoxification. It creates an opportunity for patients to begin accumulating and practicing the behaviors, beliefs and experiences that form the foundation of a recovery lifestyle.

Q. Is disulfiram recommended as a treatment for AUD in the Military Health System (MHS)?

A. Yes. The 2015 *VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders* gives a "Strong For" strength of recommendation to disulfiram for patients with moderate-severe alcohol use disorder.

The MHS relies on the VA/DoD CPGs to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q. Do other authoritative reviews recommend disulfiram as a treatment for AUD?

A. No. Other authoritative reviews have not substantiated the use of disulfiram as a treatment for AUD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency

for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: A 2014 AHRQ comparative effectiveness review of pharmacotherapy for adults with AUD in the outpatient setting included four trials investigating disulfiram (Jonas et al., 2014). Review authors concluded that the evidence does not support the efficacy of disulfiram, with the possible exception of patients with excellent adherence. The strength of evidence was rated as low for return to any drinking, and insufficient for all other outcomes.

Q. What conclusions can be drawn about the use of disulfiram as a treatment for AUD in the MHS?

A. Along with acamprosate, topiramate, and naltrexone, disulfiram has met the burden of evidence for inclusion in VA/DoD guidelines and is considered a front-line pharmacological treatment for AUD. The CPG states that there is insufficient evidence to recommend one of these medications over another, and that these medications should be used in conjunction with a psychosocial intervention. Providers should take into account factors such as potential adverse effects (for disulfiram these include optic neuritis, peripheral neuritis, and hepatitis), comorbidities, and availability to inform treatment choice for patients with AUD.

References

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