



Alcohol Use Disorders: A Clinical Update

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Editorial

Alcohol remains the most widely abused substance world-wide with 86.8% of American adults having endorsed a lifetime use in 2013. Of these 8% meet criteria for an alcohol use disorder (AUD) [1]. The opioid epidemic has been the face of public health crisis due to its visible effects through overdose deaths however the number of individuals quietly dying from alcohol-related problems is high. In managing alcohol use disorders psychosocial modalities are strong adjuncts however when delivered alone, without pharmacotherapy, there is a 70% relapse risk. Unfortunately this is the case for a significant number of sufferers as only 3% receive FDA approved medications [2]. Alarming, 20% of healthcare providers never prescribed any. Reasons include lack of provider knowledge of available medications, dosing and guidelines and also lack of screening for alcohol use [3,4]. It is quite shocking that a medication class such as the statins with a NNT>100 [5] are widely used in our healthcare yet Naltrexone (NNT=12 in reducing heavy drinking and 20 for return to any drinking) and Acamprosate (NNT=12 for return to any drinking) are so underutilized [6].

In providing a short update on the topic of alcohol use disorders, here I will describe the emerging issue of benzodiazepine resistant alcohol detoxification and discuss several new pharmacological modalities with evidence for mitigating alcohol use.

Benzodiazepine-resistant alcohol withdrawal

The majority of individuals with AUD have comorbid psychiatric and medical conditions and inpatient admissions to manage them are common. Approximately 20% of hospitalized patients end up experiencing alcohol withdrawal during their stay [7]. The majority of problem drinkers are binge drinkers and during withdrawal experience only minor symptoms. More severe withdrawal however, although occurring only in a small percentage, requires prompt identification, early intervention, close observation and aggressive management since it carries significant risk of mortality. The traditional gold standard with benzodiazepine dosed by guidance from CIWA protocols has been effective in mitigating this risk. Recent years have seen a significant number of withdrawal symptoms poorly responsive to >40 mg of Diazepam equivalents delivered over the course of 1 hour [8]. This "benzodiazepine resistant alcohol withdrawal" or RAW seems to be more prevalent in individuals having experienced past detoxification and withdrawals and is more prominent and difficult to manage with each subsequent occurrence. The risk of seizures and delirium tremens is increased and permanent cognitive difficulties may emerge [9]. Plausible explanations for this kindling effect include permanent alterations in GABA-A [10], and glutamate receptors, to where benzodiazepines are no longer able to bind. These individuals require ICU admissions and have a lengthy and complicate course

[11]. RAW management requires non-benzodiazepine alternatives such as: escalating benzodiazepine doses with Phenobarbital [12], Propofol [13], Dexmedetomidine [14] or adjunctive Ketamine [15].

The PAWSS tool developed by Maldonado [16] to identify those at risk for withdrawal (sensitivity and PPV of 93%, specificity and NPV of 99.5%) and provide guidance on early prophylaxis during their hospital stay requires an honest self-report and is mainly subjective. A recent retrospective case control study has identified several objective factors linked to RAW that clinicians could use in predicting the risk [8]. Thrombocytopenia and psychiatric history were found to double the likelihood of RAW. Caucasian race and male gender as well as abnormal liver function tests were also found to have some predictive value. Combined with the PAWSS, these hold importance in potentially increasing the ability to identify those at risk for RAW and hence prompting clinicians to provide aggressive prophylaxis sooner.

Novel clinically feasible pharmacological options

To date there has been little motivation for pharmaceutical companies to develop medications for substance use disorders in general since the existing options are not utilized by healthcare providers. This may change due to the success noted when medications are implemented as well as the cost effectiveness shown for the healthcare system. Insurance companies are already seeing reduced costs and reduced ED visits. In the meantime, the focus has shifted to what is already existent with a stronger emphasis on the more patient-accepted harm reduction model (reduced drinking) rather than complete abstinence (ie. Disulfiram).

One area of increased interest is the use of alpha-1 noradrenergic antagonists that cross the brain blood barrier to limit drinking. Prazosin is an alpha-1 adrenergic receptor antagonist [17] recently found to have such drink reduction benefit in 92 non-PTSD diagnosed participants over the course of 12 weeks. Given its short half-life the titration occurred in three times daily dosing towards: 4 mg in the morning, 4 mg in the afternoon and 8 mg in the evening. The outcome measure reported was a reduction in heavy drinking and number of drinks per week over time. The number of drinking days per week however was not impacted. This may have significant implication especially in those with PTSD where this agent is utilized and may thus serve a dual role.

Another pharmacological agent with newly reported evidence for AUD is Varenicline. In a 16 week randomized placebo controlled double blind trial, 131 participants were prescribed this standard smoking cessation agent with titration to 2 mg daily dose. Aside from the expected benefit in helping smokers quit which was secondary it also was found to impact heavy drinking days particularly in men with AUD [18]. Poor adherence and side effects rendered it ineffective for women, a majority of which ended up discontinuing. In our daily

practice this represents a potential agent that could have a dual role when considering smoking cessation options.

We have seen agents such as Gabapentin being favored when choosing a pain regimen for individuals with comorbid AUD (given its drink reduction benefit) and Topiramate when deciding on a mood stabilization or seizure control regimen (again given its effect in mitigating alcohol consumption). In a world of individualized medicine where patients favor harm-reduction over complete abstinence and desire simplified regimens, Prazosin and Varenicline hold promise and provide clinicians with yet two more off-label options to consider based on the patients' specifics.

References

1. Bayard M, McIntyre J (2004) Alcohol withdrawal syndrome. *American Family Physician* 69: 1443-1450.
2. Substance Abuse and Mental Health Services Administration (2014) Results from the 2013 national survey on drug use and health: Mental health findings, NSDUH Series H-49, HHS Publication No. (SMA) 14-4887. Rockville, MD: Substance Abuse and Mental Health Services Administration.
3. Stanciu C, Penders T (2017) Underutilization of pharmacotherapy for treatment of alcohol use disorders part II—results from a survey of practices among North Carolina Mental Health Providers and Brief Review of Efficacy of Available Pharmacotherapies. *Journal of Alcoholism and Drug Dependence*. 5(5).
4. Stanciu C, Penders T (2017) Underutilization of screening tools for alcohol use disorders—part I: Results from survey of practices among North Carolina Mental Health Providers and Brief Review of Available Instruments 5(5).
5. Taylor F, Ward K (2011) Statins for the primary prevention of cardiovascular disease. *Cochrane Database of Systematic Reviews* 2011, Issue 1. Art. No.: CD004816.
6. Jonas D, Amick H (2014) Pharmacotherapy for adults with alcohol use disorders in outpatient settings: A systematic review and meta-analysis. *JAMA* 311:1889-1900.
7. McKeon A, Frye M (2008) The alcohol withdrawal syndrome. *J Neurol Neurosurg Psychiatry* 79: 854-862.
8. Benedict N, Wong A (2018) Predictors of resistant alcohol withdrawal (RAW): A retrospective case-control study. 2018. *Drug and Alcohol Dependence*.
9. Howard C (1998) Kindling in alcohol withdrawal. 1998 *Alcohol Health & Research World (NIAAA)* 22 (1).
10. Malcolm R (2003) GABA systems, benzodiazepines, and substance dependence. *J Clin Psychiatry* 64 Suppl 3: 36-40.
11. Sarff M, Gold J (2010) Alcohol withdrawal syndrome in the intensive care unit. *Crit Care med* 38: S494-S501.
12. Gold J, Rimal B (2007) A strategy of escalating doses of benzodiazepines and phenobarbital administration reduces the need for mechanical ventilation in delirium tremens. *Crit Care Med* 35: 724-730.
13. McCowan C, Marik P (2000) Refractory delirium tremens treated with propofol: A case series. *Crit Care med*. 28: 1781-1784.
14. Darrouj J, Puri N (2008) Dexmedetomidine infusion as adjunctive therapy to benzodiazepine for acute alcohol withdrawal. *Ann Pharmacother* 42: 1703-1705.
15. Wong A, Benedict N (2015) Multicenter evaluation of pharmacological management and outcomes associated with severe resistant alcohol withdrawal. *J Crit Care* 30: 405-409.
16. Maldonado J, Sher Y (2014) The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): Systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. *Alcohol* 48: 375-390.
17. Simpson T, Saxon A (2018) Double-blind randomized clinical trial of prazosin for alcohol use disorder. *Am J Psychiatry*.
18. O'Malley S, Zweben A (2018) Effect of varenicline combined with medical management on alcohol use disorder with comorbid cigarette smoking: A randomized clinical trial. *JAMA Psychiatry* 75: 129-138.