Letters to the Editor

Alcohol Use Disorder and Expectation-Based Medicines

To the Editor: Poorman and colleagues highlighted in their article on alcohol use disorder (AUD) that "excessive alcohol use is a leading cause of preventable death in the United States… [but] only 7.3% of Americans with AUD received any treatment, and only 1.6% were prescribed medications to treat the disorder."[1]

This treatment gap does not warrant promoting off-label use of baclofen and gabapentin for AUD. Promoting off-label use without robust data on the benefit-to-harm ratio of relevant clinical outcomes hinders evidence-based medicine and therapeutic innovation, raises health care costs, and increases the risk of adverse events, including mortality, with uncertain benefit.[2] The two pivotal trials (NCT01738282: https://clinicaltrials.gov/study/NCT01738282; NCT01604330: https://clinicaltrials.gov/study/NCT01604330) with baclofen showed no benefit.[3] In addition, baclofen use has been associated with a dose-dependent increase in mortality, including intentional self-poisoning, compared with acamprosate and oral naltrexone (Revia) in several real-world settings in France.[3] Patients taking gabapentinoids have a high potential for misuse, which may be greater in patients with AUD.[4] Adverse effects include sedation, risk of serious breathing problems, suicidal behavior, and decreased bone mineral density, which increases the risk of fractures.

Poorman and colleagues state that antidepressants "may help patients who meet criteria for depression to decrease their alcohol intake," ignoring that these drugs have modest benefit, if any.[1] Antidepressants can exacerbate drinking outcomes, interacting with alcohol to produce pathological intoxication characterized by loss of self-control, memory impairment, and occasionally, serious violence.[5]

Meta-analyses and reviews have confirmed the net benefits of using oral naltrexone and acamprosate, concluding that with psychosocial interventions, oral naltrexone and acamprosate are first-line pharmacotherapy options for patients with AUD.[6]

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In Reply: We appreciate Dr. Braillon's attention to the potential risks of medications for treating AUD and the opportunity to provide additional nuance to the recommendations we shared in our article. The risks of not treating AUD, including the high morbidity associated with untreated AUD, must be weighed against the risks of treatment. Physicians often underestimate the risk of continued drinking and overestimate the risk of medication, which is demonstrated by low prescribing rates. This may also translate to physicians' low risk tolerance for adverse effects or deviation from a narrow reading of medication indications that is not applied to any other class of treatments. For example, up to 1 in 3 medications is prescribed off-label, which is occasionally the standard of care.[1]

We found less consistent evidence to support the use of baclofen when treating AUD, but we noted that a Cochrane review of 17 randomized controlled trials found a small benefit.[2] In our article, we also stated that "serious safety concerns have been raised regarding the risk of sedation and overdose."[3] With those precautions in mind, our conclusion remains that there is sufficient evidence to support the use of baclofen for AUD.

Concerns about gabapentin misuse are often cited in medical literature, but the definition of misuse often has a strong overlap with treatment goals for AUD, specifically when treating prolonged withdrawal symptoms. Gabapentin use disorder is rare. In 2017, researchers found only a few case reports publishing consistent symptoms of gabapentin use disorder, including craving, loss of control, consequences, and compulsion.[4] We reiterate that physicians should consider the risks of untreated AUD compared with the rare risk of gabapentin use disorder.

We acknowledge Dr. Braillon's theory regarding the severe risks of prescribing antidepressants to treat AUD. However, after reviewing real-world data, we did not find evidence supporting this theory.[5] Data show improved drinking outcomes for patients with AUD and depression who are prescribed antidepressants.[5] We stand by our assertion that the use of

antidepressants can benefit patients with comorbid AUD and depression. Given existing evidence, antidepressants should not be withheld from patients who meet criteria for their use as treatment for AUD.

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