Best Meds for Alcohol Dependence Revealed

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The effectiveness of antialcohol medications used treat alcohol use disorders (AUDs) in outpatients varies, according to an updated systematic review and meta-analysis of published studies. Acamprosate (*Campral*, Forest Laboratories, Inc) and oral naltrexone (50 mg/d), which are approved by the US Food and Drug Administration for AUDs, have the best evidence for decreasing alcohol use, whereas evidence for disulfiram (*Antabuse*, Odyssey Pharmaceuticals, Inc) another approved agent available since the 1950s, is lacking, the researchers found. Among medications used off label, they found moderate evidence to support the efficacy of nalmefene and topiramate for helping patients reduce drinking.

"We have several medications that can help people with AUDs to maintain abstinence or to reduce drinking. Acamprosate and oral naltrexone have the best evidence supporting their benefits," lead investigator Daniel E. Jonas, MD, MPH, of the University of North Carolina, Chapel Hill, told *Medscape Medical News*.
The study is published in the May 14 issue of *JAMA*.

AUDs Undertreated
AUDs are common, cause substantial illness, and raise the risk for premature death 3-fold, yet they remain "greatly undertreated," the authors note. Antialcohol medications can help but are "considerably underused," they add.
To determine the efficacy of medications for adults with AUDs, the investigators reviewed 122 randomized controlled trials and 1 cohort study involving a total of 22,803 patients. "The last comprehensive review of medications for AUDs was published in 1999," said Dr. Jonas."Since then, there has been more than a 10-fold increase in the number of individuals studied in controlled clinical trials of naltrexone and acamprosate, and many trials of medications that are not FDA-approved. Thus, providers were left with some uncertainty about what medications have good evidence supporting their effectiveness and which medications do not."

Most of the studies the researchers reviewed assessed acamprosate (27 studies, 7519 patients), naltrexone (53 studies, 9140 patients), or both. In all of them, the treatment period lasted at least 12 weeks, and most evaluated AUD medications when added to psychosocial interventions in patients who were abstaining when the medication was started.

Both acamprosate and oral naltrexone (50 mg/d) were associated with a reduction in return to any drinking. For acamprosate, the number needed to treat (NNT) was 12 (95% confidence interval [CI], 8 - 26). For oral naltrexone, it was 20 (95% CI, 11 - 500). Meta-analyses of trials comparing acamprosate with naltrexone found no statistically significant difference between them for return to any drinking (risk difference [RD], 0.02; 95% CI, −0.03 to 0.08) or heavy drinking (RD, 0.01; 95% CI, −0.05 to 0.06).

Treatment with injectable naltrexone (*Vivitrol*, Alkermes, Inc) was not associated with return to any drinking (RD, −0.04; 95% CI, −0.10 to 0.03) or heavy drinking (RD, −0.01; 95% CI, −0.14 to 0.13), and it curbed the number of heavy drinking days (weighted mean difference [WMD], −4.6%; 95% CI, −8.5% to −0.56%).

"Because it has been around since the 1950s, providers may be most familiar with disulfiram (brand name Antabuse), but evidence from well-controlled trials does not support an association between its use and improvement in drinking outcomes," Dr. Jonas said. However, in a subgroup analysis of the largest disulfiram trial, there were fewer drinking days for patients who returned to drinking and who had a complete set of assessments, suggesting that this drug may be helpful in some AUD patients, the authors say. Among medications used off label, there is "moderate evidence" that nalmefene can help reduce heavy drinking days per month (WMD, −2.0; 95% CI, −3.0 to −1.0) and drinks per drinking day (WMD, −1.02; 95% CI, −1.77 to −0.28). There is also moderate evidence that topiramate can reduce the percentage of heavy drinking days (WMD, −9.0%; 95% CI, −15.3% to −2.7%) and drinks per drinking day (WMD, −1.0; 95% CI, −1.6 to −0.48).

In terms of safety, the researchers point out that it is tough to accurately judge the risks associated with these medications, owing to "insufficient evidence" regarding many potential adverse events. In most cases, wide confidence intervals made it impossible to arrive at conclusions about medication risk.
They did calculate that the number needed to harm for withdrawal from trials due to adverse events was 48 for naltrexone (95% CI, 30 - 112) and 12 for nalmefene (95% CI, 7 - 50). The risk was not significantly increased for acamprosate or topiramate, they report.

Dr. Jonas noted that the "health implications of preventing return to drinking and reducing alcohol consumption are substantial. Modeling studies have shown that such improvements would result in significant reductions in alcohol-attributable mortality, costs from healthcare, arrests, and motor vehicle accidents."

Toward Patient-Centered Care

This review has the potential to increase awareness and use of drug therapy for AUD, state Katharine A. Bradley, MD, MPH, from the Group Health Research Institute in Seattle, Washington, and Daniel R. Kivlahan, PhD, Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, in an accompanying editorial.
"The most important benefit of this review, however, will be if it leads to more patient-centered care for AUD," they write. They note that under healthcare reform, treatment of AUD is considered an essential health benefit.
"More patients with AUDs will have insurance, which could increase their access to evidence-based treatments for AUDs," they point out. The article by Dr. Jonas and colleagues "should encourage patients and their clinicians to engage in shared decision-making about AUD treatment options."

"By identifying 4 effective medications for AUD, the authors highlight treatment options for a common medical condition for which patient-centered care is not currently the norm. Patients with AUDs should be offered options, including medications, evidence-based behavioral treatments, and mutual support for recovery. Moreover, patients should expect shared decision making about the best options for them," the editorialists conclude.

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