Baclofen for Alcohol Dependence: Does It Have Efficacy or Not?

The effectiveness of screening and brief intervention (SBI) for alcohol in the emergency department (ED) is uncertain. Prior negative findings may be due, in part, to lower levels of at-risk drinking among participants or assessment reactivity among controls. In this study, researchers randomized 446 ED patients with at-risk* or dependent** drinking to 1 of 3 groups: screen-only (n=147, 83% men), assessment (n=152, 86% men), or intervention (n=147, 85% men). The intervention group received a 15–20 minute brief motivational intervention by a nurse. The assessment and intervention groups received follow-up assessments at 3 and 12 months; the screen-only group received follow-up assessment at 12 months only.

- Twelve-month follow-up rates were 63%, 65%, and 59% in the screen-only, assessment, and intervention groups, respectively.
- At-risk drinking decreased from baseline to 12 months in each group (screen-only, 87% to 54%; assessment, 89% to 65%; intervention, 88% to 64%) as did dependent drinking (screen only, 25% to 21%; assessment, 35% to 24%; intervention, 43% to 24%).
- All 3 groups had significant reductions in drinks per drinking day at 12 months.
- No significant difference in drinking outcomes was found among the 3 groups at 12 months.

Comments: All 3 groups improved at 12 months, suggesting that neither intervention nor assessment were responsible for the improved outcomes. A single brief intervention may be insufficient for heavier drinking populations, particularly those with dependence. Whether booster sessions or other approaches will make brief interventions effective for such patients remains to be seen.

Kevin L. Kraemer, MD, MSc


Baclofen for Alcohol Dependence: Does It Have Efficacy or Not?

A 3-month randomized placebo-controlled trial (N=84 men) found efficacy for baclofen in people with cirrhosis (71% versus 29% abstinence). Because of this finding and findings of other preclinical and clinical studies, investigators randomly assigned 80 men and women with alcohol dependence (on average, they drank 7 drinks per drinking day) to 10 mg baclofen 3 times daily or placebo. All participants were also offered 8 therapy sessions. Follow-up was at 12 weeks.

- About one-quarter of subjects were lost to follow-up.

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Efficacy of Baclofen for Alcohol Dependence (continued from page 1)

- Although baclofen was generally well tolerated, there were no differences in heavy drinking days (26%), time to first drink, time to relapse to heavy drinking, or craving between groups.

Comments: This small study may not be the last word on baclofen. In fact, the authors suggest that it may be effective in people with more severe dependence or at a higher dose. But the results do indicate that the medication will not likely have dramatic efficacy across diverse populations of people with alcohol dependence.

Richard Saitz MD, MPH


No Reduction in Cocaine Use with Disulfiram in Opioid- and Cocaine-Dependent Patients

Co-occurring cocaine dependence is a frequent problem for opioid-dependent patients entering methadone-maintenance therapy (MMT). Some small studies have demonstrated decreased cocaine use among cocaine users treated with disulfiram, normally a treatment for alcohol dependence. To determine whether disulfiram reduces cocaine use in patients with both opioid and cocaine dependence initiating MMT, researchers conducted a placebo-controlled randomized trial in which 152 patients received either 0 mg, 62.5 mg, 125 mg, or 250 mg disulfiram daily (combined with their daily methadone dose) for 12 weeks following a 2-week MMT induction period.

- Sixty-five percent of subjects completed the study protocol. Retention did not differ between the 4 groups.
- The mean number of alcoholic drinks per week at baseline was less than 1 in all groups, which did not change significantly during the study in any group.
- The percentage of cocaine-positive urine tests increased in the 62.5 mg and 125 mg groups over 12 weeks but decreased (at similar rates) in the placebo and 250 mg groups.

Comments: In this trial, disulfiram did not reduce cocaine use in MMT patients with co-occurring cocaine and opioid dependence. In fact, patients taking low doses of disulfiram increased their cocaine use over the study period. These findings do not support disulfiram treatment for cocaine dependence in MMT patients. Additional trials are required to determine which cocaine-using populations may benefit from disulfiram treatment.

Alexander Y. Walley, MD, MSc


Patients with Chronic Pain and a Substance Use Disorder May Have Better Pain Outcomes with More Intensive Treatments

Many patients with chronic pain have a current or past substance use disorder (SUD). This study included patients recruited from Veterans Administration primary-care clinics for a clinical trial comparing treatment as usual (TAU) with a collaborative care initiative (continued on page 3)
Effect of Buprenorphine/Naloxone Treatment on HIV Risk Behaviors in Opioid-Dependent Youth

Buprenorphine/naloxone (BUP) treatment is an effective component of HIV prevention and has been shown to decrease opioid use in opioid-dependent adolescents, who are at particularly high risk for HIV infection. This analysis compared HIV, drug, and sexual risk behaviors based on gender and treatment condition (12-week BUP treatment versus 2-week BUP detoxification) among opioid-dependent treatment-seeking adolescents enrolled in a multisite randomized clinical trial. Eighty-nine participants were male, and 61 were female; 72% were white, and the median age was 19 years (range, 15–21 years).

- Fifty-one percent of females and 45% of males reported injection drug use (IDU) at baseline. Of these, 77% of females and 35% of males engaged in injection risk behavior (e.g., using dirty needles, sharing injection equipment, splitting drug solution).
- Eighty-two percent of females and 74% of males were sexually active at baseline. Of these, 14% of females and 24% of males had multiple partners, and 68% of females and 65% of males reported noncondom use.
- In contrast, no difference in improvement was detected between those with and without an SUD in the CCI group (although the confidence interval was wide) (AOR, 1.06; 95% CI, 0.37–3.01).

Comments: This study reinforces the challenges of treating chronic pain in patients with a coexisting SUD, but it also provides hope that more intensive treatment models may be effective for this population. In fact, it appears that in the CCI group, having an SUD no longer decreased the likelihood of a good outcome. This was not true for the TAU group. This finding stresses the need for additional studies specifically targeting this population.

Jeanette M. Tetrault, MD


Do Antidepressants Improve Opioid Agonist Treatment Outcomes?

Both chronic opioid use and opioid withdrawal can induce symptoms that are difficult to distinguish from mood disorders. This 12-week randomized clinical trial sought to determine whether treatment of depressive symptoms with escitalopram during opioid agonist treatment (OAT) with buprenorphine improved treatment retention compared with placebo. A total of 147 opioid-dependent individuals with depressive symptoms were randomized to either escitalopram or placebo at study initiation and began OAT induction 5 days later. Mean age of participants was 38 years; 76% were male, and 80% were white. Fifty-six percent of participants met criteria for a major depression at baseline.

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Do Antidepressants Improve OAT Outcomes? (continued from page 3)

- Thirty-nine percent of patients did not complete treatment (33% in the escitalopram arm and 44% in the placebo arm).
- Mean Beck Depression Inventory scores improved throughout treatment, with greatest improvements within the first 2 weeks. Escitalopram had no effect on treatment retention, depression outcomes, or illicit drug use compared with placebo.

Comments: These results suggest contemporaneous initiation of antidepressants and OAT does not improve retention, and depressive symptoms improve early in OAT regardless of antidepressant treatment. As stated by the authors, the decline in depressive symptoms may be related to OAT itself and the resultant improvement of psychosocial stressors.

Jeanette M. Tetrault, MD


HEALTH OUTCOMES

Light Alcohol Consumption May Increase Risk of Breast Cancer Recurrence But Not Risk of Death from All Causes

The Life After Cancer Epidemiology (LACE) study included 2269 women diagnosed with early-stage breast cancer between 1997 and 2000 and recruited approximately 2 years following breast cancer diagnosis. Researchers evaluated the association between alcohol intake, breast cancer recurrence, and death among the 1897 participants (84%) who provided alcohol consumption data at baseline. Most of the women were light drinkers (median, 5.96 g alcohol per day). Average follow-up was 7.4 years.

- There were 293 breast cancer recurrences and 273 deaths during the follow-up period.
- Compared with no drinking, consuming ≥6 g alcohol per day (about ½ a US standard drink) was associated with an increased risk of breast cancer recurrence (hazard ratio [HR], 1.35) and death due to breast cancer (HR, 1.51).
- The risk of recurrence was greater among postmenopausal women (HR, 1.51) and overweight or obese women (HR, 1.60).

Comments: Most previous large studies, as in this one, have shown no increase in all-cause mortality for women who drink moderately following a breast cancer diagnosis. Most have also shown no increased risk for breast-cancer recurrence, although one involving women with estrogen-receptor-positive tumors found an increased risk with consumption of >7 drinks per week. Because of these conflicting results, the question of whether light drinking increases breast cancer recurrence or death remains unanswered.

R. Curtis Ellison, MD


Prenatal Alcohol Exposure and Risk of Birth Defects

To investigate the association between prenatal alcohol use and birth defects, researchers in Australia studied maternal alcohol consumption in a population-based cohort of 4714 women (singleton births only). Alcohol use was classified as none (abstinence throughout pregnancy), low (<7 drinks* per week and no more than 2 drinks in a day), moderate (≤7 drinks per week but >2 standard drinks per occasion, including consumption of ≥5 drinks per occasion less than weekly), and heavy (≥5 drinks per occasion 1 or more times per week or >7 drinks per week). Consumption was assessed for the 3-month period prepregnancy, for the first trimester, and for late pregnancy (second and third trimesters). Information regarding birth defects was obtained through the Western Australia Birth Defects Registry and grouped into 2 categories: any birth defect and alcohol-related birth defects (ARBDs) as defined by the US Institute of Medicine.

- Alcohol intake was not associated with death from all causes.
- Forty-one percent of women abstained throughout pregnancy. Twenty-eight percent reported low consumption, 11% reported moderate consumption, and

*In Australia, 1 standard drink = 10 g ethanol.
Alcohol and Birth Defects (continued from page 4)

3.7% reported heavy consumption during the first trimester. Thirty-eight percent reported low consumption, 11% reported moderate consumption, and 2% reported heavy consumption during late pregnancy.

- Fifty-one children (1.1%) with at least 1 ARBD were identified; of these, 4 had 2 birth defects.
- In analyses adjusted for maternal age, marital status, parity, income, smoking, and drug use during pregnancy, compared with women who abstained, women who drank heavily in the first trimester had higher odds of giving birth to infants with an ARBD (odds ratio [OR], 4.57).
- There was no significant association between low, moderate, or heavy alcohol consumption in late pregnancy and any birth defects, including ARBDs.

Comments: In this study, the prevalence of birth defects was low (although only defects evident shortly after birth were studied), and no evidence was found for an association between low or moderate drinking and ARBDs. These results add to the evidence that heavy drinking in early pregnancy is associated with the occurrence of ARBDs. As such, it is important to provide information on the effects of heavy alcohol use on the fetus to women of childbearing age, stressing that, although safe drinking levels during pregnancy are unknown, alcohol exposure is one of the preventable causes of birth defects.

Nicolas Bertholet, MD, MSc


Is Crack Cocaine Linked to More Violent Behavior than Powdered Cocaine?

Crack cocaine use has been blamed for a variety of societal ills, including violent behavior. However, little is known about that link. Researchers analyzed data from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) to compare the frequency of self-reported violent behavior between users of crack or powdered cocaine. Subjects were divided into 2 categories: those who had ever used crack cocaine, and those who had ever used the powdered form only. Violent behaviors were measured using 10 items from the antisocial personality disorder (APD) module of the Alcohol Use Disorder and Associated Disabilities Interview, Schedule-IV.

- Compared with those who used powdered cocaine, people who used crack cocaine were more likely to be male and African American. They also had lower educational levels and lower income.
- People in the crack cocaine group reported engaging in a greater number of violent behaviors; however, the association was attenuated after adjusting for sociodemographic factors. Only 1 of the 10 APD behaviors was statistically significant after adjustment.

Comments: The study suggests that crack cocaine is not uniquely responsible for more violent behavior than powdered cocaine, and that the observed association is largely due to other factors. Unfortunately, the results provide little insight into the role cocaine use plays in violent behavior, and there are no data on the temporal relationship (if any) between the two. However, they do support the argument that we should not single out crack cocaine use as a greater societal ill than other forms of cocaine use.

Darius A. Rastegar, MD