Alcohol, Other Drugs, and Health: Current Evidence

MAY–JUNE 2010

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INTERVENTIONS & ASSESSMENTS

Adverse Events Are Not Increased with Beta-Blockers in Cocaine Chest Pain

Although beta-blockers improve outcomes in patients with myocardial infarction, cardiology guidelines recommend against using beta-blockers in cocaine-associated chest pain because of concerns about the unopposed alpha-adrenergic stimulation shown in case reports and animal studies. To determine whether beta-blockers are safe to administer to patients with chest pain and recent cocaine use, researchers reviewed the National Death Index and patient records of 331 patients with chest pain and cocaine-positive urine test results admitted to San Francisco General Hospital between 2001 and 2005.

- One hundred fifty-one patients received beta-blockers in the emergency department (ED). Of these, 85% received metoprolol as their first dose.
- During the hospitalization, systolic blood pressure decreased more in patients who received a beta-blocker in the ED. No differences in electrocardiograph results, troponin levels, intubation rates, vasopressor use, malignant ventricular arrhythmia rates, or death were found.
- There were 45 deaths (14% of the total sample) over a median follow-up of 972 days. In adjusted analyses, discharge on a beta-blocker regimen was associated with a lower risk of cardiovascular-specific death but not associated with all-cause mortality.

Comments: Although this retrospective observational study does not definitively settle the debate regarding the safety of beta-blockers for patients with cocaine-related chest pain, it does credibly challenge guidelines that recommend against the use of beta-blockers for such patients at risk for myocardial infarction. Resolving this controversy will require further study, including a randomized controlled trial.

Alexander Y. Walley, MD, MSc

Reference: Rangel C, Shu RG, Lazar LD, et al. Beta-blockers for chest pain associated with recent cocaine use. *Arch Intern Med.* 2010;170(10):874–9.

Extended-Release Naltrexone for Alcohol Dependence: Feasibility in Primary-Care Settings

Pharmacotherapies for alcohol use disorders are seldom prescribed in primary-care practices, despite the fact that patients with these disorders are more likely to be seen in general medical settings than in specialty care. This case series evaluated the feasibility of implementing a combination of extended-release naltrexone (XR-NTX) and medical management (physician-led counseling with a focus on medication adherence and abstinence) in a primary-care setting. The sample included 72 alcohol-dependent patients recruited through advertising and from other clinics who presented to 2 urban hospital primary-care clinics for treatment.

- Ninety percent of patients (n=65) received 1 planned XR-NTX injection, 75% (n=49) received a second planned injection, and 62% (n=40) received a third planned injection.
- Sixteen of the 65 patients who initiated treatment were lost to follow-up. An additional 5 patients discontinued

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Extended-Release Naltrexone in Primary Care (continued from page 1)

treatment due to side effects, and 4 patients reported no treatment effect and continued heavy drinking.

- Two serious adverse events occurred (a severe injection-site reaction and an unexpected pregnancy).
- Mean drinks per day decreased from 5.4 to 3.4 in intention-to-treat analyses; however, among the 40 patients who received all 3 injections, mean drinks per day decreased from 4.1 to 0.5.

Comments: Injectable pharmacotherapies for addiction are designed to address concerns about adherence. This study suggests that the combination of XR-NTX and medical management to treat alcohol-dependent patients in primary care is feasible. Larger controlled trials including patients recruited primarily from general medical settings and powered to detect changes in drinking outcomes over time should be conducted to lend further support for this treatment modality in primary care.

Jeanette M. Tetrault, MD

Reference: Lee JD, Grossman E, DiRocco D, et al. Extended-release naltrexone for treatment of alcohol dependence in primary care. *J Subst Abuse Treat.* 2010;39(1):14–21.

Injectable Diacetylmorphine for Second-Line Treatment of Opioid Addiction

Opioid agonist therapy (OAT) is the most effective treatment for opioid addiction, but some patients continue using illicit opioids even during treatment with optimal doses of oral methadone. In a randomized trial, UK investigators compared open-label treatment with supervised titrated doses of oral methadone, daily injected methadone, or twice-daily injected diacetylmorphine (heroin) among 127 patients receiving OAT who continued to use illicit opioids. The injectable treatments were supplemented with oral methadone when patients were unable to come to a participating clinic for injections.

- At 26 weeks, 80% of subjects remained on their assigned treatments.
- The primary outcome was 50% or more urine specimens negative for opioids and impurities associated with street heroin. More patients assigned to diacetylmorphine achieved this outcome (72%) than did those receiving injectable methadone (39%) or oral methadone (27%).
- Abstinence or near abstinence (2 or fewer positive urine tests in 12 weeks) was also more common in the diacetylmorphine group.

Comments: To interpret these results without distraction, it may be useful to call the medication used a "novel pharmacotherapy," which significantly reduced illicit heroin use among opioid-addicted patients who continued to inject heroin despite receiving OAT. A major study limitation, aside from the open-label design, is the lack of outcome measures beyond drug use; a short-acting agonist may not be the best treatment for patients with opioid addiction because of the need for frequent administration and the physiologic effects of fluctuating serum opioid levels. Even so, the treatment described here would likely improve outcomes among those for whom current best treatments are inadequate. The likelihood of even supervised heroin treatment of opioid addiction being allowed in the US, however, seems low. What happens clinically in countries where such trials have taken place (e.g., the UK, the Netherlands, Spain, Switzerland, Canada, and Germany) should be of great interest.

Richard Saitz MD, MPH

Reference: Strang J, Metrebian N, Lintzeris N, et al. Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial. *Lancet.* 2010;375(9729):1885–95.

Brief Intervention May Reduce Drinking in Injured Emergency Department Patients with Alcohol Dependence but Not in Those with Nondependent Unhealthy Use

Few studies have examined the impact of screening, brief intervention, and referral to treatment (SBIRT) on alcohol-dependent patients. This secondary report from a larger randomized controlled trial (n=1493) compared brief motivational intervention (BMI) with treatment as usual (TAU)* among a subgroup of 1336 patients who were evaluated for dependence and who reported to an emergency department with injuries. Five hundred eighty-eight patients in the subgroup met criteria for alcohol dependence. Outcomes were assessed telephonically at 6 and 12 months by blinded interviewers with follow-up rates of 77% and 66%, respectively. Because this subgroup analysis loses the benefits of randomization, analyses were adjusted for potential confounders.

- Brief intervention was not significantly associated with any drinking outcomes among those without dependence.
- At 12 months, among patients with alcohol dependence,
  - average standard drinks† per week decreased by 12 in the BMI group compared with 9.5 in the TAU group.
  - maximum drinks consumed in a single day decreased by 9 in the BMI group compared with 7 in the TAU group.
  - number of days abstinent averaged 73% in the BMI group compared with 64% in the TAU group.
  - BMI had no effect on alcohol-related problems nor did it increase attendance at specialty-treatment or self-help meetings.
- Fewer alcohol-dependent patients assigned to BMI met dependence criteria at 6 months compared with patients assigned to TAU (45% versus 33%), but this effect was not significant at 12 months.

*Assessment of drinking plus informational handout.

†In this study, 1 standard drink was equal to 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of hard liquor.

Comments: These results suggest BMI may have a positive impact on patients with, but not without, alcohol dependence. This finding is surprising, however, and may be the result of the use of adjusted subgroup analyses. The greater response to intervention by people with more severe drinking problems in the BMI group also raises the possibility of a social-desirability bias. Finally, as this study included only injured patients, whether BMI helps alcohol-dependent patients without an injurious event also remains uncertain.

Hillary Kunins, MD, MPH, MS

Reference: Field CA, Caetano R. The effectiveness of brief intervention among injured patients with alcohol dependence: Who benefits from brief interventions? *Drug Alcohol Depend.* May 19, 2010 [Epub ahead of print].

Brief Alcohol Treatment in a Hepatitis-C Clinic: Results from an Observational Study

The combination of alcohol use and hepatitis-C (HCV) infection is thought to increase the risk for liver cirrhosis, while heavy alcohol use can limit the effectiveness of HCV antiviral therapy. Yet, many patients with HCV drink risky amounts. In this retrospective medical-record review study conducted at an HCV treatment clinic, investigators assessed the impact of a brief integrated alcohol intervention on drinking outcomes and HCV antiviral treatment* eligibility among 47 heavy-drinking† men entering HCV treatment. The intervention was delivered by clinicians and followed by a within-clinic referral to a specialized mental health nurse for alcohol treatment. At the time of record review, patients had been followed for 8–22 months.

- Seventy-two percent of patients who received the intervention agreed to further alcohol treatment.
- At the last follow-up, 62% of patients reported a >50% drinking reduction, including 36% who achieved abstinence.
- The mean quantity of drinks per drinking day fell from 9.5 at baseline to 3.8 at the last follow-up ($p<0.001$).
- Only 6% of patients were excluded from HCV antiviral treatment because of drinking or drug use.

*Interferon plus ribavirin.

†Alcohol Use Disorders Identification Test—Consumption (AUDIT-C) scores ≥4.

Comments: This small uncontrolled trial showed that integrating HCV and alcohol treatment is feasible in real-world settings. Within-clinic referral has the potential to improve linkage of patients with alcohol use disorders to specialized treatment who may not otherwise have access to it. This, in turn, could lead to significant decreases in drinking, thus improving HCV antiviral treatment eligibility and slowing disease progression. However, these results cannot be considered definitive until they are replicated in controlled trials.

Nicolas Bertholet, MD, MSc

Reference: Dieperink E, Ho SB, Heit S, et al. Significant reductions in drinking following brief alcohol treatment provided in a hepatitis C clinic. *Psychosomatics.* 2010;51(2):149–56.

Retention in Naltrexone Implant Treatment: Promising, but Not Conclusive

By increasing adherence, sustained-release formulations of naltrexone are hypothesized to be more effective than oral formulations, which by-and-large have shown little advantage over placebo among opioid-dependent patients. In this observational study from Norway, 61 patients recruited at discharge from medication-free residential drug treatment or prison received sustained-release naltrexone implants lasting 5–6 months. The main outcome measure was retention in treatment, defined as receiving a second implant 4–6 months after the first. Multivariable analyses of pretreatment participant factors associated with retention were also conducted.

- Thirty-one participants (51%) received a second implant. An additional 6 (10%) initiated opioid maintenance (3 patients) or long-term residential treatment (3 patients).
- Factors associated with retention included less injection drug use in the 30 days prior to study entry (OR 0.9, p=0.007), duration of longest employment (OR 1.4, p=0.017), and fewer days of worry about family problems (OR 1.7, p=0.034).

Comments: Adding to promising evidence from 2 previous trials, this observational noncontrolled study suggests that sustained-release naltrexone may retain patients in treatment at rates approaching those observed in opioid-agonist treatment programs. However, comparative effectiveness trials, with opioid-agonist therapy as the comparison arm, are still needed before widespread use of sustained-release naltrexone can be recommended.

Hillary Kunins, MD, MPH, MS

Reference: Kunøe N, Lobmaier P, Vederhus JK, et al. Retention in naltrexone implant treatment for opioid dependence. *Drug Alcohol Depend.* May 28, 2010 [E-pub ahead of print].

Patient Satisfaction with Methadone Maintenance Is Associated with Treatment Retention and Positive Outcomes

Methadone maintenance is an effective treatment for opioid dependence, but many patients drop out of treatment. Little is know about the role of patient satisfaction in treatment outcomes. Researchers studied 283 opioid-dependent subjects entering treatment in 1 of 6 Baltimore area methadone maintenance programs. Patient satisfaction was measured at 3 months using the Texas Christian University Client Evaluation Form (CEF) and was divided into three subscales: Treatment Needs, Treatment Satisfaction, and Counselor Services. Researchers analyzed the relationship between satisfaction and 3-month Addiction Severity Index (ASI) scores, 3-month drug test results, and 12-month treatment retention.

- Participants who remained in treatment for 12 months reported more satisfaction with treatment at 3 months than those who dropped out.
- The CEF Treatment Satisfaction and Counselor Services subscales were inversely related to ASI Drug and Legal composite scores as well as to the number of days of heroin and cocaine use reported on the ASI.
- Participants who reported lower satisfaction on the Treatment Needs subscale were more likely to have drug tests that were positive for heroin or cocaine.

Comments: It is not surprising that patient satisfaction correlates with outcomes, and the CEF may be a useful tool for identifying individuals who need additional services. It would be of interest to see if there were differences in patient satisfaction between programs or individual counselors. The important question is whether steps to improve satisfaction will improve outcomes.

Darius Rastegar, MD

Reference: Kelly SM, O'Grady KE, Brown BS, et al. The role of patient satisfaction in methadone treatment. *Am J Drug Alcohol Abuse.* 2010;36(3):150–4.

Buprenorphine Treatment in an HIV Clinic Is Effective for Opioid Dependence but Does Not Improve HIV Outcomes

Providing office-based buprenorphine treatment in HIV clinics may improve both HIV and opioid-addiction outcomes. In this study, researchers randomly assigned 93 opioid-dependent HIV-infected adults attending an urban HIV clinic to either office-based buprenorphine (BUP) or referral to outside treatment. Subjects were followed for 12 months. Outcome measures included urine test results, participation in addiction treatment, visits with HIV care providers, CD4 cell counts, and HIV RNA levels.

- Compared with subjects in the referral group, those in the BUP group:
  - initiated opioid agonist treatment more rapidly;
  - were more likely to be in treatment over the 12 months of follow-up;
  - had fewer opioid- or cocaine-positive urine test results (44% versus 65% and 54% versus 76%, respectively); and

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Buprenorphine Treatment for Opioid Dependence: Effect on HIV Outcomes (continued from page 4)

  - had more visits with their HIV care provider (median, 3.5 versus 3.0 visits).
- There was no significant difference between the 2 groups in months of antiretroviral treatment, CD4 cell counts, HIV RNA levels, emergency department visits, or hospitalizations.

Comments: This small study supports the feasibility and effectiveness of providing office-based buprenorphine in an HIV clinic but failed to show a benefit in terms of HIV outcomes. A greater impact might have been seen in areas where other opioid-addiction treatment options are not readily accessible. Moreover, in this study, BUP and HIV care were provided in the same setting but by separate providers; it is possible that having a single physician provide both services would improve outcomes further.

Darius A. Rastegar, MD

Reference: Lucas GM, Chaudhry A, Hsu J, et al. Clinic-based treatment of opioid-dependent HIV-infected patients versus referral to an opioid treatment program. *Ann Intern Med.* 2010;152(11):704–11.

Pain Characterization and Prior Pain Treatment among Patients Initiating Opioid Agonist Therapy for Opioid Dependence

Unalleviated pain is common in patients receiving opioid agonist treatment (OAT) for opioid dependence and is related to poor psychosocial functioning and increased psychological distress. Additionally, few OAT programs have dedicated pain-treatment services. This needs-assessment study explored the prevalence and nature of pain and prior pain treatment among patients enrolling in OAT, focusing specifically on complementary and alternative approaches to pain management. The sample included 293 opioid-dependent participants consecutively enrolled in OAT over a 6-month period at a private community-based addiction treatment center.

- Eighty-eight percent of participants (n=257) reported having pain within the last week. Of these, 17% reported mild pain, 44% reported moderate pain, and 39% reported severe or unbearable pain.
- Sixty-seven percent of participants reporting moderate, severe, or unbearable pain described a lifetime history of chronic pain.
- Participants reporting recent pain of at least moderate intensity used conventional pain-management approaches more often than complementary or alternative approaches. The most common conventional approach was over-the-counter pain medication (>40%), and the most common alternative approach was prayer (>20%).
- Nearly 30% of all participants reported past-week use of opioid medication. Thirteen percent of participants who did not have a lifetime history of chronic pain and 20% of those who did reported using benzodiazepines in the past 7 days for pain relief.
- Sixty-seven percent of participants supported integrating pain-treatment services into the OAT program.

Comments: Despite concerns over generalizability, response bias, and the failure to include physical and psychiatric comorbidity and prior drug-treatment information, these results suggest the need for further investigation into chronic pain comorbidity and pain management among opioid-dependent patients. More conclusive evidence could have an impact on OAT-program resource planning.

Jeanette M. Tetrault, MD

Reference: Barry DT, Beitel M, Cutter CJ, et al. Conventional and nonconventional pain treatment utilization among opioid dependent individuals with pain seeking methadone maintenance treatment: A needs assessment study. *J Addict Med.* 2010;4(2):81–7.

HEALTH OUTCOMES

Is the Presence of an Alcohol-Attributable Admitting Diagnosis Associated with Decreased Drinking after Hospitalization?

To assess whether physical health status is associated with drinking after hospitalization, researchers conducted a secondary analysis of data from a randomized trial of hospital-based BI in 341 medical inpatients with unhealthy alcohol use. Separate adjusted models were used to test the association between 5 physical health measures (recent medical comorbidities, lifetime medical comorbidities, physical health status, any alcohol-attributable medical diagnosis, and alcohol-attributable principal admitting diagnosis) and number of heavy drinking days (HDDs*) in the 30 days prior to the 3-month post-hospitalization assessment.

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*Defined as >14 standard drinks per week or ≥5 drinks per occasion for men and >11 drinks per week or ≥4 drinks per occasion for women and people aged 66 or older.

Alcohol-Attributable Diagnosis and Drinking Post-Hospitalization (continued from page 5)

- Overall, there was no association between the 5 measures of physical health and HDDs.
- In analyses testing for interactions, an alcohol-attributable principal admitting diagnosis was associated with significantly fewer HDDs among participants with low perception of an alcohol problem at hospital admission (adjusted incidence rate ratio [aIRR], 0.36) or with nondependent drinking (aIRR, 0.10).
- An alcohol-attributable principal admitting diagnosis was present in 4 nondependent drinkers and 9 individuals with low perception of an alcohol problem.

Comments: These interesting results suggest that an alcohol-attributable principal admitting diagnosis may serve as a "wake-up call" to medical inpatients with low perception of an alcohol problem or nondependent drinking. The results imply that hospital-based interventions may be more successful if they focused on the link between alcohol-attributable diagnoses and alcohol use in appropriate patients. However, it is important to note that, depending on a hospital's proportion of dependent to nondependent inpatients and alcohol-attributable admitting diagnoses, this may apply to only a small minority of hospitalized patients with unhealthy alcohol use.

Kevin L. Kraemer, MD, MSc

Reference: Williams EC, Palfai T, Cheng DM, et al. Physical health and drinking among medical inpatients with unhealthy alcohol use: a prospective study. *Alcohol Clin Exp Res.* 2010;34(7):1–9.

Is the Inverse Association between Moderate Drinking and Type 2 Diabetes the Result of Other Healthy Lifestyle Habits?

To determine whether the association between moderate alcohol consumption and the reduced risk of type 2 diabetes might be the result of a combination of lifestyle behaviors, researchers in the Dutch European Prospective Investigation into Cancer and Nutrition (EPIC-NL) prospectively analyzed data from 35,625 participants aged 20–70 years who were free of diabetes, cardiovascular disease, and cancer at baseline (1993–1997) and categorized them into groups based on the following low-risk lifestyle factors: moderate alcohol consumption, optimal weight, regular physical activity, nonsmoking, and healthy diet.* Scores ranged from 0 (no low-risk behaviors) to 4 (all low-risk behaviors).

- Over a median follow-up of 10.3 years, 796 incident cases of type 2 diabetes occurred.
- Compared with nondrinkers, hazard ratios (HRs) for risk of type 2 diabetes among moderate alcohol consumers, after multivariable adjustments, were as follows:
  - 0.35 for participants of normal weight,
  - 0.65 for people who were physically active,
  - 0.54 for nonsmokers,
  - 0.57 for people eating a healthy diet, and
  - 0.56 for people with 3 or more low-risk lifestyle behaviors combined.

*Moderate alcohol consumption = 5.0–14.9 g alcohol per day for women and 5.0–29.9 g per day for men; optimal weight = BMI <25; being physically active = ≥30 minutes of activity per day; and healthy diet = general adherence to Dietary Approaches to Stop Hypertension [DASH] guidelines.

Comments: In this study, compared with abstaining, moderate alcohol consumption was associated with an approximately 40% lower risk for type 2 diabetes in subjects already at low risk due to multiple low-risk lifestyle behaviors. Whether the lower risk in moderate drinkers is due to the alcohol itself or to other lifestyle factors is a continuing question for epidemiologists; however, these results indicate that the association is not likely to be explained solely by the healthier lifestyle of moderate drinkers.

R. Curtis Ellison, MD

Reference: Joosten MM, Grobbee DE, van der A DL, et al. Combined effect of alcohol consumption and lifestyle behaviors on risk of type 2 diabetes. *Am J Clin Nutr.* 2010;91(6):1777–83.

Does the Alcohol Use of Family and Friends Influence Individual Use?

Health risks such as smoking, obesity, and sexually transmitted disease can travel through social networks. To determine whether and how alcohol use travels through such pathways, researchers analyzed longitudinal data from 12,067 Framingham Heart Study participants assessed every 2–4 years between 1971 and 2003. Social network ties for 5124 principals (i.e., the focal individuals of the network) and self-reported alcohol consumption for principals and their contacts were assessed at each time point.

- Twenty-two percent of principals were heavy drinkers,* and 15% were abstainers.
- Principals were 50%, 36%, and 15% more likely to be heavy drinkers if individuals between 1–3 degrees of

*Defined as consuming, on average, more than 1 drink per day for women and more than 2 drinks per day for men.

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Family, Friends, and Alcohol Use (continued from page 6)

separation,† respectively, were also heavy drinkers.The likelihood that a principal drank heavily increased by 18% for each heavy-drinking social contact.

- The likelihood that a principal drank heavily increased by 154% if a *female* friend started drinking heavily but did not increase significantly if a male friend started drinking heavily.
- Principals were more likely to drink heavily if their spouse or sibling drank heavily but not if a neighbor or coworker drank heavily.
- Abstinence in principals was associated with abstinence in social contacts in a pattern similar to the heavy drinking results.

†Defined as follows: 1=close friend, 2=friend of a friend, and 3=friend of a friend of a friend.

Comments: These interesting results suggest that alcohol use behaviors (both heavy drinking and abstinence) are influenced not only by family and close friends but also by more distant social contacts. Thus, public-health and clinical interventions to promote safe alcohol use should target both individuals and social groups.

Kevin L. Kraemer, MD, MSc

Reference: Rosenquist JN, Murabito J, Fowler JH, et al. The spread of alcohol consumption behavior in a large social network. *Ann Intern Med.* 2010:152(7): 426–33.

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A free multimedia training curriculum on screening and brief intervention for unhealthy alcohol use

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- Learn skills for addressing unhealthy alcohol use (e.g. screening, assessment, brief intervention, and referral) in primary care settings. Includes a free PowerPoint slide presentation, trainer notes, case-based training videos, and related curricula on health disparities/cultural competence and pharmacotherapy.

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Many others periodically reviewed (see www..aodhealth.org).

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