Alcohol, Other Drugs, and Health: Current Evidence

NOV–DEC 2008

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Interventions & Assessments

Oral Naltrexone Decreases Use and Extends Time to Relapse in Amphetamine Dependent Patients

Currently, no medications are FDA-approved to treat amphetamine dependence. Naltrexone, an opioid antagonist, has shown efficacy in reducing relapse among subjects with opioid or alcohol dependence. Investigators from Sweden, where amphetamine is the most commonly abused stimulant, conducted a 12-week randomized double-blind controlled trial among 80 amphetamine-dependent subjects to determine whether daily oral naltrexone decreased amphetamine use compared with placebo. Fifty-five patients completed the trial. Two weeks of abstinence from amphetamine were required to enter the trial, and subjects with dependence on alcohol or other drugs were excluded. Both groups attended once-weekly relapse prevention counseling and underwent twice-weekly urine toxicology testing. Missing urine tests were considered positive.

- In intent-to-treat analysis, 65% of urine tests in the naltrexone group and 48% in the placebo group were negative for amphetamines ($p<0.05$).
- The mean number of urine tests prior to first relapse was 13 in the naltrexone group and 6 in the placebo group.

Comments: In this study, oral naltrexone reduced amphetamine use and extended time to relapse in recently abstinent amphetamine dependent patients. Clinical trials of naltrexone for cocaine dependence have not shown this efficacy, and its effectiveness for methamphetamine dependence is not known. Studies in larger and more diverse populations, especially those who have not attained abstinence prior to initiating the medication, are needed to confirm naltrexone's effectiveness for amphetamine and other stimulant dependence.

Alexander Y. Walley, MD, MSc

Reference: Jayaram-Lindström N, Hammarberg A, Beck O, et al. Naltrexone for the treatment of amphetamine dependence: a randomized, placebo-controlled trial. *Am J Psychiatry.* 2008;165(11):1442–1448.

Alcohol Counseling Can Reduce Blood Pressure

Unhealthy alcohol use is associated with hypertension. Two recent articles examined whether reductions in drinking can decrease blood pressure among hypertensive heavy drinkers.

Analyzing data from 1383 alcohol dependent persons enrolled in the Combining Medication and Behavioral Interventions for Alcoholism (COMBINE) study, Stewart and colleagues found that, over a 4-month treatment period,

- systolic blood pressure (SBP) decreased by 12 mm Hg in patients whose SBP was >132 mm Hg at baseline.
- diastolic blood pressure (DBP) decreased by 8 mm Hg in patients whose DBP was >84 mm Hg at baseline.
- adjusting for age, gender, and baseline blood pressure, a 50% decrease in days of alcohol consumption decreased SBP by 2.4 mm Hg and DBP by 1.9 mm Hg in non-African Americans ($p<.001$).

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Alcohol Counseling Reduces Blood Pressure (continued from page 1)

Rose and colleagues performed a randomized trial of quality improvement measures to increase alcohol screening and brief intervention among 27,591 hypertensive patients in 21 primary care practices. The intervention included electronic medical records and reminders, site visits, annual meetings, and quarterly performance reports. Over the 2-year study period,

- hypertensive patients in intervention practices were 8 times more likely to be screened for alcohol use.
- patients with unhealthy drinking* were 5.5 times more likely to be counseled.
- no differences in blood pressure were found between the randomized groups, but SBP decreased by 4.2 mm Hg and DBP by 3.3 mm Hg (both $p<.05$) among hypertensive patients who received counseling.

*Alcohol Use Disorders Identification Test consumption score ≥4.

Comments: Counseling to reduce alcohol consumption may help reduce blood pressure in hypertensive patients with unhealthy drinking. The inclusion of alcohol screening and brief interventions in quality improvement efforts for hypertensive populations might facilitate their implementation in primary care settings.

Peter D. Friedmann, MD, MPH

References: Stewart SH, Latham PK, Miller PM, et al. Blood pressure reduction during treatment for alcohol dependence: results from the Combining Medication and Behavioral Interventions for Alcoholism (COMBINE) study. *Addiction.* 2008;103(10):1622–1628.

Rose HL, Miller PM, Nemeth LS, et al. Alcohol screening and brief counseling in a primary care hypertensive population: a quality improvement intervention. *Addiction.* 2008;103(8):1271–1280.

Longer Treatment with Buprenorphine-Naloxone Improves Outcomes in Opioid-dependent Young Adults

The use of long-term opioid agonist and partial agonist medication (e.g., methadone or buprenorphine) is often reserved for older opioid-dependent individuals, while short medication tapers or medication-free treatment is offered to younger individuals. In a randomized trial, researchers evaluated the efficacy of buprenorphine-naloxone tapers of 2 versus 12 weeks in 152 younger subjects (mean age, 19 years) at 6 community programs around the country. Subjects had a median of 1 year of opioid dependence. All were offered weekly individual and group counseling. The primary findings were as follows:

- Twelve-week treatment with buprenorphine-naloxone was associated with greater treatment retention and decreased illicit opioid use—but only during the period that medication was provided.
- Patients in the 2-week taper group had higher proportions of opioid-positive urine test results at weeks 4 and 8 but not at week 12.
- Rates of self-reported opioid use were higher in the 2-week taper group than in the 12-week taper group (55% versus 38%) at 12 weeks, but a loss of this difference was seen at 6-month follow-up (63% versus 72%).

Comments: This well-designed and well-conducted study demonstrates that young opioid-dependent patients do better with longer, rather than shorter, periods of buprenorphine-naloxone treatment. The relatively high rate of relapse following discontinuation of

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Longer Buprenorphine-Naloxone Treatment for Young Adults (continued from page 2)

medication supports longer term use, even in young patients with relatively short durations of opioid dependence. In young patients who undergo buprenorphine-naloxone taper, strategies to improve treatment outcomes, including counseling, contingencies, and alternative pharmacotherapies, may be needed to promote long-term abstinence and avoid the comorbid and fatal complications of opioid dependence.

David A. Fiellin, MD

Reference: Woody GE, Poole SA, Subramaniam G, et al. Extended vs short-term buprenorphine-naloxone for treatment of opioid-addicted youth: a randomized trial. *JAMA.* 2008;300(17):2003–2011.

Brief Intervention Decreases Risky Alcohol Use in Postpartum Women

To determine whether the postpartum period is an effective time to counsel women about alcohol use, researchers in this study screened 8706 women at their 45-day postpartum visit and randomized 235 women who met inclusion criteria* to either usual care (receipt of a booklet on general health issues but no specific counseling) or brief intervention (BI). The intervention consisted of two 15-minute counseling visits with a nurse or obstetrician, each 1 month apart, and a follow-up phone call 2 weeks after each visit. Past 28-day alcohol use was assessed at baseline and by phone interview at 6 months.

- Twenty-three of 122 women (19%) in the BI group did not receive an intervention because they failed to show up for scheduled counseling visits. An additional 23 women (19%) in the intervention group and 5 women (4%) in the usual care group (n=113) did not complete the 6-month follow-up interview.
- In intent-to-treat analyses, women in the BI group, compared with controls, reported significantly greater reductions from baseline to 6 months in number of standard drinks consumed (14.2-drink reduction versus 5.1), number of drinking days (3.4-day reduction versus 1.2), and number of heavy drinking days** (1.8-day reduction versus 0.5).

*Eligible women reported at least 1 of the following in the 28 days prior to baseline interview: ≥20 standard drinks, ≥4 drinks on 4 or more occasions, or ≥20 drinking days.
**4 or more drinks per day.

Comments: These findings suggest that BI can decrease alcohol use in postpartum women. It is important to note that 1209 women (14%) screened positive for at-risk drinking (including before and during pregnancy) but did not have sufficient alcohol use in the 28 days prior to the postpartum visit to meet the study criteria. This indicates that many women with at-risk drinking may be slow to return to drinking after delivery and will need to be rescreened periodically during the postpartum period and beyond.

Kevin L. Kraemer, MD, MSc

Reference: Fleming MF, Lund MR, Wilton G, et al. The Healthy Moms Study: the efficacy of brief alcohol intervention in postpartum women. *Alcohol Clin Exp Res.* 2008;32(9):1600–1606.

Rapid Test for Ethylene Glycol Poisoning

Ethylene glycol poisoning is often suspected when an anion gap and osmolar gap are both present in a patient with alcohol dependence or ingestion. But confirmation of the diagnosis, desirable because treatment is expensive and not without risk, usually requires sending a blood sample to an outside laboratory and waiting for results. In a prospective observational study, researchers employed a rapid qualitative test already in use by veterinarians to test for ethylene glycol in 24 blood samples from human subjects with suspected toxic alcohol poisoning. Gas chromatography was the reference standard.

- The qualitative test detected ethylene glycol in all 15 samples that were positive for ethylene glycol by gas chromatography (sensitivity, 100%).
- The qualitative test was negative in 5 samples that tested positive for methanol but not ethylene glycol.
- One of 4 samples negative for methanol and ethylene glycol by gas chromatography tested positive by the qualitative test (specificity, 89%).

Comments: Clearly, a larger study regarding this test's operating characteristics is needed before it can be recommended for widespread use in humans. I suspect the sensitivity and specificity will not be as good. But the results look promising, and having a rapid test would be a great help to clinicians who currently have to decide whether to institute treatment with fomepizole, ethanol, or hemodialysis based on nonspecific clinical findings.

Richard Saitz MD, MPH

Reference: Long H, Nelson LS, Hoffman RS. A rapid qualitative test for suspected ethylene glycol poisoning. *Acad Emerg Med.* 2008;15(7):688–690.

Overdose Management Training and Take-home Naloxone for Opiate-Using Persons May Save Lives

Opiate overdose is the cause of most drug-related mortality, and witnesses are commonly present. An initiative to provide training in the management of overdose was delivered to staff in 20 drug treatment facilities across England during 2005/2006. These staff then provided 239 opiate-using addiction treatment patients with training in management of overdose and a take-home supply of naloxone. The patients completed surveys before, immediately after, and 3 months after the training. At baseline, more than 90% of patients could recognize signs of opioid overdose. Among the 186 patients (78%) who completed 3-month follow-up,

- 90% reported still using illicit opiates.
- over 96% recalled the correct intramuscular injection sites for the naloxone, 77% retained knowledge of the recovery breathing position, and >97% remained confident in their ability to recognize and manage an overdose.
- close to 80% retained their naloxone, and 28% had trained a friend or family member to administer it should the participant overdose.
- 18 reported witnessing or experiencing an overdose during the 3-month period. Patients used their naloxone to revive other people on 10 occasions, and 2 received naloxone from ambulance staff.
- 1 death resulted among the 6 overdoses where naloxone was not administered.
- no adverse reactions were reported.

Comment: Despite the brief follow-up period and lack of a control group, this study suggests that addiction treatment patients can recognize and treat opiate overdose with intramuscular naloxone, which is easy to administer, safe, and life-saving. Overdose management training and naloxone distribution is a promising strategy to reduce the high rates of mortality among persons with opiate use disorders, especially those who have lost their tolerance as a result of detoxification or imprisonment. Although more definitive studies are needed, physicians are well-positioned to offer this very safe, life-saving option to opiate-dependent patients.

Peter D. Friedmann, MD, MPH

Reference: Strang J, Manning V, Mayet S, et al. Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. *Addiction.* 2008;103(10):1648–1657.

Buprenorphine for Opioid Dependence: Why Is It Underprescribed?

Overwhelming evidence has demonstrated that opioid agonist treatment reduces adverse consequences of opioid dependence. To improve access to pharmacotherapy, the Food and Drug Administration approved buprenorphine, a partial μ-opioid agonist, to treat patients with opioid dependence in 2002. To date, however, there has been limited uptake of buprenorphine by physicians, particularly in general practices. In this study, investigators asked 172 physicians involved in 1 of 2 buprenorphine initiatives to complete surveys assessing factors likely to affect their willingness to prescribe buprenorphine. Respondents included 49 trained nonprescribers, 45 novice prescribers (prescribed buprenorphine to 30 or fewer patients), and 78 experienced prescribers.

- Factors rated by all respondents as strongly affecting their willingness to prescribe buprenorphine included
  - lack of clinical training on buprenorphine,
  - lack of behavioral health services support (such as substance abuse counseling and mental health services),
  - absence of an effective referral system for additional drug treatment,
  - lack of adequate time per patient visit,
  - limited availability of buprenorphine, and
  - concerns about patients on chronic pain medications.
- Experienced prescribers were less concerned than novice or nonprescribers about most factors, particularly induction logistics, access to consultation with a buprenorphine expert, and access to clinical guidelines.
- Experienced prescribers were more concerned than novice or nonprescribers about reimbursement.

Comments: These data indicate that experience prescribing buprenorphine alleviates many associated concerns. Similarities in responses between novice and nonprescribers suggest that substantial experience is required before these concerns are significantly reduced. The desire for guidelines, expert support, and expanded training in this area is not surprising given the limited attention paid to drug addiction and treatment in medical school and residency training curricula.

Julia H. Arnsten, MD, MPH

Reference: Netherland J, Botsko M, Egan J, et al. Factors affecting willingness to provide buprenorphine treatment. *J Subst Abuse Treat.* 2008 [Epub ahead of print].

Alcohol Contributes to Fall Risk among Working-aged Individuals

The public-health impact of falls at home is substantial, resulting in a number of emergency department visits, hospitalizations, and deaths among working-aged individuals. Investigators conducted a population-based case-control study to investigate the role of acute alcohol use* in falls at home among individuals aged 25–60. Individuals who were admitted to a hospital or died as a result of a nonoccupational fall injury at home (n=335) were compared with controls (n=352) randomly selected from the same geographic region in New Zealand. Analyses were adjusted for various factors likely to explain falls, including hazardous alcohol use (Alcohol Use Disorders Identification Test score ≥8).

- A significant association was seen between acute alcohol consumption and risk of fall injury in the next 6 hours:
  - Individuals who consumed 2 drinks were 3.7 times more likely to have a fall injury compared with individuals who did not drink (95% CI, 1.2–10.9).
  - Individuals who consumed 3 or more drinks were 12.9 times more likely to have a fall injury compared with individuals who did not drink (95% CI, 5.2–31.9).
  - Assuming a causal relationship, 20% of all fall injuries in the study population were attributable to acute alcohol consumption.

*Consumption of 2 or more standard alcoholic drinks in the preceding 6 hours.

Comments: Clinicians should raise awareness of the potential risk for fall injuries at home when counseling working-aged individuals regarding alcohol consumption.

Nicolas Bertholet, MD, MSc

Reference: Kool B, Ameratunga S, Robinson E, et al. The contribution of alcohol to falls at home among working-aged adults. *Alcohol.* 2008;42(5):383–388.

Can Sexual Risk Reduction Be Addressed in Substance Use Treatment Programs?

Human immunodeficiency virus/sexually transmitted disease (HIV/STD) risk reduction has become a central goal of substance use treatment programs, but its implementation with regard to sexual risk reduction lacks successful pragmatic models. Tross and colleagues studied the implementation of safer sex skills building (SSB) groups among 515 women in 12 drug treatment programs participating in the NIDA Clinical Trials Network. Women who had unprotected vaginal or anal intercourse in the past 6 months were randomized to either SSB (5 ninety-minute groups using problem solving and skills rehearsal to increase HIV/STD risk awareness and condom use including partner negotiation) or HIV/STD education (HE) (1 sixty-minute group covering HIV/STD disease, testing, treatment, and prevention). Participants were assessed at 3 and 6 months for the occurrence of unprotected sex in the past 3 months.

- Although only 60–70% of participants were available for follow-up and less than two-thirds of each group received the intervention, the following significant effects were noted:
  - Unprotected sex decreased from a baseline median of 19 episodes in 3 months to 15 and 17 episodes in the SSB and HE groups, respectively (no significant difference between groups).
  - Unprotected sex further decreased to 14 episodes in the SSB group at 6-month follow-up (a 29% decrease) but increased to 24 in the HE group ($p<0.0377$).

Comments: Despite low intervention participation and follow-up assessment, this clinical trial provides encouraging if modest evidence that desired changes can be achieved using behavioral interventions to address sex risk in substance use treatment. Additional studies including men, using interventions briefer than 7.5 hours, and measuring STD outcomes will further contribute to this important component of HIV prevention.

Jeffrey H. Samet, MD, MA, MPH

Reference: Tross S, Campbell AN, Cohen LR, et al. Effectiveness of HIV/STD sexual risk reduction groups for women in substance abuse treatment programs: results of NIDA Clinical Trials Network Trial. *J Acquir Immune Defic Syndr.* 2008;48(5): 581–589.

HEALTH OUTCOMES

Alcohol, Liver Enzymes, and Risk for Type 2 Diabetes

Moderate alcohol consumption decreases the risk of type 2 diabetes (DM), but elevated liver enzymes increase the risk. This study examined the association between DM; alcohol consumption; and two liver enzymes, γ-glutamyltransferase (GGT) and alanine aminotransferase (ALT). Researchers followed a cohort of 8576 Japanese men aged 40–55 years enrolled in the Kansai Healthcare Study, an ongoing investigation of risk factors for cardiometabolic disease. Four years following baseline examination, DM was diagnosed in 878 subjects. Results in multivariable

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Alcohol, Liver Enzymes, and Type 2 Diabetes Risk (continued from page 5)

models were as follows:

- Alcohol intake of 16–43 g per day (1½–3½ drinks) decreased the risk of DM, while higher levels of GGT and ALT increased the risk.
- In joint analyses of alcohol and enzymes, moderate drinkers with the lowest tertile of GGT had the lowest risk of DM, while nondrinkers with the highest tertile of GGT or ALT had the highest risk (odds ratio, 3.18 and 2.37, respectively).
- At every level of GGT, moderate or heavy alcohol drinkers had a lower risk of DM than nondrinkers.

Comments: Although these findings indicate that GGT, ALT, and alcohol consumption are independently associated with DM risk and point to an inverse association between alcohol and DM (30–35% lower risk for moderate drinkers), interpreting the results is problematic in that multivariable analyses were not adjusted for liver enzymes. The raw data suggest a higher risk of DM not only among nondrinkers but also among heavier drinkers. Once liver enzyme data are entered into the analysis, however, even heavier drinkers show a marked decrease in risk. In addition, the highest risk of DM was almost always in nondrinkers with abnormal liver tests, raising the question of whether some subjects who were nondrinkers at baseline were former heavy drinkers. Although prospective epidemiologic studies consistently show a much lower risk of developing DM among moderate drinkers, analytic problems in the present paper make it difficult to conclude that the effect of alcohol on risk of DM is independent of liver function.

R. Curtis Ellison, MD

Reference: Sato KK, Hayashi T, Nakamura Y, et al. Liver enzymes compared with alcohol consumption in predicting the risk of type 2 diabetes: the Kansai Healthcare Study. *Diabetes Care.* 2008;31(6):1230–1236.

National Survey Reveals Increased Drug Use by Adults, with Few Receiving Treatment

The National Survey on Drug Use and Health (NSDUH) provides data on prevalence and correlates of substance use, mental illness, related problems, and treatment among a representative sample of the US general population aged 12 years and older. Results of the study for 2007, representing interviews with 67,870 participants using computer-assisted techniques to maximize truth-telling about sensitive topics, identify several important findings.

- Eight percent of the population had used an illicit drug in the preceding month.
- Illicit drug use among person 55–59 years old has more than doubled since 2002.
- Prescription drug abuse decreased among 12–17 year olds but increased among young adults aged 18–25.
- The illicit drug categories with the largest number of past year initiates among persons aged 12 or older were nonmedical use of pain relievers (2.1 million) and marijuana use (2.1 million).
- Pain relievers used nonmedically were most often obtained from a friend or relative, and from a drug dealer, stranger, or over the Internet only 5% of the time.
- Twenty-nine percent of the population used a tobacco product in the prior month. Smoking rates among youth declined, but their use of smokeless tobacco increased.
- Only 1 in 10 persons eligible for treatment for illicit drug or alcohol use received treatment in a dedicated program. Of those not receiving treatment, 1.3 million reported feeling a need for it.

Comments: These prevalence data highlight the public health potential of more widespread implementation of screening and brief intervention for substance use. Rates of substance use among older persons may continue to increase as the baby boom cohort, with its higher lifetime rates of use, ages. The gulf between treatment eligibility and participation poses a major challenge to clinicians in office-based practice, where the need to improve strategies for engaging drug and alcohol users in effective treatment remains high.

Marc N. Gourevitch, MD, MPH

Reference: Substance Abuse and Mental Health Services Administration. *Results from the 2007 National Survey on Drug Use and Health: National Findings.* Rockville, MD: Office of Applied Studies, NSDUH Series H-34 (DHHS Publication No. SMA 08-4343); 2008.

Provider Discussions May Improve Substance Abuse Treatment in HIV-infected Persons

Substance abuse treatment (SAT) is a critical component in preventing the spread of HIV infection and is associated with improved HIV outcomes. This study examined factors associated with SAT, including patient–provider discussions of substance abuse, among people with HIV. Researchers conducted interviews with 951 HIV-infected adults receiving care at 14 sites in the HIV Research Network, a consortium of HIV research centers. Seventy-one percent of

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Patient/Provider Discussions Improve SAT (continued from page 6)

respondents reported current (past 6-month) (36%) or lifetime (35%) drug use.

- Twenty-four percent of current or former users reported receiving SAT in the preceding 6 months.
- Less than half (46%) of current or former users reported discussing substance use with their provider, with current users having such discussions more frequently than former users (56% versus 35%, p<.001).
- Patients who participated in such discussions were more than twice as likely to have received SAT than those who did not (odds ratio, 2.12; confidence interval, 1.31–3.41).
- Current users who participated in such discussions received treatment more frequently than those who did not (26% versus 14%, p=.006). This was also true of former users (38% versus 21%, p=.002).

Comments: These findings reinforce the need to increase the opportunities for linkage between substance abuse treatment and HIV primary care. Although HIV primary care providers are faced with many demands, they should be encouraged to screen for and counsel patients about substance use.

Julia H. Arnsten, MD, MPH

Reference: Korthuis PT, Josephs JS, Fleishman JA, et al. Substance abuse treatment in human immunodeficiency virus: the role of patient-provider discussions. *J Subst Abuse Treat.* 2008;35 (3):294–303.

The major journals regularly reviewed for the newsletter include the following:

Addiction
Addictive Behaviors
AIDS
Alcohol
Alcohol & Alcoholism
Alcoologie et Addictologie
Alcoholism: Clinical & Experimental Research
American Journal of Drug & Alcohol Abuse
American Journal of Epidemiology
American Journal of Medicine
American Journal of Preventive Medicine
American Journal of Psychiatry
American Journal of Public Health
American Journal on Addictions
Annals of Internal Medicine
Archives of General Psychiatry
Archives of Internal Medicine
British Medical Journal
Drug & Alcohol Dependence
Epidemiology
European Addiction Research
European Journal of Public Health
European Psychiatry
Journal of Addiction Medicine
Journal of Addictive Diseases
Journal of AIDS
Journal of Behavioral Health Services & Research
Journal of General Internal Medicine
Journal of Studies on Alcohol
Journal of Substance Abuse Treatment
Journal of the American Medical Association
Lancet
New England Journal of Medicine
Preventive Medicine
Psychiatric Services
Substance Abuse
Substance Use & Misuse

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

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