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Alcohol and Health: Current Evidence

JAN - FEB 2006

Alcohol and Health Outcomes

Alcohol Likely Worsens Adherence to Diabetes Preventive Care

In addition to its effects on morbidity and mortality, alcohol use influences the self-management of chronic illness. Using data from a national survey, researchers examined whether alcohol use worsens adherence to diabetes care. Analyses were adjusted for potential confounders (e.g., age, race, diabetes duration, insulin use).

- Among 10,980 adults with self-reported diabetes, 70% were current nondrinkers, 28% were moderate drinkers (average ≤ 1 drinks per day for women, ≤ 2 drinks for men) and 2% were heavy drinkers (average > 1 drink per day for women, > 2 drinks for men).
- Heavy drinkers were significantly more likely than nondrinkers to not perform daily glucose self-monitoring and to not have had an eye exam in the past year (odds ratios 1.8 and 2.2, respectively).
- Moderate drinkers were significantly more likely than nondrinkers to not perform daily glucose self-monitoring and to not

have had a provider visit for diabetes in the past year (odds ratios 1.3 and 1.8, respectively).

- Annual self-reported hemoglobin A1c monitoring, annual foot exams, and formal diabetes education did not significantly differ by levels of alcohol consumption.

Comments: Though unable to prove causality, this cross-sectional study illustrates that alcohol use is associated with less self-care among adults with diabetes. Subsequently, these patients likely increase their risk of adverse outcomes. Clinicians should assess alcohol use in patients with diabetes and inform them of the many ways alcohol can harm their health.

Joseph Conigliaro, MD, MPH

Reference: Chew LD, et al. Association between alcohol consumption and diabetes preventive practices. *Fam Med.* 2005;37(8):589–594.

Withdrawal May Trigger Alcoholic Pancreatitis

It is generally assumed that ethanol toxicity is entirely responsible for alcoholic pancreatitis. However, withdrawal may also play a role given that few patients hospitalized for pancreatitis are intoxicated and that pancreatitis-associated protein appears in the serum after drinking stops. To investigate this possibility, Finnish researchers studied 100 patients with a first episode of acute alcoholic pancreatitis.

- Most patients had already stopped drinking before they began to feel nausea or to vomit (69 of 76 patients [91%] with nausea and vomiting) or to feel abdominal pain (54 of 79 [68%] with abdominal pain).
- Of 83 patients able to be assessed, only 24 (29%) had developed some pancreatitis

symptoms before they consumed their last drink; 36 (43%) had developed symptoms on the first day they stopped drinking and the remainder developed symptoms later (usually the second or third day).

Comments: This study cannot answer whether direct toxicity or withdrawal from alcohol causes pancreatitis because serum alcohol levels were likely greater than zero in most patients when symptoms developed. And perhaps patients chose to drink less as they became ill but before they recognized specific pancreatitis symptoms.

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Withdrawal May Trigger Alcoholic Pancreatitis (continued from page 1)

Nonetheless, it is interesting that most patients with acute pancreatitis stopped drinking before, and not after, developing symptoms. This observation suggests that there may be a window of time during which an episode of alcoholic pancreatitis can be predicted and perhaps prevented.

Richard Saitz, MD, MPH

Reference: Nordback I, et al. Is it long-term continuous drinking or the post-drinking withdrawal period that triggers the first acute alcoholic pancreatitis? *Scand J Gastroenterol.* 2005;40(10):1235–1239.

Alcohol Consumption and Lung Cancer: Are They Connected?

Few studies have explored whether alcohol independently increases the risk of lung cancer or modifies the risk conferred by smoking. To examine these possibilities, researchers conducted a pooled analysis of data from 7 prospective studies of diet and cancer. Of 399,767 subjects, 3137 developed lung cancer. Analyses were adjusted for potential confounders (e.g., smoking, education).

- The risk of lung cancer was slightly greater in subjects who consumed ≥ 30 g of alcohol (approximately 2 drinks) per day than in those who abstained (pooled relative risk [RR] 1.2; P for trend=0.03).
- Among smokers, risk did not significantly differ between those who drank and those who did not drink (e.g., RR 1.0 for men drinking 5 to <15 grams per day).
- However, among men who never smoked, those who drank had a significantly greater risk of lung cancer than those who did not drink (RR 2.5 for 5 to <15 g per day; RR 6.4 for ≥ 15 g per day).

- There were no significant findings for women who never smoked.

Comments: This study is notable for its analysis of a large number of subjects. However, the diversity of cohorts examined and difficulty adjusting for smoking (since smoking is common in drinkers) make drawing clear conclusions challenging. Nonetheless, this study, like others, suggests a weak, positive association between consuming larger amounts of alcohol (>2 drinks a day) and lung cancer risk. Notably, the association was limited in subgroup analyses to non-smokers and relatively small amounts of alcohol, though these findings need to be replicated before they can be definitively interpreted.

R. Curtis Ellison, MD

Reference: Freudenheim JL, et al. Alcohol consumption and risk of lung cancer: a pooled analysis of cohort studies. *Am J Clin Nutr.* 2005;82(3):657–667.

Alcohol Use Decreases Platelet Activation and Aggregation in Men

The lower risk of myocardial infarction in moderate drinkers may be partially due to alcohol's positive effects on platelet activity and high-density lipoprotein cholesterol. Large-scale studies examining these possibilities, however, have not included women and have not evaluated how alcohol consumption affects measures of platelet function.

Investigators examined alcohol use, platelet activation, and platelet aggregability in men and

women without cardiovascular disease who were enrolled in a prospective study of cardiovascular disease risk factors. They measured platelet activation (i.e., response to adenosine diphosphate [ADP]) in 1037 subjects and platelet aggregability (i.e., responses to ADP, epinephrine, and collagen) in 2013 subjects. Analyses were adjusted for potential confounders (e.g., age, body mass index, smoking).

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Alcohol Use Decreases Platelet Activation and Aggregation in Men (continued from page 2)

As alcohol consumption increased from 0 drinks to ≥ 20 drinks per week,

- platelet activation significantly decreased in men but not in women;
- most measures of platelet aggregation significantly decreased in men;
- only platelet aggregation induced by ADP significantly decreased in women.

Beverage type was not consistently associated with platelet activation or aggregability.

Comments: Alcohol use appears to decrease platelet activation (in men) and aggregation (in both men and women). These decreases may partially explain the possible protective effects of alcohol on cardiovascular events.

Joseph Conigliaro, MD, MPH

Reference: Mukamal KJ, et al. Alcohol consumption and platelet activation and aggregation among women and men: the Framingham Offspring Study. *Alcohol Clin Exp Res*. 2005;29(10):1906–1912.

Drinking Frequency, Mediating Biomarkers, and Myocardial Infarction

To examine the associations between drinking frequency and the risk of myocardial infarction (MI), researchers analyzed data from 32,826 female and 18,225 male participants of 2 large cohort studies. A total of 515 subjects with incident MI were matched to 1030 controls on sex, age, smoking, and date of study entry.

- Drinking at least 3–4 days per week was associated with a lower risk of MI in both men and women.
- In adjusted analyses, high-density lipoprotein (HDL) cholesterol, hemoglobin A1c, and fibrinogen accounted for 75% of the association between drinking frequency and MI risk in women and 100% of the association in men.

Comments: Like other studies, this study found that drinking fre-

quency is associated with a lower risk of MI in both men and women. The authors state that the attenuated results in analyses adjusted for HDL cholesterol, hemoglobin A1c, and fibrinogen—3 biomarkers beneficially affected by alcohol—suggest that alcohol may in fact have a causal role. This role may be largely—or even entirely—mediated by these factors. However, whether alcohol truly decreases MI risk can only be determined through long-term randomized trials.

R. Curtis Ellison, MD

Reference: Mukamal KJ, et al. Drinking frequency, mediating biomarkers, and risk of myocardial infarction in women and men. *Circulation*. 2005;112(10):1406–1413.

Heart and Mind: Is Moderate Alcohol Consumption Good for Your Brain, Too?

Recent neuropsychological studies suggest that moderate drinkers experience less cognitive dysfunction than abstainers do. Researchers in Australia sought to replicate this observation in 7485 community-dwelling people across 3 age cohorts (20–24, 40–44, and 60–64 years). Analyses were adjusted for age and sex.

- Moderate drinkers (up to 14 drinks per week for men and 7 drinks for women) performed significantly better on all cognitive measures than did abstainers and occasional drinkers.* They also performed better than did hazardous drinkers, but only among men and on approximately half of the measures.
- When analyses were controlled for education and race, these results were attenuated and became nonsignificant for male hazardous drinkers.

In additional analyses, these researchers explored whether factors associated with both drinking levels and cognitive performance could explain the observed differences between abstainers and moderate drinkers.

- The oldest cohort had the most confounders while the youngest cohort had the fewest.
- Sex, education, and extroversion were confounders shared among the age groups. Lung function and grip strength were

confounders in both the older cohorts.

Comments: Moderate drinkers had better cognitive functioning than did nondrinkers, occasional drinkers, and heavier drinkers. The evaluated confounders only partially explain the differences reported among these groups. Though these cross-sectional associations are intriguing, one cannot yet know if alcohol consumption is the cause, the effect, or an epiphenomenon. Ongoing follow-up of these samples should provide stronger evidence to support any causal inference.

Peter Friedmann, MD, MPH

*Abstainers did not drink alcohol in the past year, occasional drinkers drank alcohol monthly or less, and hazardous drinkers drank >28 drinks per week (>14 for women).

Reference: Rodgers B, et al. Non-linear relationships between cognitive function and alcohol consumption in young, middle-aged and older adults: the PATH Through Life Project. *Addiction*. 2005;100(9):1280–1290; Anstey KJ, et al. Lower cognitive test scores observed in alcohol abstainers are associated with demographic, personality, and biological factors: the PATH Through Life Project. *Addiction*. 2005;100(9):1291–1301.

Does Alcohol Use Increase Hepatitis C Virus Replication?

Among patients with hepatitis C, those who drink heavily have more severe liver disease than those who abstain. However, the mechanism by which alcohol use worsens liver disease among these patients is not known. To examine one possible mechanism, researchers performed a meta-analysis of studies that assessed the cross-sectional association between alcohol use and hepatitis C virus replication.

- Three of 9 studies showed significantly higher hepatitis C viral levels in heavy drinkers (defined variably) than in nondrinkers. However, when data from all 9 studies were combined, this difference was no longer significant.
- Hepatitis C viral levels did not increase as alcohol use increased, according to combined data from 4 studies that examined nondrinkers, moderate drinkers, and heavy drinkers.

Comments: This meta-analysis did not find a consistent association between alcohol use and hepatitis C virus replication. The conclusions from this study are limited due to its small sample size, differences in how studies defined heavy drinking, the cross-sectional analyses, and lack of control for the quality of the studies, duration of alcohol use, and antiviral treatment. However, while the mechanism of liver damage from co-occurring hepatitis C and heavy alcohol use remains uncertain, the recommendation for patients with hepatitis C to abstain or minimize alcohol use remains unchanged.

Kevin L. Kraemer, MD, MSc

Reference: Anand BS, et al. Alcohol has no effect on hepatitis C virus replication: a meta-analysis. *Gut*. 2005;54(10):1468–1472.

Interventions

Vitamin K May Reduce Risk of Alcohol Dependence

Vitamin K helps prevent brain injury in newborns. If alcohol dependence is associated with brain development in infancy, giving babies vitamin K might reduce their future risk of dependence. To explore this possibility, researchers studied a 30-year prospective cohort of male infants in Denmark.

Of 238 men, 18% had received 1 mg of vitamin K intramuscularly at birth, 16% had alcohol dependence (assessed at age 30), and 68% had fathers with alcohol dependence. Receipt of vitamin K was not significantly associated with gestational age, birth weight, birth complications, or signs of neurological impairment at birth.

- Only 5% of men who had received vitamin K at birth had alcohol dependence compared with 18% of men who had not received the vitamin.
- In an analysis adjusted for birth weight and having a father

with alcohol dependence, men who had received vitamin K had significantly fewer symptoms of alcohol dependence.

Comments: The results of this analysis suggest that perinatal brain injury (e.g., hemorrhage, which is now much less common due to universal administration of vitamin K to neonates) increases the risk of alcohol dependence. These results also imply that preventive interventions that reduce neurological trauma early in life may lower vulnerability to dependence later.

Richard Saitz, MD, MPH

Reference: Manzardo AM, et al. Neonatal vitamin K might reduce vulnerability to alcohol dependence in Danish men. *J Stud Alcohol*. 2005;66:586–592.

AA: Attend Early and Often

Participation in Alcoholics Anonymous (AA) concurrent with professional treatment appears to improve alcohol outcomes in people with alcohol use disorders. Whether AA alone or the timing of participation (e.g., before or after entering treatment) affects these outcomes is unclear.

In this study, researchers assessed remission (no heavy drinking or related problems in the past 6 months) in 362 people with an alcohol use disorder who entered treatment (inpatient or outpatient), AA, or both in the year after they sought help. Subjects were surveyed at baseline and 4 subsequent times over 16 years.

- Remission was more common in people who had participated in both treatment and AA (e.g., 65% at 16 years) followed by AA only (57%) and treatment only (50%). Differences were significant between the two treatment groups (for 3 of 4 time points).
- Remission did not significantly differ between people in treatment only and those who initially received treatment but later entered AA.
- As duration of AA participation increased, the likelihood of remission significantly increased.

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AA: Attend Early and Often (continued from page 5)

Comments: This study supports the notion that long-term participation in AA, particularly when begun soon after seeking help, is an important adjunct to professional treatment for alcohol use disorders. Treatment of alcohol dependence should include referral to mutual help groups and encouragement for patients to continue their participation.

Rosanne Guerriero, MPH

Richard Saitz, MD, MPH

Reference: Moos RH, et al. Paths of entry into Alcoholics Anonymous: consequences for participation and remission. *Alcohol Clin Exp Res.* 2005;29(10):1858–1868.

Topiramate May Help People With Alcohol Dependence to Quit Smoking

Smoking and alcohol dependence cause poor health, frequently co-occur, and can be difficult to treat simultaneously. A drug that can effectively treat both conditions would be of great clinical interest.

Researchers who found that oral topiramate improved alcohol outcomes* in people with alcohol dependence examined whether the drug could also promote smoking cessation. Using data from their previous randomized controlled trial, they compared smokers** with alcohol dependence who had received topiramate (escalating dose of 25–300 mg per day for 12 weeks; n=45) with those who had received placebo (n=49).

- At 12 weeks, 17% of the topiramate group and 7% of the placebo group reported abstinence from smoking.
- In analyses adjusted for potential confounders, the topiramate group was significantly more likely than the placebo group to report abstinence from smoking (odds ratio 4.5) and to have lower serum cotinine levels.
- Although serious adverse effects were not observed, the topiramate group was significantly more likely than the

placebo group to report paresthesia and weight loss.

Comments: This small post-hoc analysis of a subgroup of subjects in a randomized trial indicates that oral topiramate has the potential to treat both alcohol dependence and smoking. Larger randomized trials should be completed to confirm the short-term effects of oral topiramate and to assess long-term efficacy after the drug has been discontinued.

Kevin L. Kraemer, MD, MSc

*3 fewer drinks per day and 26% more abstinent days in subjects assigned to topiramate versus placebo (*Lancet* 2003;361[9370]:1677–1685)

**Smoked ≥ 1 cigarette per day

Reference: Johnson BA, et al. Use of oral topiramate to promote smoking abstinence among alcohol-dependent smokers: a randomized controlled trial. *Arch Intern Med.* 2005;165(14):1600–1605.

Assessments

The Validity of Biomarkers in Detecting Alcohol Dependence

Because of concerns about denial in the clinical history, the search continues for biomarkers for chronic alcoholism. To help identify valid biomarkers, researchers examined the performances of carbohydrate-deficient transferrin (%CDT),* gamma-glutamyltransferase (GGT), and mean corpuscular volume (MCV) in 101 current drinkers with alcohol dependence, 117 patients with liver disease (e.g., hepatitis, nonspecific elevated GGT, and nonalcoholic cirrhosis), and 115 social drinkers.

- The percent of patients with dependence who had a positive %CDT (sensitivity) was 73%. The sensitivities of GGT and MCV were 71% and 64%, respectively.*

- Sensitivity increased to 83% when %CDT was combined (through a mathematical equation) with GGT and to 88% when MCV was added to the combination.
- The percent of patients without dependence who had a negative test of %CDT (specificity) was 94% in those with elevated GGT, 88% in those with hepatitis, and 70% in those with nonalcoholic cirrhosis. Specificities of GGT and MCV in these patients were much lower.

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The Validity of Biomarkers (continued from page 5)

Comments: The %CDT assay had better sensitivity in patients with alcohol dependence and better specificity in patients with various forms of liver disease than did the GGT and MCV. The combination of %CDT with GGT and MCV increased sensitivity to 88% without loss of specificity. Before widespread adoption of these biomarkers occurs, further study is needed to understand their costs and real-world performance alone and in combination with a skilled clinical interview.

Peter Friedmann, MD, MPH

*Tina-quant® second generation test from Roche Diagnostics (who funded this study)

**The %CDT cut-off was 3% (set for 95% specificity in social drinkers), the GGT cut-off was 33 U/L for women and 56 U/L for men, and the MCV cut-off was 95 fL.

Reference: Hock B, et al. Validity of carbohydrate-deficient transferrin (%CDT), γ -glutamyltransferase (γ -GT) and mean corpuscular erythrocyte volume (MCV) as biomarkers for chronic alcohol abuse: a study in patients with alcohol dependence and liver disorders of non-alcoholic and alcoholic origin. *Addiction*. 2005;100(10):1477–1486.

Do PCPs Use Laboratory Tests and the AUDIT to Screen for Unhealthy Alcohol Use?

The extent that primary care physicians use laboratory tests and the AUDIT* to assess patients' alcohol use has not been reported. In this study, researchers surveyed all primary care physicians in Finland (n=3193) to determine use of "conventional" alcohol laboratory tests (i.e., MCV, GGT, AST, ALT),** the AUDIT, and/or CDT*** to screen for unhealthy alcohol use. Sixty-six percent of those surveyed responded and anonymously reported whether they never, occasionally, or regularly used these tests.

- Regular use of any of the 3 tests was low: 33% regularly used laboratory markers, 18% regularly used the AUDIT, and 6% regularly used CDT.
- Occasional use was more common (64%, 50%, and 38%, respectively).

Comments: The authors' claim that "almost all respondents ... used some laboratory marker to detect alcohol abuse" is an overstatement given that use was occasional and that the markers were probably obtained for other purposes. Also, the appropriate-

ness of using laboratory tests to screen for unhealthy alcohol use is not broadly accepted. Nonetheless, the low frequency of screening with the AUDIT is disappointing (but consistent with that reported in other studies of screening questionnaires). These findings from Finland suggest once again that improving implementation of alcohol screening in primary care remains an ongoing challenge.

Jeffrey Samet, MD, MA, MPH

*Alcohol Use Disorders Identification Test

**Mean corpuscular volume, gamma-glutamyltransferase, aspartate aminotransferase, alanine aminotransferase

***Carbohydrate-deficient transferrin

Reference: Aalto M, et al. Use of laboratory markers and the AUDIT questionnaire by primary care physicians to detect alcohol abuse by patients. *Alcohol Alcohol*. 2005;40(6):520–523.

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