

## Aggressive Intervention Needed for Some Drinkers

BY DOUG BRUNK

SAN DIEGO — Alcohol-dependent patients who were older than age 30 and met certain DSM-IV criteria for alcohol dependence—including tolerance and continuing to drink despite its negative impact on important events—had less dramatic reduction in heavy drinking over time.

The findings suggest that alcohol-dependent patients with those characteristics may benefit from more aggressive intervention efforts, according to results from an analysis of data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

“There have been a number of studies that examined the predictors of change in heavy drinking status over time in the general population,” Khaled Sarsour, Ph.D., said in an interview after presenting the findings in a poster at the annual scientific conference of the Research Society on Alcoholism.

“However, to the best of our research team’s knowledge, this was the first study that examined the predictors of change in the number of heavy drinking days within a U.S. nationally representative population of alcohol-dependent patients.”

Dr. Sarsour, a research scientist in the epidemiology and health services research group at Eli Lilly & Co., and his associates examined predictors of the change in frequency of heavy drinking among 1,053 alcohol-dependent patients from baseline (NESARC Wave 1, conducted in 2001-2002) to about 3 year later (NESARC Wave 2, conducted in 2004-2005). Frequency of heavy drinking was defined as the number of heavy drinking days (five drinks or more per day for men; four drinks or more per day for women) in the past year.

The researchers used an analysis of covariance model, adjusting for baseline heavy drinking days, to examine factors associated with change in the frequency

of heavy drinking. More than half of patients (64%) were younger than age 39 years, 63% were male, 61% were white, and 37% were married.

Overall, the mean number of heavy drinking days among patients with alcohol dependence fell from 114 per year during NESARC Wave 1 to 84 per year during NESARC Wave 2.

**The predictors of change in heavy drinking status over time were age and the meeting of certain DSM-IV criteria for alcohol dependence.**

Dr. Sarsour and his associates reported that the factors significantly associated with an increase of heavy drinking days between the two time periods were being older than age 30, being a current smoker, and fulfilling three DSM-IV criteria for dependence: tolerance, giving up or cutting back on important activities to drink, and drinking despite

having physical and/or psychological problems.

Alcohol-dependent patients diagnosed with comorbid depression and/or dysthymia reported an additional significant mean decrease of 19 heavy drinking days, compared with their counterparts who were not diagnosed with those conditions.

“We were expecting sociodemographic variables such as level of education, marital status, gender, and ethnicity to be associated with change in heavy drinking over time,” Dr. Sarsour said. “However, in this study, none of these variables were significant predictors of change in heavy drinking status over time. This may have been due to the fact that the study population consisted of alcohol-dependent patients. We will do a follow-up analysis to see if these predictors are significant in predicting change in heavy drinking in non-alcohol-dependent patients from the same national data set.”

Dr. Sarsour and four other members of the research team are employees of Eli Lilly. The other member of the research team was Dr. Howard B. Moss of the National Institute on Alcohol Abuse and Alcoholism, which sponsored the study. ■

## Diacetylmorphine Compares Favorably With Methadone

BY MARY ANN MOON

Treatment with injectable diacetylmorphine, the active ingredient in heroin, compared favorably with methadone treatment in a phase III clinical trial reported in the *New England Journal of Medicine*.

Patients who received diacetylmorphine through the North American Opiate Medication Initiative were more likely to stay in treatment, reduce their use of illegal drugs, and scale back other illegal activities than were those given methadone. They also showed greater improvements in medical, psychiatric, and economic status, and in their family and social relationships, which “suggests a positive treatment effect beyond reduction in illicit-drug use or other illegal activities,” said Eugenia Oviedo-Joekes, Ph.D., of the University of British Columbia, Vancouver, and her associates (*N. Engl. J. Med.* 2009;361:777-86).

“Methadone, provided according to best-practice guidelines, should remain the treatment of choice for the majority of patients. However, there will continue to be a subgroup of patients who will not benefit even from optimized methadone maintenance.

Prescribed, supervised use of diacetylmorphine appears to be a safe and effective adjunctive treatment for this severely affected population of patients who would otherwise remain outside the health care system,” the investigators said.

Injectable diacetylmorphine has been used in several European countries for many years. To assess its performance in a North American population, Dr. Oviedo-Joekes and her colleagues performed an open-label, randomized, controlled trial in Montreal and Vancouver.

A total of 115 patients were randomly assigned to receive diacetylmorphine, 111 to receive standard oral methadone, and 25 to receive injectable hydromorphone for validation of the self-reported use of illicit heroin by means of urine testing. All the study subjects had long histories of injectable drug use and extensive involvement in

criminal activity, and all had undergone multiple attempts at treatment.

The medications were administered daily and under supervision in clinics, and patients were allowed to switch, partially or totally, to oral methadone if they wished. Twenty-three of the diacetylmorphine patients switched to methadone.

To ensure safety, all study subjects who received injectable medications were observed for 30 minutes after each injection.

After 1 year of follow-up, 67% of the diacetylmorphine group improved in illicit drug use and other illegal activities, compared with 48% of the methadone group. Scores improved on more subscales on a measure of this outcome, and they improved to a greater degree, with acetylmorphine than with methadone.

The rate of retention in treatment also was better with diacetylmorphine (88%) than with methadone (54%). Rates of response and retention with hydromorphone were 64% and 88%, respectively.

The mean number of days of illicit heroin use during the preceding month declined from 27 to 5 with diacetylmorphine and from 27 to 12 with methadone. At baseline, both groups had spent a median of \$1,200 (U.S.) per month on illicit drugs, which was reduced to \$320 with diacetylmorphine and to \$400 with methadone.

A total of 54 patients reported 79 serious adverse events—18 with methadone, 51 with diacetylmorphine, and 10 with hydromorphone. Overdoses and seizures were the most common serious adverse events associated with diacetylmorphine.

“Sixteen of the 115 patients randomly assigned to receive diacetylmorphine had a life-threatening overdose or seizure during the study. Because the study included close medical supervision, these serious adverse events were promptly treated, and all patients recovered,” the investigators noted.

No potential conflicts of interest were reported. ■

## Saliva Test May Guide Smoking Cessation Treatment

BY KATE JOHNSON

MONTREAL — A simple saliva test to assess a smoker’s degree of nicotine dependence could become the first step of a smoking cessation treatment, a study has shown.

Light or heavy nicotine dependence can predict a person’s success in quitting or risk of relapse, Caryn Lerman, Ph.D., said at the annual meeting of the Society of Behavioral Med-

icine. Clinicians could use this information to guide treatment choices for their patients.

“We could decide whether someone needs smoking cessation counseling only, or whether they would do better with a patch, or if they need a medication such as bupropion or varenicline,” said Dr. Lerman of the Transdisciplinary Tobacco Use Research Center at the University of Pennsylvania, Philadelphia.

The saliva test measures the ratio of two nicotine metabolites, 3'-hydroxycotinine and cotinine, to determine a person’s rate of nicotine clearance or metabolism, Dr. Lerman said.

A new study by her group has validated that smokers with the slowest nicotine metabolism are about twice as likely to quit as are smokers with faster nicotine metabolism (*Pharmacol. Biochem. Behav.* 2009;92:6-11). The study enrolled 568 smokers

who were given counseling and 8 weeks of a 21-mg nicotine patch. The saliva test measured the metabolite ratio pretreatment to distinguish fast from slow nicotine metabolizers. Eight weeks after the quit date, fast metabolizers were approximately 50% less likely to be abstinent, compared with slow metabolizers (28% vs. 42%).

The findings support the value of the saliva test as a biomarker to predict success with

transdermal nicotine for smoking cessation, the authors concluded. “We are developing a treatment algorithm which suggests that slow metabolizers may need nothing more than counseling or nicotine patch, but fast metabolizers are candidates for more nonnicotine medications which may be more costly and have more side effects than the patch,” they wrote (*Clin. Pharmacol. Ther.* 2008;84:320-5). ■