Physicians Reluctant to Prescribe for Alcoholism

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SANTA BARBARA, CALIF. — Newer pharmacologic treatments for alcohol dependence roughly double abstinence rates and significantly reduce heavy alcohol use among patients who return to drinking, a growing body of evidence suggests.

But skepticism and, to a lesser extent, philosophical objections, may be undermining adoption of medications as part of the treatment regimen for alcohol-dependent patients, speakers agreed at the annual meeting of the Research Society on Alcoholism.

"Why are these medications not more widely prescribed [when metaanalyses show they are clearly efficacious]?" asked Henry Kranzler, M.D., professor of psychiatry and assistant dean of clinical research at the University of Connecticut Health Center, Farmington. "It's an interesting conundrum."

Dr. Kranzler noted there are nearly 8 million alcohol-dependent people in the United States at any time. "Only a fraction of them are being treated, and a small fraction of those are receiving medications approved for alcoholism treatment."

In contrast, depression strikes about 20 million adults per year in the United States. However, depressed patients are 100 times more likely to be prescribed an antidepressant than alcoholics are to be prescribed an FDA-approved medication to treat alcoholism.

The reasons are myriad, according to David R. Gastfriend, M.D., of Massachusetts General Hospital and Harvard Medical School, Boston, and vice president of medical affairs for Alkermes Inc.

The reasons include:

- ► Perceived ineffectiveness of medications and a deep concern about noncompliance rates.
- ► A sense among counselors that medications might diminish patients' motivation to help themselves or to participate in 12-step program activities.
- ► Worries about side effects and costs.
- ► A belief among providers that patients "may want to reject any treatment that prevents the relief sought from alcohol."

In some cases, providers' doubts may be justified. Dropout rates are high—even among highly motivated participants in clinical trials. Strong placebo response rates sometimes muddy final results. Medications add expense to alcohol-dependence treatment regimens that are already costly and often underfunded by the government and private insurers.

Perhaps most importantly, the best use of medications may be in combination with one another and with traditional psychosocial support—in ways only now being assessed, Dr. Gastfriend said.

An immediate boost in acceptance of medications may come from a monthly, injectable formulation of an existing drug—naltrexone. If patients did not have the daily responsibility of taking an oral drug, compliance rates might improve, Dr. Kranzler said.

Robert M. Swift, M.D., professor of psychiatry at Brown University in Providence, R.I., noted that although acamprosate (Campral) doubles the abstinence rate in most studies, "the absolute number of patients who continue to be abstinent [following the study period] is not great. Most effects come even in the placebo group. The average clinician is not going to see that much difference."

A 2003, three-state survey of physicians and nonphysicians who treat alcohol addiction found that nearly 40% of physicians and 70% of nonphysicians said they "never" or "rarely" used naltrexone to assist in the treatment process, even though the survey was taken 4 years after the drug's approval (J. Subst. Abuse Tr. 2003;24:1-11).

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DR. KRANZLER

When asked why, physicians cited inconsistent compliance, cost, efficacy issues, and side effects. Nonphysicians cited lack of knowledge as their top reason, followed by cost, the inability to predict which patients would benefit, and insufficient efficacy, said Dr. Swift, who has received research support or consulting fees from Pfizer Inc., Ortho-McNeil Pharmaceutical Inc., Bristol-Myers Squibb Co., Forest Laboratories Inc., and Alkermes.

This year, Food and Drug Administration approval is expected for a long-acting depot formulation of naltrexone, to be called Vivitrex.

Phase III trials found a 25% reduction in heavy-drinking days among subjects receiving a 380-mg monthly, injected dosage of naltrexone in combination with a low-intensity psychosocial intervention during the 6-month trial (JAMA 2005;293:1617-25).

Follow-up studies presented at the meeting found a much larger effect size (74%, compared with 19%) among subjects who entered the trial having been abstinent (even though abstinence was not a requirement for entry into the study) and also found that mental health–related quality of life scores paralleled the reduction in heavy drinking among subjects.

An open-label extension study directed by Dr. Gastfriend—an employee of Alkermes, maker of long-acting naltrexone—found that the treatment effect persisted for a year among patients who continued to receive injections.

An Internet marketing survey suggests that patients may be amenable to considering injectable long-acting naltrexone.

Among 176 problem drinkers who responded to the survey, 57% expressed positive or at least neutral opinions about whether such a drug would be helpful. Just 14% said they had no expectation that the drug would be helpful, reported Dr. Gastfriend at the meeting.

Other drugs may be on the horizon as well, said Dr. Kranzler, who disclosed that he has received research support and consulting fees from Ortho-McNeil Pharmaceutical, Bristol-Myers Squibb, Forest Pharmaceuticals, and DrugAbuse Sciences Inc.—all of which are involved in manufacturing and/or developing medications for alcohol-dependence treatment.

Phase III trials are underway to test the efficacy of the anticonvulsant topiramate (Topamax) for treating alcohol dependence. An antipsychotic medication, aripiprazole (Abilify), is also being studied in a multicenter trial.

Dr. Kranzler termed both agents "promising," although their use in clinical practice may be several years away. ■

Ups and Downs Of Alcohol Drugs

Pharmacology for alcohol treatment has followed a somewhat rocky path.

The first FDA-approved medication for alcohol treatment, disulfiram (Antabuse), was not a blockbuster drug in terms of efficacy. In the largest study of the drug, a 1-year trial, noncompliance with the medication was 80% and was associated with a lower rate of abstinence, Dr. Kranzler said.

A short-acting naltrexone formulation (Revia) came next, in 1994, initially demonstrating a "pretty robust effect" on abstinence and heavy drinking. But a meager 3-year exclusivity arrangement provided little incentive for the manufacturer to market the drug at that time.

Acamprosate (Campral), approved in 2004, may show a healthier acceptance rate. Studies in the United States and Europe suggest that the oral agent may not only double abstinence rates but also may have a meaningful effect on abstinence for as long as a year after discontinuation. Acamprosate is being heavily marketed to primary care physicians as well as psychiatrists and alcohol-dependency treatment specialists.

The Combining Medications and Behavioral Interventions (COMBINE) trial sponsored by the National Institute on Alcohol Abuse and Alcoholism is nearing completion. The trial will evaluate a multifaceted approach to alcohol-dependency treatment, comparing a placebo with two FDA-approved medications.