

Rethinking Total Abstinence

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of Connecticut, Farmington.

The old concept—that total abstinence could be the only goal for treatment of alcohol abuse—stemmed from two sources: the influence of Alcoholics Anonymous, and the fact that for many years the only medication for treatment was disulfiram (Antabuse), which makes a person feel very sick when he or she drinks.

But research conducted with naltrexone since the 1990s and with acamprosate for its approval in 2004 have begun opening investigators' eyes to the possibility that there can be other successful outcomes to treatment besides total abstinence, which is traditionally what studies have considered their prime end point, said Dr. Richard N. Rosenthal, chairman of the department of psychiatry at St. Luke's-Roosevelt Hospital Center, New York.

And that recognition, in turn, opens up the prospect of medical treatment to a greater number of potential patients with an alcohol problem, not just those who are diagnostically dependent or alcoholic. "It becomes about reducing the harm from drinking behavior, rather than thinking about the diagnosis per se," Dr. Rosenthal said.

At any one time, about 18 million people in the United States are alcohol dependent, the most recent survey shows. But a small percentage seeks alcohol treatment, and an even smaller proportion gets medication treatment—perhaps 140,000 people at any one time. Even among those who get treatment and try to become abstinent, relapse is far more common than success. Treatment of these people might be encouraged if the treatment goal was something short of abstinence, Dr. Rosenthal said.

Moreover, there is another group of individuals, over and above those who are dependent, who drink heavily or binge and may have impaired control. And these individuals could benefit from medical assistance, since it has been shown many times that heavy drinking creates health problems. "This continuous model opens up the idea that there may be other targets rather than stopping drinking as a potential target, and as a result, there may be increased social utility," Dr. Rosenthal said. Dr. Kranzler said it is not clear which medication might be best for patients who try to be abstinent but relapse, or who do not want to be abstinent. But acamprosate and naltrexone have potential.

In one trial of acamprosate used to gain its approval in this country, the drug doubled the percentage of patients who remained abstinent for a year, and the abstinence achieved largely persisted into the

second year of the study, during which the medication was discontinued, Dr. Kranzler said.

But it has also been shown, in a recent review and analysis of 15 clinical trials, that even among patients who do not remain completely abstinent, acamprosate reduces total drinking days by 28%, reduces heavy drinking days by 12%, and cuts overall alcohol consumption by 50% (J. Psychopharmacol. 2003;17:397-402). Naltrexone appears to have little impact on increasing abstinence, but it clearly does help prevent individuals from returning to heavy drinking, according to an analysis of 14 studies (Addiction 2004;99:811-28).

In a recent study of the long-acting, injectable form of naltrexone that is being investigated, the mean number of drinking days of the subjects dropped from 19 days per month at baseline to 6 days per month for the placebo patients and to only 3 days for the treated patients (JAMA 2005;293:1617-25).

An intriguing aspect of that study was that patients were not required to be abstinent when they started on the drug, as has been conventional in clinical use and with other naltrexone studies, Dr. Kranzler noted.

Therefore, naltrexone may be the drug that should be used for a harm reduction approach, said Dr. Kranzler, who is now involved in studies in which patients use naltrexone on a declining schedule and eventually only on an as-needed basis. But more study is needed.

Very little research exists specifically on the harm reduction approach, Dr. Kranzler and Dr. Rosenthal said. It has not yet been demonstrated that patients who would be appropriate for this type of treatment can be identified, or whether reduced drinking in these patients truly results in fewer medical and social problems.

"All of the medications approved in the U.S. to treat alcohol dependence reduce drinking, even among nonabstinent individuals," Dr. Kranzler said. "Clearly, we need research to identify the individuals for whom medications may help modify impaired control over drinking, to get a better handle on who we can work with responsibly around a goal of reduced drinking."

The new openness about what constitutes successful treatment for alcohol abusers is a welcome development, Dr. Edward V. Nunes added.

"Twenty years ago, if anyone suggested a goal of less than abstinence, they would have met a lot of hostility," said Dr. Nunes, a research psychiatrist at the New York State Psychiatric Institute, New York City. "Now we can have a much more reasoned discussion about it." ■

Incentive System May Keep Substance Abusers in Treatment

BY TIMOTHY F. KIRN

Sacramento Bureau

PHOENIX — Small awards for good attendance and clean urine tests can help keep more addicts in treatment longer, greatly improving their chances of staying drug free, a federally sponsored study shows.

The feasibility and benefit of this "motivational incentives" approach has been demonstrated before. But in previous trials, the awards were rather large. They could equal \$1,000 total, said Maxine Stitzer, Ph.D., in presenting the new study at the annual meeting of the American Academy of Addiction Psychiatry.

The new trial used a door-prize-like system, in which patients who met attendance and abstinence milestones drew chips from a hat. Some chips had value, but half had none at all, and the patients had only a 0.2% chance of drawing a chip with the highest value, worth \$80-\$100 toward merchandise. The longer a patient stayed on the straight and narrow, the greater the number of draws they earned—and relapses set them back. The chips were redeemed for items such as kitchenware, cordless telephones, and DVD players, all of which were kept on site at the clinic.

The door-prize system makes this rewards approach much cheaper than previous systems, said Dr. Stitzer, a professor of behavioral biology at Johns Hopkins University, Baltimore. The most a patient could win was merchandise worth \$400.

The aim of the system is to change the culture of the treatment environment to some extent, Dr. Stitzer said. "Rather than looking for ways to punish people who are doing wrong, what this program is trying to do is to catch people doing good and to reward them for their successes. "My conclusion is that everybody should be using in-

centives, because they work so well."

The study was conducted at eight outpatient clinics, and the patients were followed for 12 weeks, during which time they had twice-weekly urine testing. A total of 415 methamphetamine and cocaine abusers were randomized to either usual care or usual care plus the incentive system.

At 12 weeks, retention in the incentive-system patient group was 49%, compared with only 35% in the control group. The patients were also more likely to test negative for drug use. Almost 40% of the patients in the incentive group had 18-24 negative urine tests, a range known to be associated with a higher rate of long-term success, compared with less than 25% of the control group patients.

The study also sought to determine if the incentives would work as well for methamphetamine abusers as for cocaine abusers, who were the sole subjects of previous experiments with the system, Dr. Stitzer said. On the West Coast, stimulant abusers tend to be methamphetamine abusers; on the East Coast, they tend to be cocaine abusers. A subanalysis of the study data did find that the results with the methamphetamine abusers mirrored those for the study as a whole.

The study had 113 methamphetamine abusers, 51 of whom were randomized to the incentive system and 62 of whom were controls. Full, 12-week retention was 55% for the incentive group and 39% for the control group. Fifty-eight percent of the urine tests submitted by the incentive group patients were negative for stimulants, compared with 42% of the control group's tests, and 18% of the incentive group had 24 negative tests, compared with only 6% of the control group. Because of this and previous research, the National Institute on Drug Abuse plans to spread the word about the incentive system to drug abuse clinic administrators, Dr. Stitzer said. ■

Memantine May Have Alcoholism Use

SCOTTSDALE, ARIZ. — Memantine, the Alzheimer's drug, could have a new use: alcohol-dependence treatment.

In a small pilot study of 16 people who met Diagnostic and Statistical Manual criteria for alcohol dependence and who were treated with memantine for 8 weeks, drinking behavior declined, Dr. Albert J. Arias said in a poster presentation at the annual meeting of the American Academy of Addiction Psychiatry.

The mean number of drinking days reported by the subjects declined 18% during the 8 weeks of the study, compared with the weeks before treatment. The mean number of heavy drinking days declined 22%, and the mean number of drinks per drinking day declined by two.

Moreover, all except three people had a decrease in the number of drinks per drinking day, all except four people had a decrease in drinking days, and all except five had a decrease in heavy drinking days.

The trial was promising more than it was definitive, since there were no control subjects for comparison. The participants also received seven sessions of counseling and were enrolled because they had a stated desire to reduce their alcohol intake.

The investigators would have liked to have seen a bigger impact, said Dr. Arias, of the Al-

cohol Research Center at the University of Connecticut, Farmington, in an interview.

"Our impression is that we significantly underdosed," he said.

The dose used started at 5 mg per day and was titrated up by 5 mg a week to 20 mg a day. All except one of the 16 patients completed the study. That patient complained of fatigue, the most common adverse effect of the medication. A dosage reduction did not alleviate his fatigue.

Still, overall, the drug was well tolerated.

The other patients who initially experienced fatigue reported that their fatigue diminished over time, Dr. Arias said.

Some of the participants reported that the drug seemed to produce a rapid improvement in their cognitive functioning and in their sleep patterns. Dr. Arias said he believes that a dose of 60-80 mg a day might be more effective. That dose has been shown to be tolerable.

At Columbia University, New York, another research group has already begun a trial using a dose of 60 mg a day, he added.

Memantine is an N-methyl-D-aspartate (NMDA) receptor antagonist, and NMDA receptor function has been implicated in alcohol dependence. In human laboratory studies, it has been found to reduce alcohol craving.

—Timothy F. Kirn