Risperdal May Help

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treatment (Mayo Clin. Proc. 2007;82:1170-8). "These are medications that I expect are either being studied or will be studied in controlled trials," Dr. Saxon said at the annual meeting of the American Academy of Addiction Psychiatry. "We may have some information on these in a year or two."

In a 20-week randomized study of aripiprazole (15 mg/day) versus slow-release methylphenidate (54 mg/day) versus placebo for amphetamine dependence, urine toxicology for amphetamine during treatment was positive in 82% of specimens given by patients in the placebo group, compared with 91% of those who received aripiprazole and 67% of those who received methylphenidate (Am. J. Psychiatry 2007;164:160-2).

"None of those was a very good percentage," Dr. Saxon said. "However, the aripiprazole did much worse than placebo, and methylphenidate did a little better than placebo. Any day when we can get someone not to use methamphetamine is a victory, so there is some evidence that methylphenidate might be a useful treatment if we have the fortitude to give a stimulant-dependent person another psychostimulant."

Abstinence from methamphetamine is not the only outcome desired by researchers. In a small study Dr. Saxon and his associates conducted at the Kitsap Recovery Center in Bremerton, Wash., they found that verbal memory impairments in methamphetamine users worsen during short-term abstinence.

"A lot of the behavioral, psychosocial treatments that we are delivering rely on verbal content we're asking people to absorb and remember," he said. "If their verbal memory is impaired, how can we expect them to respond well to these interventions?"

Patients in the study were administered a neuropsychological test battery during days 3-10 of treatment and again 3 weeks later. The researchers found that on average, patients performed in the impaired range on tests of visual memory and verbal memory, "and they do not improve on these measures with short-term abstinence," Dr. Saxon said. "That led to my thought that if we're going to be delivering psychotherapies, maybe our pharmacotherapies should be an attempt to improve [the patients'] cognition so they can respond better to their psychotherapies. That's what led me to risperidone."

Dr. Saxon chose risperidone (Risperdal) because it works on areas of the brain "that would be expected to attenuate the effects of methamphetamine. It blocks dopamine D_2 receptors, the 5-hydroxytryptamine$_{2A}$ receptors, and it has activity at α_1- and α_2-adrenergic receptors." He chose long-acting, injectable risperidone to minimize concerns about medication adherence in this unstable patient population.

In an open-label study, 34 patients began a 7-day run with oral risperidone before the first injection. Of the 34 patients, 22 received one or more injections of long-acting risperidone, reported Dr. Saxon, who is also professor of psychiatry and behavioral sciences at the University of Washington, Seattle. Neuropsychological assessments were conducted twice at baseline to minimize practice effects, then repeated at 4 and 8 weeks after the initial injection. The 22 subjects receiving injections had a mean age of 38, and 86% were male. The mean number of days they used methamphetamine in the past 30 days was 17, and they had been taking the drug for a mean of 12 years.

The researchers observed a significant increase between baseline and week 4 in mean scores on the Hopkins Verbal Learning Test delayed-recall component. In this test, patients are given a list of 10 items; 30 minutes later, they are asked to repeat as many items as they can from that list.

"At baseline, they averaged just fewer than seven items, and at week 4, they averaged almost nine, so they were remembering almost two more items," he said. "That was a statistically significant effect. There's a little trail off to week 8, when they averaged slightly over seven items, but this shows some promise. Risperidone might help their memory and help them respond to psychotherapy."

Scores on other measures of neuropsychological function, including the Brief Visual Memory Test delayed-recall component, the symbol search, letter-number sequencing, and simple reaction time, did not significantly change from baseline.

Dr. Saxon disclosed that he has received research support from the Alcohol and Drug Abuse Institute at the University of Washington, Seattle, and from Ortho-McNeil Janssen Scientific Affairs LLC. The symposium was sponsored by the National Institute on Drug Abuse. ■

Proven Cocaine Dependence Tx Also May Work for Meth

BY DOUG BRUNK
San Diego Bureau

CORONADO, CALIF. — Mounting evidence suggests that behavioral and psychosocial interventions proven successful for cocaine dependence—such as cognitive-behavioral therapy and contingency management—may work equally well for methamphetamine dependence.

"We haven't looked at community reinforcement or 12-step facilitation with methamphetamine users, but I would argue that the treatments that we have evidence for cocaine efficacy should be considered very promising if not effective for the treatment of methamphetamine dependence," Richard Rawson, Ph.D., said at the annual meeting of the American Academy of Addiction Psychiatry. "I don't think we need to redo all the studies we did during the 1980s and 1990s with cocaine treatment again for methamphetamine."

In a 16-week study led by Dr. Rawson, a psychologist who is associate director of the integrated substance abuse programs at the University of California, Los Angeles, 171 stimulant-dependent patients were randomized to received either contingency management, cognitive-behavioral therapy (CBT), or combined contingency management and CBT. Contingency management condition participants received vouchers for stimulant-free urine samples, while CBT condition participants attended three 90-minute group sessions each week (Addiction 2006;101:267-74).

Self-reported stimulant use was reduced from baseline levels at all follow-up points for all groups, and urinalysis data did not differ between groups at follow-up. Contingency management produced better retention and urinalysis results; CBT produced comparable longer-term outcomes. No evidence was found of an additive effect when the two treatments were combined.

"This study suggests that contingency management is an efficacious treatment for reducing stimulant use and is superior during treatment to a CBT approach," Dr. Rawson said. "Contingency management is useful in engaging substance abusers, retaining them in treatment, and helping them achieve abstinence from stimulant use. CBT also reduces drug use from baseline levels and produces comparable outcomes on all measures at follow-up."

In the 1980s, Dr. Rawson and his associates developed a 16-week, nonresidential drug dependence treatment method known as the Matrix Model. This method incorporates several psychosocial elements, including individual counseling, CBT, motivational interviewing, positive reinforcement for behavior change, family education groups, urine testing, and participation in 12-step programs.

In a study the researchers conducted at eight sites nationwide, 978 methamphetamine-dependent patients were randomly assigned to receive either treatment as usual or the Matrix Model and were followed for 12 months (Addiction 2004;99:708-17). In six of the eight sites, patients who were assigned to the Matrix study attended more clinical sessions, compared with those who received treatment as usual (27 vs. 13, respectively), had a higher treatment completion rate (40% vs. 34%, respectively), provided significantly more methamphetamine-free urine samples during the treatment period (a mean of 6.25 weeks vs. 3.12 weeks, respectively), and had longer periods of methamphetamine-free abstinence (3.8 weeks vs. 2.6 weeks, respectively).

Dr. Rawson went on to note that a key predictor of no methamphetamine use at treatment discharge and at the 6- and 12-month study follow-up was methamphetamine use for 15 days or fewer at baseline. "That's been the single most important predictor of treatment outcome," he said. "We've seen that in about eight different studies. If you have to ask people one question to figure out what kind of treatment they need, that's the most important one. People who use more have more difficulty."

Other predictors of success include lifetime meth use of less than 2 years, no previous drug abuse treatment, and providing three consecutive methamphetamine-free urinalyses during treatment.

In a yet-to-be-published trial that assessed the treatment impact on HIV risk behavior among methamphetamine users in the aforementioned Matrix study, the mean number of people who injected in the past 30 days fell from 13.1% at baseline to 5.4% at treatment end. According to repeated measures on 193 people who injected over the past 30 days, changes in injection practices also improved. The mean number of times they injected fell from 19.7 at baseline to 7.8 at treatment end, and the mean number of times they used dirty needles fell from 3.9 to 0.91.

In addition, Matrix program enrollment had a positive effect on most risky sexual practices. For example, the mean number of times Matrix program enrollees had sex without a condom with a methamphetamine user in the past 30 days user fell from 6.5 at baseline to 1.4 at treatment end.

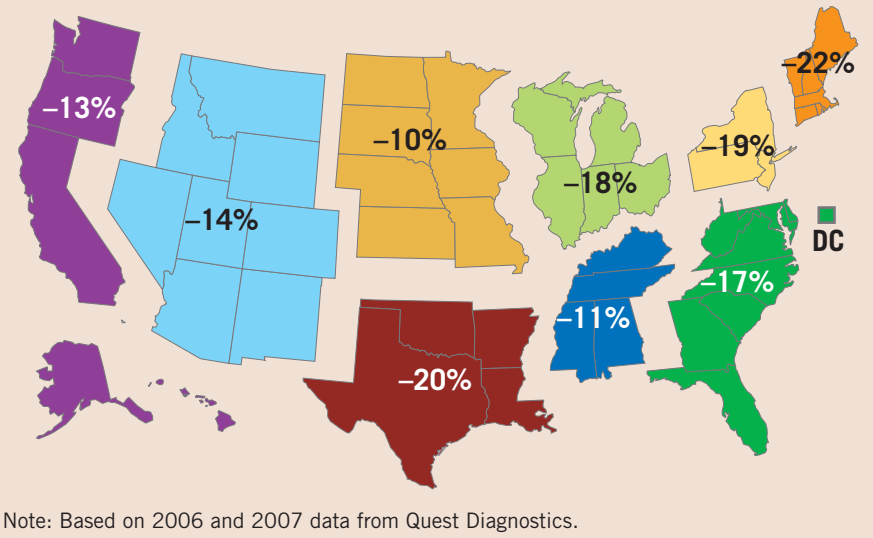
"Methamphetamine treatment is associated with substantial reductions in HIV risk behaviors," Dr. Rawson concluded. "Retention and treatment play a critical role in preventing the escalation of HIV risk behaviors."

The symposium was sponsored by the National Institute on Drug Abuse. ■

A manual about the Matrix Model program can be downloaded for free at the Substance Abuse and Mental Health Services Administration Web site, www.samhsa.gov.

DATA WATCH

Decline in Positive Tests for Cocaine in U.S. Workforce



Note: Based on 2006 and 2007 data from Quest Diagnostics.
Source: Executive Office of the President, Office of National Drug Control Policy