

Antipsychotics' Effects Differ in Substance Abusers

Activation of cytochrome P-450 system by cigarette smoke appears to play a role in drug metabolism.

BY DAMIAN McNAMARA
Miami Bureau

SAN JUAN, P.R. — Risperidone and ziprasidone increased adherence to inpatient substance abuse treatment for people with schizophrenia or schizoaffective disorder in a comparison that also included olanzapine and typical neuroleptic agents, Elizabeth B. Stuyt, M.D., said at the annual meeting of the American Academy of Addiction Psychiatry.

In the retrospective study, the risperidone (Risperdal) and ziprasidone (Geodon) groups experienced increased length of stay in substance abuse treatment, a higher completion rate, and greater behavioral improvements.

Cigarette smoking may play an important role, said Dr. Stuyt, lead researcher. All 55 participants smoked at baseline, and constituents of cigarette smoke activate the same cytochrome P-450 system enzyme that metabolizes olanzapine (Zyprexa), haloperidol decanoate (Hal-

dol), and fluphenazine decanoate. This enzyme does not metabolize risperidone or ziprasidone, said Dr. Stuyt of the University of Colorado, Denver.

"We thought smoking made the difference," Dr. Stuyt said in an interview. "The implication is when getting someone to quit smoking, it is good to know which meds they are on."

All of the patients—31 with schizophrenia and 24 with schizoaffective disorder—had a cooccurring substance abuse disorder.

Most were referrals to the Circle program, a fully integrated, 90-day inpatient dual-diagnosis treatment program for adults who have failed previous attempts to treat substance dependence. The Colorado Mental Health Institute at Pueblo runs the program.

A majority of the participants are referred as a condition of criminal court (75%-80%); others are referred by civil court (5%-10%), and the rest attend voluntarily (10%-20%).

Fifteen of the 55 study patients took olanzapine (mean dose, 18.78 mg/day), 16 took risperidone (mean dose, 3.9 mg/day), 14 took ziprasidone (mean dose, 132.8 mg/day), and 10 took a typical neuroleptic (5 each took haloperidol decanoate and fluphenazine decanoate).

"We knew there were differences [between medications], but we noticed in our program that people on olanzapine were not doing well," Dr. Stuyt said. "So we looked retro-

spectively at psychotic diagnoses at admission, what drug they were on, and the outcome."

The Circle program uses up to 90 days of cognitive-behavioral treatment. Five objectives are assigned at admission based on existing behaviors. Patients are started at a precontemplative stage regarding their substance abuse, even if they say they are committed to quitting. "They have not demonstrated it by their behavior," she said.

"It's very hard," Dr. Stuyt said. "I've had medical students say they don't think they could do it."

As behaviors improve, participants advance up levels in the program. "They are here to 'gift.' They are not snitches, but

they write up reports if they break the rules or they see other people doing something wrong," she said.

The longer the length of stay, the better the outcome, Dr. Stuyt said. The average length of stay was about the same for

risperidone (82 days) and ziprasidone (74 days), but stays were shorter for patients taking olanzapine (44 days) or a typical neuroleptic (47 days).

Participants were considered completers if they completed their homework and strategies for self-improvement, Dr. Stuyt said.

There was a 56% success rate overall: 88% of risperidone patients were completers, versus 64% of ziprasidone and 33% of olanzapine patients, she added. ■

'We knew there were differences [between medications], but we noticed in our program that people on olanzapine were not doing well.'

Combined Approach Boosts Medication Compliance

BY DAMIAN McNAMARA
Miami Bureau

SAN JUAN, P.R. — Patients who are struggling with medication compliance for alcohol dependence may benefit from a clinical intervention that combines medical management and brief counseling sessions, Helen M. Pettinati, Ph.D., said at the annual meeting of the American Academy of Addiction Psychiatry.

The compliance-enhancing intervention for physicians comes from an ongoing combination drug and behavioral treatment study sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), said Dr. Pettinati, a research director at the Center for Studies of Addiction, University of Pennsylvania, Philadelphia.

During a lengthy initial session, the physician educates the patient about alcohol dependence, explains medication effects and treatment success rates, and emphasizes the importance of adherence.

Follow-up is a series of 15- to 30-minute sessions that include a brief check on medical functioning and whether the patient is drinking and/or medication adherent.

The NIAAA publishes a medical management manual, available for \$6 at www.niaaa.nih.gov/publications/combine-text.htm, that includes standardized dialogues for education and counseling, she said.

For example, if a patient is nonadherent with medication and drinking, the

"support and advice" dialogue reviews the benefits of alcohol abstinence and pharmacotherapy.

"If the patient has a poor response to treatment, ask first about treatment non-adherence. Many times in a clinical setting someone will tell me their patient does not respond to that agent, but they haven't asked the patient if they were taking the treatment," Dr. Pettinati explained.

"There are a lot of reasons for nonadherence—only a small percentage actually forget and need help with reminders," Dr. Pettinati said at a symposium funded by an educational grant from Alkermes Inc. Among her disclosures was receipt of grant research support from the company.

The NIAAA study assessing the medical management approach is a phase III study of Alkermes' injectable, long-acting naltrexone. One aim of the study was to assess if the 30-day form improves compliance. The study included 624 patients with DSM-IV-defined alcohol dependence.

At a higher dose (380 mg), long-acting naltrexone reduced heavy drinking 25% more than did placebo. The 190-mg dose had a 17% advantage over placebo.

"Reductions were seen in the placebo group as well—remember, this is an injectable placebo," Dr. Pettinati pointed out.

People were compliant—the median number of injections was six. In addition, participants attended a median of 11 out of 12 psychosocial support sessions, she reported. ■

Improved Sleep Quality Could Aid Recovery From Alcohol Dependence

BY HEIDI SPLETE
Senior Writer

WASHINGTON — If sleep disturbance can be managed, patients in the early stages of treatment for alcoholism may be less likely to relapse, said Peter D. Friedmann, M.D.

A growing literature suggests that the sleep abnormalities that accompany both acute and chronic abstinence from alcohol may contribute to craving and urges to resume drinking. "We became interested in this notion of whether we could intervene in sleep and therefore improve abstinence," said Dr. Friedmann of Brown University in Providence, R.I.

Dr. Friedmann found significant associations between poor sleep quality and the presence of risk factors for relapse among 130 sleep-disturbed adults in recovery from alcohol dependence. He presented a cross-sectional analysis of baseline patient data at the annual conference of the Association for Medical Education and Research in Substance Abuse. The data stem from a recently initiated study in which the patients are taking 50-150 mg of trazodone for 12 weeks to improve sleep quality.

Overall, patients who reported poor sleep quality were significantly more likely to be in worse physical health based on the SF-12 Health Survey physical health subscale, to have worse depressive symp-

toms based on the Beck Depression Inventory, and to report a desire to drink when they couldn't fall asleep, Dr. Friedmann said at the conference, which was sponsored by Brown Medical School.

Most of the patients were male (84%) and white (83%), with an average age of 41 years. They were highly dependent drinkers who had consumed alcohol on approximately 25 of the 30 days before they were admitted to the detox program. The average score on the Beck in-

ventory was 20.8, and the average global score on the Pittsburgh Sleep Quality Index—in which sleep disturbance is a score higher than 5—was 11.7.

The study excluded people with brain disorders and those who were actively suicidal, as well as patients who had medical conditions that affected sleep, those taking psychotropic medications, or those with contraindications to trazodone. The patients completed a 19-item

self-report questionnaire, with variables including the number of drinks per day and questions about depression, physical health, and psychiatric status.

Despite the limitation of the self-reports, "I'm going to conclude that sleep disturbances relate to some significant factors for relapse [in alcohol-dependent patients], including depression," Dr. Friedmann said. However, separating the antidepressant effects from the sleep-inducing effects of trazodone at the study's end will be a challenge, he noted. ■

Highly dependent drinkers who reported poor sleep quality were significantly more likely to report a desire to drink when they couldn't fall asleep.