Modafinil Helps Some Cocaine Dependence

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VIENNA — Modafinil has now been found to be effective for the treatment of cocaine dependence in two randomized clinical trials, Frank J. Vocci, Ph.D., reported at the annual congress of the European College of Neuropsychopharmacology.

The caveat is that modafinil (Provigil) does not appear to work in individuals who are both cocaine and alcohol dependent, which is a common situation among cocaine users, said Dr. Vocci, director of the division of pharmacotherapies and medical consequences of drug abuse at the National Institute of Mental Health, Bethesda, Md.

Modafinil is approved by the Food and Drug Administration to promote wakefulness in adults who have excessive daytime sleepiness that is associated with sleep apnea/hypopnea syndrome, narcolepsy, or shift work sleep disorder.

The drug has several effects making it of interest as a potential treatment for cocaine dependence, including increases in brain glutamate and gamma amino butyric acid (GABA).

In laboratory studies, modafinil produced clinical effects opposite to those seen in cocaine withdrawal, reduced cocaine self-administration, diminished cocaine-induced euphoria, attenuated the cardiovascular effects of large doses of cocaine, and showed no untoward effects in combination with the drug of abuse. However, "we still don't have any idea how it's working [as a treatment for cocaine dependence] in terms of mechanisms," Dr. Vocci said.

The first clinical trial to demonstrate efficacy was an 8-week, randomized double-blind study involving 62 treatment-seeking cocaine-dependent patients at the University of Pennsylvania. Participants received a single daily morning dose of 400 mg of

modafinil or placebo plus twice-weekly manual-guided cognitive-behavioral therapy (CBT).

The primary outcome—the mean proportion of clean urine samples during the 8 weeks—was 42% in the modafinil group and 24% with placebo. Moreover, 33% of the patients in the modafinil arm achieved 3 consecutive weeks of clean urine samples at some point during the study period, compared with 13% of the controls.

There were, however, no significant differences between the two study groups in any secondary outcome measures, including craving scores and patient-reported cocaine use (Neuropsychopharmacology 2005;30:205-11).

In a recently completed, not yet published phase II multicenter double-blind trial, 210 cocaine-dependent patients were randomized to receive modafinil at 200 mg or 400 mg once daily or placebo for 12 weeks. All subjects received manualized CBT once a week. A total of 122 participants completed the study.

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DR. VOCCI

The primary outcome measure was the maximum number of consecutive days without cocaine use as determined by urine testing and patient self-report.

The mean maximum was 8.8 days with placebo, 12.6 days with 200 mg/day of modafinil, and 12 days with modafinil at 400 mg daily.

That is a less robust treatment effect than had been seen in the earlier single-center trial. But patients with comorbid alcohol dependence were excluded from that earlier trial while roughly 40% in the larger trial were both cocaine and alcohol dependent.

Upon closer analysis of the multicenter trial data, researchers found a statistically significant benefit for modafinil in reducing cocaine use that was confined to the non–alcohol-dependent subgroup, Dr. Vocci said.

Both trials were funded by the National Institute on Drug Abuse.

Despite several decades of research, there remains no approved pharmacotherapy for cocaine dependence. ■