Entacapone Blunts Cravings in Marijuana Users

BY FRAN LOWRY

BOCA RATON, FLA. — In an open-label pilot study of 36 marijuana-dependent individuals, 12 weeks of treatment with the catechol *O*-methyltransferase inhibitor entacapone significantly decreased craving for marijuana in 19 (53%) of the study participants.

These 19 patients were able to abstain from smoking marijuana for the full 12 weeks of the trial, Dr. Rahim Shafa said at the annual meeting of the American Academy of Addiction Psychiatry.

The drug represents a potential safeguard against marijuana addiction in some individuals, said Dr. Shafa of the Metrowest CNS Research Center, Natick, Mass.

Entacapone (Comtan) has been approved by the Food and Drug Administration for use in the treatment of Parkinson's disease as an adjunct to levodopa/carbidopa therapy.

The 19 patients who experienced significantly decreased craving were able to abstain for the full 12 weeks.

DR. SHAFA

In the current study, which was presented as a poster, 30 patients were treated with entacapone 2,000 mg/day for 12 weeks, and 6 patients took 3,000 mg/day. Clinical efficacy was evaluated using the clinical global impression (CGI) improvement scale, which was based on absolute abstinence criteria.

The CGI was divided into four scores, ranging from 0 to 4. Patients who did not improve got a score of 0. Patients who were abstinent for up to 4 weeks got a score of 1, patients who were abstinent for up to 8 weeks got a score of 2, and those who were abstinent for the full 12 weeks of the study got a score of 3.

The patients' ages ranged from 15 to 55 years, with most of them in their mid-20s.

In addition to the 19 patients who were totally abstinent for the 12-week duration of the pilot study, 7 patients were abstinent for 8 weeks, and 3 were abstinent for 4 weeks. There was no improvement noted in the remaining 7 subjects.

The subjects who took up to 3,000 mg/day of entacapone did not report any toxicity and claimed improved efficacy, said Dr. Shafa, who also is in private practice in Natick.

Side effects associated with entacapone in this study were mild, and included palpitations (one patient), somnolence (two patients), sweating (one patient), and nausea (one patient). All of the patients reported urine discoloration.

Dopamine deficiency has been shown to play a major role in drug craving. The catechol *O*-methyltransferase (COMT) gene plays a pivotal role in regulating homeostatic dopamine neurotransmitter levels. COMT overactivity is related to an increased rate of dopamine degradation, which results in certain disorders, including social withdrawal personality trait, disturbance in attention, and drug abuse.

Drugs that inhibit this overactivity, such as entacapone, may help reduce craving for marijuana by correcting the dopamine imbalance, Dr. Shafa said.

Marijuana is the most commonly used illicit drug in the United States, and first-time use of the drug occurs early.

According to a 2006 National Institute on Drug Abuse survey, 63% of people who used marijuana for the first time were under the age of 18. This is very alarming, Dr. Shafa said.

"The adolescent brain, because of the yet unfulfilled process of myelination, is more vulnerable to permanent structural damage. This makes the increasing problem of tetrahydrocannabinol-containing substance abuse in younger people very worrying," he said. "As of now, there is no pharmacological treatment recognized for marijuana abuse. COMT-inhibitors may be a promising tool to combat marijuana addiction."

Dr. Shafa disclosed relationships with AstraZeneca, Bristol-Myers GlaxoSmith-Kline, Janssen, Squibb, and Eli Lilly. ■