Smoking Cessation Strategies Now Numerous

Try nicotine replacement therapy plus bupropion or high-dose NRT plus nicotine gum or lozenges.

BY BRUCE JANCIN

ESTES PARK, COLO. — Three major drug classes with diverse mechanisms of action are now approved for smoking cessation, providing an unprecedented array of options in terms of sequential and combination therapies.

Trying different agents, recycling them, combining them, and providing more intensive behavioral support are all important strategies, Dr. Allan Prochazka said at a conference on internal medicine sponsored by the University of Colorado.

Combination drug therapy is usually more effective than monotherapy, particularly for more heavily tobacco-dependent patients, Dr. Prochazka said. His go-to combinations are nicotine replacement therapy (NRT) plus bupropion (Zyban), or high-dose NRT using a nicotine patch plus nicotine gum or lozenges.

There is a definite need for more studies aimed at defining the optimal drug combinations, according to Dr. Prochazka, professor of medicine at the university and acting associate chief of staff at the Denver VA Medical Center.

The third class of drugs approved by the Food and Drug Administration for smoking cessation, in addition to NRT and the antidepressant bupropion, is varenicline (Chantix), a nicotine receptor partial agonist and the first designer drug for tobacco dependence.

A Cochrane Review of the pivotal clinical trials leading to varenicline's 2006 marketing approval concluded it had a 52% better quit rate than did long-acting bupropion, and there was a suggestion of moderately greater efficacy than NRT, although there were few trials comparing the two (Cochrane Database Syst. Rev. 2008;doi:10.1002/14651858.CD006103.pub3).

And varenicline has a relatively low discontinuation rate. But because of varenicline's psychiatric morbidity and hefty price, Dr. Prochazka reserves it as second-line therapy in patients who have failed NRT and bupropion.

The VA smoking cessation guidelines also categorize varenicline as second-line therapy.

In July, the FDA ordered a black box warning for both varenicline and bupropion, urging prescribers to watch for the development of hostility, agitation, depression, and suicidality. The VA guidelines now call for varenicline to be avoided in psychiatric patients unless the smoking cessation intervention is done in collaboration with a mental health professional. For the time being, the best approach to smoking cessation in psychiatric patients remains unclear, Dr. Prochazka said.

In a generally healthy population of smokers, however, all three FDA-approved types of medication are safe and effective, he stressed. Nearly all smokers—even those who don't meet formal diagnostic criteria for tobacco dependence—will benefit from drug treatment along with brief counseling to quit the habit, he added.

Dr. Prochazka cited a clinical trial of triple combination treatment with bupropion, an NRT patch, and a nicotine inhaler that produced a 35% quit rate at 26 weeks, compared with 19% for the patch alone.

Side effects of the combination therapy were acceptable. There was less weight gain with triple therapy than with the patch alone (Ann. Intern. Med. 2009;150:447-54).

Varenicline has been combined with bupropion in a 38-patient, open-label, phase II trial. The result was a 58% cessation rate at 6 months (Nicotine Tob. Res. 2009;11:234-9).

Varenicline costs about $370 for 12 weeks' worth of 1-mg tablets, a price similar to 3 months' worth of Marlboro cigarettes, the general internist noted. In contrast, 3 months of generic long-acting bupropion runs $210.

Transdermal nicotine costs $70-$100 per month; nicotine gum retails for $35-$50 for 108 pieces, with most patients using 5-8 pieces daily; and nicotine inhaler cartridges cost up to $160 for a 2- to 4-week supply. Nicotine lozenges run $30-$40 for a box of 72; the maximum dose is 20 per day. And nasal nicotine spray costs about $47 per 100 doses, with the typical patient using 3-6 doses per day.

The Agency for Healthcare Research and Quality smoking cessation guidelines are an excellent resource, according Dr. Prochazka.

"It's probably the most evidence-based guideline in medicine," he said.

The guidelines, updated in April 2008 (www.ahrq.gov/clinic/tobacco), are based on a review of more than 3,000 studies, nearly all randomized, controlled trials. The guidelines advocate the "5 A's" approach to smoking cessation:

- ► Ask all patients aged 18 and older at each visit about whether they smoke.
- ► Advise to quit in clear, strong, personalized language.
- ► Assess the smoker's willingness to try to quit now.
- ► Assist the quit attempt with medications, counseling, and other help.
- ► Arrange for follow-up.

A 10%-15% long-term quit rate is realistic for smokers in motivated primary care practices that use the AHRQ guidelines, Dr. Prochazka said. ■

Gabapentin Shows Promise for Cannabis Dependence

BY DAMIAN McNAMARA

HOLLYWOOD, FLA. — Gabapentin significantly decreases weekly cannabis use while significantly improving craving, depression, and sleep quality symptoms, compared with placebo, the results of a phase II, double-blind, randomized study show.

Cannabis dependence is the most common illicit substance disorder in the United States, Barbara J. Mason, Ph.D., said. However, there are no medications approved by the Food and Drug Administration for withdrawal or relapse prevention in this population.

Dr. Mason placed an advertisement in a free newspaper in San Diego in which she invited potential participants to contact her. She received 745 telephone inquiries. Of those, almost half—350 people—did not return a subsequent telephone call. After excluding a similar number (for example, for comorbid depression and/or anxiety), the final cohort was 50 treatment-seeking outpatients who met DSM-IV criteria for cannabis dependence.

The cohort was "solidly dependent," according to Dr. Mason. "Nearly every one of the seven criteria for dependence were met, despite a need for only three," she said at a meeting of the New Clinical Drug Evaluation Unit sponsored by the National Institute of Mental Health.

Compared with placebo, gabapentin significantly reduced cannabis use and tetrahydrocannabinol (THC)/creatinine levels, improved mood and sleep quality, and improved executive function.

The participants reported an average 12-year history of daily marijuana smoking. At baseline, they had average urine TCH/creatinine ratio of 673 ng/mg and reported smoking an average 11 grams a week. Dr. Mason said this amount was equivalent to about one to two marijuana cigarettes a day. The gabapentin group demonstrated significant decreases in grams/week of cannabis smoking (*P* less than .01) and in THC/creatinine levels (*P* less than .02), compared with placebo.

Similarly, those in the gabapentin group showed significantly greater improvements in marijuana craving severity (*P* less than .01), Beck Depression Inventory scores (*P* less than .05), and the Pittsburgh Sleep Quality Index components. "Gabapentin had a rather dramatic effect on daytime dysfunction for week 1 to 8," said Dr. Mason, professor and member of the Committee on the Neurobiology of Addictive Disorders at the Scripps Research Institute in La Jolla, Calif.

A neuropsychologist joined the study to assess executive function. There was a statistically significant higher number of improvements on the various executive function tasks in the gabapentin group than in the placebo group.

The participants were equally randomized to 12 weeks of 1,200 mg/day gabapentin (available as a generic) or placebo. Men comprised 92% of the treatment and 84% of the placebo cohort. The mean age was 34 years, and 76% of the participants were white. Participants were not paid.

Dr. Mason was surprised at how motivated participants were to quit cannabis use. "Over the course of 12 weeks, between screening and week 0, people cut back on grams-per-week use, with a decrease in THC/creatinine ratio," Dr. Mason said. "So they were motivated to cut down from their first call to their clinic."

Before randomized, they underwent 4 weeks of motivational interviewing to set a quit date. This cognitive-behavioral relapse prevention therapy was included "because we thought there would not be a willingness to set a quit date, and we were wrong," said Dr. Mason, who plans to change the protocol in future study.

Before randomized, the cohort underwent a cognitive-behavioral relapse prevention therapy involving 4 weeks of motivational interviewing to set a quit date.

"We are not starting with 4 weeks of motivational interviewing. This is a group already coming in willing to start, and it's a mixed signal to tell them to wait 4 weeks."

A meeting attendee asked Dr. Mason why she chose to study gabapentin.

"It normalizes some CRF [corticotrophin-releasing factor] systems associated with drug withdrawal, as well as the profile with mood and sleep, so we thought we would give it a try," Dr. Mason said. When it came to sleep, somnolence associated with gabapentin could improve the protracted insomnia typically experienced when people stop using marijuana.

"This is one area where a side effect of a drug … was in the service of the greater good in this population," Dr. Mason said.

Gabapentin was well tolerated, Dr. Mason said. Dizziness was the only adverse event significantly higher in the treatment group and was reported by 22%, compared with none of the placebo participants.

Dr. Mason said she had no relevant financial disclosures. The study was funded by National Institute on Drug Abuse. ■

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