'Poor' Data Support Cholinesterase Inhibitor Use

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CARMEL, CALIF. — The evidence for using cholinesterase inhibitors in patients diagnosed with Alzheimer's disease "is pretty darned poor," Dr. Laura Mosqueda said at the Western regional meeting of the American Federation for Medical Research.

She based her remarks on two recent meta-analyses of the topic. The first was a systematic review of randomized clinical trials of the cholinesterase inhibitors donepezil, rivastigmine, and galantamine.

In a search of the Medline, Embase, and Cochrane databases, researchers led by Dr. Hanna Kaduszkiewicz of Hamburg, Germany, evaluated 412 references published between 1989 and 2004 (BMJ 2005;331:321-7). Of these, 22 were included in the study.

In the 14 trials that used the Alzheimer's disease assessment scale–cognitive subscale, the mean difference be-



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DR. MOSQUEDA

tween treatment and placebo groups ranged from 1.5 points to 3.9 points, which is a modest effect at best, said Dr. Mosqueda, director of geriatrics and a professor of family medicine at the University of California, Irvine.

In the 12 trials that used the Clinician's Interview-Based Impression of Change scale with caregiver input, the mean differences ranged from 0.26 to 0.54, "which is below what you're even allowed to score on the test," she said, explaining that the rater is allowed to use only whole integers.

The incidence of adverse effects from the medications was 20% among those in the treatment group and 7% among those who took placebo. The most common adverse events were nausea, vomiting, diarrhea, and weight loss.

"How many times have we had somebody who comes in with Alzheimer's disease, they're losing weight and going through a major work-up, only to realize that they're on donepezil, and that this may be the cause of the weight loss?" Dr. Mosqueda asked.

She also highlighted a more recent Cochrane Review led by Dr. Jacqueline Birks of the University of Oxford (England). It was a meta-analysis of studies also involving the cholinesterase inhibitors donepezil, rivastigmine, and galantamine (Cochrane Database Syst. Rev. 2006;DOI: 10.1002/14651858.CD005593). The meta-analysis concluded that although these three cholinesterase inhibitors are modestly efficacious for mild to moderate Alzheimer's disease, there are no differences among them in terms of efficacy, even though the three drugs work in slightly different ways.

Despite the paucity of data showing efficacy, one factor that motivates physicians to prescribe cholinesterase inhibitors for Alzheimer's patients is the sense that they "really want to do something" for patients and their families, Dr. Mosqueda said. "It's much faster to write that prescription than to sit down, review the evidence, and go over the pros and cons with the patient and family. That takes time to do, but I think it's so important for people to understand, so that they can make an informed decision."

The cost of medication can also be a downside for some Alzheimer's patients who have to pay out of pocket for cholinesterase inhibitors.

Dr. Mosqueda noted that for families faced with making a financial decision between paying for a cholinesterase inhibitor prescription and enrolling their loved one in an adult day care program, "that adult day care program is much more efficacious. Other, more important issues may not be addressed [with the medication

alone]. Sometimes you can spend your time prescribing medicines instead of talking about other issues related to Alzheimer's disease."

She concluded by saying that cholinesterase inhibitors "are nice, but all of us need comfort, identity, joy, and a big dose of love. That goes a long way when we're caring for people who have Alzheimer's disease and their families. Cholinesterase inhibitors may or may not be an adjunct to that."

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