Evidence-Based Medicine Does Not 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 darn poor,” said Dr. Laura Mosqueda 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 between treatment and placebo groups ranged from 1.5 points to 3.9 points, with 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 Assessment of Change scale with caregiver input, the mean differences ranged from 0.26 to 0.54. “This is pretty much what you’d expect if you 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 heard how 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 drugs work in slightly different ways. Despite the paucity of data showing efficacy, one factor that motivates physicians to prescribe cholinesterase inhibitors “are nice, but it’s much faster to write that prescription than to sit down and 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.”

Medication cost is a downside for some patients who have to pay out of pocket for cholinesterase inhibitors. Dr. Mosqueda noted that “families faced with making a financial decision between a cholinesterase inhibitor pre-scription 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 be not addressed [with the medication alone] sometimes you can spend your time prescribing medicines instead of talking about issues related to Alzheimer’s disease.”

“Cholinesterase inhibitors are not a cure,” she said. “They are 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.”

Heresy Simplex May Play a Role in Some Alzheimer’s Cases

SALZBURG, AUSTRIA — Heresy simplex virus type 1 may be the root cause of some cases of Alzheimer’s disease, according to research presented at an international conference on Alzheimer’s and Parkinson’s diseases.

Dr. Matthew Wozniak and Dr. Ruth Itzhaki of the University of Manchester (England) found that human neural cells infected with HSV-1 had contained far more amyloid β than had uninfected cells. “We’ve examined both neuronal and glial cells, and the increase occurs in both cell types,” said Dr. Wozniak.

HSV-1 causes several diseases, including cold sores and herpes simplex encephalitis. Most humans are infected, usually in infancy, and in some the virus is woken from its dormant phase in times of stress.

Previously, researchers from Dr. Itzhaki’s laboratory demonstrated that HSV-1 DNA is present in brain tissue and that antibodies to the virus can be found in the cerebral spinal fluid in a high proportion of patients with Alzheimer’s disease (AD) and elderly patients who do not show signs of the disease (J. Med. Virol. 2005;75:300-6). The study included 27 AD patients and 11 age-matched controls. Importantly, these same markers are generally absent in the brains of younger people.

Subsequently, the researchers increased the study population to 61 AD patients and 48 age-matched controls (Lancet 1997;349:241-4). They found that HSV-1 DNA in the brain and possession of an apolipoprotein E-4 allele is a strong risk factor for AD (odds ratio 12).

More recently, the researchers demonstrated that HSV-1 infection decreases the concentration of full length amyloid precursor protein, Dr. Wozniak explained.

“HSV-1 DNA in AD patients is linked to the use of antiviral agents as a treatment for the symptoms of the disease,” he suggested.