Minimize Drugs in Managing Patients With Alzheimer's

BY HEIDI SPLETE
Senior Writer

BALTIMORE — Recent estimates suggest that by the year 2050, one in four Americans either will have Alzheimer's disease or will be caring for someone who does, Dr. Thomas Finucane said at a meeting sponsored by the American Geriatrics Society and Johns Hopkins University.

"This is a big problem and [it's] going to get bigger," said Dr. Finucane, a professor in the division of geriatric medicine and gerontology at Johns Hopkins University, Baltimore. The burden of Alzheimer's disease (AD) is daunting, especially in long-term care settings. In addition, few government programs exist to ease this burden in part because the federal government considers AD a social problem rather than a medical problem, he said.

When evaluating a patient for Alzheimer's disease, it is important to understand the definition of the disease, Dr. Finucane said. Dementia is defined as an acquired, severe loss of cognitive function. Sometimes the patient is not delirious and speaks coherently, but he or she still exhibits some evidence of cognitive impairment. The impairment must be global to meet the criteria for dementia, which means the patient suffers from amnesia, plus at least one of the following: aphasia (has a speech disorder), apraxia (can't perform a learned task), agnosia (can't recognize a familiar object), and disturbance of executive function (is unable to recognize a problem, plan, monitor, and execute a solution, and stop when the task has been completed).

Nonpharmaceutical strategies can help manage AD symptoms and behavioral problems. Simple empathy and thinking outside the box can work wonders.

Families of Alzheimer's patients should seek counseling and information about useful interventions, Dr. Finucane said. Many think of drug treatment first, but cholinesterase inhibitors, the drugs most often suggested for AD, do not benefit the daily lives of most patients, he noted. Yet many patients and family members insist on trying drug therapy, despite the expense and the potential side effects.

When family members or other caregivers insist on drug therapy, propose an end point for drug use, at which time the patient will discontinue the drug treatment if symptoms have not meaningfully improved, Dr. Finucane suggested.

Data on cholinesterase inhibitors from the medical literature show two important facts. First, the drugs have been associated with a statistically significant improvement in scores on psychometric tests, such as the Mini-Mental State Examination (MMSE). Second, patients, however, have been unable to tell whether they are taking the study drug or a placebo, and in any trials that ask about the quality of life of the patient and the caregiver, it is impossible to distinguish the effects of the drug from those of a placebo, Dr. Finucane said. "The science in some of these studies may be good, but the rhetoric of the research is purely promotional."

He cited a non-industry-supported metaanalysis of 22 double-blind, randomized, controlled trials (RCTs) that included the use of donepezil, rivastigmine, and galantamine for AD (BMJ 2005;331:321-7). Overall, patients with AD who took any of these drugs showed improvements ranging from 1.5 to 3.9 points in favor of the drugs on the Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog), a 70-point scale. Improvement on the 30-point MMSE was less than 2 points in the RCTs. However, the investigators reported methodologic flaws and minimal clinical benefits, which led them to question the effectiveness of cholinesterase inhibitors for AD.

The American Academy of Neurology's position on AD is that treatment with cholinesterase inhibitors should be considered (not mandated), and that the current evidence shows only a small degree of benefit, Dr. Finucane noted.

Also, the evidence does not support arguments that drug therapy stabilizes AD. In a randomized, double-blind trial of nearly 500 elderly patients, there was no significant difference in the progression of disability after 3 years between patients who took either 5 or 10 mg of donepezil daily or a placebo (58% vs. 59%, respectively). There was a significant difference in scores on the Mini-Mental State Examination in favor of donepezil (in this case, 0.8 points) and a small (1 point on a scale of 18) benefit on the Bristol Activities of Daily Living Scale (Lancet 2004;363:2105-15).

"You will hear over and over that you can't afford to stop these drugs in a stable AD patient, because there is a risk of catastrophic reaction," Dr. Finucane said. However, several studies were designed with a washout period, the subjects stopped taking the medications at the end of the trials, and no adverse events were reported.

"If there was a serious risk of catastrophic reactions from stopping the donepezil, it would have been evident during the washout period at the end of the study," he said.

In a retrospective study of 22,890 patients aged 65 years and older in Pennsylvania (N. Engl. J. Med. 2005;353:2335-41), atypical antipsychotics and conventional antipsychotics were equally associated with risk of death in elderly patients, and the investigators wrote that use of any antipsychotics for AD should be avoided. In April 2005, the Food and Drug Administration issued a black box warning on the use of atypical antipsychotics to treat Alzheimer's.

Given the lack of evidence to support a genuine benefit from drug therapy, other nonpharmaceutical strategies can be used to help manage the symptoms and behavioral problems associated with AD. Simple empathy and thinking outside the box can work wonders. For example, simply positioning a person's wheelchair in a different direction so he or she is not looking at a person or object that triggers bad behavior can be amazingly helpful, Dr. Finucane said. "Don't confront the patients. Try to talk civilly to them," he explained. For example, when Mom says she wants to go home, rather than arguing with her, suggest, "We are just fixing your dinner now. Why don't we finish that and then talk about this request of yours."

Bad behavior toward caregivers is a chronic problem in long-term care facilities. However, education can be as helpful as medication in addressing this problem, Dr. Finucane said. The same is true for patients who touch caregivers inappropriately; try education before medication.

Finally, some AD patients have enough insight into their condition to become extremely depressed, and antidepressants can be helpful for managing their depressive symptoms, Dr. Finucane said. However, the bottom line remains that drug treatments for AD symptoms rarely are significantly helpful in improving the quality of patients' lives and their caregivers' lives. ■

Use of Potassium-Sparing Diuretics Cuts AD Risks

BY MARY ANN MOON
Contributing Writer

Elderly patients who took potassium-sparing diuretics had a 70% lower rate of developing Alzheimer's disease than those who did not take antihypertensive drugs in a population-based study of dementing illnesses, reported Ara S. Khachaturian, Ph.D., and his colleagues.

Antihypertensive agents in general reduced the risk for Alzheimer's disease (AD), but the potassium-sparing diuretics were particularly beneficial, said Dr. Khachaturian of Potomac, Md., and his colleagues.

To assess whether protection against AD might be specific to individual classes of antihypertensive drugs, the investigators analyzed data from the Cache County study, an ongoing investigation of dementias in the elderly population of Cache County, Utah (Arch. Neurol. 2006 March 13 [Epub doi:10.1001/archneur.63.5.noc60013).

They studied medication usage in 3,227 patients who were aged 65 years or older when they enrolled in the study in 1995, including 104 who developed AD during follow-up. Of the 3,217 patients who provided drug information, nearly half of the patients (45.3%) took antihypertensive drugs, including ACE inhibitors (13.0%); β-blockers (11.5%); calcium channel blockers (14.9%); diuretics (26.5%); or some combination of these (18.2%).

The risk of developing AD was significantly smaller in those who took antihypertensive medications than in those who did not (adjusted hazard ratio [aHR] 0.64). When the results were broken down by drug class, diuretics showed the greatest protective effect against AD (aHR 0.61), whereas β-blockers showed a statistical trend toward a significant protective effect (aHR, 0.53); ACE inhibitors (aHR, 1.13) and calcium channel blockers (aHR, 0.86) showed no effect. Closer analysis showed the potassium-sparing diuretics accounted for all the risk reduction attributed to their drug class (aHR, 0.26); thiazide diuretics and loop diuretics were not protective (aHR, 0.72 and 1.45, respectively). Analysis also showed that the dihydropyridine subclass of calcium channel blockers cut the risk of AD (aHR, 0.53), but other subclasses did not, said the researchers.

The finding that antihypertensive agents that protect against AD seem to do so independently of controlling blood pressure was of particular interest. It's not known why the diuretics cut the AD risk. Other diuretics reduce potassium concentrations, and low potassium levels have been tied to oxidative stress, inflammation, platelet aggregation, and vasoconstriction, possible contributors to AD pathogenesis, they said. ■

Initiative Wants Volunteers For Neuroimaging Study

Researchers with the Alzheimer's Disease Neuroimaging Initiative are recruiting 800 older adults to participate in a landmark study to identify biologic markers of memory decline and Alzheimer's disease.

The National Institutes of Health study is the most comprehensive effort to date to identify biochemical and brain imaging changes associated with memory decline. The study is expected to last 5 years.

The researchers are seeking adults aged 55-90 years, who are in good general health with no memory problems or who are in good general health but have memory problems/concerns or a diagnosis of early Alzheimer's disease (AD). The researchers expect to enroll 400 patients with mild cognitive impairment (MCI), 200 cognitively normal controls, and 200 with early AD.

The researchers will be performing serial MRI and PET scans, and measuring various biologic compounds in the blood, cerebrospinal fluid, and urine. The participants will also undergo clinical and neuropsychologic assessments to track MCI and early AD progression. Healthy volunteers and patients with MCI will be followed for 3 years, while those with early AD will be followed for 2 years. Patients will be evaluated at 58 study sites in the United States and Canada.

For more information about participating in the study and to obtain a list of sites, contact the National Institute on Aging's Alzheimer's Disease Education and Referral Center by visiting www.alzheimers.org/imagine or calling 800-438-4380.

—Kerri Wachter