Minimize Drugs in Managing Patients With Alzheimer’s

BY HEIDI SPLETER
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Baltimore — Recent estimates suggest that by the year 2050, one in four Americans either will have Alzheimer’s disease (AD) 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 begin before the age of 65 years or older, which means the patient suffers from amnesia, at least at one of the following: aphasia (has a speech disturbance that prevents him or her from understanding words); agnosia (does not 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).

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. “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 taken or 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 there are no currently accepted disease 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 study, 8.8 points): the benefits were 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 reaction, anyone using 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 2003, the Food and Drug Administration issued a black box warning on the use of atypical antipsychotics to treat Alzheimer’s disease. Given the lack of evidence to support a genuine benefit from drug therapy, other nonpharmacologic 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.

Nonpharmacologic strategies can help manage AD symptoms and behavioral problems. Simple empathy and thinking outside the box can work wonders. For example, you may be able to get people to stop taking their antipsychotic if you share with them the natural appetite for a walk, a card game, and so forth. Do not push people beyond their abilities, Dr. Finucane said. “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 reaction, anyone using donepezil, it would have been evident during the washout period at the end of the study,” he said.

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The neural changes associated with AD can be global to meet the criteria for dementia, said Dr. Finucane. Many think of drug treatments for AD symptoms rarely are significant, Dr. Finucane said. However, the bottom line remains that the use of any antipsychotics for AD should be avoided (N Engl J Med. 2005;353:2335-41), and the investigators wrote that use of any antipsychotics for AD should be avoided.

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