Severe Alzheimer's Responds to Donepezil

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Patients with severe Alzheimer's disease showed improved cognition and function when treated with donepezil in a 24-week, placebo-controlled trial, Dr. Sandra Black and her associates reported in a poster at the annual meeting of the American Geriatrics Society.

The results are consistent with a Swedish nursing home study in a similarly institutionalized population (Lancet 2006;367:1262-70), suggesting that even patients with severe disease can benefit from treatment with donepezil.

"The two studies taken together suggest that this stage of disease can show measurable benefits of treatment with donepezil," Dr. Black, professor of medicine and head of neurology at Sunnybrook Health Sciences Centre, University of Toronto, said in an interview.

Donepezil (Aricept) is approved for mild to moderate Alzheimer's disease. In February 2006, the U.S. Food and Drug Administration accepted a supplemental new drug application for donepezil in severe Alzheimer's disease.

Doses of 5 mg and 10 mg of donepezil are typically administered once daily.

Dr. Black and her colleagues study randomized 343 patients with severe Alzheimer's disease to an initial dose of donepezil 5 mg/day for 6 weeks and then 10 mg/day donepezil (176 patients) or placebo (167 patients) for 24 weeks. Patients resided in the community or in assisted-living facilities. Baseline characteristics were similar in both groups. Overall, 117 of the 176 donepezil-treated patients and 127 of the 167 placebo patients completed the study, which was supported by Eisai Inc. and Pfizer Inc. Dr. Black holds no financial interest in either firm, but has been a study investigator for both. She is an ad hoc consultant and speaker, and has received honoraria from Pfizer.

Primary end points were change from baseline in Severe Impairment Battery (SIB) total score and Clinician's Interview-Based Impression of Change-Plus (CIBIC-plus) at 24 weeks.

The primary analysis was based on the intent-to-treat population using a last-observation-carried-forward analysis at 24 weeks. Categories in the CIBIC-plus analysis were collapsed (1-3 equals improved; 4 equals no change; and 5-7 equals worsened) because the distribution of values was sparse in categories 1, 2, and 7.

Donepezil was significantly superior to placebo on the SIB score at week 24 in the intent-to-treat population (mean difference 5.3), and at weeks 8, 16, and 24 in patients who completed the study. Most reported adverse events were mild to moderate (74%), the most common of which were diarrhea, nausea, and insomnia. ■

Ritalin Lifted Dementia-Related Apathy in a 13-Patient Study

CHICAGO — Methylphenidate may be effective in the treatment of apathy associated with dementia of the Alzheimer type, Dr. Prasad Padala and associates reported in a poster at the annual meeting of the American Geriatrics Society.

Results from an open-label study in 13 patients suggest that methylphenidate (Ritalin) has a substantial effect on apathy, with smaller but significant positive effects on mood, cognition, and independent activities of daily living.

The findings warrant further testing with a double-blind, placebo-controlled trial, he noted.

Apathy is the most common behavior problem reported in persons with Alzheimer's disease, affecting about 70%-90% of patients.

All patients in the study had dementia of the Alzheimer type, Mini-Mental State Examination (MMSE) scores greater than 18, and Apathy Evaluation Scale (AES) scores greater than 30. Their mean age was 69 years.

All patients were started on methylphenidate 5 mg twice daily; the dose was titrated to 10 mg twice daily over a 2-week period. Follow-up visits were scheduled at 4, 8, and 12 weeks.

Significant improvement in apathy (AES 52.6 vs. 31.6) was reported from baseline over 12 weeks, reported Dr. Padala, of the department of psychiatry at the University of Nebraska, Omaha, and a psychiatrist at the Omaha division of the VA (Veterans Affairs) Nebraska Western Iowa Health Care System.

Less robust but significant improvement was noted at 12 weeks in Geriatric Depression Scale scores (93 vs. 63), MMSE scores (24.2 vs. 25.5) and Independent Activities of Daily Living criteria (13.7 vs. 16).

—Patrice Wendling

CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Dementia

BY NEIL SKOLNIK, M.D. AND PAMELA ANN FENSTEMACHER, M.D.

A person who has progressive dementia experiences decline in multiple areas of cognitive function, and eventually manifests significant deficits, usually beginning in occupational function, progressing to social function, and eventually affecting self-care. Guidelines developed by the American Medical Directors Association (AMDA) are based on research and expert opinion. Although the document is aimed at treating long-term care residents, it illustrates a systematic approach to the identification and management of dementia that is applicable to other settings as well.

Guidelines are most useful when they are available at the point of care. A concise yet complete handheld computer version of this guideline is available for download, compliments of FAMILY PRACTICE NEWS, *at www.redi-reference.com.*

Assessment

Review all available information and speak with the patient, family, and other caregivers to investigate the patient's physical, functional, cognitive, and behavioral status. Evaluate any current signs or symptoms of dementia in the patient by performing a formal functional-status and cognitive assessment, including, if possible, the observations of an interdisciplinary team. If a patient has many somatic symptoms and performs well on automatic processing tasks (such as writing her name, eating a meal), depression should be considered as a possible cause or contributor to the patient's cognitive decline. An altered level of consciousness combined with increasing cognitive impairment can be caused by delirium. Any recent or abrupt changes in the level of consciousness, behavior, or function usually are the result of an acute condition, not dementia.

Evaluate the patient's risk factors for dementia, such as atherosclerosis, alcohol abuse, or vitamin B_{12} deficiency. Often a specific cause is undetectable, or the dementia may be so far advanced in the long-term care facility that additional diagnostic testing—beyond a complete blood count, thyroid function test, metabolic screen, B_{12} level, and syphilis serology—is not helpful. Tests to consider include imaging studies of the head, a screen for depression, and testing for HIV. Neuropsychological testing or a consultation with a psychologist, psychiatrist, or neurologist may be helpful.

Management

Identify the patient's strengths and deficits and determine the significance of any deficits, impairments, or symptoms. Concise and accurate documentation by using tools like the Minimum Data Set are encouraged. Treatment should take an interdisciplinary approach that optimizes function and quality of life while capitalizing on the patient's strengths. Vigilantly address inadequately treated or unrecognized medical conditions, adverse medication effects, and psychological and environmental problems. Socially unacceptable behaviors are a manifestation of disease that can be anticipated and should be accommodated whenever possible. Identifying the triggers for disruptive behavior will allow for targeted behavioral interventions that can prevent or help to manage the disruptive behavior. When an individual becomes more impaired, the environment plays an even greater role in the patient's functional ability. If a patient has a significant condition change, is newly admitted, or was recently hospitalized, medical factors may be contributing to the disruptive behavior. Only when a patient's impairment leads to excessive disruption or has dangerous effects—and after behavioral and environmental management fail—should medication be considered.

Medical Interventions

Before any drug therapy is initiated to treat dementia or disruptive behavior, the goals, risks, and anticipated benefits of therapy should be addressed with the family. The use of antihypertensive, antiplatelet or lipid-lowering agents in multi-infarct dementia may prevent worsening of symptoms. Cholinesterase inhibitors may reduce the rate of cognitive decline and may improve behavioral symptoms in mild to moderate dementia. Memantine is approved to treat moderate to severe dementia of the Alzheimer type. It is reasonable to consider using these agents if the patient's dementia is consistent with Alzheimer-type dementia. The atypical antipsychotics—trazodone, carbamazepine, and divalproex—are used to manage behavior and psychological symptoms in patients with dementia, but these medications have only modest effectiveness and associated risks that make close monitoring necessary.

After initiation of any management, including drug therapy, the patient's condition must be monitored in order to maximize the beneficial interventions and minimize adverse drug reactions and interventions that may no longer be appropriate or working.

The Bottom Line

AMDA's clinical practice guideline on dementia—although aimed at long-term care facilities—describes useful steps that can be implemented in all settings to help identify patients who are at risk for dementia and the progression of dementia, as well as steps that can be used to manage dementia. Management is aimed at optimizing the patient's function and quality of life while minimizing the preventable complications and negative consequences of the condition.

DR. SKOLNIK *is an associate director and* DR. FENSTEMACHER *is an assistant director of the family medicine residency program at Abington (Pa.) Memorial Hospital.* DR. SKOLNIK *is also a coauthor of the "Redi-Reference Clinical Guidelines" handbook for handheld computers.*