

# Interventions Work for Alzheimer's Caregivers

BY KATE JOHNSON  
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ORLANDO — The quality of life among caregivers of Alzheimer's patients can improve significantly when interventions are tailored to their needs, according to the first randomized trial of such interventions.

"Physicians are in a position to identify highly stressed caregivers and intervene," said Richard Schulz, Ph.D., the principal investigator on the Resources for Enhancing Alzheimer's Caregiver Health (REACH) II trial.

Speaking at the annual meeting of the Gerontological Society of America, Dr. Schulz and several other of the trial's investigators noted that a goal of the REACH team is to develop a brief assessment for use by physicians to evaluate caregivers' depressive symptoms. "This would be something a caregiver could fill out in the waiting room and would give the doctor an indication that there may be problems," he said in an interview.

The REACH II trial randomized 642 family member caregivers of Alzheimer's patients to either usual care (control group) or a tailored intervention aimed at improving their quality of life. The primary outcome, measured after 6 months, was a multivariate quality of life indicator that assessed

caregiver burden (how extensively their lives were disrupted as a result of caregiving), depressive symptoms, self-care, social support, and patient problem behaviors, said Dr. Schulz, a professor of psychiatry at the University of Pittsburgh.

The group's racial and ethnic backgrounds were equally divided among whites, blacks, and Hispanics. Most caregivers were female, in their late 50s, and living with the Alzheimer's patient.

Prior to randomization, all caregivers underwent an extensive baseline evaluation, which assessed their risk for poor or decreasing quality of life. Those in the intervention arm then received a series of 12 intervention visits tailored specifically to their areas of concern.

When reassessed at the end of the study period, whites and Hispanics showed significant improvement after the intervention, whether the caregiver was a spouse or an adult child, while blacks showed improvement only when the caregiver was a spouse.

The study also measured clinical depression among caregivers as well as their intentions of placing the Alzheimer's patient in an institution. Caregivers who received the intervention were significantly less likely than the control group to consider institutionalization (4% vs. 7%) and to be clinically depressed (13% vs. 23%). ■

# Alzheimer's Study Identifies Biomarkers in Early Stages

BY JONATHAN GARDNER  
Contributing Writer

**B**iomarkers in cerebrospinal fluid may indicate whether patients with mild cognitive impairment will progress to Alzheimer's disease and could assist in the development of new screening tools or treatments, according to Dr. Oskar Hansson of Lund University, Malmö, Sweden, and his associates.

The investigators followed 137 patients with mild cognitive impairment who had consulted the memory disorder clinic at the university hospital between July 1998 and June 2001. A control population of 39 healthy volunteers with no memory complaints, good cognitive functioning, and without neurologic or psychiatric disease was recruited from Malmö.

The researchers followed the populations for 4-6 years after scientists took cerebrospinal fluid from a lumbar puncture.

A total of 57 patients with mild cognitive impairment at baseline

developed Alzheimer's disease during the study period, and 21 developed other forms of dementia. Those patients with abnormal concentrations of the biomarkers  $\beta$ -amyloid, total tau, and phosphorylated tau at the beginning of the study were more likely to have progressed to Alzheimer's disease (Lancet Neurol. 2006;5:228-34).

Concentrations of total tau greater than 350 ng/L and of  $\beta$ -amyloid less than 530 ng/L at baseline were defined as pathologic. Patients with pathologic levels of the biomarkers were more than 20 times as likely to progress to Alzheimer's disease as those with mild cognitive impairment but without the pathologic levels of biomarkers, reported the authors.

Earlier studies followed those biomarkers in patients for only 1-2 years. Because of this study's long follow-up, "the diagnosis of stable [mild clinical impairment] is more reliable in this study, compared with previous investigations," the investigators said. ■

## EVIDENCE-BASED PSYCHIATRIC MEDICINE

### Donepezil for Alzheimer's Dementia

#### The Problem

You are working with the family of a patient who has been diagnosed with probable Alzheimer's disease. The family asks about possible medications.

#### The Question

Can treatment with Aricept (donepezil) improve the patient's well-being?

#### The Analysis

Before conducting an extensive Medline search, we decided to look for a review at the Cochrane Collaboration's Web site (Cochrane Database Syst. Rev. 2006 Jan 25;(1):CD001190; www.cochrane.org/reviews/en/ab001190.html).

#### The Evidence

The Cochrane review of this topic by investigators was updated June 12, 2005. In conducting this review, the researchers included all double-blind, randomized controlled trials that compared donepezil with placebo in patients with mild, moderate, or severe dementia caused by Alzheimer's disease.

Mild dementia was defined as "impairment of attention and memory; forgetting of recent information; occasional confusion or disorientation; some help needed with everyday activities." Moderate dementia was defined as "amnesia for recent events, some disorientation for time and place, impairment of reasoning and ability to understand events, and dependency on others in personal care and routine daily tasks." Severe dementia was defined as "incoherent speech; disorientation for time, place, and person; failure to recognize close relatives; incontinence of urine and feces; complete dependence on others for basic personal care."

Mild to moderate dementia was also defined as scoring 10-26 on the Mini-Mental State Examination (MMSE). For this Cochrane review, 23 trials with a total of 5,272 patients were included.

Global assessment of function was evaluated using the Clinician's Interview-Based Impression of Change scale (CIBIC-plus); the 7-point Gottfries-Brane-Steen scale (GBS); or the Clinical Dementia Rating-Sum of the Boxes scale (CDR-SB), which measures both cognitive function and everyday function in a single score: 0.5, 1, 2, or 3.

Studies that used the CIBIC-plus showed the benefits of donepezil doses of 5 mg/day (odds ratio [OR] 2.10 at 12 weeks and 2.38 at 24 weeks) and 10 mg/day (OR 2.70 at 12 weeks and 2.18 at 24 weeks). Studies using the GBS showed benefits of donepezil 5 mg/day at 24 weeks (mean difference  $-2.56$ ) and donepezil 10 mg/day at 52 weeks (mean difference  $-6.01$ ). Studies using the CDR-SB showed benefits of donepezil 5 mg/day at 24 weeks (weighted mean difference [WMD]  $-0.51$ ), 10 mg/day at 12 weeks (WMD  $-0.23$ ), and 10 mg/day at 24 weeks (WMD  $-0.53$ ).

Cognitive function was evaluated using the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) and MMSE.

The ADAS-Cog total score ranges from 0 to 70, with a higher score indicating greater impairment. Studies that used the ADAS-Cog showed benefits of donepezil 5 mg/day (WMD  $-2.15$  at 12 weeks and  $-2.02$  at 24 weeks) and 10 mg/day (WMD  $-2.45$  at 12 weeks and  $-2.81$  at 24 weeks).

Studies using the MMSE showed the benefits of donepezil 5 mg/day (WMD  $+1.08$  at 12 weeks and  $+1.44$  at 24 weeks) and 10 mg/day (WMD  $+1.26$  at 12 weeks,  $+1.45$  at 24 weeks, and  $+1.84$  at 52 weeks).

Activities of daily living were evaluated, in part, using the Disability Assessment for Dementia (DAD) scale and the Instrumental Activities of Daily Living (IADL) scale.

The DAD is scored on a scale from 0 to 100, with higher scores equating to higher levels of functioning. In studies applying the DAD, donepezil 10 mg/day at 12 weeks showed a mean difference of  $+4.83$ . After 24 weeks, the patients taking a dose of 10 mg/day showed a mean difference of  $+8.00$ .

The IADL is based upon eight criteria (use of telephone, traveling via car or public transportation, food or clothes shopping, meal preparation, housework, laundry, medication use, and money management) and each criterion is graded on a three-part scale (independent, assistance needed, or dependent). In the studies that applied the IADL, patients who took donepezil at a dose of 10 mg/day for 12 weeks showed a mean difference of  $-4.31$ . After 24 weeks, the mean difference in IADL score was  $-6.32$  for patients taking 10 mg per day.

One study evaluated the level of behavioral disturbance using the Neuropsychiatric Inventory, which is scored from 1 to 144, with a lower score indicating improvement. After 6 weeks of treatment, patients who received 10 mg/day dose of donepezil had a mean difference of  $-6.20$ , and after 24 weeks, the mean difference in Neuropsychiatric Inventory score was  $-3.26$ .

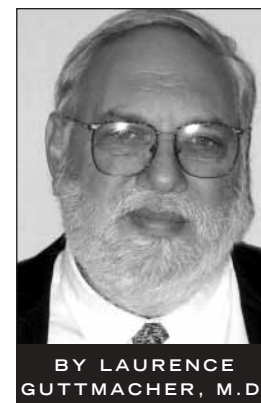
#### The Conclusion

The data that are currently available indicate that global function and cognitive function improve with donepezil in a dose-related manner and that the improvement increases with length of time treated for periods of 12, 24, and 52 weeks. Although fewer data are available evaluating activities of daily living and behavioral disturbance, they show benefit for treatment with donepezil, mostly at a dose of 10 mg/day.

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