Small Trial Finds Donepezil Effective in African Americans With Alzheimer's

BY DOUG BRUNK
San Diego Bureau

San Diego — Donepezil is safe and effective in African Americans with mild to moderate Alzheimer's disease, a 12-week open-label study demonstrated.

The finding is important because African Americans are underrepresented in clinical trials even though they have a higher risk for Alzheimer's disease, compared with whites, Patrick Griffith, M.D., said during a poster session at the annual meeting of the American Association for Geriatric Psychiatry.

This trial uses the Fuld Object Memory Evaluation (FOME), a culturally unbiased evaluation of memory. "The test has been validated in African Americans, and it operates independent of educational level or [social background]," Dr. Griffith, chief of the division of neurology at Morehouse School of Medicine, Atlanta, said in an interview. "It relies on touch and vision. We may have a measuring tool for future clinical trials that will avoid previous reports of educational or cultural bias."

He added that the FOME was designed for elders who may have problems with hearing or attention.

Incidences of diarrhea, hypertension, and urinary tract infection were similar between untreated patients with Alzheimer's and those on donepezil.

Dr. Griffith and his associates enrolled 125 community-dwelling African Americans aged 51-98 from 30 sites in the United States with a clinical diagnosis of mild to moderate Alzheimer's disease and Mini-Mental State Examination (MMSE) scores of 10-26. The patients received donepezil (Aricept) 5 mg/day at the conclusion of their baseline visit; the dose was increased to 10 mg/day after 4 weeks—according to clinician judgment.

At weeks 4, 8, and 12, the investigators administered the FOME, the MMSE, and the Clinician Interview-Based Impression of Change with Caregiver Input (CIBIC-plus).

Patients demonstrated significant improvement on the FOME storage and retrieval scores, the MMSE scores, and the CIBIC-plus scores during 12 weeks of therapy.

The most common treatment-emergent adverse events were diarrhea, hypertension, and urinary tract infection, and the incidences were similar to those reported previously in patients with mild to moderate Alzheimer's. Lab results were unremarkable.

Pfizer Inc., donepezil's maker, supported the study. ■

Low Plasma N-3 Fatty Acids Linked to Dementia

BY KERRI WACHTER
Senior Writer

Washington — Higher intake of n-3 fatty acids may have a protective effect against cognitive impairment, according to data presented at the annual meeting of the Gerontological Society of America.

In a study of almost 1,000 people aged 65 years and older, those with dementia had significantly lower plasma levels of n-3 fatty acids, said Antonio Cherubini, M.D., of the Institute of Gerontology and Geriatrics in Perugia, Italy.

The n-3 fatty acids are an important component of the neuronal membrane, influencing membrane fluidity and all the related functions, such as signal transduction and enzyme function. Fish—particularly fatty fish, such as mackerel and albacore tuna—are the primary source of n-3 fatty acids.

Dr. Cherubini presented data from the Aging in Chianti (InCHIANTI) study conducted between 1998 and 2000 in the Chianti region of Italy.

The 935 volunteers were categorized as having normal cognition (725 subjects), cognitive impairment without meeting criteria for dementia (153 subjects), or dementia (57 subjects). Cognitive function was screened using the Mini-Mental State Examination. The subjects with age- and education-unadjusted scores lower than 26 on the examination underwent more detailed tests. The diagnosis of dementia was made according to DSM-IV criteria. Plasma fatty acid levels were determined using gas chromatography.

Subjects with dementia had the lowest n-3 fatty acid plasma concentrations—as a percentage of total fatty acid plasma concentrations in mg/L—with a mean of 2.7% vs. 3.0% for the cognitively impaired group and 3.2% for the normal cognition group. Subjects with dementia had the highest plasma concentrations of saturated fatty acids—as a percentage of total fatty acid plasma concentrations in mg/L—with a mean of 31.4% vs. 30.1% for the cognitive impairment group and 30.3% for the normal cognition group.

"Subjects in the second group—those who have cognitive impairment but not dementia—tended to have intermediate values in many of the fatty acids," Dr. Cherubini said.

The finding of lower n-3 fatty acid plasma concentrations in subjects with dementia persisted even after adjusting for age, gender, education, smoking status, cholesterol and triacylglycerol levels, alcohol, fatty acid and total energy daily intakes, and total plasma levels of fatty acids. The difference between normal subjects and those with mild cognitive impairment was not ignificant after adjustment.

Previous studies have examined the relationship between n-3 fatty acid consumption and the development of dementia, but the results have been conflicting, Dr. Cherubini said. ■

Cognitive Decline Unchecked in Some After One Stroke

Bal Harbour, Fla. — Cognition declines in the years after a single stroke for a substantial minority of patients, according to a study presented at the annual meeting of the American Neuropsychiatric Association.

After the initial poststroke period, most experts would expect cognition to improve or remain static, according to the literature. However, some studies with a longer follow-up now suggest cognitive decline is possible after a single stroke, even in younger patients. The current research supports that finding and shows the utility of screening patients with the Mini Mental State Examination (MMSE).

The cognitive impairment due to stroke is not static. "Our findings suggest there is a subpopulation that continues to decline as they age," Gregory Kellermeyer, M.D., said in an interview.

The investigators assessed 16 men and 10 women at least 1 year following a single known stroke. The mean follow-up was almost 6 years. Participants were relatively young with a mean age of 58 years. Pretreatment data for the stroke survivors came from a study of constraint-induced movement therapy for upper extremity motor impairment.

Cognitive deficits can occur independent of motor decline. The implication is that "even a single stroke may in some persons incite a progressive neurodegenerative process that preferentially affects cognition," the investigators wrote.

There was possible cognitive impairment in 6 of 27 participants (22%) and definite cognitive impairment in 2 of 27 (7%). Possible cognitive impairment was defined as a greater than 1 standard deviation on the adjusted MMSE; definite cognitive impairment was defined as greater than 2 standard deviations.

"The Mini Mental State Examination is a possible way to identify this subpopulation," said Dr. Kellermeyer, fourth year resident in psychiatry at the University of Colorado, Denver.

Patient age, gender, handedness, stroke laterality, and severity of motor impairments were not significantly associated with raw or adjusted MMSE results.

—Damian McNamara

Memantine May Ease Agitation In Alzheimer's

BY DOUG BRUNK
San Diego Bureau

San Diego — Use of memantine in patients with moderate to severe Alzheimer's disease significantly reduced their behavioral disturbances and psychiatric symptoms, compared with placebo, Jeffrey L. Cummings, M.D., reported in a poster session at the annual meeting of the American Association for Geriatric Psychiatry.

"We think this represents an important, newly recognized benefit for the use of memantine in patients with Alzheimer's disease," Dr. Cummings, director of the University of California, Los Angeles, Alzheimer's Disease Research Center, said in an interview. "The question we posed was, does a drug like memantine, which is used for cognitive improvement, have any effect on agitation? What we saw was that in several analyses—whether we looked at week 12 or week 24, whether we looked at patients who were asymptomatic at baseline or symptomatic at baseline—memantine reduced agitation."

For the 24-week study, Dr. Cummings and his associates randomized 403 patients at 37 clinical centers who had moderate to severe Alzheimer's disease to receive either memantine 10 mg b.i.d. or placebo. The memantine was titrated up weekly in 5-mg increments from a starting dose of 5 mg/day during week 1 to 20 mg/day at week 4. All patients remained on donepezil throughout the study.

The investigators used the Neuropsychiatric Inventory (NPI) to assess behavioral symptoms at baseline, week 12, and week 24.

Of the 403 community-dwelling patients, 202 received memantine and 201 received placebo. The mean age of study participants was 76 years, and 65% were female. Most (91%) were white.

When compared with patients in the placebo group at 12 weeks, those in the memantine group had significant improvements on the NPI domains of agitation/aggression (–0.4 vs. 0.2), irritability/lability (–0.4 vs. 0.1), and appetite/eating change (–0.4 vs. 0.1), where a negative value denotes improvement and a positive value signifies worsening of symptoms. Improvements in all of these NPI domains remained statistically significant at 24 weeks.

"I was surprised by the magnitude and consistency of the effect," Dr. Cummings told Clinical Neurology News.

The investigators also observed that in patients who were asymptomatic at baseline, memantine treatment resulted in significantly less emergence of agitation/aggression and appetite/eating changes by week 24, compared with those on placebo.

According to Dr. Cummings, this is the first study to look at the effect of memantine on behavior in Alzheimer's disease.

Forest Laboratories Inc., manufacturer of memantine, supported the study. ■