Depression Intensifies Stroke Risk in the Elderly

BY MITCHEL L. ZOLER
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DALLAS — Depression boosted stroke risk in a study of more than 4,000 elderly people followed for 10 years.

People with the highest depression scores at baseline had twice the incidence of a cerebrovascular event or transient ischemic attack during follow-up, compared with people who had no depression, Dr. Abraham A. Ariyo reported at the annual scientific sessions of the American Heart Association.

The finding that depression is a risk factor for stroke follows a prior analysis of the same group of people showing that depression boosted coronary artery disease risk, said Dr. Ariyo, director of HeartMasters in Dallas.

The Cardiovascular Health Study Collaborative Research Group enrolled 4,483 men and women aged 65 or older who were completely free of any clinical sign of cardiovascular disease at baseline. The study also excluded patients who were treated with an antidepressant.

All participants were assessed for depression using a modified version of the Center for Epidemiologic Studies Depression Scale. The participants were categorized into quartiles based on their scores. Those with a score of zero had no depression. The next quartile included people with a score of 1-5, followed by quartiles with scores of 6-10, 11-15, and 16 and over.

During 10.3 years of follow-up, 533 people had a stroke, and 1,359 died.

In a multivariate analysis that controlled for baseline differences, the incidence of stroke was related to depression scores.

Compared with people who had a score of zero, those with a score of 1-5 had 19% more strokes, those with a score of 6-10 had 57% more strokes, those with a score of 11-15 had 78% more strokes, and people with a score of 16-30 had twice as many strokes. The increased stroke rates seen in patients with depression scores of six or higher were significantly different from the rate for people with no depression.

An analysis of death rates showed a similar pattern. People with scores of 6-10 had a 27% higher death rate; those with scores of 11-15 had a 73% higher mortality; and those with scores of 16 or more had 86% more deaths.

Several mechanisms may explain how depression affects stroke rates and mortality, Dr. Ariyo said. Depressed people are less physically active and engage in more unsafe behaviors, such as smoking. Also, depressed people have increased levels of circulating platelets, fibrinogen, and other factors that raise thrombogenicity. ■

Depression Scores and Stroke Risk in the Elderly

Depression Score	Relative Risk Of Stroke	Relative Risk Of Death
≥16	2.02	1.86
11-15	1.78	1.73
6-10	1.57	1.27
1-5	1.19	1.10
0	1.00	1.00

Note: Depression scores are measured in 4,483 patients aged 65 or older using a modified Center for Epidemiologic Studies depression scale. Relative risks are from multivariate models that adjusted for several variables.
Source: Dr. Ariyo

Duloxetine Beats Placebo at Easing Arthritis Pain, Improving Cognition

BY JANE SALODOF MACNEIL
Southwest Bureau

SANTA ANA PUEBLO, N.M. — Elderly people with depression and arthritis experienced significant pain relief with duloxetine in a placebo-controlled trial reported at the annual meeting of the Academy of Psychosomatic Medicine.

Conducted by investigators from Eli Lilly & Co., the research findings also documented significant improvement in cognitive functions, primarily verbal learning and memory, for depressed patients treated with duloxetine (Cymbalta) in the 8-week, multicenter study.

"I think (these findings are) very encouraging," investigator Dr. Michael J. Robinson, a clinical research physician at Lilly's medical division in Indianapolis, said in an interview. "Duloxetine may be advantageous for those specific cognitive symptoms."

The results suggest duloxetine can alleviate arthritis pain, a common comorbidity in depressed elderly patients. An inhibitor of serotonin and norepinephrine reuptake, duloxetine is known to have analgesic properties and is approved for treatment of peripheral neuropathic pain in patients with diabetes.

Cognition was a primary outcome in the trial, which randomized 207 depressed elderly patients to 60 mg daily of duloxetine and 104 to placebo. The two cohorts were similar, with an average age of 73 years, slightly more women than men, and more than three-fourths the population being white. All patients were at least 65 years old and had previous episodes of depression.

Similar proportions of patients withdrew because of adverse events. The most common in the duloxetine group were dry mouth, nausea, and constipation.

Duloxetine produced faster and more significant reductions than placebo on the Geriatric Depression Scale (GDS) and the Hamilton Rating Scale for Depression (HAMD 17). On average, the GDS fell 4.07 in patients on duloxetine vs. 1.34 in the placebo cohort. HAMD 17 scores declined 6.49 with duloxetine and 3.72 with placebo.

The duloxetine cohort demonstrated significantly greater improvement in a composite score based on four cognitive tests: a mean change of +1.95 vs. +0.76 for the placebo group.

At baseline, the mean composite cognitive scores were 22.70 for the duloxetine group and 23.17 for the placebo group. Most of the improvement could be due to changes in scores on verbal learning and recall tests.

Visual analog scale scores for all 311 patients in the trial demonstrated greater improvement in back pain and "time in pain while awake" for the duloxetine cohort. In a subgroup analysis limited to patients with comorbid arthritis, 117 patients on duloxetine had significantly greater improvement in four of six pain measures, compared with 55 placebo patient scores.

At the outset, all patients with arthritis had significantly higher baseline scores on five of six pain categories assessed with visual analog scales. Overall severity was 38.3 for patients with arthritis vs. 22.5 in patients who did not have arthritis.

Arthritis patients in the duloxetine cohort had greater improvements in overall pain, back pain, time in pain while awake, and interference with daily activities. Arthritis patients in the placebo group had more headache and shoulder pain; the difference was not significant.

The mean change in overall pain scores was –6.70 for arthritis patients on duloxetine vs. –1.89 for arthritis patients on placebo. The most dramatic effect was for back pain, which fell by a mean of more than 20% with duloxetine while increasing more than 10% with placebo.

"We don't know if this is their pain due to arthritis or their pain due to depression," Dr. Robinson said. "This is just looking at general pain outcomes."

Baseline scores for depression and improvements in mood were similar for arthritis patients in the two arms of the trial.

In another poster at the meeting, analysis of pooled data from seven randomized, multicenter, double-blind trials of duloxetine showed symptom improvement to be similar for white, Hispanic, and African American patients. Dr. John M. Plewes of Eli Lilly was the principal investigator. ■

Acetaminophen Improves Social Interaction in Dementia Patients

BY MARY ANN MOON
Contributing Writer

Regular administration of acetaminophen raises levels of general activity, social interaction, engagement with media, and worklike activity in elderly patients with moderate to severe dementia, reported John T. Chibnall, Ph.D., of St. Louis University School of Medicine, and his associates.

Regular dosing with the analgesic presumably addresses untreated pain in these patients, who often cannot report pain and who have a high prevalence of comorbidities, which can generate significant pain, the researchers said.

Their study findings imply that untreated pain inhibits dementia patients' active engagement with the environment and promotes their withdrawal, Dr. Chibnall, a professor of psychiatry at the university, and his associates added (J. Am. Geriatr. Soc. 2005;53:1921-9).

Behavioral changes in 25 elderly (mean age 85.9 years) nursing home residents with moderate to severe dementia during an 8-week study were evaluated. The subjects had degenerative dementia, Alzheimer's disease, or multi-infarct dementia and had resided in nursing homes for a mean of 35 months. All had moderate to severe cognitive decline and impairment in daily living activities.

The subjects were given either two 500-mg tablets of acetaminophen or two placebo tablets at mealtimes every day for 4 weeks, then switched to the other treatment for 4 weeks, following a 1-week washout period between the two phases. Their behavior was evaluated under both conditions using the Dementia Care Mapping (DCM) tool, in which trained "mappers" observed patients for 5 hours between 9 a.m. and 2 p.m., when subjects were likely to be most active. At 5-minute intervals, the observers quantified a wide range of behaviors across 24 domains such as direct or passive social involvement, creative activities, exercise, listening to music, sleeping, and eating.

They also were evaluated using the Cohen-Mansfield Agitation Inventory (CMAI), a 29-item scale in which personnel assessed how often the patients displayed a variety of agitated behaviors during the preceding 2 weeks.

With acetaminophen, subjects clearly showed higher levels of general activity, spent more time in direct social interactions and in engagement with media, and participated more in worklike activity. They also spent significantly less time alone in their rooms.

However, subjects also spent more time in passive social involvement, and slightly more time experiencing unattended distress.

Agitation did not decrease, and the use of psychotropic medications did not decrease, while patients were taking acetaminophen. However, the levels of agitation and the frequency of agitated behaviors were quite low in this study, which may have confounded the results. Similarly, the use of psychotropic drugs was quite low overall, leaving little room for the intervention to show an effect, the researchers noted. ■