

# Rivastigmine Good Choice For Parkinson's Dementia

BY MICHELE G. SULLIVAN  
Mid-Atlantic Bureau

MADRID — Rivastigmine should be the first option for treating dementia and associated behavioral symptoms in Parkinson's disease, with the atypical antipsychotics reserved for unresponsive patients, Dr. Murat Emre said at the 10th International Conference for Alzheimer's Disease and Related Disorders.

"There is evidence from our studies and from other, smaller studies that behavioral symptoms can improve with cholinergic treatment," said Dr. Emre, a professor of neurology at the University of Istanbul (Turkey).

"If the symptoms are not massive, acute, or destructive, and are combined with dementia, the wise thing is to first try a cholinesterase inhibitor, because the atypical antipsychotics are associated with an increased risk of cerebrovascular or cardiovascular events."

Up to 78% of Parkinson's patients eventually will develop dementia, Dr. Emre said. The prototypic syndrome consists of impaired or fluctuating attention and lessened visuospatial and executive function. There may be moderate memory impairment, although language is usually preserved. Depression, apathy, delusions, and hallucinations also can occur.

Clozapine and quetiapine are often prescribed for these symptoms in Parkinson's patients, Dr. Emre said. However, these drugs, like all atypical antipsychotics, carry a black box warning of increased mortality in elderly patients with dementia. The Food and Drug Administration, which reviewed 17 studies before issuing the warning, said most of the excess

deaths were cardiovascular or infectious.

Because Parkinson's, like Alzheimer's, is a disease of the cholinergic system, cholinesterase inhibitors are a sound alternative for Parkinson's dementia, Dr. Emre said. Many small studies—all with fewer than 30 patients—have investigated the use of anticholinergics in Parkinson's dementia, concluding that the drugs can improve cognition without further impairing motor function. Only one large, placebo-controlled, randomized trial has addressed the issue, however.

That 2004 study by Dr. Emre and colleagues randomized 541 patients to either rivastigmine (titrated from 3 mg to 12 mg over 16 weeks) or placebo for 24 weeks. The trial found significant improvements in cognition, activities of daily living, and clinical impression among the active group, compared with the placebo group (N. Engl. J. Med. 2004;351:2509-18).

There were significantly more adverse events in the group on active treatment than in the placebo group, most of which were mild to moderate gastrointestinal upset. However, 10% of patients on active treatment did experience new or worsening tremor.

A 12-month follow-up crossover trial assessed the long-term effects of the drug. Published this year, the study concluded that rivastigmine maintained efficacy over time in the original group on active treatment, and that placebo patients switched to the drug showed improvements similar to those seen in the trial's initial group on active treatment (Mov. Disord. 2006;21:456-61).

However, the lag time for the original placebo patients did affect their improvements. ■

# High Copper and Fat Intake Accelerates Cognitive Decline

BY MARY ANN MOON  
Contributing Writer

High dietary copper intake markedly accelerated the rate of cognitive decline in people whose diet was also high in saturated and trans fats, reported Dr. Martha Clare Morris of Rush University Medical Center, Chicago, and her associates.

In their analysis of data on 3,718 community residents who were enrolled in the Chicago Health and Aging Project (CHAP), the increase in the rate of cognitive decline "for the high-fat consumers whose total copper intake was in the top 20% (more than 1.6 mg/day) was equivalent to 19 more years of age." This is "an extraordinarily large estimate of effect," the researchers said.

Previous studies using data from the CHAP study population had shown that subjects who consumed high levels of saturated or trans fats had two to three times the risk of incident Alzheimer's disease and more rapid cognitive decline than people whose diets were lower in those fats. After noting the results of animal and other human studies that suggested dietary copper may induce the accumulation of amyloid-beta in the brain and cause memory deficits, Dr. Morris and her associates looked at the data on copper intake in the CHAP population.

The subjects were 65 years and older at entry into the study, and were as-

sessed using four different measures of cognitive function at 3- and 6-year follow-up. Among the 604 subjects (16% of the entire cohort) who consumed a diet high in saturated and trans fats, there was a 143% increase in the rate of cognitive decline for those in the highest quintile of copper intake (median 2.75 mg/day), compared with those in the lowest quintile (median 0.88 mg/day).

**Among those who consumed a high-fat diet, a 143% increase in the rate of cognitive decline was seen for those in the highest quintile of copper intake.**

In contrast, there was no association between copper intake and cognitive decline in subjects who had lower consumption of saturated and trans fats, the investigators said (Arch. Neurol. 2006;63:1085-8).

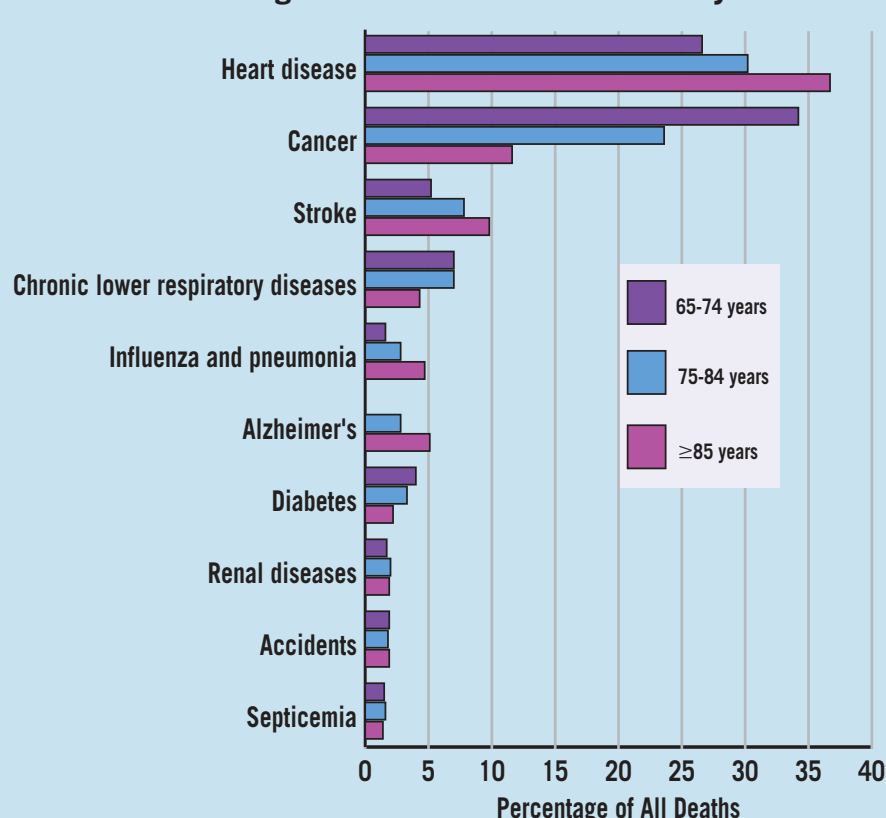
Copper, zinc, and iron are essential for normal brain function, but the "dyshomeostasis of these metals is thought to play a central role in the formation and neurotoxicity of amyloid-beta and neurofibrillary tangles," they noted.

In this study, the link with accelerated cognitive decline was specific to copper. Zinc and iron levels showed no interactions with dietary fats.

In a further analysis of data on the subset of 602 subjects who took vitamin supplements containing copper, high copper intake again was associated with faster cognitive decline, but only in those whose diets were high in saturated and trans fats. These results "must be viewed with caution" because the study design was observational rather than prospective, and "the supporting evidence on this topic is limited," Dr. Morris and her associates said. ■

## DATA WATCH

### Leading Causes of Death in the Elderly



Source: 2002 data, Centers for Disease Control and Prevention

## New Dementia Risk Score Targets Factors Modifiable in Midlife

Age, education and cholesterol levels, high blood pressure, and obesity at midlife are significantly associated with the later development of dementia, according to findings from a 20-year follow-up study.

A new, simple dementia-risk prediction tool may allow for the earlier detection of the disease based on these midlife factors, Miia Kivipelto of the Karolinska Institute in Stockholm and colleagues reported in *Lancet Neurology* (Aug. 3, 2006; Epub ahead of print; doi: 10.1016/S1474-4422(06)70537-3). The detection technique highlights the role of vascular factors in the development of dementia "and could help to identify individuals who might benefit from intensive lifestyle consultations and pharmacological interventions," the investigators reported.

Data were derived from the population-based Cardiovascular Risk Factors, Aging, and Dementia (CAIDE) study, in which 1,409 patients were studied in midlife and reexamined 20 years later. Of these patients, 4% were diagnosed with dementia.

Based on the prediction model, future dementia was associated with an age of 47 years or older, less than 10 years of education, systolic blood pressure greater than 140 mm Hg, high cholesterol levels greater than 6.5 mmol/L, and obesity (body mass index over 30 kg/m<sup>2</sup>).

Gender, smoking, and physical activity were not significantly associated with dementia. In a second model that factored in apolipoprotein ε4 status (carriers vs. noncarriers), age and education became more predictive of risk and cholesterol less so, the investigators reported.

Potential risk factors not examined in this study include a family history of dementia, serum triglyceride levels, HDL and LDL levels, waist-to-hip ratio, and diabetes (insulin resistance). "There is much evidence that diabetes is associated with an increased risk of dementia, and thus its inclusion in future risk scores is important," the investigators noted. Further research is needed to validate their dementia risk score in other populations.

—Bruce K. Dixon