Vitamin E May Increase Survival in Alzheimer's

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CHICAGO — Vitamin E supplementation at doses of 2,000 IU/day appeared to be associated with improved survival in a retrospective case analysis of patients who had Alzheimer's disease.

The results, presented at the annual meeting of the American Academy of Neurology, were seen in a retrospective case analysis of 847 patients seen between 1990 and 2004 at the Alzheimer's Disease and Memory Disorders Center at Baylor College of Medicine, Houston.

The results do not indicate that high-dose vitamin E was associated with an increased risk of death in Alzheimer's patients, as has been seen in large studies of vitamin E for prevention of cardiovascular events.

All of the patients studied had probable or mixed Alzheimer's disease. About two-thirds of the subjects took 2,000 IU of vitamin E, with or without a cholinesterase inhibitor; less than 10% took vitamin E alone; and approximately 15% did not take any antidementia drug.

For those taking vitamin E, with or without a cholinesterase inhibitor, there was a 26% reduction in risk of dying (statistically significant at $P = .009$) at any time interval of the analysis, compared with those not taking vitamin E.

The prescribing of high-dose vitamin E in Alzheimer's disease gained popularity after a 1997 study indicated that vitamin E at doses of 2,000 IU/day appeared to slow the disease's progression. That approach fell into disfavor, however, when a meta-analysis of 19 randomized controlled trials involving more than 135,000 participants found that vitamin E supplementation for at least 1 year at doses greater than 400 IU/day was associated with increased all-cause mortality (Ann. Intern. Med. 2005;142:37-46).

Valory Pavlik, Ph.D., one of the investi-

gators in the Baylor study, said that many of the studies in the meta-analysis examined vitamin E for prevention of cardiovascular events. Vitamin E was not being used for treatment as it was in the Baylor patients with Alzheimer's disease.

To determine whether the risk of death was greater for Alzheimer's patients, Dr. Pavlik and her associates undertook their analysis based on patients who were taking vitamin E during the time before high-dose vitamin E fell into disfavor.

In the Baylor study, patients averaged 74 years old and ranged in age from 65 to 83 years at their first visit to the Baylor center. Two-thirds of the patients were women; they were followed up for a median time of 5 years, with a range of 1-15 years.

Neuropsychological scores, clinical assessments, and medication histories were collected using standardized protocols. Vital status was ascertained through contact with family members or death index searches. Time-dependent Cox proportional hazards modeling was used to calculate all-cause mortality hazard ratios for vitamin E alone, or in combination with a cholinesterase inhibitor, adjusting for demographics, duration of symptoms at diagnosis, and baseline disease severity.

The adjusted hazard ratio associated with vitamin E (with or without a cholinesterase inhibitor) was 0.74 (95% CI = 0.59-0.92, $P = .008$), and for cholinesterase inhibitor use (with or without vitamin E), was 0.91 (95% CI = 0.72-1.14, $P = .393$).

The hazard ratios corresponding to mutually exclusive treatment categories (reference group = no drug treatment) were 0.79 ($P = .069$) for vitamin E with another drug, 1.1 ($P = .515$) for cholinesterase inhibitor use only, and 0.82 ($P = .341$) for vitamin E only.

Dr. Pavlik emphasized that this was an observational study and not a randomized controlled trial.

Alternatively, this group of patients was followed for longer times than were many of the patients in clinical trials. Further, survival rates were comparable or better among patients on cholinesterase inhibitors who also took vitamin E supplements at doses of 2,000 IU/day than they were among patients on cholinesterase inhibitors alone.

During a press conference, Dr. Pavlik said the lowest effective dose for vitamin E in Alzheimer's disease has not been determined. A dose-response study conducted at Vanderbilt University, Nashville, Tenn., has indicated that the antioxidant action of vitamin E begins to occur at doses exceeding 1,000 IU/day. ■