Ginkgo biloba and vitamin E for Alzheimer’s disease
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ABSTRACT
Alzheimer's disease affects an estimated 35 million people worldwide, with over 5 million affected in the United States. Few medications are currently approved by the Food and Drug Administration (FDA) for the treatment of Alzheimer’s disease; subsequently, patients and caregivers often look for additional treatment options. This article reviews studies evaluating the use of Ginkgo biloba and vitamin E for the treatment of Alzheimer’s disease.

KEYWORDS
Ginkgo biloba, vitamin E, Alzheimer’s disease

CASE
Mary presents to your community pharmacy to fill prescriptions for her 73-year-old mother. She has been filling prescriptions for her mother at your pharmacy for several years. Three years ago, her mother was diagnosed with Alzheimer’s disease (AD) and was prescribed donepezil (Aricept®) 5mg once daily. After six weeks of therapy, the dose was titrated to 10mg once daily. At her mother’s most recent medical appointment, the primary care physician mentioned the possibility of initiating a second medication, memantine (Namenda®), for the treatment of Alzheimer’s disease. Mary wanted to ask the primary care physician questions about alternative treatments, including Ginkgo biloba and vitamin E, after watching a syndicated “doctor show” on daytime television. Unfortunately, Mary forgot to ask at the appointment. She presents today requesting a refill on her mother’s donepezil prescription as well as information on Ginkgo biloba and vitamin E.

DISCUSSION
An estimated 35 million people worldwide have Alzheimer’s disease, with over 5 million people affected in the United States alone. The prevalence of Alzheimer’s disease is expected to exceed 80 million worldwide and 10 million in the United States by the middle of the century. Despite efforts in drug development, few medications are currently approved by the U.S. Food and Drug Administration for the treatment of dementia. These include memantine, donepezil, galantamine (Razadyne®), rivastigmine (Exelon®), and tacrine (Cognex®). Consequently, patients and/or caregivers often search for other treatment options. An estimated 38% of Americans use some form of complementary and alternative medicine (CAM). Examples of CAM therapies for the treatment of AD include antioxidants, omega-3 fatty acids, huperzine A, and Ginkgo biloba. Ginkgo biloba and vitamin E have amassed a considerable amount of data.

Ginkgo biloba
Ginkgo biloba is the seventh most commonly used natural product among Americans. Ginkgo leaf extracts contain flavonoids, terpenoids, and terpene lactones which are thought to exert beneficial effects on blood flow and neurotransmitter systems as well as possess antioxidant and anti-amyloid aggregation properties. Observational studies have demonstrated variable results. Le Bars and colleagues conducted a 52-week, randomized, double-blind trial comparing Ginkgo biloba (120 mg/day) versus placebo in patients with AD or multi-infarct dementia. Ginkgo biloba appeared safe and improved cognitive performance on the Alzheimer’s Disease Assessment Scale-Cognitive subscale (ADAS-Cog). Similarly, Yancheva and colleagues conducted a 22-week, randomized, double-blind trial comparing the effects of Ginkgo biloba (240mg/day), donepezil, or combination therapy in AD patients. The authors concluded that Ginkgo biloba and donepezil were similar with regard to the outcomes measured; however, they acknowledged a small sample size along with other limitations hindered the generalizability of their results.

On the contrary, McCarney and colleagues conducted a randomized, double-blind trial comparing Ginkgo biloba (120 mg/day) versus placebo. Upon completion of the trial, Ginkgo biloba was not shown to have a significant effect on the ADAS-Cog and provided no benefit in mild-to-moderate dementia over the course of six months. Similarly, van Dongen and colleagues also found no difference between Ginkgo biloba (160 or 240mg/day) and placebo on any outcome measures during a 24-week,
randomized, double-blind trials. Two additional randomized, placebo-controlled trials examined whether Ginkgo biloba reduced the incidence of cognitive decline or dementia in normal elderly or those with mild cognitive impairment. In each study, Ginkgo biloba did not prevent or delay cognitive decline or dementia. In addition to negative results, each study uncovered potentially serious adverse effects. In the first study, significantly more ischemic strokes and transient ischemic attacks occurred in the Ginkgo biloba group. In the second study, twice as many hemorrhagic strokes occurred in the Ginkgo biloba group; however, the overall number was small and not statistically significant.

Vitamin E

Vitamin E is a lipid-soluble vitamin that interacts with cell membranes, acts as a free radical scavenger, and interferes with the chain reaction that damages cells. Results are mixed with regard to its use in dementia. Sano and colleagues conducted a randomized, double-blind trial of 341 patients and compared vitamin E (2000 IU/day), selegiline, the combination, and placebo. Unadjusted comparisons were not found to be statistically significant; however, when baseline scores on the Mini-Mental State Examination were included as a covariate, both selegiline and vitamin E were found to significantly decrease the progression of dementia.

In contrast, a larger and more recent trial conducted by Petersen and colleagues studied the effects of vitamin E (2000 IU/day), donepezil, or placebo in patients with mild cognitive impairment. The primary outcome at the end of three years was clinically possible or probable AD. No benefit was observed with vitamin E in preventing the development of dementia. In a small trial by Lloret and colleagues, the authors examined whether vitamin E prevented oxidative stress as well as worsening cognition in AD. In participants where vitamin E was found to lower measured markers of oxidative stress, cognitive test scores were maintained. In participants where vitamin E was not shown to alter oxidative stress, cognitive test scores worsened in several patients. Lastly, a meta-analysis of over 130,000 participants with chronic diseases concluded that high dose vitamin E supplementation, defined as greater than or equal to 400 IU/day for at least one year, increased all-cause mortality. However, many of the trials analyzed included patients with, or at high risk for, cardiovascular disease.

CONCLUSION

A number of CAM therapies have been utilized for the treatment of AD, including Ginkgo biloba and vitamin E. Neither Ginkgo biloba nor vitamin E has demonstrated consistent results with regard to prevention or treatment of AD. Troubling signals of serious adverse effects require additional research, as well. Until further research is available, Ginkgo biloba and vitamin E cannot be recommended for the prevention or treatment of AD.

REFERENCES