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File: ■ Ginkgo (*Ginkgo biloba*)
■ Vertigo
■ Efficacy and Safety

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RE: Ginkgo Comparable to Betahistine in Treating Vertigo and Has a Superior Safety Profile

Sokolova L, Hoerr R, Mishchenko T. Treatment of vertigo: A randomized, double-blind trial comparing efficacy and safety of *Ginkgo biloba* extract EGb 761 and betahistine. *Int J Otolaryngol*. 2014;2014:682439. doi: 10.1155/2014/682439.

Vertigo (dizziness) associated with cerebrovascular disorders is most commonly treated with drugs that improve cerebral blood flow. According to an international survey, betahistine is the most frequently prescribed medication, followed by piracetam, and then ginkgo (*Ginkgo biloba*). Research suggests that impaired neuronal plasticity prevents compensation for vestibular disturbances, and EGb 761® (manufactured by Dr. Willmar Schwabe GmbH & Co. KG; Karlsruhe, Germany) has been shown to enhance neuronal plasticity. The purpose of this randomized, controlled, double-blind, multi-center study was to compare the efficacy and safety of ginkgo to that of betahistine in the treatment of patients with vertigo.

Eligible patients (n = 160, ≥ 45 years old) diagnosed according to the International Classification of Diseases, 10th edition (ICD-10) with peripheral vertigo or vertiginous syndrome not otherwise specified were enrolled in this study conducted at 10 outpatient hospital clinics in the Ukraine. Included patients had symptoms of vertigo for ≥ 3 months, scored ≥ 3 on a 1-to-10 numeric analogue scale (NAS) of vertigo severity at screening, and could respond to interview questions and complete questionnaires in Russian or Ukrainian. Included females had a negative pregnancy test and adequate birth control. Excluded patients had specific vertiginous syndromes (e.g., Ménière's disease, Lermoyez syndrome, and benign paroxysmal positional vertigo), vertigo due to specified somatic diseases (except cerebrovascular disease), other severe disorders, contraindications for ginkgo or betahistine, gastrointestinal disorders with uncertain absorption of the active agents, or needed drugs that might interfere with efficacy assessments.

Patients were randomly assigned to receive either 240 mg/day ginkgo extract EGb 761 (60% ginkgo leaf acetone extract standardized to contain 22-27% ginkgo flavonoids, 5-7% terpene lactones, 2.6-3.2% bilobalide, and < 5 ppm ginkgolic acids) or 32 mg/day

betahistine dihydrochloride for 12 weeks. Efficacy and safety were evaluated at 4, 8, and 12 weeks. Efficacy was evaluated using: (1) the vertigo NAS; (2) the short form of the Vertigo Symptom Scale, which assesses the frequency and severity of vertigo within the last month; (3) the Sheehan Disability Scale, which evaluates the extent psychological symptoms disrupt a patient's work, social life, and family life; and (4) the Clinical Global Impressions (CGI) Scale. Safety was monitored via measurement of vital signs, physical examination, 12-lead electrocardiogram (ECG), and laboratory tests. There were no significant differences between groups at baseline.

Both groups improved compared to baseline on all measures. There were no significant differences between groups on any measurement, although "numerically, the improvements of patients receiving EGb 761 were slightly more pronounced on all scales." On the CGI, physicians rated 79% of the patients receiving EGb 761 and 70% of the patients receiving betahistine as "much improved" or "very much improved."

Blinded review could not rule out a causal relationship for 6 adverse events (AEs) in 5 patients in the EGb 761 group and 18 AEs in 16 patients in the betahistine group. In the EGb 761 group, both the total number of AEs and the number of patients reporting AEs were lower compared to the betahistine group.

The authors conclude that EGb 761 is at least as effective as betahistine, the world's most frequently prescribed drug in the treatment of vertigo. Although not statistically significant, numerically the EGb 761 group had more pronounced improvements in all outcome measures. And in terms of safety and tolerability, EGb 761 was superior to betahistine.

Despite the fact that there were 80 patients per group, the study did not have sufficient statistical power to prove equivalence between EGb 761 and betahistine. The study had several other limitations: (1) there was no negative control (placebo group) to provide an objective measure of the true effect size of both treatments because it would be unethical to deny treatment to the placebo group; (2) although assessments were conducted at 4 and 8 weeks, the interim data were not reported so the elapsed time till onset of measurable improvements cannot be compared; and (3) there was no follow-up to determine how long the therapeutic benefit lasted after treatment discontinuation. Given comparable efficacy, the latter 2 factors are important considerations when choosing a treatment. The patients were not queried as to whether they would choose to continue the treatment after the trial ended.

Nonetheless, the data are encouraging because EGb 761 compared favorably to the most frequently used drug for vertigo, it had fewer AEs in fewer patients, and might be less expensive than betahistine [Note: Pharmacoeconomics were not discussed in this report]. A larger, sufficiently powered clinical trial is needed to prove equivalence and confirm ginkgo has a superior safety profile to betahistine.

—Heather S. Oliff, PhD

Referenced article can be found at http://www.hindawi.com/journals/ijoto/2014/682439/.