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File: ■ Ginkgo (*Ginkgo biloba*, Ginkgoaceae)
■ Attention-deficit/Hyperactivity Disorder (ADHD)
■ Methylphenidate

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RE: Adjunct Ginkgo Improves Inattention Symptoms in Children with ADHD

Shakibaei F, Radmanesh M, Salari E, Mahaki B. *Ginkgo biloba* in the treatment of attention-deficit/hyperactivity disorder in children and adolescents. A randomized, placebo-controlled, trial. *Complement Ther Clin Pract*. May 2015;21(2):61-67.

Attention-deficit/hyperactivity disorder (ADHD) is characterized by persistent inattention, hyperactivity, and impulsivity. It is one of the most common neuropsychiatric disorders in children. ADHD is treated pharmacologically and behaviorally. Approximately 30% of patients with ADHD do not successfully respond to pharmacological drug treatment, so many seek herbal treatment. Well-designed, randomized, controlled clinical trials evaluating herbal treatments for ADHD are lacking. Several open-label studies indicate that ginkgo (*Ginkgo biloba*, Ginkgoaceae) leaf extract is useful for treating ADHD in children. However, a randomized, controlled study reported that ginkgo was not effective compared with methylphenidate (Ritalin®; Novartis; Basel, Switzerland).[1] The purpose of this randomized, double-blinded, placebo-controlled study was to evaluate the efficacy of ginkgo as an adjunct therapy to methylphenidate in children and adolescents with ADHD.

Children and adolescents (n=66, aged 6-12 years; mean age, 8 years) diagnosed with ADHD according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) and referred to the Department of Child and Adolescent Psychiatry at the Noor University Hospital in Isfahan city, Iran participated in the study. Included patients had a Children's Global Assessment Scale (CGAS) score of < 80 indicating decreased general function. Excluded patients had mental retardation (IQ ≤ 70), type I bipolar disorder, psychosis, pervasive developmental disorders, organic brain disease, seizure, or cardiovascular disease. To establish baseline, there was a 2-week run-in where patients were psychiatric drug-free. Then patients were randomly assigned to receive either methylphenidate plus ginkgo (Ginko TD™; TolidDaru Co.; Tehran, Iran) or methylphenidate plus placebo for 6 weeks. The placebo contained starch and lactose, and was the same shape and color as the ginkgo preparation. The dose of methylphenidate was 20 mg/day for patients with body weight of < 30 kg, and 30 mg/day for those > 30 kg. The methylphenidate dosage was increased 10 mg/week up to the assigned total dose. The ginkgo dose was 80 mg/day for those with body weight of < 30

kg and 120 mg/day for those > 30 kg. The ginkgo dosage was increased by 40 mg/week up to the assigned total dose.

The primary outcome was the amount of change in ADHD Rating Scale-IV (ADHD-RS-IV) scores after treatment. ADHD-RS-IV is used to assess 18 symptoms of ADHD and includes 2 subscales to assess inattention and hyperactivity/impulsivity; the parent (completed in interview with clinicians) and teacher form of the instrument was used. Treatment response was considered a ≥ 27% improvement from baseline in the ADHD-RS-IV total score. The secondary outcome was a change in global functioning as assessed by parents in interview with clinicians using the CGAS. The CGAS measures general (psychosocial) functioning of children. ADHD-RS-IV and CGAS were measured at baseline and after 2 and 6 weeks of treatment.

Baseline characteristics were similar between groups. For the ADHD-RS-IV parent rating after 6 weeks of treatment, the ginkgo group had a significantly greater improvement in inattention (P=0.001), total score (P=0.001), and clinical response rate (P=0.002) compared with the placebo group. However, according to the ADHD-RS-IV teacher rating, the only significant improvement observed was inattention (P=0.004). Both the parent and teacher ratings showed that ginkgo did not improve hyperactivity-impulsivity. There was no significant difference between groups on the CGAS. Side effects were mild, and there were no significant differences between groups in side effects.

The authors conclude that adding ginkgo to standard methylphenidate treatment is a safe and effective adjunct therapy. "Although the additional effect of the herb on ADHD symptoms was actually minimal and limited to the inattention symptoms, it resulted in a significant increase in overall clinical treatment response." The mechanism of action is not clear. Acknowledged limitations of the study were the lack of a pure placebo arm (it would be unethical to deny treatment), the short study duration (it is not clear if the benefits would be maintained long-term), and the lack of patient follow-up after they stopped taking ginkgo (it would be valuable to see whether the benefit of ginkgo was lost when ginkgo treatment ended). "Further trials with larger sample size, various drug dosages, and longer treatment and follow-up duration are warranted."

—Heather S. Oliff, PhD

Reference

[1]Salehi B, Imani R, Mohammadi MR, et al. *Ginkgo biloba* for attention-deficit/hyperactivity disorder in children and adolescents: a double blind, randomized controlled trial. *Prog Neuropsychopharmacol Biol Psychiatry*. 2010;34(1):76-80.

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