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File: ■ Ashwagandha (*Withania somnifera*, Solanaceae)
■ Subclinical Hypothyroidism

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RE: Pilot Study Finds Ashwagandha Normalizes Thyroid Indices in Patients with Subclinical Hypothyroidism

Sharma AK, Basu I, Singh S. Efficacy and safety of ashwagandha root extract in subclinical hypothyroid patients: a double-blind, randomized placebo-controlled trial. *J Altern Complement Med*. August 22, 2017; [epub ahead of print]. doi: 10.1089/acm.2017.0183.

Subclinical hypothyroidism (SCH), also known as mild thyroid failure, affects up to 8% of the population and is characterized by elevated serum thyroid-stimulating hormone (TSH) and normal serum thyroxine (T4) levels. Left untreated, SCH may progress to overt hypothyroidism. In addition, SCH may worsen other conditions such as type 2 diabetes mellitus, cardiovascular disease, and neuromuscular disorders. For patients with SCH who have TSH levels > 10.0 µIU/L, there is a clear consensus that the synthetic hormone levothyroxine should be prescribed. However, the risk/benefit ratio for this treatment is equivocal for patients with SCH who have TSH levels between 4.5 and 10.0 µIU/L. The adaptogen ashwagandha (*Withania somnifera*, Solanaceae) root is used in traditional medicine to treat hormonal imbalances such as thyroid disorders. Ashwagandha has been found to reduce serum levels of T4 and triiodothyronine (T3) in animal models of hypothyroidism, and a clinical study of patients with bipolar disorder found that improved thyroid indices were a secondary benefit of ashwagandha therapy. The purpose of this prospective, randomized, double-blind, placebo-controlled pilot study was to evaluate the efficacy and safety of ashwagandha in the treatment of SCH.

Patients (n = 50, aged 18-50 years) with elevated TSH levels (4.5-10 µIU/L) and normal T3 and T4 levels participated in this study conducted from May to September 2016 at Sudbhawana Hospital; Varanasi, India. Included patients had no significant medical history. Excluded patients had a history of smoking within the past year; hypersensitivity to ashwagandha and related herbal products; were under treatment with any thyroid medications, nutritional/energy supplements, hypotensives, beta-blockers, inhaled beta agonists, hormonal contraceptives, or corticosteroids within the prior 3 months or psychotropics within the prior 8 weeks; were diagnosed with heart disease, diabetes, stroke, depression, or other neurologic/psychiatric disorders; had psychiatric hospitalization within the past year; or had a body mass index < 30 kg/m^2.

The ashwagandha treatment (KSM-66®; Ixoreal Biomed; Los Angeles, California) consisted of a 100% aqueous root extract containing 5% withanolides. Patients were randomly assigned to receive capsules containing placebo (not described) or 600 mg of ashwagandha daily for 8 weeks. The primary efficacy measures were serum TSH, T3, and T4 levels. Safety assessments included the monitoring of vitals (systolic and diastolic blood pressure, pulse rate, respiratory rate, and body temperature) and hematologic (hemoglobin, hematocrit, platelet count, red blood cell count, and white blood cell count) and physical (cardiovascular, respiratory, musculoskeletal, genitourinary, and nervous system) parameters. Assessments were made at baseline, 4 weeks, and 8 weeks.

Both groups were similar at baseline. Four patients (2 in each group) withdrew consent. The following results of the intent-to-treat (ITT) analysis were calculated using the last observation carried forward (LOCF) method.

T3 levels were significantly increased in the ashwagandha group at 4 weeks ($P = 0.002$) and 8 weeks ($P = 0.0011$) compared with the placebo group. Compared with baseline, serum T3 increased by 18.6% at 4 weeks ($P = 0.0121$) and 41.5% at 8 weeks ($P < 0.0001$) in the ashwagandha group. In contrast, in the placebo group, T3 levels significantly decreased by 15.9% at 4 weeks ($P = 0.0067$) and nonsignificantly decreased by 0.03% at 8 weeks ($P = 0.7387$).

T4 levels were significantly increased in the ashwagandha group at 4 weeks ($P = 0.0110$) and 8 weeks ($P = 0.0394$) compared with the placebo group. Compared with baseline, serum T4 significantly increased by 9.3% at 4 weeks ($P = 0.0027$) and 19.6% at 8 weeks ($P < 0.0001$) in the ashwagandha group. In contrast, in the placebo group, T4 levels did not significantly change over time ($P = 0.466$).

TSH levels in the ashwagandha group were significantly decreased compared with the placebo group at 4 weeks ($P = 0.0006$) and 8 weeks ($P = 0.0002$).

There were no significant changes in any of the physical, hematologic, or vital parameters that were assessed. Only 1 ashwagandha-treated patient (4%) and 3 placebo-treated patients (12%) reported adverse events (fever, asthenia, cough, and headache), which were mild and temporary.

The authors conclude that 8 weeks of treatment with 600 mg/day of ashwagandha root extract containing 5% withanolides safely normalized thyroid indices in patients with SCH. It is hypothesized that ashwagandha may exert these effects by modulating the activity of the hypothalamic-pituitary-thyroid axis. As this was a pilot study of a relatively small population, the authors point out that a larger trial with a longer duration is required to confirm efficacy and to further assess safety, as there has been 1 case report of thyrotoxicosis attributed to ashwagandha consumption. Another limitation is that blood samples were not screened for the presence of the anti-thyroid antibodies which are indicative of the chronic autoimmune disorder Hashimoto's thyroiditis (HT). Epidemiological evidence suggests that the progression to overt hypothyroidism is catalyzed in patients with HT compared to non-HT patients and these 2 sub-populations (HT and non-HT) may respond differently to ashwagandha treatment.

This pilot study is registered in the Clinical Trial Registry of India and the report conforms with the CONSORT (Consolidated Standards of Reporting Trials) guidelines. The

authors report no conflict of interest. They thank the manufacturer (Ixoreal Biomed) for supplying the study material.

—Heather S. Oliff, PhD

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