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File: ■ Ashwagandha (*Withania somnifera*, Solanaceae)
■ Osteoarthritis
■ Knee Joint Pain

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RE: Clinical Efficacy of Ashwagandha for Knee Joint Pain

Ramakanth GSH, Uday Kumar C, Kishan PV, Usharani P. A randomized, double blind placebo controlled study of efficacy and tolerability of *Withaina* [*sic*] *somnifera* extracts in knee joint pain. *J Ayurveda Integr Med*. July-September 2016;7(3):151-157.

Osteoarthritis (OA) is a common condition in the aging population. It is characterized by a decrease in joint cartilage which leads to stiffness, pain, and disability. Many patients use non-steroidal anti-inflammatory drugs and opioid drugs, but these can cause adverse side effects. Ashwagandha (*Withania somnifera*, Solanaceae) is used to treat arthritis in Ayurvedic medicine, and has been reported to alleviate pain in patients with OA. Extracts of the root have been shown to have anti-inflammatory and analgesic properties. This prospective, randomized, double-blind, placebo-controlled study tested the efficacy of a water extract of ashwagandha roots and leaves (Sensoril®; Natreon Inc.; New Brunswick, New Jersey) in patients with knee OA.

This study took place at the Department of Clinical Pharmacology and Therapeutics, Nizam's Institute of Medical Sciences, Hyderabad, India. Included patients were between 40 and 70 years old, had experienced knee pain for at least 6 months with a class I to III designation by the American Rheumatology Association (mild to moderate physical limitations), and had a baseline pain score of 40 mm using a visual analog scale (VAS). Patients were instructed to stop any pain medication 7-10 days before the study. The exclusion criteria were as follows: functional class IV designation (severe physical limitations); using an "alternative system of medicine"; psychiatric disorders; use of steroids within 12 weeks of the study; use of hyaluronic acid in the prior 9 months; needing joint replacement; recent knee trauma; uncontrolled high blood pressure or diabetes; problems with kidney or liver function; and pregnancy or lactation.

Included patients were randomly assigned to receive either Sensoril, administered in 125-mg or 250-mg capsules, or placebo capsules, also provided by Natreon Inc. The Sensoril capsules were standardized to contain ≥ 10% withanolide glycosides, ≥ 32% oligosaccharides, and ≤ 0.5% withaferin A. Patients took 2 capsules with water daily after meals for 12 weeks. Rescue pain medication was acetaminophen (650-mg tablets),

and compliance was gauged by pill count. Screening for adverse side effects also was conducted.

This study's primary outcomes were any change in pain or stiffness measured using the Modified Western Ontario and McMaster University Osteoarthritis Index (WOMAC) from baseline to endpoint. This system uses numerical assessments similar to a VAS, where lower scores indicate better physical condition. Secondary outcomes were any changes in the score after 4 and 8 weeks, changes in the Knee Swelling Index (KSI, determined by knee circumference), and VAS of pain, disability, and stiffness, after 4, 8, and 12 weeks of treatment or placebo. Also assessed were the use of rescue medication and the Physician Global Assessment scale, which gauged symptom relief.

In total, 60 patients (43 men and 17 women; average age, 57.78 ± 4.49 years) were randomly assigned equally into 3 groups. There were no dropouts in this study and no significant differences among groups at baseline in demographic parameters or WOMAC, KSI, or VAS scores. After 12 weeks of treatment, the WOMAC score significantly decreased in both treatment groups, indicating improvement (250 mg ashwagandha, $P<0.001$; 125 mg ashwagandha, $P<0.05$). Also, the percent decrease in WOMAC score from baseline to endpoint was significantly greater in those in the 250-mg group as compared with both the 125-mg group ($P<0.001$) and the placebo group ($P<0.001$). This also was significantly greater in those taking 125 mg of ashwagandha as compared with the placebo group ($P<0.01$).

The KSI score significantly decreased from baseline to endpoint in those taking 250 mg of ashwagandha ($P<0.001$), as well as in those taking 125 mg ($P<0.05$). The percent decrease was also significantly greater in those taking 250 mg as compared with both 125 mg ($P<0.001$) and placebo ($P<0.001$). The VAS scores for pain, stiffness, and disability were all significantly decreased in those taking 250 mg ($P<0.001$ for all) and 125 mg ($P<0.05$ for all). The changes in these scores were all significantly greater in those taking 250 mg as compared with those taking 125 mg ($P<0.001$) and placebo ($P<0.001$). The changes in scores were also significantly greater in those taking 125 mg as compared with placebo ($P<0.01$).

Acetaminophen use was an average of 10 tablets in the 250-mg group, 13 tablets in the 125-mg group, and 17 tablets in the placebo group. According to the Physician Global Assessment, 15 patients taking 250 mg thought the treatment was excellent, and 5 thought it was good. In those taking 125 mg, 17 thought it was good, and 3 thought it was fair; in those taking the placebo, 1 patient thought treatment was fair, and 19 thought it was poor. After 4 weeks of treatment, only those in the 250-mg group had significant reductions in WOMAC score, KSI, and VAS of pain, stiffness, and disability ($P<0.01$ for all). After 8 weeks, this was still observed in the 250-mg group, and those in 125-mg group had a significant reduction in VAS of stiffness ($P<0.05$). It is mentioned that 4 patients taking 250 mg of ashwagandha had nausea and 1 patient had gastritis; 2 patients taking 125 mg had nausea and headaches. No adverse side effects were reported in the placebo group.

This study suggests the use of ashwagandha in treating mild and moderate knee OA. The authors note that as withaferin A has been shown to modulate pain, this may explain the significant reduction of pain in those taking ashwagandha. The significant decrease in KSI scores also supports that ashwagandha may be working as an anti-

inflammatory agent. While further studies are needed to understand its therapeutic efficacy, this botanical may be an effective adjuvant treatment in those with OA.

—*Amy C. Keller, PhD*

Referenced article can be accessed at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5052364/.