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File: ■ Saw Palmetto (*Serenoa repens*)
■ Benign Prostatic Hyperplasia
■ Dosage

HC 111151-437

Date: November 30, 2011

RE: Symptoms of Benign Prostatic Hyperplasia Unaffected by High Doses of Saw Palmetto Ethanolic Extract

Barry MJ, Meleth S, Lee JY, et al. Effect of increasing doses of saw palmetto extract on lower urinary tract symptoms: a randomized trial. *JAMA*. 2011;306(12):1344-1351.

Benign prostatic hyperplasia (BPH)—enlargement of the prostate—causes lower urinary tract symptoms. Saw palmetto (*Serenoa repens*) fruit extract is a popular treatment. A 2002 Cochrane meta-analysis concluded that saw palmetto extract is efficacious for improving BPH-related lower urinary tract symptoms of nocturia and reduced urine flow.[1] However, a 2009 Cochrane meta-analysis including 9 new trials concluded that saw palmetto extract was not efficacious for BPH-related lower urinary tract symptoms.[2] The largest placebo-controlled trial (n = 220 men), known as the Saw Palmetto Treatment for Enlarged Prostates (STEP) study, concluded that 320 mg daily of a saw palmetto carbon dioxide extract was not significantly better than placebo.[3] The purpose of the current double-blind, multicenter, placebo-controlled, randomized study was to see if a dose greater than that used in the STEP study would be efficacious.

In an attempt to make the study more real-world, the enrollment criteria was broad. Participants were recruited at 10 sites in the United States and 1 site in Canada. Men were eligible if they were aged ≥ 45 years, had a peak uroflow rate of at least 4 mL/s, and an American Urological Association Symptom Index (AUASI) score of between 8 and 24 at 2 screening visits. Men were ineligible if they had prior invasive treatment for BPH; recent treatment with an α-blocker, 5α-reductase inhibitor, phytotherapy including saw palmetto extract, or other medications affecting lower urinary tract symptoms; creatinine level > 2.0 mg/dL; liver function test results > 3 times normal; coagulopathy or anticoagulation; recent unstable medical conditions; neurological conditions affecting urination; recent prostatitis or repeated urinary tract infections; prostate or bladder cancer or a prostate-specific antigen (PSA) level of more than 10 µg/L; recent or planned genitourinary instrumentation; severe incontinence; recent diuretic initiation or dose change; or medical conditions likely to prevent completion. Patients received placebo or a lipidic ethanolic extract of dried, ripe saw palmetto berries (Prosta-Urgenin Uno capsules; Rottapharm/Madaus; Cologne, Germany) of 320 mg/day, with a dose escalation to 640 mg/day at 24 weeks and another dose escalation to 960 mg/day at 48 weeks. The placebo group also received an escalation, but dummy capsules were used. The study was completed at 72 weeks. The primary outcome measure was the change in AUASI score from baseline to 72 weeks. Secondary outcome measures

included global assessments of improvement and satisfaction, the BPH Impact Index, quality of life as assessed with the International Prostate Symptom Score, nocturia item from the AUASI, peak uroflow, post-void residual volume, PSA level, indices of erectile and ejaculatory function, the International Continence Society male Incontinence Scale, the Jenkins Sleep Dysfunction Scale, and the National Institutes of Health Chronic Prostatitis Symptom Index. Assessments were made at baseline and 12, 24, 36, 48, 60, and 72 weeks.

A total of 357 patients (mean age = 61 years) were randomized, and 306 patients completed the entire study and were included in the analysis. The study was well-blinded, with a similar number of patients responding that they thought they were taking placebo/saw palmetto when they were actually taking the other treatment (P = 0.36).

The primary outcome measure (the AUASI score) showed no greater improvement with saw palmetto extract than with placebo (P = 0.22). In addition, there was no significant difference using saw palmetto extract compared with placebo at any dose level. Further, saw palmetto was not more efficacious than placebo on any of the secondary outcome measures. An exploratory subgroup analysis stratified by race/ethnicity and other baseline parameters such as symptom severity did not reveal any clinically important responses compared with placebo. Aside from physical injuries or trauma, there were no significant differences in adverse events (AEs) between groups, at any dose.

The authors conclude that this saw palmetto extract at doses up to 960 mg/day was not more effective than placebo for treating lower urinary tract symptoms related to BPH or for secondary symptoms. The strengths of the study were: (1) use of a well-characterized product, (2) adequate sample size, (3) multicenter design to increase generalizability, (4) adequate dose and duration of treatment (24 weeks at each dose level), (5) excellent adherence with study medication and visits, (6) comprehensive outcome measures, and (7) adequate blinding. The authors point out that earlier studies did not have all of these strengths. A limitation of the study is that the results may not apply to other products. However, there have been negative studies that use other products, so the authors think that "it is increasingly unlikely a dose of some preparation will be identified that is better than placebo." Nonetheless, since the potential active components and mechanism(s) are not known, the best preparation is uncertain.

This study was conducted as part of an Investigational New Drug Application for the US Food and Drug Administration. The drug company donating the product had a vested interest that the results would be positive, even though they did not sponsor the study financially. This adds to the credibility of the findings, since the outcome was negative.

—Heather S. Oliff, PhD

References

[1]Wilt T, Ishani A, MacDonald R. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev*. 2002;(3):CD001423.

[2]Tacklind J, MacDonald R, Rutks I, Wilt TJ. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev*. 2009;(2):CD001423.

[3]Bent S, Kane C, Shinohara K, et al. Saw palmetto for benign prostatic hyperplasia. *N Engl J Med*. 2006;354(6):557-566.

The American Botanical Council has chosen not to reprint the original article.