

Jason Ricco, MD, MPH;
Shailendra Prasad, MBBS,
MPH
North Memorial
Family Medicine Residency,
University of Minnesota,
Minneapolis

PURLS EDITOR

John Hickner, MD, MSc
Cleveland Clinic

The shrinking case for saw palmetto

Findings of this study should make physicians and patients alike reconsider the popularity of this herbal remedy for BPH symptoms.

PRACTICE CHANGER

Advise men with benign prostatic hyperplasia (BPH) not to take saw palmetto for urinary symptoms. Explain that it has not been found to alleviate symptoms, even at triple the standard dose.¹

A: Based on evidence from a high-quality randomized controlled trial (RCT)¹ and a 2009 meta-analysis.²

1. 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;306:1344-1351.

ILLUSTRATIVE CASE

A 66-year-old man comes to your office complaining of urinary frequency and straining to begin urination. He was recently diagnosed with BPH by a urologist, but is hesitant to begin taking a prescription drug. The patient, who is on a fixed income, asks you if saw palmetto extract might relieve his urinary symptoms. What should you tell him?

Roughly 40% of American men older than 60 years and nearly 90% of men older than 80 suffer from BPH and the troublesome lower urinary tract symptoms (LUTS) that it causes.³ Established medical and surgical options, as well as over-the-counter (OTC) plant-based products, are used for symptom relief. The OTC remedy most commonly used for BPH is *Serenoa repens*, derived from the saw palmetto dwarf

palm tree. In a 2007 survey, 1.6 million US adults reported using saw palmetto extract, often as a treatment for BPH, in the 30 days prior to the survey.⁴

Until now, more questions than answers

As a family physician, you undoubtedly have many patients who are taking or considering taking saw palmetto for relief of BPH symptoms. The significant adverse effects of alpha-blockers and 5-alpha-reductase inhibitors, which are typically prescribed for LUTS—including decreased libido and dizziness—may help account for their interest in this alternative treatment.^{5,6}

Until recently, evidence of saw palmetto's efficacy has been limited and conflicting, despite widespread use of the extract. That has left many of us wondering whether we should recommend that men with BPH try saw palmetto despite the limited evidence; whether it is effective for some, but not all, BPH symptoms; and whether an increase in dose would increase its efficacy.

A 2002 Cochrane meta-analysis of 21 trials of saw palmetto extract for LUTS reported reduced nocturia, improved self-reported symptoms, and increased peak uroflow compared with placebo, without significant adverse effects.⁷ An updated Cochrane review published in 2009 included several more rigorous trials—and had very different results: This meta-analysis, which was based on 30 trials, found a reduction in nocturia,

but failed to show improvement in other self-reported symptoms or peak uroflow.²

The largest trial included in the 2009 review was the Saw Palmetto Treatment for Enlarged Prostates (STEP) study,⁸ a one-year study with 225 participants. Its findings: no improvement in the treatment group compared with the placebo group in symptom scores or any secondary endpoints, and no important toxicity.⁸ Of note, the STEP study and most trials included in the 2009 Cochrane review used the standard saw palmetto extract dose of 160 mg twice daily.^{1,2}

STUDY SUMMARY

Saw palmetto is ineffective, even at triple the dose

Barry et al conducted a 72-week double-blind, multicenter placebo-controlled trial to assess the effect of double (640 mg/d) and triple (960 mg/d) the standard dose of saw palmetto extract on BPH symptoms.¹ The study included 369 men with moderate LUTS who had not recently received treatment for BPH. Exclusion criteria included a history of invasive BPH treatment, recent treatment with either an alpha-blocker or a 5-alpha-reductase inhibitor; recent phytotherapy, including saw palmetto; and a history of prostate or bladder cancer. Participants were randomized to receive either saw palmetto extract or an identical-looking placebo gel cap. Doses started at 320 mg/d and were increased to 640 mg/d at 24 weeks and 960 mg/d at 48 weeks.

The primary outcome was the change in the American Urological Association Symptom Index (AUASI) score from baseline to 72 weeks. AUASI, a scale of 0 to 35 in which higher numbers represent increased symptoms, is the same scoring tool used in both the Cochrane review and the STEP trial. Secondary measures included other symptom scales, peak uroflow, and poststudy satisfaction. The treatment and placebo groups had statistically identical baseline characteristics, and the sample size was large enough to detect clinically significant differences.

The AUASI score decreased by a mean of 2.20 points (95% confidence interval [CI], -3.04 to -0.36) in the group that received saw

palmetto and by 2.99 points (95% CI, -3.81 to -2.17) in the placebo group—a mean difference of 0.79 in favor of the placebo group ($P=0.91$). The proportion of participants achieving a 3-point reduction in AUASI score was statistically similar between the 2 groups ($P=0.66$). There was no significant dose response difference between the 2 groups, and saw palmetto proved to be no better than placebo for any of the secondary outcomes.

Subgroup analysis did not reveal any results that differed from the main outcomes. The only adverse events that were significantly different between the 2 groups related to physical injury or trauma, which were unlikely to be due to the intervention.¹

By using the same symptom scoring system (AUASI) as many studies in the previous Cochrane reviews, Barry et al were able to compare their findings with those of other high-quality studies with similar methodologies and outcome measures. Despite using an even higher dose of the extract, the results of this trial are remarkably consistent with previous conclusions: Saw palmetto is not an effective treatment for symptoms associated with BPH. Moreover, this trial had a broad base of participants similar to the population in a primary care practice, including patients who would typically choose a natural remedy for LUTS.¹

WHAT'S NEW

We now have answers to queries about saw palmetto

This trial is the first to compare higher doses of saw palmetto with placebo to assess a dosage threshold for effectiveness. While the study found no evidence of saw palmetto toxicity even at these higher doses, the extract did not outperform placebo for any measured outcome.¹

This high-quality study confirmed the recent series of rigorous studies with negative outcomes by showing that the use of a standard dosage was not a study limitation and that saw palmetto extract is not effective for treating LUTS at any dosage. This trial should substantially affect future guideline recommendations that were limited by methodological concerns in the past.⁹⁻¹¹

CONTINUED



INSTANT POLL

What do you tell men with BPH who ask about saw palmetto?

- It often helps alleviate urinary symptoms
- It probably won't help, but it's worth a try
- It is ineffective
- Other _____

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CAVEATS

In theory, individual preparations could work differently

It is not possible to be absolutely certain that these findings apply to all saw palmetto extract preparations, given the unknown active ingredients and unknown mechanism of action. However, the researchers used a high-quality preparation (a proprietary lipidic ethanolic extract) of saw palmetto at higher doses than the STEP trial and came to a similar conclusion, making it highly unlikely that another preparation would perform differently.

CHALLENGES TO IMPLEMENTATION

There are none

We see no challenges to implementation of this recommendation. **JFP**

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References

1. 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;306:1344-1351.
2. Tacklind J, MacDonald R, Rutks I, et al. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev*. 2009;(2):CD001423.
3. Roehrborn CG, McConnell JD. *Etiology, Pathophysiology, Epidemiology, and Natural History of Benign Prostatic Hyperplasia*. 8th ed. Philadelphia, Pa: Campbell's Urology; 2002.
4. Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007. *Natl Health Stat Report*. 2008;(12):1-23.
5. Traish AM, Hassani J, Guay AT, et al. Adverse side effects of 5-alpha-reductase inhibitors therapy: persistent diminished libido and erectile dysfunction and depression in a subset of patients. *J Sex Med*. 2011;8:872-884.
6. Clifford GM, Farmer RD. Medical therapy for benign prostatic hyperplasia: a review of the literature. *Eur Urol*. 2000;38:2-19.
7. Wilt T, Ishani A, MacDonald R. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev*. 2002;(3):CD001423.
8. Bent S, Kane C, Shinohara K, et al. Saw palmetto for benign prostatic hyperplasia. *N Engl J Med*. 2006;354:557-566.
9. Benign prostatic hyperplasia: treatment [saw palmetto]. In: DynaMed. Available at: <http://www.DynamicMedical.com>. Accessed April 16, 2012.
10. Saper R. Clinical use of saw palmetto [saw palmetto]. In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate 2012. Available at: <http://www.uptodate.com>. Accessed April 16, 2012.
11. Agency for Healthcare Research and Quality. Guidelines on the treatment of non-neurogenic male LUTS. Available at: <http://www.guideline.gov/content.aspx?id=34066>. Accessed June 17, 2012.

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