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File: ■ Saw Palmetto (*Serenoa repens*, Arecaceae)
■ Prostate Cancer
■ Serum Prostate-specific Antigen (PSA)
■ Lower Urinary Tract Symptoms (LUTS)
■ Radiation Therapy

HC 081662-564

Date: March 15, 2017

RE: Saw Palmetto's Safety and Efficacy in Treating LUTS in Patients with Prostate Cancer Undergoing Radiation

Wyatt GK, Sikorskii A, Safikhani A, McVary KT, Herman J. Saw palmetto for symptom management during radiation therapy for prostate cancer. *J Pain Symptom Manage*. June 2016;51(6):1046-1054.

Prostate cancer affects many men across the world, and lower urinary tract symptoms (LUTS) are prevalent in men treated with radiation therapy (a standard cancer treatment). Studies with saw palmetto (*Serenoa repens*, Arecaceae) have suggested its use in treating benign prostatic hyperplasia (enlarged prostate)[1]; however, its safety and efficacy in the treatment of LUTS in those undergoing radiation is unclear. As other treatments for this condition, namely alpha-adrenergic blockers, can cause adverse side effects (ASEs), saw palmetto may be an alternative. This clinical study tested increasing doses for safety. The maximum tolerated dose of saw palmetto was then used to test efficacy for LUTS treatment in a randomized, double-blinded, controlled trial in those suffering from prostate cancer.

This study took place in the United States from 2011-2014, and men with early-stage prostate cancer and eligible for radiation therapy were included. Patients were 21 years or older with a Karnofsky Performance Status score of ≥ 70% (this assesses quality of life in patients with cancer, with 100% indicating cancer-free status and 0% indicating death), a Gleason score of ≤ 8 (this measures tumor differentiation, with a score of 10 meaning less differentiated tumors and 1 indicating highly differentiated tumors), and a serum prostate-specific antigen (PSA) of ≤ 40 ng/ml (elevated concentrations are indicative of disease).

Those who had T4 or M1 (certain types of prostate cancer), were using other botanicals, had undergone radiation in the area previously, had liver or kidney function problems, or had systemic conditions were excluded. Radiation therapy was done for 5 days per week for 8 weeks. Saw palmetto treatment was begun 2 weeks prior to radiation and continued 2 weeks after radiation was ended, for a total of 12 weeks of treatment. Follow

up was conducted up to 22 weeks. There were no restrictions on the use of other drugs for LUTS.

Patients took a health-related quality of life (HRQOL) assessment at baseline and weeks 12, 14, and 22. It is unclear how this was measured, and no details were given regarding a questionnaire. At baseline and from weeks 3-22, LUTS assessment was made using the International Prostate Symptom Score (IPSS). This consists of 6 symptoms rated from 0 (indicating no symptom) to 5 (always present). Assessed at baseline and from weeks 2-22, the Common Terminology Criteria for Adverse Events (CTCAE) data were obtained. The CTCAE is a questionnaire of certain symptoms such as fatigue, nausea, and hemorrhoids, among other factors. It ranges from 0-4 for each symptom, where higher numbers indicate increased severity. The Functional Assessment of Cancer Therapy-Prostate (FACT-P; weeks assessed not given) also was used to measure factors such as emotional and social well-being. This scale ranged from 0 for "not at all" to 4 for "very much."

Blood parameters (nitrogen, white blood cell count, etc.) were measured at baseline and 6 weeks, and serum PSA was assessed at baseline and week 22. The initial part of the study was a dose-finding phase, where the first 3 patients were given the dosage of 320 mg daily of saw palmetto. Since no ASEs were noted during the 12-week treatment, the dosage of the next 4 patients for the same time period was 640 mg daily, after which 20 men took the highest dose of 960 mg daily for 12 weeks. The parameter for ASEs (particularly nausea, gastritis, and anorexia, based on previously reported ASEs and assessed as scoring 2 or higher using the CTCAE) was a prevalence of 10%. [Note: It is not specified whether the prevalence refers to ASEs or patients.] Saw palmetto was distributed in gel capsules (320 mg), with instructions to take 1 at a time with food in accordance with a patient's prescribed dose. No information on the source, preparation, or plant part used was given. Placebo is also not defined.

For the dose-finding phase, 27 patients participated, with 3 taking 320 mg saw palmetto daily, 4 taking 640 mg daily, and 20 patients taking 960 mg daily. With the exception of 1 patient dropping out due to gastritis, no ASEs were observed during this phase; 17 patients finished the 12-week dose-finding phase—dropout reasons other than gastritis were delay in receiving saw palmetto, scheduling conflicts, and too many medications. In total, 5 patients took alpha-adrenergic (antitumor) drugs.

For the randomized controlled trial (RCT), patients were randomly assigned into either a saw palmetto (960 mg) group (10 patients) or a placebo group (11 patients). None of the patients in the saw palmetto group took alpha-adrenergic drugs, but 2 patients in the placebo group did. Blood parameters and PSA levels were not significantly different between the herb-supplemented and placebo groups at baseline or week 6 or 22.

At baseline of the exploratory RCT phase, the functional well-being section of the FACT-P questionnaire was significantly higher in the saw palmetto group as compared with the placebo group (23.60 ± 4.12 vs. 19.33 ± 4.59, P = 0.04), indicating a more healthy status in the saw palmetto group. [Note: It is mentioned that this was adjusted statistically when analyzing final results.] At the end of the study, the FACT-P prostate-specific concerns part of the questionnaire reflected a significantly higher score in the saw palmetto group as compared with the placebo group (35.13 ± 1.92 vs. 33.81 ± 1.82, P = 0.03). No other significant differences were observed.

In summary, this study suggests that the final dosage of saw palmetto used here (960 mg) may be well tolerated. Discussed limitations include a modest sample size. It is mentioned that those in the saw palmetto group in the trial did not use standard medication for LUTS, suggesting that further work may be necessary in establishing the potential efficacy of this treatment for remediating symptoms.

—Amy C. Keller, PhD

Reference

[1]Blumenthal M, Goldberg A, Brinckmann J, eds. *Herbal Medicine: Expanded Commission E Monographs*. Austin, TX: American Botanical Council; Newton, MA: Integrative Medicine Communications; 2000.