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File: ■ Saw Palmetto (*Serenoa repens*, Arecaceae)
■ Lower Urinary Tract Symptoms
■ Benign Prostatic Hyperplasia
■ Quality of Life

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RE: Saw Palmetto Shows Equivalent Efficacy to Prescribed Medications in Improving Lower Urinary Tract Symptoms Associated with Benign Prostatic Hyperplasia

Alcaraz A, Carballido-Rodríguez J, Unda-Urzaiz M, et al. Quality of life in patients with lower urinary tract symptoms associated with BPH: change over time in real-life practice according to treatment—the QUALIPROST study. *Int Urol Nephrol*. 2016;48(5):645-656.

A common condition in older men, benign prostatic hyperplasia (BPH) can cause lower urinary tract symptoms (LUTS) that can have a significant impact on quality of life (QoL). A longitudinal, prospective, observational, multicenter study called the Quality of Life in Benign Prostatic Hyperplasia (QUALIPROST) examined the QoL changes and symptom relief in a large cohort of patients with moderate-to-severe LUTS/BPH being managed by therapeutic approaches typically found in real-world clinical practice. The study was conducted in centers throughout Spain from September 2009 to June 2011.

Patients were included in the study if they were aged 40 years or older, had been diagnosed with LUTS/BPH, and had an International Prostate Symptom Score (IPSS) of 8 or greater. Patients were excluded if they had received drug treatment for BPH during the 6 months prior to the study, if they had received drug treatment with a known effect on BPH symptoms during the 4 weeks before the study, if they had other urinary disorders, or if they had undergone surgery of the lower urinary tract. One hundred nineteen urologists participated in the study, with 1,888 patients recruited, and 1,713 included in the intention-to-treat analysis.

QoL and BPH symptoms were measured at baseline and after 6 months. The primary endpoint was change in QoL, assessed by using the validated Spanish version of the 4-question BPH Impact Index (BII), which asked each patient about the impact of urinary symptoms on physical discomfort, any worries about one's health, how bothersome the symptoms are, and whether the symptoms interfered with usual activities during the preceding month. Scores ranged from 0 (best QoL) to 13 (worst QoL). Symptoms of LUTS/BPH were evaluated by using the validated Spanish version of the IPSS, for which scores range from 0 to 35 (a higher score indicates more severe symptoms). At

baseline, the mean time from diagnosis of BPH was 1.3 ± 2.8 years. Regarding treatment, 8.9% of patients were on watchful waiting (WW), 70.3% received monotherapy, and 20.8% were being treated with combined therapy.

As this was a real-world study of patient management, the investigators were allowed to prescribe commercially available treatments. Of the several brands of alpha-blockers (ABs) prescribed, tamsulosin was the most frequent (88.7% of all ABs), followed by finasteride. Dutasteride was the most frequently prescribed 5α-reductase inhibitor (5ARI) (53.2% of all 5ARIs), and hexanic extract of saw palmetto (*Serenoa repens*, Arecaceae) (HESr) was the most common phytotherapy (95.2% of all phytotherapy) used.

At baseline, patients on WW and those treated with phytotherapy had slightly lower prostate volume and IPSS scores and higher peak urinary flow rate compared with patients on the other treatments. Patients receiving combination therapy (AB + 5ARI, AB + HESr, or 5ARI + HESr) had higher mean BII and IPSS scores compared with those treated with monotherapy or WW. After 6 months, patients in all medical treatment categories reported a relevant improvement in BII and IPSS scores. In the treated patients, BII scores improved by 2.3 points and IPSS scores improved by 5.0 points. In the WW group, which reported the smallest improvements, BII scores improved by 1.0 point and IPSS improved by 2.5 points. Accounting for the severity of symptoms at baseline and comparing changes in BII and IPSS among groups receiving different monotherapies (AB, 5ARI, and HESr), no statistically significant differences were observed. All monotherapies showed significant improvements compared with the WW group ($P<0.05$ for all comparisons).

In the patients with more severe symptoms at baseline, improvements in QoL and IPSS scores were similar among those treated with AB, 5ARI, and HESr. In patients receiving monotherapy, the incidence of adverse effects was highest with AB therapy (16.3%) and lowest for HESr (0.8%). Among the combination therapies, the highest rate of adverse effects (30.5%) was seen in the AB + 5ARI group. Erectile dysfunction and reduced libido were the most frequent adverse effects reported proportionally. Looking at absolute numbers, the authors report that retrograde ejaculation, occurring in 31 of the 424 patients in the AB group, was the most common adverse effect. In all medical treatment groups, 90% of patients reported no difficulty taking the medication.

Although not recommended by the American Urological Association BPH guideline,[1] extracts of saw palmetto are considered a treatment option. The European Medicines Agency states "that only the hexanic extract of *S. repens* has sufficient evidence to support its use as a well-established medicinal product with recognized efficacy and acceptable safety."[2]

The authors acknowledge several limitations, including data obtained under real-world practice conditions, no randomization or blinding, and patients allocated based on clinical judgment possibly leading to selection bias. The short follow-up period also could be a limitation in a study of a chronic disease. A placebo arm was not used because the authors were interested in outcomes seen under conditions of current clinical practice. Despite the limitations, the authors state that real-world practice studies contribute useful information on day-to-day patient management strategies and are a useful complement to clinical trials, in which the results do not always transfer to real-life practice.[3]

The authors conclude that improvements in QoL and IPSS scores were similar across the medical treatments most often used to manage patients with moderate-to-severe LUTS/BPH, and all treatments led to greater improvements than that seen with WW. The use of hexanic extract of saw palmetto led to efficacy equivalent to AB and 5ARI with fewer adverse effects.

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—*Shari Henson*

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[3]Mishra V, Emberton M. To what extent do real life practice studies differ from randomized controlled trials in lower urinary tract symptoms/benign prostatic hyperplasia? *Curr Opin Urol*. 2006;16(1):1-4.

Referenced article can be accessed at http://link.springer.com/article/10.1007%2Fs11255-015-1206-7.