Lower urinary tract symptoms (LUTS) are prevalent in adult men and are often associated with benign prostatic hyperplasia (BPH) and bladder outlet obstruction (BOD) due to benign prostatic enlargement.

Different Serenoa repens extracts (5% repens) are the phytotherapeutic agents most commonly used to treat LUTS/BPH. Systematic reviews and meta-analyses of S. repens data from RCTs have reported different results. In a Cochrane meta-analysis Tacklind et al. concluded that different extracts of S. repens do not improve LUTS or maximum urinary flow rate (Qmax) compared to placebo in men with LUTS/BPH (1). It was found that different brand extracts of S repens is different by composition and free fatty acid concentration table 1, fig 2 [2,3].

Adapted with permission from Haddad FK, Wylie MG. Not all brands are created equal: a comparison of formulated components of five commercial Serenoa repens preparations. Prostate Cancer Prostatic Dis 2004;7:195-203.

Introduction

The assessment report of the S. repens by European Medicine Agency (EMA) 2015 found out that the activity can differ from one extract to another, probably dependent upon type of extraction and the content of fatty acids [4]. Only hexane extract of S repens (HESr) was recognized EMA as a well-established medicinal product was with proved efficacy and acceptability safety. Systematic review and meta-analysis Vela-Navarro et al. (2019) [5] concluded that HESr improve LUTS or maximum urinary flow rate (Qmax) compared with placebo in men with LUTS/BPH and has comparable symptomatic and objective effects with alfalpha blockers [6]. It was shown that treatment by alfalpha-blockers or 5 alpha reductase inhibitors lead to decreased bladder outlet obstruction on 20-35%. But there is lack data of urodynamic effects HESr. The aim of our study was to evaluate the urodynamic and symptomatic impact of the HESr (Permixon) in the treatment of patients with LUTS/BPH.

Methods

This study was pilot, single center, prospective, randomized, single blinded, placebo controlled. A total of 75 patients, aged 51±7.9 years with mild-moderate LUTS according International Prostate Symptom Score (I-PSS) were included for the study, in which 60 patients received Permixon 320mg daily for 12 weeks. The control group (n=15) receive placebo and did not receive any medical treatment for LUTS. Patients were randomized into the study groups by investigator. Patients were included in the study if they had mild-moderate BPH according to their mean International Prostate Symptom Score (I-PSS) (<19 points), a residual urine volume less than 100 ml, maximum urinary flow rate (Qmax) more than 5 ml/s but less than 15 ml/s, no indications for emergency BPH treatment. Exclusion criteria were the presence of urinary tract infections, suggestion of prostate cancer (PSA>4 ng/ml), urological disease affecting micturition, previous urological surgery, detrusor overactivity, neurogenic bladder, concomitant neurogenic disease and men or liver insufficiency. Patients were also excluded if they were taking concomitant medication that might interfere with study medication, including other 5alpha- reductase inhibitors, alfalpha blockers, antiinflammatories and antidepressants.

At the initial visit, each patient completed the I-PSS questionnaire and their medical history and concomitant medications were recorded. Prostate volume evaluation, free flow uroflowmetry were assessed at baseline and at the end of the 12-week treatment. Cystometry and pressure/flow study with a 7F urethral catheter was performed in Medtronic Duet urodynamic equipment. The methods used conformed to the standards of the International Continence Society.

Results

There was no significant difference between the two treatment groups at baseline in age or duration of BPH. The mean age of the control group was 62.5 (SD 7.8) years, while the mean age of the control group was 62.9 (53.7 8.6) years. The mean duration of BPH in both groups was 18.33 (3 4) months.

Treatment with HESr resulted in a significant improvement in symptoms from baseline: I-PSS total score decreased by 25.6% from a baseline of 8.3 points (P<0.001), and the quality of life (QoL) score decreased by 18.5% from a baseline of 3.3 points (P<0.001). In addition there was a significant decrease of 12.6% from baseline 59.4 centimeters of water (P<0.001) in detrusor opening pressure and of 12.9% from baseline 72.3 centimeters of water (P<0.001) in Pdet at maximum flow in patients receiving HESr. None of these parameters improved significantly in control patients. Qmax increased by 5.2% (0.7 ml/s) from a baseline value of 11.7 (P<0.001) in the HESr group. The volume of residual urine in this group also decreased by 12.4% from a baseline value of 49.4 (P<0.05). Prostate volume after HESr treatment (71.6 ml) did not change. There were also improvement in maximum DP (5.2%) in the HESr group which did not reach significance (p=0.07). After 12 weeks there was no significant difference in mean I- PSS score, QoL score, Qmax, residual volume, urodynamic parameters in the control group. Two patients receiving HESr experienced gastrointestinal disturbances but these did not lead to withdrawal or require additional therapy.

Interpretation of results

HESr therapy produced a rapid and significant improvement in the majority of urodynamic and symptomatic assessments carried out in this study. There were significant reductions in the I-PSS and QoL scores, which were accompanied by significant improvements in two urodynamic parameters DP at maximum flow and OP opening pressure. Considered together with the signiﬁcant improvement in Qmax and residual urine, these data conﬁrm that HESr produced an improvement in I/O. There were no signiﬁcant improvements for any of these parameters in the control group despite the fact that both groups were comparable at baseline. The rapid improvement in I/O seen with HESr conﬁrms the positive effects of the drug on urinary function and this may be mainly due to its anti-inflammatory and antiedematous action. Although this was an open-label study, the degree of improvement in the best parameter suggests that HESr may have greater efficacy when evaluated under well-controlled conditions in future trials. In contrast to our findings, a previous study which included 50 men with LUTS suggestive of BPH found that another commercially available Saw palmetto (Serenoa repens) extract did not show a significant effect on urodynamic parameters (1). However, plant extracts strongly differ in composition according to their method of manufacture.

Conclusions

Treatment of LUTS/BPH with HESr produced a improvement in urodynamic parameters and symptoms, illustrating a reduction in bladder outlet obstruction. These data demonstrate that HESr is well tolerated and support its efficacy as first-line phytotherapeutic agent in patients with uncomplicated symptomatic BPH.

References