LETTERS TO THE EDITOR

Phytotherapy in Urology. Current scientific evidence of its application in benign prostatic hyperplasia and prostate adenocarcinoma

Fitoterapia en Urología. Evidencia científica actual de su aplicación en hiperplasia benigna de próstata y adenocarcinoma de próstata

Dear Editor:

A review article was recently published in this journal that deserves our recognition for its goal of trying to clarify the utility of herbal medicine in the treatment of prostate conditions.

However, in that article there are statements that might seem confusing or apparently contradictory.

Thus, when addressing the treatment of benign prostatic hyperplasia and it is indicated that ‘there are over 100 plant derived preparations …’ it is not hard to imagine that with such a great number of extracts from different plants, their composition must necessarily be different and, therefore, trying to group them into one therapeutic family, herbal medicine, to assess its efficacy and safety, seems unreasonable.

Indeed, the EAU Guidelines on the management of LUTS point out that even ‘the extracts of the same plant produced by different companies do not necessarily have the same biological or clinical effects, so that the effects of a brand cannot be extrapolated to others’. Thus, it is observed that different extracts of the same plant, Serenoa repens, have a different composition, and also the extracts of S. repens produced by different manufacturers show a significantly different in vitro activity.

It therefore seems clear that for proper therapeutic evaluation within a group as heterogeneous as phyotherapy, it would be necessary to evaluate each plant extract individually, based on the extraction process and brand, rather than evaluating them together.

It is, therefore, understandable that in this review, by evaluating together studies conducted with different extracts of S. repens (Debruyne, Bent, Gerber, Shi, etc.), a wrong conclusion can be drawn.

On the other hand, the authors note that in the PERMAL study, Debruyne et al. observed therapeutic equivalence between tamsulosin and the hexanic extract of S. repens, no clinically significant differences being observed in the efficacy variables of both study groups, which would support the clinical efficacy of both drugs. However, the authors of this review suggest that one of the limitations of this study is not to include the sample size calculation. In this regard, it should be noted that Debruyne et al. described, on page 499 of their article, the methodology with which they have made the calculation of the sample size.

Another limitation that is mentioned in the review, and in connection with the PERMAL study, is the absence of a placebo group. In this regard, some authors suggest that the existence of a placebo group in patients that come their doctor seeking medical treatment to relieve their LUTS and that can be associated with a risk of progression, could be considered little ethical. In this sense, the mean baseline values of the following variables of the patients included in the PERMAL study (IPSS: 15.5; PSA: 2.8 ng/ml; prostate volume: 48 cm3; Qmax: 10.9 ml/s) would exceed the lower threshold of those associated with risk of progression.

In relation to the importance of assessing each extract individually, a meta-analysis is noteworthy, conducted exclusively with a single trademark of S. repens (lipido hexanic extract, Permixon®), concludes that this extract is associated with significant improvement of the maximum urinary flow (p = 0.042) and nocturia (p < 0.001), higher than those observed with placebo, and an improvement of about 5 points in the IPSS.

In conclusion, the effort made by the authors of this review is commendable, but it is necessary to analyze individually each of the brands associated with a particular plant extract in order to draw conclusions that are useful in clinical practice.

Conflict of interest

The authors are part of the scientific area of Pierre Fabre Laboratories, a company that produces an extract of S. repens.

References


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Reply to 'Phytotherapy in Urology. Current Scientific Evidence of its Application in Benign Prostatic Hyperplasia and Prostate Adenocarcinoma’

Dear Editor:

In our work we try to summarize in a few paragraphs, due to the limitation of space required by the rules of publication, the existing scientific evidence about Serenoa repens for the treatment of LUTS caused by benign prostatic enlargement. Our main objective was to synthesize the usefulness of phytotherapy in various urological pathologies and not that of a particular compound. However, in our work, and focusing it to the greatest clinical relevance in BPH of certain products, we only analyze S. repens and Pygeum africanum.

Drawing conclusions about the clinical efficacy of a particular product in a particular disease must be based on evidence-based medicine. And in this regard, we should always use the greatest evidence provided by well-designed and high-quality clinical trials.

The analysis of efficacy or effectiveness data on BPH of different products should take into account the characteristics of the population to be analyzed, the clinical variables of specific weight in BPH, the use of validated questionnaires, the quality of the trials, and the duration of the study. One of the biggest problems when drawing conclusions with phytotherapeutic products in BPH is the great heterogeneity in the design of the studies and the products used, as well as the low quality of the design of the studies.

The latest clinical evidence has perfectly defined the population with BPH with high probability of progressing from a clinical point of view and has designed therapeutic algorithms based on the risk of progression. But one of the most important aspects in the design of treatment studies of BPH is to define the target population of the study and its duration. In this regard, the evidence found in the literature with respect to S. repens is very limited and contradictory. Most of the studies have a low sample size and the follow-up rarely exceeds 72 weeks. Taking into account that most of the great studies on BPH reach 4 years of follow-up, and considering that the BPH is a chronic disease with clinical progression in a high percentage of patients, studies designed with follow-up periods of one year or less provide limited evidence.

Initial studies of combination therapy showed no superiority of finasteride versus placebo, because the follow-ups were shorter than one year. However, the MTOPS study demonstrated the superiority of the finasteride and doxazosin combination therapy versus each of the monotherapies and versus placebo at 4 years of follow-up. Finasteride proved superior to placebo at 4 years of follow-up in this study as well. This fact of finasteride superiority was demonstrated earlier in the PLESS study, in which it was assessed at 4 years versus placebo. However, S. repens has not shown superiority to placebo in a recently published metaanalysis or in previous studies in which validated questionnaires. Therefore, the PERMAL study should have included a placebo arm, mainly because its superiority versus placebo is not completely demonstrated. On the other hand, the population selected for this study is a population at high risk of progression, candidate for combination therapy from the