

# THE EFFECTS OF MEDICAL THERAPY FOR BENIGN PROSTATIC HYPERPLASIA ON THE SEXUAL FUNCTION OF THE PATIENTS

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## REZUMAT

**Introducere:** Studiile recente au demonstrat că există o legătură strânsă între simptomele de tract urinar inferior și disfuncția erectilă, afecțiuni cu un impact semnificativ asupra calității vieții pacienților. **Obiectiv:** Scopul studiului nostru a fost de a evalua funcția sexuală a unui grup de pacienți cu hiperplazie benignă prostatică (HBP), tratați cu alfa-blocante sau cu inhibitori de 5-alfa-reductază, la momentul inițial și după 12 luni de tratament. **Material și metode:** Am selecționat un număr de 337 pacienți de sex masculin cu HBP cu indicație de tratament medicamentos, în ambulator, pe care i-am urmărit timp de un an. 215 pacienți au fost tratați cu alfa-blocante (110 cu alfuzosin și 105 cu tamsulosin) și 122 pacienți au primit dutasterid. Evaluarea funcției sexuale s-a făcut cu ajutorul scalei SHIM (Sexual Health Inventory for Men). **Rezultate:** Pacienții tratați cu alfuzosin au prezentat o ameliorare semnificativă, cu 1,78 puncte în medie, a scorului SHIM. Pacienții aflați sub tratament cu tamsulosin au avut o îmbunătățire mai modestă a funcției sexuale, de 0,24 puncte, însă scala SHIM nu a putut aprecia impactul ejaculării retrograde, principala acuza a pacienților tratați cu tamsulosin. În fine, pacienții tratați cu dutasterid au cunoscut o ușoară scădere a funcției sexuale (0,12 puncte în medie); selectând din cadrul acestui grup doar pacienții care inițial au avut o funcție sexuală normală sau disfuncție erectilă ușoară, am observat o ameliorare, cu 0,85 puncte, a scorului SHIM. **Concluzii:** Tratamentul HBP cu alfa-blocante (în special alfuzosin) are un efect pozitiv asupra funcției sexuale a pacienților, acționând atât la nivel prostatic, cât și la nivelul musculaturii netede a corpilor cavernoși. O nouă stratificare a riscului pacienților ce primesc inhibitori de 5-alfa-reductază poate fi realizată, în raport cu funcția lor sexuală inițială.

**Cuvinte cheie:** hiperplazie benignă prostatică, disfuncție erectilă, alfa-blocante, inhibitori de 5-alfa-reductază

## ABSTRACT

**Introduction:** Recent studies have demonstrated that there is a close relationship between the low urinary tract symptoms (LUTS) and erectile dysfunction (ED), diseases with significant impact on the quality of life. **Objective:** The aim of our study was to evaluate the sexual function of a group of patients with benign prostatic hyperplasia (BPH), treated with alpha-blockers or 5-alpha-reductase inhibitors, at baseline and after 12 months of therapy. **Material and methods:** We have included a number of 337 male patients with BPH with indication for medical treatment, in an outpatient setting, during a one year therapy period. 215 patients were treated with alpha-blockers (110 with alfuzosin and 105 with tamsulosin), while 122 patients received dutasteride. The evaluation protocol included the Sexual Health Inventory for Men (SHIM score). **Results:** The patients treated with alfuzosin had a significant improvement, of 1.78 points in average, of the SHIM score. The patients treated with tamsulosin had a more modest improvement of their sexual function, of 0.24 points, but the SHIM score was not able to assess the impact of retrograde ejaculation, the major complaint of this patient group. The patients treated with dutasteride had an overall slight decrease of their sexual function (0.12 points); selecting from this group only the patients with initial normal sexual function or with mild erectile dysfunction, we can observe a slight improvement (0.85 points) of the SHIM score. **Conclusions:** BPH therapy with alpha-blockers (especially alfuzosin) has a positive effect on the overall sexual function, acting at both at the prostate level and in the cavernous smooth muscle cells. A new risk stratification of patients receiving 5-alpha reductase inhibitors is possible, in relationship with their initial sexual function.

**Key Words:** benign prostatic hyperplasia, erectile dysfunction, alpha-blockers, 5-alpha-reductase inhibitors

## INTRODUCTION

The interaction between the low urinary tract symptoms (LUTS) and erectile dysfunction (ED) has been extensively studied in the last twenty years, because both conditions have a high associated incidence in elderly males, with significant impact on their quality of life.<sup>1</sup>

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There are several theories that try to establish pathophysiological links between the two diseases, opening new common therapeutic opportunities.<sup>1</sup> Additionally, the urologists should know as much as possible about this association, because the existing drugs used for the therapy of LUTS/benign prostate hyperplasia (BPH) might have adverse effects at the sexual function level.<sup>2</sup>

Selective alpha-receptors antagonists, used currently for BPH therapy, block also the action of norepinephrine at the level of alpha-1 receptors of the cavernous smooth muscle cells. The normally released norepinephrine produces smooth muscle contraction and penile detumescence, so the alpha blockers might have a pro-erectile effect.<sup>3</sup>

On the other hand, during the studies realized using 5-alpha-reductase inhibitors for BPH therapy, several sexual side effects were observed, in different proportions, ranging from decreased sexual desire and ejaculation disorders to complete impotence.<sup>4</sup>

## **OBJECTIVE**

The aim of our study was to evaluate the sexual function of a group of patients with BPH, treated with alpha-blockers and 5-alpha-reductase inhibitors, at baseline and after 12 months of therapy.

## **MATERIAL AND METHODS**

We have included in our initial evaluation a number of 385 male patients with benign prostatic hyperplasia with indication for medical treatment, in an outpatient setting, which accepted to take the medication for one year. The inclusion criteria were: age over 50 years, moderate to severe low urinary tract symptoms (LUTS) with duration of at least six months, prostate volume over 30 cm<sup>3</sup>. Among the most significant exclusion criteria we can cite: previous low urinary tract surgery, major cardiovascular or systemic diseases, diabetes mellitus, bladder stones or recent history of urinary tract infections.

Following this evaluation process, a number of 337 patients were selected for the one year clinical study, after signing an informed consent form, according to the Good Clinical Practice (GCP) regulations. The baseline and one year assessments included: the International Prostate Symptom Score (IPSS), the ultrasonographic measurement of prostate volume, urinary peak flow rate (Q<sub>max</sub>), the total Prostatic Specific Antigen (PSA) value, and the Sexual Health Inventory for Men (SHIM), containing five questions.<sup>5</sup>

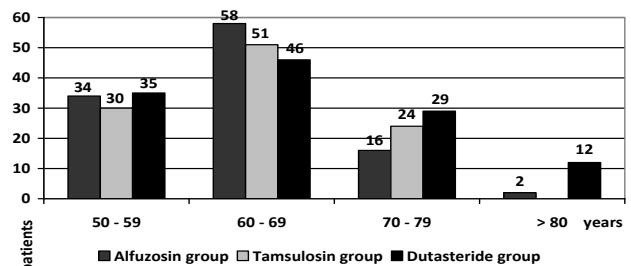
A number of 215 patients (with prostate volumes lower than 40 cm<sup>3</sup>) were treated with alpha-blockers, being randomized into two groups: 110 have received alfuzosin (10 mg extended release tablets) and 105 were prescribed tamsulosin (0.4 mg oral controlled absorption tablets). The remaining 122 patients, with prostate volumes higher than 40 cm<sup>3</sup>, have been treated with dutasteride (0.5 mg capsules), a novel 5-alpha-reductase inhibitor.

### **Statistical analysis**

The obtained data was analyzed using the NCSS 2007 software application for Windows; mean values and standard deviations were calculated and various correlations between the parameters, using the paired two-sample t-Test, were analyzed.

## **RESULTS**

The age distribution in the study groups was relatively homogenous for the two alpha-blocker groups, but different from the dutasteride group. The explanation for this difference resides from the direct proportionality between the prostate volumes and the patients' age (a significant number of the patients with prostates larger than 40 cm<sup>3</sup>, treated with dutasteride were over 70 years old). (Fig. 1)



**Figure 1.** The age distribution of the three study groups.

### **Therapy effects on benign prostatic hyperplasia**

As we can observe from Table 1, therapy with the two alpha-blockers and the 5-alpha-reductase inhibitor had favorable effects on all parameters of BPH, as expected, taking into account the fact that our study was designed as open label, without a placebo arm, using already known drugs, indicated for BPH.

We have also observed the following differences between the study groups:

- The patients from the tamsulosin and dutasteride groups had a similar decrease of the IPSS, with a slight advantage for dutasteride, while the patients treated with alfuzosin had a lower IPSS decrease; we may also observe that this group of patients had the initial IPSS value with at least two points lower than the other

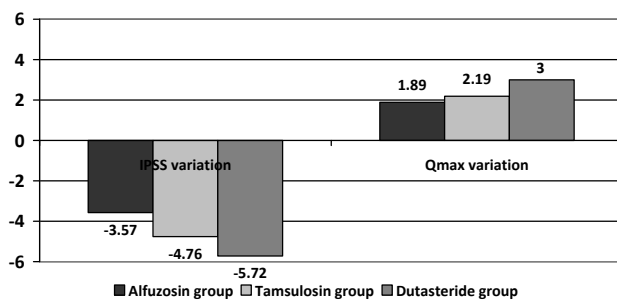
**Table 1.** Effects of the therapy on BPH parameters.

	Initial IPSS (± SD)	Final IPSS (± SD)	Initial Q <sub>max</sub> (± SD)	Final Q <sub>max</sub> (± SD)	Initial prostate volume (± SD)	Final prostate volume (± SD)	Initial PSA (± SD)	Final PSA (± SD)
<b>Group A (Alfuzosin)</b>	15.87 ± 4.91	12.3 ± 4.96	9.07 ± 1.59	10.96 ± 1.68	N/A	N/A	N/A	N/A
<b>Group B (Tamsulosin)</b>	19.14 ± 6.75	14.38 ± 6.81	9.09 ± 1.79	11.28 ± 1.96	N/A	N/A	N/A	N/A
<b>Group C (Dutasteride)</b>	19.87 ± 5.62	14.15 ± 5.56	8.37 ± 2.03	11.37 ± 2.05	52.34 ± 9.28	43.53 ± 6.13	2.39 ± 1.05	1.30 ± 0.56

group (this was due to randomization and it was not intended), so the final IPSS score was also the lowest.

- The patients from the two groups receiving alpha-blockers (A and B) had a similar increase of the maximum urinary flow (1.89 vs. 2.19 ml/s), which is consistent with other studies, while the patients treated with dutasteride had a slightly bigger increase (3 ml/s); despite this difference, we must take into account that the initial average Q<sub>max</sub> was with 1 ml/s lower than in the other two groups, so the final Q<sub>max</sub> was around 11 ml/s in all types of therapy. (Fig. 2)

- In the dutasteride group the average reduction of the prostate volume was 8.81 cm<sup>3</sup>, while the average PSA value was reduced with 45.6%, values which are also consistent with previous studies.



**Figure 2.** Variations of IPSS score and maximum urinary flow.

### Evolution of sexual function

Let's now examine the evolution of the SHIM score in the three study groups.

- Group A (of patients treated with alfuzosin) had a significant improvement, of 1.78 points; the improvement of sexual function was constant in all patients, regardless of the initial erectile function (ranging from normal sexual function to severe erectile dysfunction), which makes alfuzosin a first intention drug, especially for patients having BPH associated with ED.

- Group B (of patients treated with tamsulosin) had a modest improvement of their sexual function, of 0.24 points (p = 0.03). From the data already known from the literature, this could be the consequence

of ejaculatory problems induced by tamsulosin (i.e., retrograde ejaculation). Unfortunately, the SHIM questionnaire is not assessing ejaculatory function, so we are not able to evaluate the impact of retrograde ejaculation on the overall sexual function of the patients from this group. We intend to realize further studies with tamsulosin (placebo-controlled, if possible, to increase the level of clinical significance), using other questionnaires, which should assess the ejaculatory dysfunction too.

**Table 2.** The evolution of the SHIM score in the three study groups.

	Initial SHIM (± SD)	Final SHIM (± SD)	SHIM variation
<b>Group A (alfuzosin)</b>	12.77 ± 4.13	14.55 ± 3.52	1.78
<b>Group B (tamsulosin)</b>	13.30 ± 5.01	13.54 ± 5.07	0.24
<b>Group C (dutasteride)</b>	13.96 ± 4.79	13.84 ± 5.64	-0.12

Group C (patients treated with dutasteride) have an overall slight decrease of their sexual function, as measured by the SHIM questionnaire (0.12 points, p = 0.13). These results indicate that dutasteride has a negative impact, but their statistical significance is very low, so we have tried to further stratify the patient group: we divided it into two subgroups, one with initial normal sexual function, or mild erectile dysfunction (SHIM score of 16 – 25) and the other with initial moderate, or severe erectile dysfunction (SHIM score of 5 -15). The results are presented in Table 3.

**Table 3.** Risk stratification of the patients treated with dutasteride.

Group	Initial SHIM (± SD)	Final SHIM (± SD)	SHIM variation	P
<b>No initial ED or mild ED</b>	19.25 ± 2.96	20.1 ± 3.18	+0.85	<0.002
<b>Initial moderate or severe ED</b>	11.38 ± 3.09	10.78 ± 3.73	-0.6	<0.006

As we can observe, the patients with initial moderate to severe sexual function impairment had a SHIM score increase of 0.6 points, more statistically significant than the whole group ( $p < 0.006$ ). In the mean time, patients with initially mild erectile dysfunction, or with normal sexual function, even had a decrease of the SHIM score, with 0.85 points, finding that represents quite a surprise; its statistical significance, confirmed by the paired two-sample t-Test ( $p < 0.002$ ), raises an attractive new question: do patients with an initial SHIM score over 16 benefit (in sexual function parameters) from the therapy with dutasteride?

This possible risk stratification should be undoubtedly explored further, in a prospective randomized, double blind clinical study, using the full IIEF questionnaire.

## **CONCLUSIONS**

Therapy with alpha-blockers has a positive effect on the overall sexual function, acting at the level of alpha-1-receptors, both in the prostate and in the cavernous smooth muscle cells.

A new risk stratification of patients receiving 5-alpha reductase inhibitors might emerge, the patients with mild erectile dysfunction or normal sexual function having the chance for improvement, while the patients with moderate to severe erectile dysfunction might expect a worsening of their sexual life.

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