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Impact of pharmacologic therapy for benign prostatic hyperplasia on prostate volume and free testosterone and consequently on urinary parameters and sexual desire in men

Uticaj farmakološke terapije benigne hiperplazije prostate na volumen prostate i slobodni testosteron i, posledično, na urinarne parametre i seksualnu želju muškaraca

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Abstract

Background/Aim. Pharmacologic therapy for benign prostatic hyperplasia (BPH) relieves disease progression and affects the androgen hormone status. A decrease in the level of free testosterone (freeT) within total testosterone (totalT) leads to symptoms of sexual dysfunction. The aim of this study was to show the impact of pharmacological treatment for BPH on prostate volume (PV) and levels of freeT and, consequently, on urinary parameters and sexual desire in men during 6 months of administration. **Methods**. This clinical prospective study included 156 BPH patients with moderate urinary symptoms – International Prostate Symptom Score (IPSS) < 19, PV > 30 mL and prostate specific antigen (PSA) value < 4 ng/mL. The average age of patients was 61.16 ± 2.97 years. The performed tests included determination of tumor markers (PSA, free PSA), hormones (totalT, freeT, freeT/totalT ratio), trans abdominal ultrasonography and uroflowmetry. Urinary symptoms were measured by IPSS and the Quality of Life (QoL) questionnaire while the changes in sexual desire were measured using the International Index of Erectile Function (IIEF) questionnaire. Four groups were formed, 39 patients each. The group 1 received alpha1-blocker (AB) tamsulosin, the group 2, 5 alpha-reductase inhibitor (5-ARI) finasteride, the group 3, combined therapy of both drugs (tamsulosin and finasteride), while the group 4 (control group) had no therapy. Follow-ups were performed every three and six months during therapy administration. **Results**. Prostate volume significantly decreased in the patients on combined therapy (-6.95 ± 2.00; $p < 0.001$) and finasteride (-6.67 ± 3.35). In the finasteride group, the levels of freeT (-4.23 ± 5.2; $p < 0.001$) and freeT/totalT ratio (-0.12 0.08; $p < 0.001$) significantly decreased as did the freeT (-2.64 ± 7.81) and freeT/totalT ratio (-0.09 ± 0.13) in the combined therapy group. Uroflowmetry showed a significant improvement in all parameters and all the therapy groups. Combined therapy provided the greatest improvement in the maximum flow rate (Qmax) (+4.06 ± 1.75; $p < 0.001$) and urinary symptoms (-10.95 ± 3.19). A significant improvement of sexual desire occurred in the patients on tamsulosin (+0.78 ± 1.00; $p < 0.001$), with a slight deterioration in the finasteride group, but without statistical significance. **Conclusion**. Hormonal component of pharmacologic therapy for BPH most effectively reduces PV and freeT levels, improves urinary symptoms with a slight decline of sexual desire in men on finasteride monotherapy.

Key words:
prostatic hyperplasia; drug therapy; urination disorders; sexual dysfunction, physiological; quality of life.

Apstrakt

Uvod/Cilj. Farmakološka terapija benigne hiperplazije prostate (BHP) ublažava progresiju bolesti i utiče na androgeni hormonski status. Opadanje nivoa slobodnog testosterona (slobodniT) unutar ukupnog testosterona (ukupniT) dovodi do simptoma seksualne disfunkcije. Cilj rada bio je da se prikažu rezultati uticaja farmakološke terapije BHP u toku 6 meseci korišćenja na volumen prostate (VP) i nivo slobodnogT kao i efekat na urianarne parametre i seksualnu želju muškaraca. **Metode**. Ova klinička prospektivna studija obuhvatila je 156 bolesnika sa BHP, sa umerenim simptomima poremećaja mokrenja – internacionalni prostata simptom skor (IPSS) < 19,VP > 30 mL i vrednošću prostata specifičnog antigena (PSA) < 4 ng/mL. Prosečna starost bolesnika bila je 61,16 ± 2,97 god. Rađene su analize krvi sa određivanjem tumorskih markera (PSA, slobodni PSA), hormona (ukupniT, slobodniT, odnos slobodniT/ukupniT), transabdominalna ultra-

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sonografija i urofloumetrija. Simptomi poremećenog mokrenja mereni su upitnicima za IPSS i kvalitet života (*Quality of Life* – QoL), a promene seksualne želje upitnikom Internacionalni indeks erektilne funkcije (IIEF). Formirane su četiri grupe sa po 39 bolesnika. Prva grupa dobijala je alfa1-blokator (AB) tamsulosin, druga grupa inhibitor 5alfa-reduktaze (5-ARI) finasterid, treća grupa kombinovanu terapiju (tamsulosin i finasterid) i četvrta, kontrolna grupa, bila je bez terapije. Kontrole su rađene na tri i šest meseci tokom terapije. **Rezultati**. Značajno je smanjen VP kod bolesnika sa kombinovanom terapijom (-6,95 ± 2,00; $p < 0,001$) i finasteridom (-6,67 3,35). U grupi sa finasteridom značajno je smanjen slobodniT (-4,23 ± 5,20; $p < 0,001$) i odnos slobodniT/ukupniT (-0,12 ± 0,08; $p < 0,001$), kao i u grupi sa kombinovanom terapijom [slobodniT (-2,64 ± 7,81) i odnos slobodniT/ukupniT (-0,09 ± 0,13)]. Urofloumetrija je pokazala značajno poboljšanje svih urinarnih parametara u svim terapijskim grupama. Kombinovanom terapijom postignuto je najveće poboljšanje maksimalnog protoka (Qmax)(+4,06 1,75; $p < 0,001$) i simptoma poremećenog mokrenja (-10,95 ± 3,19). Seksualna želja kod bolesnika sa tamsulosinom bla je značajno poboljšana (+0,78 1,00; $p < 0,001$), dok je u grupi sa finasteridom registrovano blago pogoršanje, ali bez statističke značajnosti. **Zaključak**. Hormonska komponenta farmakološke terapije za BHP najefikasnije smanjuje VP i nivo slobodnogT, poboljšava simptome poremećenog mokrenja sa blagim pogoršanjem seksualne želje muškaraca lečenih samo finasteridom.

Ključne reči:
prostata, hipertrofija; lečenje lekovima: mokrenje, poremećaji; seksualni poremećaji; kvalitet života.

Introduction

Benign prostatic hyperplasia (BPH) is the fourth most common disease in elderly men. It causes difficulties in urination and sexual function disorders. The occurrence and development of BPH are triggered by age and male sex hormones [1]. In men aged over 60 histological changes which indicate BPH are present in over 60%, while over 40% experience lower urinary tract symptoms (LUTS) [2]. Male sex hormones, testosterone, androstenedione and dehydroepiandrosterone (DHEA), are important for the formation of secondary sexual characteristics, the existence of libido, erection, and spermatogenesis process. Their influence on the development of BPH contributes to the occurrence and maintenance of LUTS [3].

The androgenic activity of testosterone is 10 times higher than that of androstenedione and 20 times higher than DHEA. Testosterone is present in plasma in free (freeT) and bound form. Free testosterone (2% of totalT), comes into contact with different cells in the body: muscle, brain, skin and hair cells, the prostate and other sex organs [4]. For the most part, bound testosterone is weakly bound to plasma albumin (38%) or strongly bound to beta globulin (60%) – sex hormone binding globulin (SHBG). Free testosterone plus albumin bound testosterone implies bioavailable testosterone, which easily enters cells and better reflects the bioactivity of testosterone. After the age of 20, there is a gradual decline in levels of totalT by 0.4% and by 1.2% in freeT *per* year [5]. If freeT starts to decrease in totalT, the symptoms of decreased sexual activity will occur. However, even in the oldest men, the blood level of testosterone is high enough to maintain libido and spermatogenesis [6].

Pharmacological treatment of BPH includes alpha 1-blockers (ABs) and 5 alpha-reductase inhibitors (5-ARIs), individually or together as a combination therapy [7]. ABs bind to alpha-receptors, relaxing the smooth muscles of the prostate and the bladder neck. They facilitate urination without affecting prostate size [8]. 5-ARIs block the conversion of inactive forms of testosterone into dehydrotestosterone (DHT), which has a 2–5 times higher affinity to androgen receptors than testosterone. Decreasing the level of DHT reduces the prostate volume (PV) thus improving urinary symptoms. At the same time, 5-ARI lead to changes in hormonal status which affects the elements of sexual function [9].

Many studies have examined the relationship between male sex hormones and BPH, but only a few analyzed the relationship between free T and LUTS in BPH finding no significant interrelationships [10].

The aim of this paper was to demonstrate the impact of pharmacologic therapy for BPH on PV and the levels of freeT during 6 months of administration and the effects of such changes on LUTS, functional urinary parameters and sexual desire in men.

Methods

A prospective clinical study was conducted at the Military Hospital in Niš with the participation of 156 BPH patients. The average age of the entire cohort of patients was 61.16 ± 2.97 years, all were in good general condition, previously not treated for BPH. The patients were informed about the course and research goals and they all signed the consent form to participate in the research. The Ethics Committee of the Military Hospital in Niš approved the implementation of the study.

The research included patients without indications for surgical treatment, with moderate urinary symptoms [7 < International Prostate Symptom Score (IPSS) < 19], PV > 30 mL and the prostatic specific antigen (PSA) value of < 4 ng/mL. Patients with residual urine > 200 mL, infections, calculosis, malfunction of the kidneys and those who had undergone prostate biopsy for suspected malignacy were excluded.

After a general check-up and a digital rectal examination of the prostate, determination of serum tumor markers (PSA, freePSA), sexual hormones – testosteron (totalT, freeT, freeT/totalT ratio), creatinine, urine and urine culture with antibiogram were performed in all the patients. Prostate volume and post-void residual (PVR) urine were measured by transabdominal ultrasonography. The functionality of the lower urinary tract was measured using uroflowmetry parameters: Qmax, average flow rate (Qave), voiding time (VT), PVR with voided volume (Vcomp) of > 150 mL.

Urinary symptoms were measured using the IPSS and Quality of life (QoL) questionnaire. The IPSS is an 8-item questionnaire, consisting of seven symptom questions in the past month and QoL question. Four questions refer to voiding symptoms (incomplete emptying, intermittency, straining, weak stream) while three deal with storage symptoms (frequency, urgency, nocturia). The effect of hormonal changes was measured by the changes in the level of sexual desire and orgasmic function as provided by the International Index of Erectile Function (IIEF) questionnaire which assesses sexual function in the previous month. The questions include: how often did you feel sexual desire and how do you rate your level of sexual desire? The following questions were used to measure the orgasmic function: how often did you ejaculate during sexual acitivity and how often did you experience an orgasm? To assess the ejaculatory function three items were used for rating the domains of ejaculation (frequency, strength and volume) as given in the Male Sexual Health Questionnaire-Ejaculatory Dysfunction (MSHQ-EjD) [11].

The patients completed the questionnaires before treatment. After three and six months of the therapy, follow-up examinations were performed like the ones performed upon entering the study. Based on the results, four groups of 39 patients were formed. The first group received AB tamsulosin 0.4mg/day, the second group received 5-ARI finasteride 5 mg daily while the third group received combination therapy (tamsulosin andfinasteride). The fourth control group consisted of patients with mild symptoms (IPSS < 7), without therapy, but provided advice on lifestyle (self-management as a part of watchful waiting). Tamsulosin was given to patients with PV < 40 mL, finasteride for PV 40–50 mL and combination therapy to patients with PV > 50 mL. Average values of urinary symptoms intensity did not differ significantly across the two groups.

Two patients from the group on tamsolusin and another two on combination therapy did not undergo the third examination. The reasons for this were of objective nature – two patients had changed their residence, the third was recovering after a road accident, while the fourth was receiving inpatient orthopedic treatment. This was taken into consideration in statistical processing.

Testing the differences between the questionnaire scores and variables before the examination, three and six months after the therapy was performed using repeated measure analysis of variance (RM ANOVA). The respondents' ages within the groups were compared using unilateral analysis of variance (one-way ANOVA) and the Tukey *post-hoc* test.

The questionnaire scores and variables were presented as mean values ± standard deviation ($\bar{x} \pm SD$). The level of statistical significance was $p < 0.05$.

Results

The average age was no statistically significantly different between the formed groups. In the group using tamsulosin it was 60.69 ± 3.22 years, 61.56 ± 3.30 years in the finasteride group, 61.76 ±2.51 years in the combination therapy group and 60.64 ± 2.70 years in the control group.

Table 1 shows changes in the parameters measured

Table 1

The values of variables during the study in the therapy groups

Therapy group	Variables	Testing (mean ± SD)			Comparison between testing *(p)*		
		Baseline (I)	After 3 mths (II)	After 6 mths (III)	I *vs* II	II *vs* III	I *vs* III
Tamsulosin	PSA (ng/mL)	1.08 ± 0.45	0.97 ± 0.48	0.87 ± 0.48	0.031*	0.097	< 0.001*
	Free PSA (ng/mL)	0.32 ± 0.19	0.28 ± 0.18	0.31 ± 0.15	0.134	0.109	0.450
	TotalT (ng/mL)	5.21 ± 1.83	5.44 ± 2.02	5.08 ± 1.96	0.531	0.169	0.704
	FreeT (pg/mL)	14.94 ± 7.18	13.37 ± 4.09	13.4 ± 6.19	0.137	0.874	0.215
	FreeT/TotalT (%)	0.30 ± 0.14	0.28 ± 0.13	0.29 ± 0.14	0.498	0.549	0.843
	Voiding time (s)	49.61 ± 21.89	45.00 ± 18.82	41.19 ± 14.58	0.128	0.133	0.010*
	Qmax (mL/s)	13.66 ± 3.19	15.54 ± 3.26	16.49 ± 3.19	< 0.001*	0.007*	< 0.001*
	Qave (mL/s)	8.69 ± 2.41	9.36 ± 2.44	9.84 ± 2.66	0.022*	0.063	0.003*
	PVR (mL)	40.44 ± 29.00	30.10 ± 21.29	23.30 ± 17.83	0.006*	0.043*	< 0.001*
Finasteride	PSA (ng/mL)	1.94 ± 0.79	1.25 ± 0.56	1.01 ± 0.48	< 0.001*	< 0.001*	< 0.001*
	Free PSA (ng/mL)	0.45 ± 0.22	0.25 ± 0.20	0.23 ± 0.14	< 0.001*	0.255	< 0.001*
	TotalT (ng/mL)	5.05 ± 1.97	6.35 ± 2.48	6.40 ± 3.41	< 0.001*	0.896	0.002*
	FreeT (pg/mL)	12.89 ± 4.27	11.94 ± 6.17	8.66 ± 5.57	0.243	0.001*	< 0.001*
	FreeT/TotalT (%)	0.26 ± 0.08	0.19 ± 0.09	0.14 ± 0.09	< 0.001*	< 0.001*	< 0.001*
	Voiding time (s)	53.03 ± 19.70	43.55 ± 17.73	41.26 ± 14.77	0.002*	0.328	< 0.001*
	Qmax (mL/s)	12.85 ± 2.59	14.54 ± 2.43	16.52 ± 2.71	< 0.001*	< 0.001*	< 0.001*
	Qave (mL/s)	7.93 ± 2.39	9.13 ± 2.84	10.14 ± 2.82	< 0.001*	0.004*	< 0.001*
	PVR (mL)	52.03 ± 26.32	33.54 ±19.24	18.54 ± 12.09	< 0.001*	< 0.001*	< 0.001*
Combination therapy	PSA (ng/mL)	2.31 ± 0.95	1.53 ± 0.91	1.22 ± 0.71	< 0.001*	< 0.001*	< 0.001*
	Free PSA (ng/mL)	0.54 ± 0.24	0.30 ± 0.20	0.28 ± 0.16	< 0.001*	0.333	< 0.001*
	TotalT (ng/mL)	5.61 ± 1.85	6.33 ± 2.65	6.46 ± 2.67	0.018*	0.784	0.051
	FreeT (pg/mL)	13.83 ± 5.91	12.43 ± 6.62	11.17 ± 7.18	0.203	0.080	0.047*
	FreeT/TotalT (%)	0.26 ± 0.11	0.20 ± 0.08	0.17 ± 0.10	0.002*	0.013*	< 0.001*
	Voiding time (s)	58.09 ± 22.34	51.75 ± 17.02	40.93 ± 12.43	0.033*	< 0.001*	< 0.001*
	Qmax (mL/s)	12.18 ± 2.60	14.44 ± 3.00	16.05 ± 2.92	< 0.001*	< 0.001*	< 0.001*
	Qave (mL/s)	7.11 ± 2.23	8.41 ± 2.46	9.42 ± 2.80	< 0.001*	< 0.001*	< 0.001*
	PVR (mL)	64.51 ± 26.23	34.77 ± 21.73	21.03 ± 14.52	< 0.001*	< 0.001*	< 0.001*

*** – statistically significant difference; SD – standard deviation; PSA – prostate specific antigen; TotalT – total testosterone; FreeT – free testosterone; PVR – post-void residual urine; Qmax – maximum flow rate; Qave – average flow rate; mths – months.**

during research. Assessment of prostate size (mL) by ultrasound showed a significant reduction in PV after 6 months of the treatment in the group on combination therapy (-6.95 ± 2.00) and the finasteride users (-6.67 ± 3.35). In the patients using only tamsulosin there were no significant changes (Figure 1).

PSA (ng/mL) significantly decreased in all therapy groups after 6 months, the most in patients on combination therapy (-1.15 ± 0.51) followed by the groups on finasteride (-0.93 ± 0.64) and tamsulosin (-0.21 ± 0.31). Free PSA (ng/mL) significantly decreased with combination therapy (-0.27 ± 0.15) and finasteride (-0.22 ± 0.14), while non-significant decrease occurred in the tamsulosin group.

Regarding the impact on hormones the significant change of totalT levels (ng/mL) from the baseline values occurred only in the finasteride group, where it was increased (+1.34 ± 2.49). Free testosterone (pg/mL) was significantly reduced in the groups on finasteride (-4.23 ± 5.20), and combination therapy of (-2.64 ± 7.81), while non-significant changes were recorded in the tamsulosin group. Free testosterone/total testosterone ratio (%) as a measure of androgen bioactivity of total testosterone decreased in all groups after 6 months of therapy, with statistical significance only in groups on finasteride (-0.12 ± 0.08) and combination therapy (-0.09 ± 0.13) (Table 1).

Uroflowmetry results showed a significant improvement of all parameters in all therapy groups compared to baseline. Voiding time (sec) decreased the most with combination therapy (-18.51 ± 17.77), then with finasteride (-11.77 ± 16.58) and the tamsulosin (-8.61 ± 19.14). The highest increase of the Qmax (mL/s) was registered in the combination therapy group (+4.06 ± 1.75), followed by the finasteride (+3.67 ± 1.84) and the tamsulosin group (+2.81 ± 2.61) (Table 2). The highest increase of the Qave (mL/s) was in the combination therapy group (+2.47 ± 1.84), followed by the groups on finasteride (+2.21 ± 2.12) and tamsulosin (+1.16 ± 2.21). Post-void residual urine (mL) decreased mostly with combination therapy (-44.22 ± 26.02), then with finasteride (-33.49 ± 26.06) and the least with tamsulosin (-16.08 ± 25.22).

Urinary symptoms (IPSS) significantly improved in all therapy groups as follows: (-10.95 ± 3.19) with combination therapy, (-9.00 ± 2.84) with finasteride and (-5.84 ± 3.08) with tamsulosin (Table 2). Quality of life also improved significantly in all the three therapy groups, the most with combined therapy (-2.95 ± 0.97), then with finasteride (-2.85 ± 1.01) and tamsulosin (-2.32 ± 1.00) (Table 2).

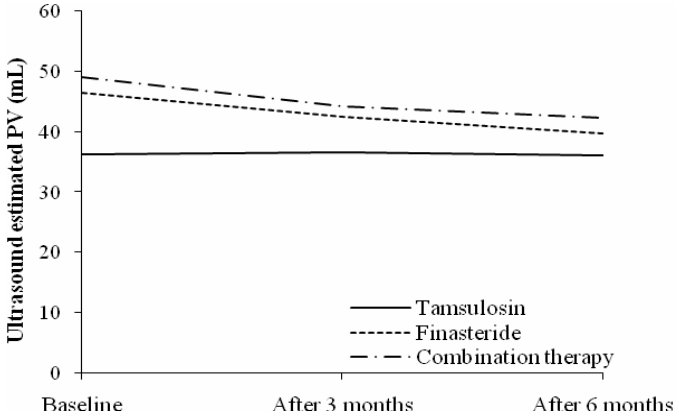

Fig. 1 – The prostate volume (PV) on ultrasound scan during the study.

Table 2

Score values of urinary symptoms and QoL during the study in all the groups

Therapy group	Score	Testing (Mean ± SD)			Comparison between testing *(p)*		
		Baseline (I)	After 3 mths (II)	After 6 mths (III)	I vs II	II vs III	I vs III
Tamsulosin	IPSS	13.64 ± 3.35	9.21 ± 2.66	7.51 ± 2.66	< 0.001*	0.001*	< 0.001*
	Voiding symptoms	7.79 ± 2.65	4.74 ± 2.06	3.70 ± 2.22	< 0.001*	0.010*	< 0.001*
	Storage symptoms	6.10 ± 1.67	4.51 ± 1.17	3.81 ± 1.29	< 0.001*	0.001*	< 0.001*
	QoL	3.74 ± 0.75	1.79 ± 0.89	1.32 ± 0.85	< 0.001*	0.006*	< 0.001*
Finasteride	IPSS	16.69 ± 2.91	10.97 ± 2.45	7.69 ± 2.62	< 0.001*	< 0.001*	< 0.001*
	Voiding symptoms	9.21 ± 2.33	6.03 ± 1.94	3.69 ± 1.78	< 0.001*	< 0.001*	< 0.001*
	Storage symptoms	7.49 ± 1.71	4.95 ± 1.45	3.97 ± 1.46	< 0.001*	< 0.001*	< 0.001*
	QoL	4.10 ± 0.64	1.97 ± 0.84	1.26 ± 0.79	< 0.001*	< 0.001*	< 0.001*
Combination therapy	IPSS	19.82 ± 3.09	12.05 ± 2.65	8.89 ± 2.60	< 0.001*	< 0.001*	< 0.001*
	Voiding symptoms	10.82 ± 2.48	6.41 ± 2.06	4.03 ± 1.91	< 0.001*	< 0.001*	< 0.001*
	Storage symptoms	9.26 ± 2.57	5.62 ± 1.63	4.84 ± 1.68	< 0.001*	< 0.001*	< 0.001*
	QoL	4.33 ± 0.70	2.10 ± 1.02	1.41 ± 0.86	< 0.001*	< 0.001*	< 0.001*
Control group	IPSS	7.21 ± 1.28		7.05 ± 1.39			0.509
	Voiding symptoms	3.49 ± 1.50		3.36 ± 1.44			0.463
	Storage symptoms	3.72 ± 1.17		3.69 ± 1.08			0.875
	QoL	1.95 ± 0.94		1.56 ± 0.79			0.017*

*** – statistically significant difference; SD – standard deviation; IPSS – International Prostate Symptom Score; QoL – Quality of Life; mths – months.**

Voiding symptoms referred to in IPSS significantly improved in all the therapy groups. The greatest improvement occured with combination therapy (-6.86 ± 2.85), followed by finasteride (-5.51 ± 2.30) and tamsulosin treatment (-3.95 ± 2.17). Storage symptoms referred to in IPSS also improved significantly in all the therapy groups. The greatest improvement was reported in the combined therapy group (-4.38 ± 2.47), followed by the finasteride group (-3.51 ± 1.50) and, finally, the tamsolusin group (-2.16 ± 1.57).

Measurement of the effects of hormonal changes on sexual desire demonstrated the presence of significant improvement in patients submitted to tamsulosin at the end of the treatment (+0.78 ± 1.00), recording no significant changes in the other two therapy groups.

Pharmacologic therapy of BPH produced significant side effects on sexual desire in patients by disrupting their orgasmic function and EjD (Table 3). A significant disruption of orgasmic function was most prominent in the group on tamsulosin (-1,03 ± 1,94), followed by the group on combined therapy (-0.76 ± 2.07), while in the finasteride group this change was insignificant (-0.54 ± 1.68).

Significant EjD was reported in all the therapy groups. It was most prominent in the group receiving tamsulosin (-4.38 ± 2.55), with the decline in the ejaculatory function in 25 (64%) patients, whereas no change was recorded in 14 (36%) patients. This is followed by the combined therapy group (-3.89 ± 2.84) and the decline of function in 23 (59%) patients, no changes in 13 (33%) patients and the improvement in 3 (8%) patients. In the finasteride group (-1.49 ± 2.52) the decline was recorded in 15 (38%) patients, no changes were found in 19 (49%) patients while the improvement was reported by 5 (13%) patients.

The complete absence of ejaculation was recorded in the group receiving combined therapy in 9 patients (23%), in 6 patients (15%) being administered tamsulosin and in 2 patients (5%) on finasteride.

The control group showed the improvement in Qmax ($p = 0.002$), QoL ($p = 0.017$) and sexual desire ($p = 0.005$), although this was not a standard control group as the patients were given recommendations on lifestyle adjustments. The values of other scores did not change significantly (Table 4).

Six months of administration of pharmacologic therapy for BPH treatment is considered short time. There were no patients with the acute urine retention during therapy, nor were they in need of prostate surgery.

Discussion

A decrease in PV by the end of the study in the groups on finasteride (by 14.4%) and combination therapy (14.2%) indicates their almost identical therapeutic effect. In patients using only tamsulosin no significant changes occurred as the drugs from the AB group do not affect the growth of prostatic glandular tissue. Alleviating subvesical obstruction by reducing PV lead to a significant increase of the Qmax and Qave. The effect of finasteride also resulted in a greater reduction in VT and PVR compared to the same effect reported for the tamsulosin group.

Table 3

Score values of sexual desire, orgasmic function and ejaculatory dysfunction (EjD) during the study across therapy groups

Therapy group	Score	Testing (mean ± SD)			Comparison between testing *(p)*		
		Baseline (I)	After 3 mths (II)	After 6 mths (III)	I *vs* II	II *vs* III	I *vs* III
Tamsulosin	Sexual desire	6.69 ± 1.49	7.31 ± 1.47	7.46 ± 1.41	0.005*	0.554	< 0.001*
	Orgasmic function	8.36 ± 1.88	7.67 ± 1.84	7.35 ± 1.72	0.043*	0.066	0.003*
	EjD	10.49 ± 2.43	7.46 ± 2.67	6.22 ± 2.31	< 0.001*	0.001*	< 0.001*
Finasteride	Sexual desire	6.56 ± 1.52	6.41 ± 1.50	6.03 ± 1.46	0.504	0.141	0.053
	Orgasmic function	7.92 ± 2.02	8.00 ± 1.45	7.38 ± 2.07	0.760	0.010	0.053
	EjD	9.26 ± 2.68	8.49 ± 2.13	7.77 ± 2.50	0.004*	0.035*	0.001*
Combination therapy	Sexual desire	5.92 ± 1.68	6.10 ± 1.55	6.19 ± 1.60	0.382	0.918	0.368
	Orgasmic function	6.79 ± 2.25	6.10 ± 2.09	5.97 ± 2.32	0.048*	0.650	0.033*
	EjD	8.56 ± 3.08	5.77 ± 2.75	4.59 ± 2.50	< 0.001*	< 0.001*	< 0.001*

*** *p* – statistically significant difference; SD – standard deviation; mths – months.**

Table 4

The values of variables during the study in the control group

Variables	Testing (mean ± SD)		Comparison between testing *(p)*
	Baseline	After 6 mths	
PSA (ng/mL)	1.09 ± 0.48	0.97 ± 0.75	0.240
Free PSA (ng/mL)	0.29 ± 0.15	0.27 ± 0.15	0.302
TotalT (ng/mL)	4.40 ± 1.60	4.59 ± 1.82	0.505
FreeT (pg/mL)	12.31 ± 4.57	13.19 ± 5.40	0.181
FreeT/TotalT (%)	0.66 ± 2.28	1.00 ± 3.09	0.302
Voiding Time (s)	39.80 ± 12.40	41.13 ± 12.08	0.468
Qmax (mL/s)	18.40 ± 4.01	19.65 ± 4.68	0.002*
Qave (mL/s)	10.62 ± 2.98	10.62 ± 2.41	0.989
PVR (mL)	20.28 ± 17.44	19.59 ± 15.97	0.780
Sexual desire	6.92 ± 1.94	7.56 ± 1.60	0.005*

*** *p* – statistically significant difference; SD – standard deviation.**
For abbreviations see under Table 1.

The largest decline in PSA and fPSA levels in the groups on combination therapy and finasteride was expected because they accompany the enlarged volume of hyperplastic tissue. The decreased PSA levels in the tamsulosin group may be explained by relieved voiding and less irritation of the prostate tissue caused by reducedi ntravesical pressure and pressure in the prostatic urethra during urination.

The Proscar Long-Term Efficacy and Safety Study (PLESS) investigated the effects of finasteride during 4 years. Finasteride reduced PV by 17.9% compared to its increase of 14.1% in the placebo group. Urinary flow significantly improved with a decreased risk of surgical treatment by 55% [12]. New analysis of Medical Therapy of Prostatic Symptoms (MTOPS) studies shows the significant reduction of clinical progression of BPH by finasteride with PV > 30 mL (decrease of 5.79 mL), and with no significant effects in patients with PV < 30 mL (an increase of 0.28 mL) [13].

In a study by Zabkowski [14] finasteride led to a decrease in PV up to 40% after 12 months. In their 5-year retrospective analysis of 5-ARI effects, Kaplan et al. [15] pointed out that finasteride and other 5-ARI dutasteride, are similarly effective in reducing PV and improving Qmax and LUTS in BPH patients after 12 months of administration. Dutasteride significantly reduces PSA and PV after just 3 months of the therapy.

Preclinical studies show that the new GhRh and LhRh antagonists can cause a decrease in PV by direct inhibitory action of GhRh and LhRh (growth hormone-releasing hormone and luteinizing hormone-relating hormone, respectively) antagonists *via* prostate receptors [10]. It is believed that the IPSS is significantly correlated with age, PV and totalT, but not with freeT or serum levels of other sex hormones [16]. The mean PSA level and the average PV significantly increase with age. The mean level of PSA increases about 0.3 ng/mL every 10 years [17].

Dihydrotestosterone levels increase after the age of 40 due to the inability of peripheral tissue to use freeT which remains in serum in DHT form. The values of freeTand freeT/totalT ratio were significantly reduced in the groups on finasteride and combination therapy. However, this did not significantly change the level of sexual desire after six months of the therapy. In two groups of patients who had used finasteride as monotherapy or as a part of combination therapy, a total of 41% had slight deterioration in sexual desire. Extremely decreased sexual desire (from the previous normal or mild dysfunction to the level of difficult function or the occasional occurrence of sexual desire) was reported by 7.7% of the patients, all in the finasteride group. Combination therapy slightly improved sexual desire probably due to the positive effect of tamsulosin on erectile function. There was no single case of complete absence of sexual desire. Only the group using tamsulosin experienced a significant improvement in sexual desire with significant improvement of urination. Opinions are divided over whether AB therapy leads to the improvement of sexual desire by improving LUTS and consequently the erectile function or whether the treatment affects the two processes separately [18].

Gur et al. [19] state that by reducing the DHT levels, finasteride results in a decrease or loss of sexual desire in 2–10%. Other data show that after 12 months of finasteride use, DHT levels decreased by 80% with no significant changes in serum testosterone while increasing Qmax by 1.6%, and decreasing the IPSS by 2.7% [9].

Primary side effects of pharmacologic treatment for BPH are decreased ejaculation and aggravated orgasmic function. They are most prevalent in the tamsulosin group and manifest themselves during sexual activity as the reduced number of ejaculations and the decreased ejaculatate volume or the complete absence thereof. The findings of other studies show that the administration of AB over a longer period leads to the higher incidence of EjD, while the combined therapy possess a three-times higher risk of EjD compared to that of an AB or 5-ARI monotherapy [20].

In the finasteride taking group, the aggravation of ejaculation occured mostly due to decreased ejaculate force. Sexual desire did not decrease significantly, as reported in major studies where administration of 5-ARI resulted in the loss of sexual desire in 2–10% and EjD in 0–8% [21]. Trost et al. [22] note that sexual desire decreases in 1.5% and EjD in 3.4% with the use of 5-ARI compared to that of the placebo.

Beneficial effect of 5-ARI on prostate is decreasing the risk of lower grade prostate cancer by changing the metabolism of androgens [9]. Despite the belief that androgens are necessary for the development and growth of the prostate, new epidemiological studies state that changes in androgen serum concentrations do not affect the processes within the gland regulated by androgens and that in older men the influence of androgens on PV and LUTS are not in harmony [3]. Only the age correlates with BPH (with a prevalence of 8% in the fourth decade to >70% in the seventh decade of life), while the potential effect of testosterone on LUTS may be indirect [23]. Kim et al. [24] reported that totalT level significantly decreased in patients with ≥ 4 episodes of nocturia and are significantly associated with the presence of expressed LUTS.

The efficacy of combination therapy compared to AB and 5-ARI monotherapy demonstrates significantly greater improvement in functional parameters and voiding symptoms by unifying common characteristics of action of two classes of drugs. The results of the recent studies demonstrated that the combination therapy leads to significant reduction of PV, PSA and IPSS and improvement of Qmax. The best effect in reducing the progression of BPH is seen in PV > 35mL and PSA > 2.0 ng/mL [25]. Symptoms improved by combination therapy and maintained after discontinuation of AB and continuous administration of 5-ARI monotherapy, whereas the risk of urinary retention due to the re-growth of the prostate is reduced [26].

Hormonal component of the pharmacological therapy in the form of finasteride as a monotherapy or as a part of combination therapy significantly reduced PV. It improved functional urinary parameters and alleviated difficulties with urination. At the same time the level of freeT and freeT/totalT ratio was reduced which led to a slight deterioration of sexual desire only in the patients from the finasteride group.

The limitations of this study lie in the fact that it is centred around a small number of respondents and that it involves a brief treatment period of six months with the absence of remote therapeutic results.

Standard pharmacologic treatment of BPH is still based on AB, 5-ARI and their combination [27]. Having in mind the preliminary findings of this paper and the findings of most other studies, this type of treatment should be personalized in the future according to the type of symptoms, the presence of sexual dysfunction and the risk of BPH progression. Patients need to be informed about any side effects the drugs might have on their sexual function, particularly if they are younger men and thus include them in the decision-making process regarding their treatment.

Conclusion

The use of pharmacologic therapy for BPH reduces the intensity of urinary symptoms and improves the QoL. The finasteride based therapy, as monotherapy or combination therapy, by the reduction of the PV may probably efficiently alleviate the disease progression. Androgenic hormone status is affected by the reduction of freeT levels which if used as finasteride monotherapy may slightly deteriorate sexual desire in men.

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