



Frequency of Common Complications During Treatment of Patients with Benign Prostate Hyperplasia

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Abstract

Background/Aim: Benign prostatic hyperplasia (BPH) is a very common disease in older men. BPH involves the presence of signs of hyperplasia of the stromal and epithelial elements in the prostate with consequent enlargement of its volume. The aim of this study is to analyse the frequency of typical complications in the treatment of patients with benign prostatic hyperplasia and the effect of medicamentous treatment.

Method: Patients diagnosed BPH were included in the prospective, one-year study. They were divided into 2 groups. The first group (30 patients) consisted of those ones, whose prostate volume was equal to or over 50 cm³, while and the second group (30 patients) comprised the subjects with prostate volume less than 50 cm³. The complications of BHP analysed are residual urine (RU), symptomatic urinary infection, haematuria, thickening of the detrusor wall, diverticulum in the bladder, ureterohydronephrosis, renal failure, bladder stone and acute urinary retention (AUR).

Results: The majority of patients in both groups were aged 60-69. There was a statistically significant difference in the average value of RU between the groups at the first, second and fifth check-ups ($p < 0.05$), as well as the complication of symptomatic urinary infection, since the same occurred earlier in the first group than in the second group ($p < 0.05$). There was no statistically significant difference in complications: haematuria, detrusor wall thickening and diverticulum ($p > 0.05$). Complications: ureterohydronephrosis, renal failure, bladder stone, and AUR were not diagnosed in patients in either group.

Conclusion: Relevant medical therapy leads to a reduction of RU and reduces the risk of complications caused by its presence. Other complications of BPH were rare or absent in both groups, suggesting that appropriate and timely applied medical therapy affects the course of BPH and reduces the risk of complications and the need for surgical treatment. Benefit from medicamentous therapy is equally represented in both analysed groups of patients.

Key words: prostate; benign hyperplasia; prostatic obstruction; complications.

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Introduction

Benign prostatic hyperplasia (BPH) is a histological term for benign prostatic enlargement and it is usually based on the gland size. The ex-

act aetiology of BPH is unknown. It is common in older men, and it is characterised by direct obstruction of the bladder outlet (the static com-

ponent) as well as increased muscle tone within the gland (the dynamic component). There are several synonyms and descriptions of several forms for the same one. These are: benign prostatic enlargement (BPE), benign prostatic obstruction (BPO) or benign outlet obstruction (BOO). It is also described through lower urinary tract symptoms (LUTS), which is a term that refers to a group of symptoms that originate from the lower urinary tract.

Prostate enlargement is a key clinical sign of the BPH and it is often accompanied by symptoms labelled as LUTS, and which significantly affect the quality of life of these patients. However, it is known that prostate size itself does not correlate well with the intensity of the BPH symptoms. Isolated prostate enlargement and the consequent compression of the posterior urethra are not the only reasons for the appearance of clinical symptoms. Detrusor dysfunction caused by various age-related changes plays an important role. At the same time, the obstruction itself (in this case caused by enlargement of the prostate) causes neural changes on the detrusor that further contribute to the formation and development of symptoms of clinical (symptomatic) BPH.1-6

The aim of this study is to analyse the frequency of typical complications in the treatment of patients with benign prostatic hyperplasia and the effect of medicamentous treatment in groups patients with two different stages of BPH.

Methods

Patients who were diagnosed with BPH were included in the prospective, one-year study. Participants were divided into 2 groups. The first group (30 patients) consisted of patients whose prostate volume was equal to or over 50 cm³ and the second group (30 patients) consisted of subjects with prostate volume less than 50 cm³.

BPH was diagnosed based on patient history, digital rectal examination, prostate specific antigen (PSA) and ultrasound (US) examination of the urinary tract. The following laboratory

parameters were monitored simultaneously: urea, creatinine, C reactive protein (CRP), PSA, erythrocyte sedimentation (ES) and blood count (BC) and urine sediment and urine culture (UC) with antibiogram. The complications of BHP analysed were residual urine (RU), symptomatic urinary infection, haematuria, thickening of the detrusor wall, diverticulum in the bladder, ureterohydronephrosis, renal failure, bladder stone and acute urinary retention (AUR).

All participants were given standard medical therapy. Patients with prostate less than 50 cm³ were given only alpha-adrenergic blocker (tamsulosin). Patients with a prostate equal to or larger than 50 cm³ were given an alpha-adrenergic blocker (tamsulosin) and a 5-alpha reductase inhibitor (finasteride). Patients were followed for 12 months with check-ups every 3 months and determination of PSA and digital rectal examination after 6 and 12 months. They were instructed to report immediately for check-up in case of acute complications (symptomatic urinary infection, acute urinary retention, haematuria) or significant exacerbation of the problems. Statistical data processing was performed by using χ^2 test, analysis of variance (ANOVA), Mann-Whitney U test and Student t-test.

Results

Table 1 shows the distribution of patients by age decades.

Table 1: Age of patients with benign prostate hyperplasia

Decade		First group	Second group	Total
From 50 to 59	N	1	3	4
	%	3.3	10.0	6.7
From 60 to 69	N	19	16	35
	%	63.3	53.3	58.3
From 70 to 79	N	6	8	14
	%	20.0	26.7	23.3
80 and more	N	4	3	7
	%	13.3	10.0	11.7
Total	N	30	30	60
	%	100.0	100.0	100.0

There was a statistically significant difference ($\chi^2 = 39.067$; $p < 0.05$) in the distribution of patients by age. Patients from aged 60 to 69 were the most common.

Results and statistical comparisons of differences in the frequency of typical complications in the treatment of patients with benign prostatic hyperplasia: residual urine (RU), symptomatic urinary infection, haematuria, detrusor wall thickening, and diverticulum are presented in Tables 2-5.

Table 2: Decrease in the average residual urine size in patients with benign prostate hyperplasia

Check-up	N	Minimum	Maximum	Mean value	Standard deviation
Residual urine – patients of the first group					
First	30	20.00	150.00	34.33	23.00
Second	30	10.00	150.00	27.00	24.37
Third	30	10.00	140.00	24.00	23.17
Fourth	30	10.00	130.00	22.17	21.44
Fifth	30	10.00	120.00	21.00	19.63
Residual urine – patients of the second group					
First	30	20.00	150.00	34.33	23.00
Second	30	10.00	150.00	27.00	24.37
Third	30	10.00	140.00	24.00	23.17
Fourth	30	10.00	130.00	22.17	21.44
Fifth	30	10.00	120.00	21.00	19.63

In the first group of patients, the average residual urine value was highest at the first check-up and lowest at the fifth check-up. There was no statistically significant difference between the check-ups compared to the average RU in the first group (ANOVA test: $F = 1.701$; $p = 0.153$; $p > 0.05$), but there was a statistically significant difference between the check-ups in the average RU in the second group ($F = 12.501$; $p = 0.000$; $p < 0.05$).

Table 3: Symptomatic urinary infection in patients with benign prostate hyperplasia

		Check-up				
		First	Second	Third	Fourth	Fifth
First group						
Yes	N	0	2	0	0	0
	%	0.0	6.7	0.0	0.0	0.0
No	N	30	28	30	30	30
	%	100.0	93.3	100.0	100.0	100.0
Total	N	30	30	30	30	30
	%	100.0	100.0	100.0	100.0	100.0
Second group						
Yes	N	0	0	2	0	0
	%	0.0	0.0	6.7	0.0	0.0
No	N	30	30	28	30	30
	%	100.0	100.0	93.3	100.0	100.0
Total	N	30	30	30	30	30
	%	100.0	100.0	100.0	100.0	100.0

There was a statistically significant difference in the average value of RU among the groups at the

first check-up ($t = 2.118$; $p = 0.038$; $p < 0.05$), second check-up ($t = 2.031$; $p = 0.047$; $p < 0.05$), fifth check-up ($t = 2.061$; $p = 0.044$; $p < 0.05$). There was no statistical difference at the third and fourth check-ups ($p > 0.05$) (Table 2). At the same time, there was no significant difference between the first and second groups in the rate of decrease of the average RU. (Mann-Whitney U test; $U = 6.500$; $p = 0.663$; $p > 0.05$).

Symptomatic urinary infection was diagnosed in two patients of the first group at the second check-up (in one patient after 36 days and in another after 61 days) and in two patients of the second group at the third check-up (in one patient after 140 days and in the other one after 141 days) (Table 3). There was no statistically significant difference (Mann-Whitney U test: $p > 0.05$) between the patients of the first and second groups in the number of symptomatic urinary infections per check-up.

An analysis of the time of diagnosing the symptomatic urinary infection showed a mean value of 48.5 days in the first group and 140.5 days in the second group, with the difference being significant (t-test; $t = -7.35$; 0.018 ; $p < 0.05$).

Table 4: Occurrence of haematuria in patients with benign prostate hyperplasia

		Check-up				
		First	Second	Third	Fourth	Fifth
First group						
Yes	N	3	0	0	1	0
	%	10.0	0.0	0.0	3.3	0.0
No	N	27	30	30	29	30
	%	90.0	100.0	100.0	96.7	100.0
Total	N	30	30	30	30	30
	%	100.0	100.0	100.0	100.0	100.0
Second group						
Yes	N	2	0	0	0	1
	%	6.7	0.0	0.0	0.0	3.3
No	N	28	30	30	30	29
	%	93.3	100.0	100.0	100.0	96.7
Total	N	30	30	30	30	30
	%	100.0	100.0	100.0	100.0	100.0

Haematuria was diagnosed in 3 patients of the first group at the first check-up and in one patient on the fourth one, after 276 days from the first check-up. In the second group of patients on first check-up haematuria was ascertained in two cases and in one patient on the fifth check-up, ie after 365 days (Table 4). There was no statistically significant difference (Mann-Whitney U test: $p > 0.05$) between the patients of the first

and second groups according to the number of episodes of haematuria per check-up (Table 4).

Table 5: Changes in detrusor thickness in patients with benign prostate hyperplasia

		Check-up				
		First	Second	Third	Fourth	Fifth
First group						
Proper wall thickness	N	23	22	22	22	22
	%	76.7	73.3	73.3	73.3	73.3
Thickened wall	N	7	8	8	8	8
	%	23.3	26.7	26.7	26.7	26.7
Total	N	30	30	30	30	30
	%	100.0	100.0	100.0	100.0	100.0
Second group						
Proper wall thickness	N	27	27	26	26	26
	%	90.0	90.0	86.7	86.7	86.7
Thickened wall	N	3	3	4	4	4
	%	10.0	10.0	13.3	13.3	13.3
Total	N	30	30	30	30	30
	%	100.0	100.0	100.0	100.0	100.0

Detrusor wall thickness was found in 7 patients of the first group at the first check-up and in one patient after 90 days at the second check-up. In the second group it was found in 3 patients at the first check-up and in one patient on the third check-up, after 319 days (Table 5). There was no statistically significant difference between the first and second group in the number of patients with thickened detrusor wall on check-ups 1-5, ($p > 0.05$).

Diverticulum was present in one patient of the first group on first check-up. In the second group there were no patients with diverticulum and there was no statistically significant difference between the patients of the first and second groups according to this parameter. (Mann-Whitney U test: $U = 430.000$; $p = 0.317$; $p > 0.05$). At the same time, complications such as ureterohydronephrosis, renal failure, bladder stone, and acute urinary retention (AUR) were not diagnosed in either of the patient groups.

Discussion

BPH is a progressive disease with a frequency that successively increases mainly after the age of 50.¹⁻⁶ This study showed that patients aged 60 to 69 were predominant. Complications of BPH can occur immediately, but they can also

occur after many years of the onset of the first symptoms. Residual urine (RU) is an important factor in the evaluation of pathology of the bladder neck, prostate or urethra. Adequate RU measurement can only be performed after spontaneous voiding. A full bladder causes distension of the wall and reduces contractility of the detrusor, making it difficult for the bladder to complete voiding.

Measurement of RU can be expressed in absolute values, in millilitres, based on measurement of bladder diameter or relatively, as a subjective estimate of RU relative to full bladder capacity. Accurate measurement of RU is achieved by measuring the largest transverse, longitudinal and anteroposterior diameter of the bladder and since the bladder is usually oval in shape, the volume is calculated by multiplying all 3 diameters by 0.5. A residue measured in this way is of importance if less urine is left behind. Subjective data on the reduction of bladder volume before and after voiding is more significant in case when is RUT larger.³⁻¹⁰

In patients from the first group, the average RU value was highest at the first check-up and the lowest at the fifth check-up. There was no statistically significant difference between the check-ups compared to the average RU in patients of the first group, but there was statistically significant difference in the average value of the RU in patients of the second group. RU was higher in the first group at all check-ups than in the second group and there was no statistically significant difference between the first and second group of patients in the rate of decrease of the average RU. This is expected since the patients from both groups were initially included an alpha-adrenergic blocker, acting by relaxing the smooth muscles of the bladder neck, urethra and prostate and it acted to reduce RU equally in patients of both groups. At the first, second and fifth check-ups there was a statistically significant difference in the average value of residual urine between the patients of the first and second groups, while at the third and fourth check-ups there was no statistically significant difference.

Urinary infection in BPH patients is a product of the presence of RU and reduced body resistance. The infection in patients with BPH and significant RU is much more serious than in patients with anatomically and functionally normal urinary tract. The bacteria causing the infection

often come ascending from the urethra and then multiply in the bladder. Bladder is infected, significantly less frequently, by haematogenous, lymphogenous or per continuitatem route from the surrounding foci (from the prostate in chronic bacterial prostatitis). Nephrolithiasis and diverticulosis of bladder also support the persistence of the infection.³⁻¹⁰ The infection can be limited to the prostate or bladder or it can affect the kidney. According to the resistance of the organism and adequate antimicrobial therapy, the infection recovers relatively quickly.³⁻¹²

In this study, there was no significant difference between patients of the first and second group regarding the number of episodes of symptomatic urinary infections per check-up. There was a (statistically significant) difference between the first and second groups when it came to the time of diagnosing these complications. In the first group, symptomatic urinary infection occurs in a shorter period of time than in the second group. This may be partly explained by higher RU in patients of the first group, which is a precipitating factor for urinary infections.

Haematuria is a common complication of BPH. It can be microscopic or macroscopic. Sometimes it is so extensive, that causes bleeding. The causes are different. Spontaneous haematuria is explained by severe congestion of the hyperplastic prostate and sclerotic changes of blood vessels. The cause is sometimes the prostate infarction. In patients of both groups, no significant difference in the number of episodes of haematuria per check-up and the mean time of finding complications was found. Haematuria did not occur in large numbers because the patients regularly used prescribed medication therapy with the proposed diet, thus reducing the possibility of congestion of adenoma and occurrence of significant hematuria.⁴⁻¹⁴

Bladder wall thickening, occurrence of trabeculae and diverticulum are changes in the bladder that occur due to obstruction. In the analysis presented here, the occurrence of complications in the form of thickening of the detrusor was monitored. The same occurs earlier in the development of complications on the bladder wall than the diverticulum, so the incidence is higher. Detrusor thickening was also found to be more common in patients in the first group than in patients in the second group, at all check-ups. This finding is expected since a larger volume of the prostate indicates prolonged, more intense

subvesical obstruction. Detrusor thickening was verified if the ultrasonographically measured detrusor thickness was over 5 mm.⁴⁻¹⁴

Diverticulum of the bladder is a common complication in the late stage of BPH and it is caused by loosening of the stretched wall. In one study of 300 patients, diverticulum was found in 10 (3.4 %) patients and secondary diverticulosis in 38 (12.6 %) patients.⁷ In patients from this study diverticulum was present in only one patient of the first group.

Renal insufficiency is often present in the late stages of BPH. It is caused by dilation of the upper urinary tract and subsequent urinary compression on the kidney parenchyma, as well as occasional kidney infections. Ureterohydronephrosis, accompanied by varying degrees of renal insufficiency, occurs in patients with large RU and decompensated bladder. Ureterohydronephrosis and renal insufficiency were not observed during this study. The patients in the present study did not have an AUR and/or RU over 300 mL, so this complication did not develop.⁶⁻¹⁷

AUR is a very common complication of BPH. It is caused by a conglomerate: sphincter spasm, detrusor hyperdistension, congestion and prostate infarction. It may develop suddenly or gradually, with the progressive enlargement of RU. Acute complete retention may occur at all stages of BPH. The causes of acute retention are complex: hyperdensity of detrusor muscle fibres, congestion and prostate infarction, sphincter spasm.^{6, 10-20} According to one study performed in 300 patients, 231 (77 %) had different forms of retention during of BPH. Complete retention as the first sign of BPH, occurred in 52 (17.6 %) patients.⁷

AUR was not present in the patients of either groups. As all patients included in the study received medical therapy (alpha-adrenergic blocker or combination therapy of alpha-adrenergic blocker + 5-alpha-reductase inhibitor). Also, the relatively short follow-up time (one year) within the analysed study should be considered.

Bladder calculi is a relatively common complication of BPH. It is mainly secondary, for urinary tract and infection.¹⁹ The incidence of this complication in the group of 300 patients was 49 (16.3 %) patients.⁷ Bladder calculi in patients with BPH occurs due to a urinary stasis com-

bined with infection. These calculi are secondary, mainly due to infection, with a basis that lies in the urinary tract.^{6,10-20} The bladder calculi were not verified in the patients presented in this study. Given that there were not many patients with a large amount of post-voiding RU and with long-term urinary infection due to the inclusion of adequate antibiotic therapy, as well as a limited time of this study, it is believed that this is the reason why this complication did not occur.

Conclusion

The majority of patients in both groups were aged 60-69. Medicamentous therapy leads to a reduction of RU and reduces the risk of complications caused by its presence. Other complications of BPH were rare or absent in both groups, suggesting that appropriate and timely applied medical therapy affects the course of BPH and reduces the risk of complications and the need for surgical treatment. Benefit from medicamentous therapy is equally represented in both analysed groups of patients.

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Conflict of interest

None.

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