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IMPACT OF SYMPTOM SEVERITY SCORE AND TYPE OF TREATMENT ON QUALITY OF LIFE IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

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Abstract: Benign prostatic hyperplasia (BPH) is the fourth most common disease in the male population aged over 50 years which results in lower urinary tract symptoms (LUTS). These symptoms lead to affect patients' quality of life (QoL) differently. Quality of life (QoL) refers to the subjective perception of a patient`s well-being in terms of physical, psychological, and socioeconomic aspects. Aging and worsening LUTS/BPH are contributing factors to decreased QoL. Several medicament options that include alpha-blockers and 5 alpha-reductase inhibitors as a "gold" standard, are available for LUTS/BPH treatment. This paper aims to evaluate the effects of pharmacological treatments used to treat LUTS /BPH in daily practice and to allow a comparison of results between treatments. We evaluated 250 patients with BPH using the International Prostate Symptom Score (IPSS) questionnaire, including the eighth question on quality of life concerning the severity of symptoms and the type of drug therapy with which they were treated. When analyzing the results, we concluded that patients with less pronounced symptoms of the disease have a better quality of life ($p<0.05$), while those patients with more severe symptoms and those who have the appearance of side effects from the therapy have a worse quality of life. ($p<0.05$). In conclusion, we provide additional evidence of the impact of two different medicament strategies for BPH treatment on patients' QoL to help further inform decision-making regarding treatment strategies in this patient population. A holistic approach is needed in the management of BPH, leading to better QoL in BPH patients.
Keywords: BPH, lower urinary tract symptoms, quality of life

1. INTRODUCTION

Benign prostatic hyperplasia (BPH) with associated lower urinary tract symptoms (LUTS) is the fourth most common disease in the male population older than 50 years (Noweir et al., 2022). According to the latest knowledge, 1 in 4 men will suffer from BPH during their lifetime (Lee et al., 2017).

The prevalence of BPH increases with age, reaching 90% in men in their ninth decade. (Berry et al., 1984). The SNAPSHOT study provided the most recent data on the prevalence of BPH, ranging from 13.84% to 23.79% in five Middle Eastern countries (Noweir et al., 2022).

Health-related QoL is defined as the subjective perception of overall well-being status in terms of physical, mental, socioeconomic, and spiritual aspects, and BPH affects it by inducing disturbance in psychological well-being due to anxiety and worsening social function (Karimi et al., 2016).

Lower urinary tract symptoms (LUTS) consist of irritative or storage symptoms such as frequency, urgency, urge incontinence, and nocturia as well as obstructive or micturition symptoms such as straining, hesitancy, postvoid dribbling, and incomplete emptying. Symptoms of the lower urinary tract caused by BPH have a disturbing effect on the overall life of patients, their habits, and socialization. (Pinto et al., 2015). Patients state that every time they leave the house with the need for the toilet, they feel uncomfortable due to frequent visits to the toilet when they are in company, or they feel tired and sleepless due to nocturia.

The medical treatment of BPH consists of the use of alpha-adrenergic blockers, a 5-alpha-reductase inhibitor, phytotherapy, combined therapy, antimuscarinic agents, and inhibitors of phosphodiesterase type 5 and beta 3 agonists, which improve the symptoms of BPH. However, the occurrence of side effects from these medications, more or less, in certain individuals limits their use. Their use sometimes negatively affects their daily activities and health-related quality of life (Gravas et al., 2015).

Studies of this type are valuable because they complement data obtained in controlled clinical trials, where patients, centers, and compliance may not be representative of wider clinical practice. (Mishra et al., 2006).

This paper aims to evaluate the impact of LUTS/BPH on the patient's QoL as well as the effects of tamsulosin and dutasteride that are used in the treatment of LUTS/BPH in daily practice allowing a comparison of results between two treatment modalities

2. MATERIAL AND METHODS

This is a prospective controlled clinical study that included a total of 250 patients aged 45-70 with no previous history nor treatment for BPH, allocated n=130 to the control group (CG) patients treated with tamsulosin and n=120 patients to investigated group (IG) treated with combination therapy with tamsulosin and dutasteride. The evaluation of lower urinary tract symptoms was done through the International Prostate Symptom Score (IPSS) questionnaire, including a question about the quality of life contained under number 8 in the IPSS questionnaire, with independent interpretation. The final symptom score obtained from the IPSS questionnaire classifies patients into three groups of BPH patients: patients with mild (1-7), moderate (8-19), and severe (20-35) symptoms. The patient's quality of life was evaluated through the eighth question of the IPSS questionnaire, which is graded from 1 to 5, where 1 indicates a “delighted”, 2 is a "satisfied” patient, 3 is "mostly satisfied”, 4 is“ half of the time satisfied, half dissatisfied”, 5 is “mostly unsatisfied” and 6 is for an “unhappy” patient.
Therapy in patients with BPH is determined depending on the volume of the prostate measured by echo sonography and the level of prostate-specific antigen (PSA). Those patients who had prostates with a volume of less than 40 g and PSA up to 4 ng/ml were prescribed tamsulosin therapy. BPH patients who had prostate size greater than 40g and PSA up to 4ng/ml were prescribed combination therapy with tamsulosin and dutasteride. The analysis of the studied parameters was done at the beginning (month 0), after 6 months, and after 12 months of therapy.
For participation in the research, all patients signed informed consent, and the same was conducted following ethical standards and the Helsinki Declaration of 1975, which was revised in Seoul in 2008. The research was approved by the ethics committee at the institution where it was conducted.

3. RESULTS

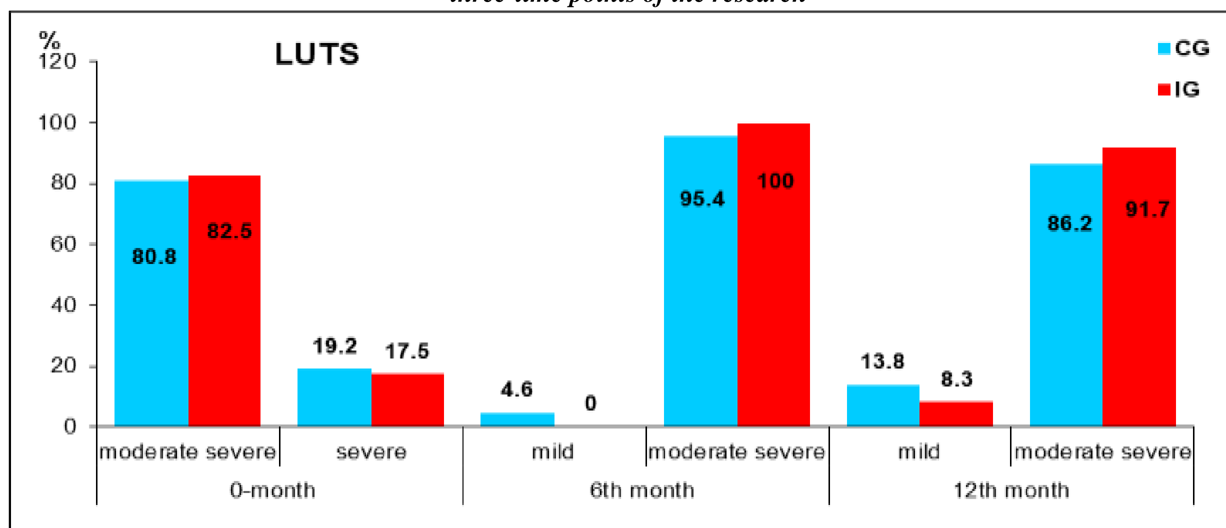
The patients included in the research had an average age of 59.84 ± 6.4 years; the youngest patient was 45 years old, and the oldest was 70 years old; most of the patients, 146 patients (58.4%) were in the sixth decade of life. Patients from the control group (CG) and the investigated group (IG) were homogeneous in terms of age, that is, they did not differ significantly in terms of average age (p=0.18) as shown in Table 1.

Table 1. Patients` age in the control (CG) and investigated (IG) group (t - Student t-test)

Group	**Age**		**p value**
	(mean ± SD)	**median (IQR)**	
CG	59.9 ± 6.7	45 – 68	t=0.3
IG	60.95 ± 5.4	45 – 69	p=0.18 ns

The severity of lower urinary tract symptoms measured by the IPSS questionnaire presented non-significantly different values in CG and IG before therapy (p=0.81), but significantly different values after 6 (p=0.000001) and 12 months of therapy (p=0.045), respectively. At both control time points after 6 and 12 months, patients treated with combination therapy had a significantly higher IPSS score than patients on monotherapy (mean 10.29 ± 1.7 vs 11.34 ± 1.4, median 10 vs 11 after 6 months of therapy; mean 9.12 ± 1.6 vs 9.32 ± 1.5, median 9 vs 10, after 12 months of therapy (graph 1).

Graph 1. Percentage display of patients according to lower urinary tract symptoms (LUTS) in both groups, at all three-time points of the research



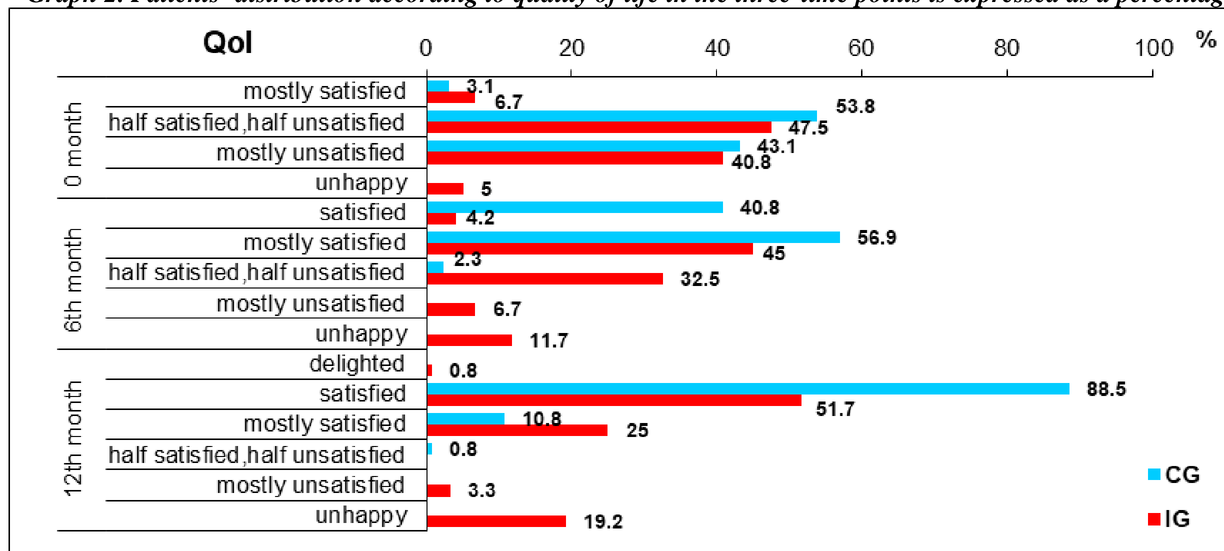
The quality-of-life assessment presented non-significantly different totals between the two groups of patients before therapy (p=0.7), and significantly different after 6 months and after 12 months of therapy (p<0.0001), because of significantly higher totals for the questionnaire obtained in patients treated with combination therapy. (Table 2).

Table 2. Comparative analysis of the values of the quality of life in CG and IG (Z - Mann-Whitney)

Group	**QoL**		**p value**
	mean ± SD	**median (IQR)**	
0 month			
CG	3.4 ± 0.5	3 (3– 4)	Z=0.4
IG	3.44 ± 0.7	3 (3 – 4)	p=0.7 ns
6th month			
CG	1.62 ± 0.5	2 (1– 2)	Z=8.8
IG	2.77 ± 1.05	3(2– 3)	p=0.000 sig
12th month			
CG	1.12 ± 0.5	1 (1-1)	Z=5.2
IG	2.11 ± 1.5	1 (1 – 2)	p=0.000 sig

In the analyzed period, patients on monotherapy and combination therapy had a significantly different quality of life, with a significance of (p=0.033) before the start of therapy, and (p<0.0001) after 6 and 12 months of therapy. Patients treated with combination therapy had a worse quality of life than patients in CG at the beginning of the study.
At the control examination after 6 months, a total of 53 (40.8%) patients from CG and 5 (4.2%) patients from IG were “satisfied” with the quality of life while “mostly unsatisfied” and “unhappy” were only 8 (6.7%) and 14 (11.7%), patients from the investigated group, respectively.
At the end of the follow-up, after 12 months, a total of 115 (88.5%) patients from CG and 62 (51.7%) from IG were “satisfied” with the quality of life. Fourteen (10.8%) patients from CG and 30 (25%) from IG were “mostly satisfied”. Twenty-seven patients from IG showed impairment of the QoL out of which 23 (19.2%) patients made qualification as “unhappy” and 4 (3.3%) patients were “mostly unsatisfied” (graph 2).

Graph 2. Patients` distribution according to quality of life in the three-time points is expressed as a percentage



The most common reasons for the worsened quality of life in 27 patients treated with combination therapy with tamsulosin and dutasteride were erectile dysfunction (ED), especially after 12 months of therapy and a combination of ED and impaired libido, while only one patient complied with disturbed ejaculation after 6 months (Table 3).

Table 3. Reasons for the deterioration of quality of life in the two control time points in the group with combined therapy (ED-erectile dysfunction)

	n (%)	**low libido +ED**	**ED**	**disturbed ejaculation**
6th month				
satisfied	**0**	**0**	**0**	**0**
mostly satisfied	**3 (11.11)**	**3**	**0**	**0**
Half satisfied-half unsatisfied	**2 (7.41)**	**2**	**0**	**0**
mostly unsatisfied	**8 (29.63)**	**2**	**6**	**0**
unhappy	**14 (51.85)**	**5**	**8**	**1**
12th month				
delighted	**0**	**0**	**0**	**0**
satisfied	**0**	**0**	**0**	**0**
mostly satisfied	**0**	**0**	**0**	**0**
Half satisfied/half unsatisfied	**0**	**0**	**0**	**0**
mostly unsatisfied	**4 (14.81)**	**0**	**4**	**0**
unhappy	**23 (85.19)**	**8**	**15**	**0**

4. DISCUSSION

The analysis of the results in this paper showed that after the inclusion of medical therapy for BPH in both groups there was a significant improvement in LUTS and as a result an improvement in the quality of life. The number of those who had a shift in the IPPS score in the direction of improvement of LUTS increased significantly after 6 months in the control group and after 12 months in both the control and the study groups ($p<0.0001$). In the studied group, side effects appeared in 27 patients, and as a result, these patients complained of a deterioration in their quality of life. Erectile dysfunction, isolated or in combination with reduced libido and impaired ejaculation, was indicated as the reason for the deterioration of QoL. This indicated that apart from the severity of the symptoms, the type of medical therapy also affects the quality of life.

According to the Guidelines, the combination therapy with alpha 1 blocker and 5ARIT is the preferred medical treatment for BPH due to the significant reduction of the risk of progression of LUTS/BPH, acute urinary retention, and need for surgical treatment but it has a higher incidence of sexual side effects (Zhou et al., 2019).

From the results obtained in our study, it was confirmed that the type of medical treatment of patients with BPH, whether only with tamsulosin or a combination of tamsulosin and dutasteride has a similar impact on the severity of lower urinary tract symptoms but it differs in the impact to the QoL regarding the side effects. Alpha-blockers (tamsulosin) act quickly and relax the smooth muscles of the lower urinary tract leading to a reduction in LUTS, especially the irritative symptoms. On the other hand, 5ARIs, acting as antiandrogens, prevent further growth of the prostate and lead to a reduction in volume by up to 30%, thus reducing the obstructive symptoms of the lower urinary tract. The combination of these two drugs has the maximum effect in reducing LUTS (Roehborn et al., 2010).

A multicenter study assessed the effect of pharmacologic treatment of LUTS/BPH on disease-specific and generic QoL measures and concluded that 5 years after symptom onset, previously treated BPH patients, had significantly impaired QoL in patients in a manner comparable to other chronic diseases (Bhatt et al., 2021).

The two large studies addressing the superiority of combination therapy for the treatment of BPH, MTOPS (McConnell et al. 2003) and CombAT (Roehborn et al., 2010) highlight the effect of combination therapy of an alpha-blocker and a 5ARIs on the severity of LUTS, reducing the risk of acute urinary retention (AUR), and the need for surgical treatment as superior to monotherapy, except for the occurrence of side effects of 5ARIs treatment.

In our analysis, we confirmed that the majority of patients on combined therapy who experienced side effects cited the occurrence of erectile dysfunction (70.3%) and combined ED with impaired libido (29.7%) as the reason for the deterioration of the quality of life, which is a clear indication that the occurrence of side effects of 5ARI therapy has a significantly deteriorates the quality of life of BPH patients.

5. CONCLUSION

The quality of life of BPH patients is significantly affected both by the severity of lower urinary tract symptoms caused by BPH significantly and the type of pharmaco-therapy. With this study, we provide additional evidence of the impact of two different medicament strategies for BPH treatment on patients' QoL to help further inform decision-making regarding treatment strategies in this patient population. A holistic approach headed towards the patient as an individual is needed in the management of BPH, leading to better QoL in BPH patients.

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