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Effect of medical treatment on outcome of benign prostatic hyperplasia in patients followed in the University Teaching Hospital of Kigali

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ABSTRACT

INTRODUCTION: Management of lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) includes watchful waiting, pharmacotherapy and surgical intervention. This study aimed to determine the effect of medical therapy on LUTS in patients with BPH in Rwanda.
METHODS: This was a one-year prospective observational study in men over 40 years with LUTS due to BPH. Patients were followed at 1, 3, and 6 months. We recorded post-void residual urine (PVR), prostate size, International Prostate Symptom Score (IPSS), and BPH medications. Logistic regression analyses were used to assess the relationship between medical treatment and outcomes of interest.
RESULTS: A total of 163 patients were enrolled. Adherence to treatment was 151/154 (98%) at one month and 133/151 (88%) at 6 months. The reason of no adherence was ignorance in 11/17 (65%), drug was not available 3/17 (18%), and 2/17 (12%) were lacking money.
Medical therapy was associated with a decrease in IPSS score of more than 4 points after 3 months and the relationship was statistically significant after adjusting to the initial prostate size as a confounder (p =0.01 and p=0.02, respectively). Medical treatment was also associated with mean decrease in PVR at 3 and 6 months, respectively (p: 0.03 at 3 month and p 0.04 at 6 months).
CONCLUSION: Medical treatment for BPH was associated with decreased IPSS and PVR in Rwanda. Medical therapy offers an alternative to surgical treatment in low-resource areas with limited surgical services. Advocacy efforts should focus on ensuring affordable access to these medications.

Keywords: Benign prostatic hypertrophy, Rwanda, lower urinary tract symptoms

INTRODUCTION

Benign Prostate Hypertrophy (BPH) is a common condition in elderly men and is characterized by an enlargement of the prostate gland. The incidence of BPH increases with age and affects almost 50% of men above 50 years [1]. BPH affects the quality of life of many men due to bothersome lower

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urinary tract symptoms (LUTS) such as urinary frequency, urgency, hesitancy, weak stream, and nocturia. Studies on BPH are challenged by lack of universal definition of clinical BPH. Some studies utilize a combination of histological diagnosis or LUTS related to it, such as post void residual (PVR) and urinary flow rate volume, to define clinical BPH [2].

Initial choices in the management of LUTS of BPH origin include watchful waiting, medical treatment and surgical intervention [3]. Treatment choice is made together with the patient and individualized to patients' circumstances and personal preference. Ultimately the choice of treatment depends upon its efficacy, speed of onset, durability, tolerability as well as the patient's preference. Because the average patient with LUTS of BPH origin has a remaining life expectancy of 15–20 years, both short-term and lifetime management outcomes should be considered [4,5].

Over recent years, medical treatment has become the primary choice for symptomatic BPH, and has been shown to improve short-term outcomes in terms of maximum flow rate and international prostate symptom scores (IPSS). Medical therapy can include alpha blockers, 5-alpha reductase inhibitors (5ARIs), or a combination of both medications. These medical treatments have been shown to improve LUTS and reduce prostate volume in clinical trials[6][7]. Different studies define BPH improvement for patient on medical treatment as decrease in IPSS of 4 points below the baseline[8]. However, the effectiveness of medical treatment in a real-world setting, particularly in low-income countries, remains unclear.

Currently, Rwanda has 12 urologists serving a population of around 13millions. BPH is one of the most common conditions managed by urologists. Previously medications for BPH were expensive, and patients relied on open prostatectomy or transurethral resection of the prostate (TURP) for management of BPH. Due to the scarcity of urologists and surgical infrastructure, there was a long list of old men waiting for BPH surgery. A study by Umuhire et al [9] showed that the prevalence of BPH among men aged 50 years and above in Rwanda was 33.6%, and that LUTS had a significant negative impact on the quality of life of affected individuals. In Rwanda, recently there has been introduction of different generic BPH drugs which caused a significant drop in cost of medication and greater access to medications for BPH. Currently medical management of BPH in Rwanda is more prevalent than surgical options.

In Rwanda, there is limited data on the management of BPH and the factors that influence the treatment outcome. This study aims to evaluate the effectiveness of medical treatment for BPH in a real-world setting and identify factors that influence treatment outcomes in patients followed at a referral hospital in Rwanda.

METHODS

Study design and settings: This was a prospective observational study conducted at Kigali University Teaching Hospital (CHUK), a referral hospital in Rwanda to evaluate the effect of medical treatment on BPH in patients. This study follows Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [10].

Study population: The study enrolled patients with BPH who were taking medical treatment. The inclusion criteria were patients diagnosed with BPH and receiving medical treatment. The exclusion criteria were patients with prostate cancer or any other malignancy, those with a history of prostate surgery or radiation therapy, and those with severe comorbidities that could affect the study outcomes. The patients were followed up at enrollment, and after 1, 3, and 6 months.

The medical treatment included monotherapy with alpha blockers, 5ARIs, or combined therapy with both. The primary outcome measure was the change in the IPSS after 1, 3 and 6 months of treatment. Secondary outcome measures included changes in post void residual (PVR) and other clinical parameters.

Data collection: Data were collected on demographic and clinical characteristics, including age, past medical history, creatinine levels, total prostate specific antigen (PSA), prostate size, PVR, LUTS, adherence to treatment and reason for non-adherence. There was no urodynamic machine available during the study period, therefore flow rate was not included in our data.

Data analysis: Data were analyzed using descriptive statistics, including mean, standard deviation (SD), median, interquartile range (IQR), frequency, and percentage. Bivariate and multivariate logistic regression analyses were

Table 1: Patient characteristics on study enrollment (N=163)

		Frequency (%)
Age, mean (standard deviation)		68 (8.6)
Past Medical History	Hypertension	36 (23)
	Diabetes	1 (1)
	Diabetes mellitus and Hypertension	12 (8)
	STD/HIV	2 (1)
	Recurrent urinary tract infections	14 (9)
	None	95 (59)
Past Surgical History	Inguinal hernia repair	20 (12)
	Transurethral resection of prostate	7 (4)
	Other	10 (6)
	None	126 (77)
Eastern Cooperative Oncology Group (ECOG)	0	10 (6)
	1	86 (53)
	2	47 (29)
	3	20 (12)
Digital rectal examination	Nodules/tender	62 (38)
	Smooth, no nodule	101 (62)
Full bladder		17 (10)
Catheter at consultation		9 (6)
Laboratory values (median, interquartile range)	Urea (Millmol/l)	4.2 (3.3, 4.8)
	Creatinine (micromol/l)	76 (67.8, 87.8)
	Total prostate specific antigen (ng/ml)	6 (1.62, 14.1)
	Free prostate specific antigen (ng/ml)	1.22 (0.48, 2.41)
Prostate volume on ultrasound (g)		67 (48, 88)
Prostate on ultrasound	Heterogeneous	43 (27)
	Homogeneous	119 (73)
Post void residual (ml)		75 (56, 126)
International Prostate Symptom Score (IPSS)		13 (10, 22)
Lower Urinary Tract Symptoms severity	Mild	23 (14.11)
	Moderate	88 (53.99)
	Severe	52 (31.90)
Quality of Life		4 (3, 5)
Treatment given	Watchful waiting	8 (5)
	Monotherapy	17 (10.4)
	Combined therapy	138 (84.6)
Adherence to treatment	1 month	151/154 (98)
	3 months	142/149(95.
	6 months	133/151 (88)
Reason for non-adherence to drug (N=17)	Ignorance	11 (64.7)
	Drug not available	3 (17.6)
	No money	2 (11.8)
	Others	1 (5.9)
Cost of drug monthly (Rwandan francs); Median (Interquartile range)		15500 (4000, 18000)

used to assess the relationship between medical treatment and the outcomes of interest, adjusting for potential confounders such as age, baseline IPSS, and prostate size.

Ethical clearance was obtained from CHUK Research and Ethic Committee, with a reference number "Ref.:EC/CHUK/146/2021".
A written informed consent was obtained from all participants before enrollment. Confidentiality was maintained throughout the study.

RESULTS

We enrolled 163 patients with BPH taking medical treatment. Patients were put on different medical treatment for BPH and follow up data were collected at enrollment, at month one, month 3 and month 6. They were evenly distributed in all Rwanda districts (Table 1). The mean age was 68 years (SD=8.6). Most patients had no significant past medical history (n=95/160, 59%) but 49/160 (30%) had diabetes and hypertension and 14/160 (9%) had recurrent urinary tract infection (UTI). The majority (n=126/163, 77%) of patients had no prior surgery. Overall, 20/163 (12%) patients had prior inguinal hernia repair and 7/163 (4%) patients had prior TURP (Table 1).

LUTS were severe in 52/163 (32%), moderate in 88/163 (54%) and mild in 23/163 (14%). Seventeen (10%) patients came with urinary retention necessitating bladder drainage whereas 9/163 (6%) consulted with a urinary catheter.
The median creatinine was 76 micromol/L (IQR: 67.8, 87.8). The median total PSA was 6ng/ml (IQR: 1.62, 14.1). The median prostate size at enrollment was 67gr (IQR: 48, 88) and PVR was 75ml (IQR: 56ml, 126ml).
The majority (n=138, 85%) were taking combined therapy (alpha blocker and 5ARIs) and 17/163 (10%) took monotherapy (alpha blocker or 5ARIs). The adherence to treatment varied from 151/154 (98%) in month 1 to 133/151 (88%) in month 6. The reason of non-adherence was ignorance (n=11/17, 65%); drug was not available in the pharmacy (n=3/17, 18%), and lacking money (n=2/17, 12%).
After the first month of treatment, the association of medical treatment and decrease in IPSS was not statistically significant. The medical treatment

Table 2: Multivariate analysis of factors associated with IPSS reduction of more than 4 units for patients on BPH medical treatment.

			Bivariate analysis		Multivariate analysis		
			IPSS decrease >=4, N (%)	Pvalue	Odds ratio	95% confidence interval	P-value
Month 1							
	Treatment	Watchful waiting	6 (75)	0.3			
		Monotherapy	14 (82)				
		Combined therapy	121 (88)				
Month 3							
	Treatment	Watchful waiting	6 (75)	0.04	Ref		
		Monotherapy	16 (94)		59.2	2.52, 1388.8	0.01
		Combined therapy	133 (96)		13.8	1.5, 128	0.02
	Prostate size	<=40g	23 (82)	0.004	Ref		
		>40g	132 (98)		22.2	3.6, 136.5	0.001
Month 6							
	Treatment	Watchful waiting	6 (75)	0.02	Ref		
		Monotherapy	16 (94)		42.1	1.2, 967.4	0.01
		Combined therapy	134 (97)		15.2	1.7, 134.5	0.01
	Prostate size	<=40g	24 (86)	0.01	Ref		
		>40g	132 (98)		14.8	2.2, 99	0.005

has significantly lowered IPSS score by 4 or more after 3 months in a bivariate analysis. Taking both monotherapy and combined therapy were associated with decrease in IPSS score of more than 4 after 3 months and the relationship was statistically significant after adjusting to the initial prostate size as a confounder [p =0.01 (OR=59.2) and p=0.02 (OR:13.8), respectively]. The IPSS score remained consistently reduced after 6 moths of medical treatment (Table 2).

Medical treatment was associated with a mean decrease in PVR of 46ml of 1 month, however it was not statistically significant (p=0.2). Medical treatment was associated with mean decrease in PVR of 61ml and 94ml after 3 months and 6 months, respectively. This association was statistically significant in a bivariate analysis (p= 0.03 at 3month and p= 0.04 at 6 months) (Table 3). However, after adjusting for baseline IPSS score in a multivariate analysis, the relationship of medical treatment and PVR reduction was not statistically significant (p=0.9 at month 3 and month 6 of follow up).

During the follow up, patients with severe LUTS (IPSS: 20-35) were likely to have reduction in PVR after 3 months and 6 months of follow up [p=0.004 (OR:7.9) at 3 months and p= 0.002 (OR:9.4) at 6 month], respectively (Table 3).

DISCUSSION

The present study evaluated the effect of medical treatment on patients with BPH over a 6-month follow up. Medical treatment was associated with a significant reduction in IPSS after 3 months, which was consistent after 6 months. The reduction in PVR was also observed after 3 and 6 months, but the relationship was not statistically significant after adjusting for the baseline IPSS score. Patients with severe lower urinary tract symptoms were likely to have a reduction in PVR at follow-up.

The findings of this study are consistent with previous studies that have shown the effectiveness

Table 3: Multivariate analysis of factors associated with progressive PVR reduction over time for patients on BPH medical treatment.

		Bivariate analysis		Multivariate analysis		
		PVR decrease*, N (%)	Pvalue	Odds ratio	95% confidence interval	P-value
Month 1						
Treatment	Watchful waiting	1 (13)	0.2			
	Monotherapy	3 (18)				
	Combined therapy	46 (33)				
Month 3						
Treatment	Watchful waiting	0	0.03	Ref		
	Combined therapy	56 (42)		5992440	0	0.9
Baseline IPSS	Mild	3(13.6)	<0.001	Ref		
	Moderate	25(28.7)		1.6	0.4, 6.1	0.5
	Severe	33(67.4)			1.9, 32.3	0.004
Month 6						
Treatment	Watchful waiting	0	0.04	Ref		
	Monotherapy	3 (18)		486392	0	0.9
	Combined therapy	50 (36)		1E+06	0	0.9
Baseline IPSS	Mild	3(13,6)	<0.001	Ref		
	Moderate	15(17.2)		0.7	0.2, 3.1	0.7
	Severe	35(71.4)		9.4	2.2, 39	0.002

*PVR: post-void residual urine; * PVR decrease at 1 month >=46ml; PVR decrease at 3 months >=61ml; PVR decrease at 6 months>=94ml*

of medical treatment for BPH in reducing IPSS and PVR [11,12]. The use of combination therapy with alpha-blockers and 5ARIs has been shown to be more effective than monotherapy in reducing IPSS and prostate volume [13,14]. This supports current practice with most Rwandan patients receiving dual therapy for treatment of BPH.

The majority of the patients had no significant past medical history, but 40% of patients had comorbidities such as diabetes, hypertension, and recurrent urinary tract infection. Almost one third of patients with LUTS secondary to BPH in Rwanda presented with severe symptoms, likely due insufficient number of urologists in Rwanda making early detection and early intervention a challenge. In contrast, studies conducted in developed countries like France found that BPH with severe symptoms were rare [15]. In a Ugandan study, 20% of patients with BPH presented with severe symptoms, similar to the Rwandan setting where access to health care is limited [16].

The adherence to treatment varied over time, with the main reason for non-adherence being ignorance. Adherence to treatment is an important factor in the effectiveness of medical treatment for BPH, and healthcare providers should focus on educating patients about the importance of adherence to treatment. Furthermore, while most patients had health insurance, cost and access to medications remained a challenge for some patients. Continued efforts to strengthen access and availability remains a focus for Rwanda.

The study has several limitations, including the lack of a control group and the short follow-up period. The relatively short follow-up period of 6 months may not be sufficient to evaluate the long-term effectiveness of medical treatment for BPH. Future studies should consider longer follow-up periods to evaluate the long-term outcomes of medical treatment for BPH.

CONCLUSION

Medical treatment for BPH was associated with a significant reduction in both IPSS and PVR and this improvement remained consistent up to 6 months of follow up. Healthcare providers should focus on educating patients about the importance of adherence to treatment. Further studies with long duration may be needed to evaluate the long-term effect and side effect of medical treatment on BPH.

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