The impact of medical therapy for benign prostatic obstruction on the health-related quality of life at Muhimbili National Hospital

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THE IMPACT OF MEDICAL THERAPY FOR BENIGN PROSTATIC OBSTRUCTION ON THE HEALTH-RELATED QUALITY OF LIFE AT MUHIMBILI NATIONAL HOSPITAL

By,

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A Dissertation Submitted in (Partial) Fulfillment of the Requirements for Degree of Masters of Medicine in (Urology) of

Muhimbili University of Health and Allied Sciences
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CERTIFICATION

The undersigned certifies that this research dissertation is the work of the candidate carried out during his Masters of Medicine Urology training under my direct and/or delegated supervision.

The undersigned certifies that he has read and hereby recommends for consideration by Muhimbili University of Health and Allied Sciences the research entitled: ***"The impact of medical therapy for benign prostatic obstruction on the health-related quality of life at Muhimbili National Hospital."*** This research dissertation is submitted in partial fulfilment of the requirements for the Degree of Masters of Medicine (Urology) of Muhimbili University of Health and Allied Sciences.

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Dr. Obadia V. Nyongole

Supervisor

_____

Date

DECLARATION AND COPYRIGHT

I, **Herry Godfrey Kibona**, declare that this dissertation is my own original work and that it has not been presented, and will not be presented, to any other university for a similar or any other degree award, and is not previously or currently under copyright.

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DEDICATION

I would like to dedicate this work to my wife Beatrice and son Brendan.

Also to my parents Godfrey and Evelyn Kibona.

ABSTRACT

Background; Benign prostatic obstruction (BPO) is a common condition in older men that can often result in lower urinary tract symptoms (LUTS). LUTS associated with BPO can cause bladder outlet obstruction may have a significant negative impact on patients' health-related quality of life as can certain treatments for the condition.

Objective: To determine the impact of medical therapy on health-related quality of life among patients on treatment for lower urinary tract symptoms due to benign prostatic enlargement at MNH.

Methodology: A prospective hospital based descriptive study was carried out in urology outpatient clinics. Both public and private clinics from April to December 2017. All diagnostic and treatment options of patients were decided by attending clinicians. Patients were ≥30 years of age on medical treatment for LUTS due to BPO. Symptom and HRQL were measured at baseline and at 3 months using the international prostate symptom score (IPSS) and the Benign Prostatic Hyperplasia Impact Index (BII) score tools.

Results: A total 150 patients were included in the analysis with median age was 54.6 years ,mean PSA of 4.45ng/ml (SD5.13) and a mean prostate volume 54.62cc (SD5.13).Majority, 144(96%) had moderate and severe LUTS. Majority, 94(63%) men received a combination of tamsulosin and finasteride and 44(29%) men received tamsulosin. Pytotherapy or its combination with finasteride were prescribed to few (7%). Medical therapy was associated with overall improvement of quality of life ($p<0.001$). Tamsulosin and combination of tamsulosin and finastride were equally effective in improving symptom and QoL. A combination of tamsulosin and finasteride was associated with more adverse effects.

Conclusion: Improvements in QoL and symptoms was noted across the medical treatments most widely used in real-life practice at MNH to manage patients with LUTS for BPO. Tamsulosin showed an equivalent efficacy to a combination of tamsulosin and finasteride at third month of therapy with fewer adverse effects than combination therapy.

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LIST OF ABBREVIATIONS

AEs	Adverse effects
AUA	American urological association
AUR	Acute urine retention
BII	Benign prostate hyperplasia impact index
BOO	Bladder outlet obstruction
BPE	Benign prostatic enlargement
BPO	Benign prostatic obstruction
BPH	Benign prostatic hyperplasia
DRE	Digital rectal examination
DM	Diabetes Mellitus
EAU	European association of Urology
HRQL	Health-related quality of life
IPSS	International prostatic symptoms score
IRB	Institutional review board
LUTS	Lower urinary tract symptoms
MMED	Masters of Medicine
MNH	Muhimbili national hospital
MUHAS	Muhimbili University of Health and Allied Sciences
OPD	Outpatient Department
PSA	Prostate specific antigen
PV	Prostate volume
QoL	Quality of life
Q8	Question eight
RUV	Residual urine volume
SPSS	Statistical package for social sciences
SI	Symptom index
UK	United Kingdom
USA	United States of America

CHAPTER ONE

1.1 DEFINITION OF TERMS

Definition of health related quality of life

The term Health-related quality of life (HRQL) emerged from the broader concept of general Quality of life (QOL), and is, by definition, more focused on aspects of life quality that are influenced by or that can influence one's health status directly. These aspects can include symptoms of disease and treatment side effects, treatment satisfaction, physical functioning and well-being, social functioning and life satisfaction, and mental health, including emotional well-being and cognitive functioning(1).

Health-related quality of life (HRQL) can be defined as: "The extent to which one's usual or expected physical, emotional and social well-being are affected by a medical condition or its treatment" (2).

Medical treatment; this term will be used to refer to various medications with their effective doses for treating LUTS due to BPO used at MNH like Tamsulosin 0.4mg or 0.8mg per day, Finasteride 5mg per day, plant extract saw palmetto(Prostacare) 320mg per day or some combination of these prescribed to patients.

Impact; this term will be used with meaning of strong or powerful effect that something, especially something new, has on somebody(3). In this study this term was used referring to effect of medical therapy to Health-related quality of life.

1.2 BACKGROUND

The prostate is a walnut-shaped gland in men, lies immediately below the base of the bladder surrounding the proximal portion of the urethra and consists of canals and follicles lined with columnar epithelial cells and surrounded by a fibromuscular stroma consisting of connective tissue and smooth muscle. The prostate contributes to seminal fluid, where its secretions are important in optimizing conditions for fertilization by enhancing the viability of sperm in both male and female reproductive tracts(4).

Different terminologies are used when describing the condition of a symptomatic enlarged prostate gland. Benign prostatic enlargement (BPE) refers to detectable enlargement of the prostate gland which is clinically not malignant. Benign prostatic obstruction (BPO) is a consequence of benign prostatic hyperplasia (BPH) which is a histological diagnosis, referring to smooth muscle and epithelial cell proliferation occurs within the prostatic transition zone(5). Benign prostatic obstruction is implicated in the pathophysiology of lower urinary tract symptoms (LUTS) like those symptoms primarily associated with overactive bladder (frequency, urgency, and nocturia) and include symptoms relating to storage and/or voiding disturbances(5,6).In the initial evaluation of a man presenting with LUTS, the evaluation of symptom severity is essential. Medical history should be taken thoroughly also focused physical examination, including a digital rectal exam (DRE)(5).A formal symptom inventory (e.g. International Prostate Symptom Score (IPSS) is recommended for an objective assessment of symptoms and for evaluation of response to treatment(7).

Therapeutic decision-making should be guided by the severity of the symptoms, the degree of bother and patient preference. Information on the risks and benefits of BPO treatment options should be explained to all patients for whom therapy is inevitable. Patients with mild symptoms (IPSS<7) should be counselled about a combination of lifestyle modification and watchful waiting, measures like fluid restriction particularly prior to bedtime, avoidance/monitoring of some drugs (e.g., diuretics), timed or organized voiding, and avoidance or treatment of constipation(5).Patients with mild symptoms and severe bother should undergo further assessment. Treatment options for patients with bothersome moderate (e.g., IPSS 8 – 18) and severe (e.g., IPSS 19 – 35) symptoms of BPO include watchful waiting/lifestyle modification, as well as medical, minimally invasive or surgical therapies.

Medical treatment for BPO has played a major role in the improvement of LUTS associated with BOO. It focuses mainly on the two aspects of pathophysiology of BPO; a dynamic component related to the tension of smooth muscle in the prostate, prostatic capsule and bladder neck and secondly on a fixed component related to bulk of the enlarged prostate impinging on the urethra. The mechanisms of action of the drugs is either to relax smooth muscle tone and/or reduce the size (bulk) of the prostate(8)**.**

Alpha 1 Receptor Blockers

Alpha-blocker therapy is based on the hypothesis that clinical BPH is partly caused by alpha1-adrenergic-mediated contraction of prostatic smooth muscle, resulting in bladder outlet obstruction(9).Alpha-adrenergic receptor antagonists such as doxazosin, tamsulosin, alfuzosin, and terazosin inhibit this process and thus relax the smooth muscles of prostate ,bladder neck and urethra and therefore the bladder outlet obstruction(10).

The primary adverse events reported with alpha-blocker therapy are orthostatic hypotension, dizziness, tiredness (asthenia), ejaculatory problems, and nasal congestion.

The 5-Alpha-reductase inhibitors

Androgens are required to maintain the size and function of the prostate in men; the androgen primarily responsible for prostatic growth and enlargement is dihydrotestosterone(11). Dihyrotestosterone is an active form of testosterone hormone where conversion is influenced by 5α-reductase enzyme. A compound that selectively inhibit 5α-reductase could therefore provide an effective treatment for benign prostatic hyperplasia. Finasteride is a competitive inhibitor of 5α-reductase(12).Administration of this drug for short period results in decreased serum dihydrotestosterone concentrations by reducing conversion of testosterone hormone, which result in a reduction in the size of the prostate, and improvement in urinary-flow rate. Reported adverse events are primarily sexually related and include decreased libido, ejaculatory dysfunction, and erectile dysfunction and are uncommon and reversible after the first year of therapy(13).

Phytotherapy

Phytotherapy belongs to the area of complementary and alternative medicine. Most of the phytotherapeutic drugs used for treatment of LUTS due to BPH are extracted from roots, seeds, barks or fruits of plants. There are available preparations which are derived from single plant while others contains extracts of two or more plants and each agent has one or more proposed mode of action(14).

Quality of life Measurement

HRQL represents a subjective appraisal of the impact of illness or its treatment; individual patients with the same objective health status can report dissimilar HRQL due to unique differences in expectations and coping abilities(15). As a result, HRQL must be measured from the individual's viewpoint rather than that of outside observers (i.e., caregivers or health care professionals) whenever possible. The importance of obtaining HRQL reports from patients, themselves, is highlighted by a substantial literature documenting disparate estimates of symptoms and HRQL between patients and their physicians(16).

This diversity in perception has led to development of specific measurements by researchers(17). Several instruments exist which are used to measure quality of life in various disease conditions some of them are disease specific. For benign prostate enlargement which is a disease causing lower urinary tract symptoms; there are various existing tools used by researchers to assess HRQL in patients with symptoms for disease or monitor treatment given for symptoms of disease. In this study IPS score was used to measure symptom severity, IPS score question 8 and BPH impact index score were used to measure perception of individual HRQL before and after three months of therapy.

CHAPTER TWO

2.1 LITERATURE REVIEW

SYMPTOMS PREVALANCE AND PROGRESSION

The causes of LUTS are multifactorial, although BPO secondary to BPH is a major contributing factor. The prevalence of LUTS in Europe varies with age, ranging from 14% for men in their fourth decade of life to > 40% for men in their sixth decade(18). Studies indicate little cultural variation in the prevalence of LUTS across Europe(19). Based on an overall prevalence of LUTS of 30%, approximately four million men aged >40 years have LUTS in the UK alone(18). In a study among African Ghanaian men which included only BPH patients, the proportion of LUTS by severity reported as thirty seven (37%) had severe symptoms, 40% moderate symptoms, and 23% mild symptoms before treatment with *C. membranaceus* root extract(20).

An expert review of published evidence regarding BPH as a progressive disease defined progression as worsening of symptoms, deterioration of urinary flow rate, increase in prostate volume (PV), and outcomes such as acute urinary retention (AUR) and the need for surgery either for AUR or symptoms(21). Clinical trials have included renal insufficiency and recurrent urinary tract infections as additional measures of BPH progression, although these outcomes were rarely observed(22).In the placebo arm of the Medical Therapy of Prostatic Symptoms (MTOPS) study the rate of overall clinical progression (defined as an increase in AUA-SI of 4 points, AUR, urinary incontinence, renal insufficiency or recurrent urinary tract infection) was 17.4% over the 4-year duration of the study. About 78% of progression events took the form of deterioration in symptoms(22).

It is important for clinicians to determine which patients are at increased risk of disease progression in order to optimize therapy and offer a treatment approach that correlates with patient preferences. Numerous factors, such as age and PV, have been linked with the risk of BPH progression events(23–25).

Several studies have demonstrated a relationship between age and markers of BPH progression. In the Olmsted County study, moderate-to-severe urinary symptoms were recorded in 13% and 28% of men aged 40–49 years and > 70 years respectively(26). An increase in symptom severity with increasing age has also been reported in Asian men(27). As previously discussed, the

incidence of AUR among men with moderate-to-severe symptoms in the Olmsted County study was shown to increase with increasing age(23).

More recently, a study of men (n = 1859) with symptomatic BPH showed an increase in PV with increasing age, from a mean of 27.7 ml in men aged 40–49 years to 52.3 ml in men aged 70–80 years(28).Prostate volume is perhaps the most extensively studied of the risk factors for BPH progression. Men with a PV of 30 ml are more likely to suffer moderate- to-severe symptoms (3.5-fold increase), decreased flow rates (2.5-fold increase), and AUR (three- to fourfold increase), compared with men with PV < 30 ml(29). An enlarged prostate is also predictive of the need for BPH-related surgery(23,25).

MEDICAL THERAPY AND OUTCOME

Over the last decade, there has been a considerable decline in the popularity of surgery to manage symptoms associated with BPH, and medical therapy is now the most frequently used treatment option in clinical practice(30). Hence, patients with mild or moderate symptoms can usually be treated in a primary care setting, with more complicated cases referred to a urologist for evaluation and management(31).Various studies have been done worldwide with aim of evaluating changes in symptom severity and health-related quality of life among individuals on various medical treatment modalities for LUTS associated with BPO. However, various published data regarding the subject are inconsistent and none has been documented in Tanzania.

Current EAU guidelines focus on alpha-blockers and 5-alpha-reductase inhibitors (5ARIs), as monotherapies or in combination, when recommending medical therapy for BPO(32). Treatment of LUTS with plant extracts (phytotherapies) has a long tradition in countries such as France and Germany, and is also popular in other parts of the world(32). However, their mode of action is unclear and the clinical efficacy of these agents is largely unproven(33).

The two principal drug classes in BPO treatment, α-blockers and 5α-reductase inhibitors (5ARIs), have both been shown to improve symptoms and QoL(34–37). The Medical Therapy of Prostatic Symptoms (MTOPS) study showed that combined therapy with the type 2 selective 5ARI finasteride and the α-blocker doxazosin was more effective than either drug alone in reducing the risk of BPH progression and improving symptoms at 4 years in men with mild-to severe BPH, reflecting the general population(22). However, neither disease-specific QoL nor any other patient-reported outcomes were assessed in this study in any detail; indeed, data on the effects of α-blocker and 5ARI combined therapy on disease-specific, patient-reported health

outcomes are limited to short-term studies. In the 1-year Veterans Affairs study, the improvement in the BPH Impact Index (BII) score and the proportion of men reporting improvement in overall assessments were significantly greater with the finasteride and terazosin combination than with finasteride alone, but not compared with terazosin monotherapy(38).

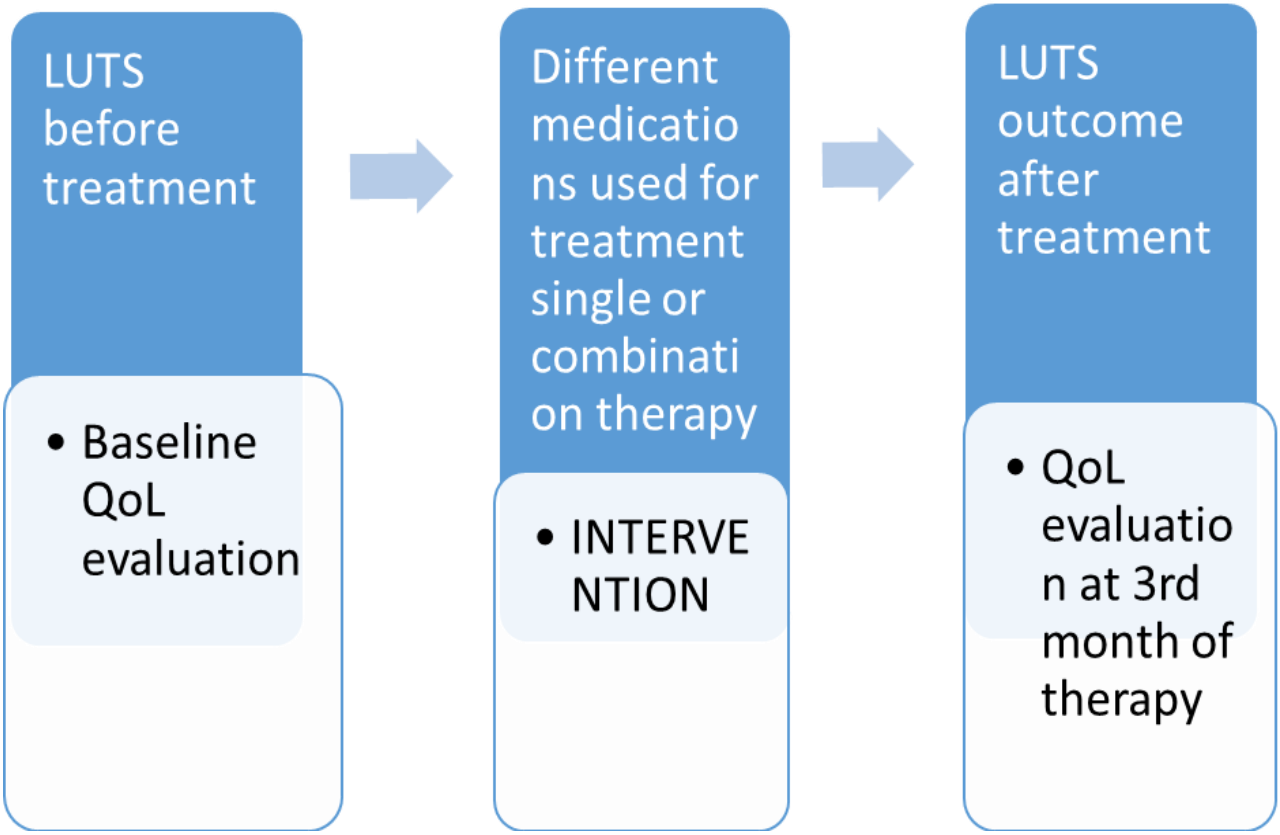
The Combination of Avodart and Tamsulosin (CombAT) study investigated the effect of the dual 5ARI dutasteride and the α-blocker tamsulosin, alone and combined, on symptoms and health outcomes over 2 years, and on the risk of AUR and surgery over 4 years, in men with moderate-to-severe urinary symptoms and prostate enlargement. The BII and question 8 of the IPSS are the two most commonly used and validated QoL instruments in BPH studies(39). The third instrument used was the Patient Perception of Study Medication (PPSM) questionnaire, which was specifically developed for use and validation in this trial to assess patient treatment satisfaction across a range of domains. Results from the CombAT pre-planned 2-year analysis were reported, and these showed significantly greater improvements in symptoms with dutasteride and tamsulosin combined therapy from 3 months versus dutasteride, and from 9 months versus tamsulosin(40). Combined therapy also provided significantly greater improvements in peak urinary flow rate (Qmax) than with each monotherapy from the first assessment after baseline at 6 months to 24 months.

In another CombAT trial done among Canadian men for 2 years a combined therapy of dutastride and tmsulosin resulted in greater improvements in BPH impact index and IPS Q8 scores from baseline than did dutastride from 3 months and compared with tamsulosin from 9 months (BII) or 12 months (IPSS Q8).Improvement with combined therapy was also observed when Patient Perception of Study Medication questionnaire was used at 24 months(41).

A most recent longitudinal, prospective, observational, multicenter study done among 1713 patients in Spain, famously known the QUALIPROST study(42). This study documented improvements in QoL and IPSS scores were equivalent across the medical treatments (monotherapy and combined therapy) most widely used in real-life practice, and all medical treatments studied were associated with considerably larger improvements in QoL and symptoms than watchful waiting at sixth month of therapy. Moreover hexanic extract of S. repens showed equivalent efficacy to alpha-adrenergic blocker and 5Alpha reductase inhibitor without the side effects on sexual function associated with those treatments(42).

The observational study among 1,098 French patients included 82.7% treated with monotherapies and 17.3% with combined therapy(43). Patients reported diminished quality of life (IPSS-Q8 C3) (42.3%), persisting symptoms (IPSS-score C12) (35.5%), symptoms worsen (VNS-score B-1) (18.8%) and high bother (BII-score C9) (2.6%). Globally 52.8% had at least one of these unsatisfactory outcomes. The results of this study suggest that all dimensions of patients' HRQL measured with EQ-5D significantly decreased with LUTS severity and were significantly altered in patients with moderate to severe symptoms(43).

2.2 CONCEPTUAL FRAME WORK



2.3 PROBLEM STATEMENT

It has been said that medical therapy for LUTS due BPO has interference with individual HRQL. The ability of therapy in reducing the impact of LUTS as well as the degree to which it interferes with lifestyle or causes embarrassment, should be the primary consideration in choosing therapy in a patient with BPO.

Fewer studies have been done to assess how drugs for treating LUTS due to BPO affect quality of life among individuals using them. There is existing gap of local published data on impact of various medical treatment modalities on HRQL among symptomatic BPO patients which brings dilemma among clinicians on choice of therapy.

Inadequate management of LUTS can trigger disease progression and lead to several complications. Also the proportion of men with LUTS due to BPO before and after initiation of specific various treatments is not known. As a consequence, patient treatment satisfaction and HRQL assessment seem to be essential criteria to ensure optimal treatment outcomes.

Therefore there is a need of such data which will provide evidence on what is the current and ongoing practice at MNH. This study will determine the impact of various available medical therapies on HRQL of patients with LUTS due to BPO attending MNH for treatment**.**

2.4 RATIONALE

The results of this study will help in knowing the impact on HRQL of various available medical treatment options for treating LUTS due BPO in the current practice at MNH. This study will attempt to provide evidence for met or unmet medical needs for a number BPO patients treated with various medications.

Moreover the result of this study will add to the evidence pool by establishing baseline data on currently used treatments and will further inform decision-making among clinicians regarding available medical treatments for BPO at MNH.

2.5 RESEARCH QUESTIONS

1. What is the difference in severity of LUTS before and after undergoing various medical treatments at MNH?

2. Are there differences of HRQOL in patients undergoing different medical treatment modalities for BPO at MNH?

3. What are the common adverse events reported by patients undertaking different treatment modalities for BPO at MNH?

2.6 OBJECTIVES

2.61 Broad objective

To determine the impact of medical therapy on health-related quality of life among patients on treatment for BPO at MNH.

2.62 Specific objectives

1. To assess the severity of lower urinary tract symptoms before and after usage of specific medical treatments for BPO.

2. To assess the HRQL among patients receiving various medical treatments for BPO before and after treatment.

3. To assess the treatment failure related events among patients on various medical therapies.

CHAPTER THREE

3.0 METHODOLOGY

3.1 STUDY DESIGN

Descriptive prospective hospital based study.

3.2 STUDY AREA

The study was conducted at urology clinics of Muhimbili National Hospital. Muhimbili is a tertiary hospital located in Dar es Salaam city Tanzania, is also a teaching hospital for MUHAS and other universities. MNH provides its services to the people living in Dar es Salaam whose population is about 5 million as well as the adjacent Pwani region with a population of about 1.099 million and being a Tertiary care Referral Hospital, it also draws patients from all over the country. Urology clinics receive public, private and health insurance covered patients with an average of 250 clinic attendees per week. Public clinics are done twice weekly and private clinics are done daily including Saturdays.

3.3; STUDY DURATION

April 2017 - December 2017.

3.4 STUDY POPULATION

The study recruited patients who were newly started on medical therapy for BPO attending urology clinics-at MNH, during the study period.

3.5 SAMPLING TECHNIQUE

Convenient sampling was employed whereby clinic attendees diagnosed with BPO by attending clinician who met criteria were recruited until sample size was reached. Attending clinicians diagnosed patients with BPO after have done evaluation and several blood and imaging investigations which were documented in patients' case files.

3.5.1 Inclusion criteria

The study included patients diagnosed with BPO with lower urinary tract symptoms categorized as mild, moderate or severe IPS scores.

3.5.2 Exclusion criteria

This study excluded all the patients

1. Who had other co-morbid conditions like diabetes mellitus (DM), neurological diseases and any patients on treatment with alpha blockers or diuretics for other medical indication, or those with kidney failure.
2. Those with history of prior surgery on the prostate.
3. All patients who were already on medical therapy

3.6 SAMPLE SIZE:

The estimated sample size N was computed using the formula below,

$$N = \frac{Z^2 \, p \, (100-p)}{e^2}$$

Where;

N = Estimated Sample Size

Z = is the standard deviation in normal population, which turns out to be 1.96 on using the 95% confidence interval.

P= proportion on outcome for quality of life for BPO patients on medical treatment

(In a study done in Ghanaian men by George Awuku Asare et al 2015 reported 94% of participants to have good quality of life post use of medication herb extract and only 6% reported poor quality of life post treatment)

Taking difference between two post treatment proportions then p will be 88%

e = margin of error will be 5%

Hence from the formula above the sample was:-

$$N = \frac{1.96 \times 1.96 \times 88 \, (100-88);}{5 \times 5} \qquad N = 162$$

Minimum estimated Sample Size patients was 162**.**

3.7 STUDY TOOLS

A structured questionnaire Swahili version was administered to each patient and filled by the investigator/data collector. Pretesting of the questionnaire and corrections was done before beginning of data collection.

A questionnaire contained questions for documenting patient's demographic data, questions specific for lower urinary tract symptoms using IPSS chart and question for assessment of health related quality of life (question 8 on IPSS) chart and also used benign prostate hyperplasia impact index score chart (Appendix 3).

3.8 DATA COLLECTION

Data was collected through personal interviews and additional information like diagnosis, pharmacy records was obtained from the electronic patient files on data base software for patient information system used by the MNH.

The Swahili version questionnaire was filled during personal interview on the first visit and completed at third month of patient visit. Informed consent was obtained from each patient before interview and if a patient agreed for interview he had to sign on a consent form.

Three people were recruited as research assistants prior to the actual work ,the assistants were registrars/intern doctors who were trained to become familiar with the subject of the study, the research tool, ethics and administration issues such as work schedule and other logistics.

3.9 STUDY VARIABLES

The primary endpoint was change in QoL assessed using the validated version of the Benign Prostatic Hyperplasia Impact Index (BII), questionnaire consisting of four questions measuring the impact of urinary symptoms on physical discomfort, worries about health, symptom bother, and interference with usual activities during the past month. Items are answered using a Likert scale, with four or five response options per item and scores range from 0 (best QoL) to 13 (worst QoL).

Symptoms of BPO were evaluated using the validated version of the International Prostate Symptom Score (IPSS). Scores on this instrument range from 0 to 35 with a higher score indicating more severe symptoms and Question 8 on IPSS chart was used to assess QOL with scores from 0(delighted) to 6(terrible). Both instruments were completed at baseline and at the 3-month follow-up visit.

Sociodemographic data collected at baseline included age, level of education and occupation. We also collected data on diagnostic tests (prostate volume, residual urine volume, PSA), and treatment received (alpha-blockers, 5-alpha-reductase inhibitors, phytotherapy, other). Adverse events associated with treatment were recorded at the follow-up visit.

3.10 ETHICAL ISSUES

Ethical clearance for doing the study was obtained from MUHAS research and publication committee. Informed consent was obtained from patients by explaining to them the aim of the study, then a form which contains all the information concerning the research was given to each patient and asked to sign the form if he agreed to participate. Patients who refused to participate were not enrolled in the study. There was no use of patients identifiers instead numbers were used and all patients' information including raw data was be kept confidential during and after study period.

3.11 DATA ANALYSIS

All questionnaires were coded with numbers then data was entered in computer. Descriptive data was analysed with the aid of SPSS (Statistical Package for the Social Sciences) computer software version 22.0.

Data was summarized with descriptive statistics, mean and respective standard deviation was calculated for continuous data and comparison was made using T-test. Categorical data was analyzed by chi square test and association between variables was made

CHAPTER FOUR

4.0 RESULTS

4.1: Response Rate

A total of 168 men were interviewed. Eighteen men were excluded for analysis due to different reasons including poor adherences to medications as reported by patients, change to other medication type and those who were lost during follow up and therefore analysis was done using 150 men.

The median age of participants was 54.6 years, mean PSA was 4.45ng/ml (SD5.13) and mean prostate size 54.62cc (SD33.60).

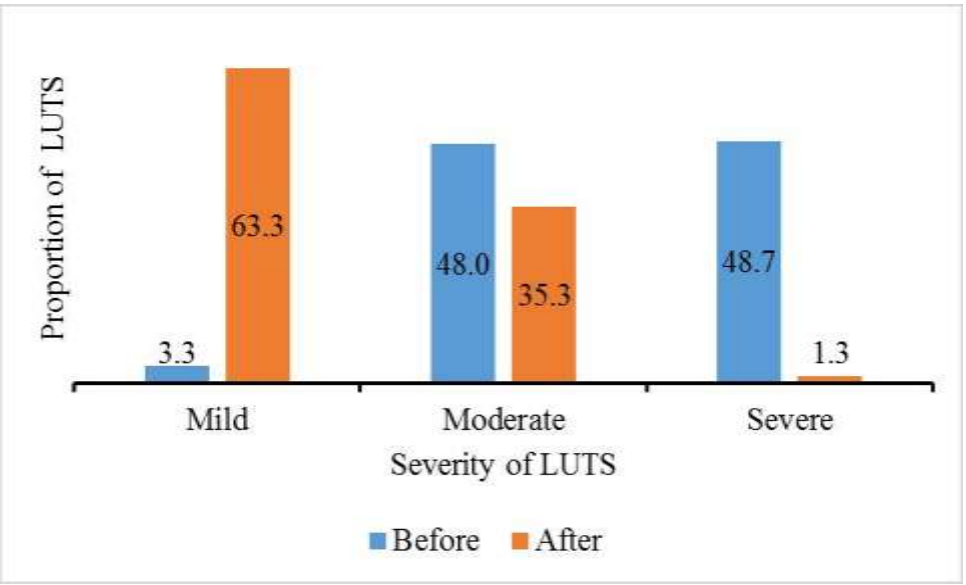
4.2: Patients' characteristics

The majority of patients 88(58.7%) were in age group 50-69 years. Of 150 men minority 5(3.3%) had no formal education, a few were unemployed 7(4.7%) while 59(39.3%) retired from formal employment.

4.3: Proportion of men by severity of LUTS before and after medical treatment.

Among 150 men, equal proportions of patients reported moderate and severe LUTS 48% and 48.7% respectively before the start of treatment. After three months of therapy more than half of men (63.3%) reported to have mild LUTS (Figure 1)

Figure 1: Proportion of men by severity of LUTS before and after medical treatment



4.4: Treatment outcome for specific medication(s).

Among 150 men, 94(62.6%) men were on combination therapy of Tamsulosin+Finasteride; and majority had severe and moderate LUTS 51.1% and 46.8% respectively at the start of therapy. At the end of third month of therapy more than half (64.9%) reported mild LUTS.

Fourty four men were on Tamsulosin monotherpy, more than half (54.5%) had moderate LUTS while 38.7% had severe LUTS at the start of therapy. At third month of therapy 70.5% reported mild LUTS.

Prostacare monotherapy and combined therapy of prostacare and finasteride were prescribed to 6 men (Table 1).

Table 1: Severity of LUTS using IPSS before and after usage of specific medical treatment for BPO (N=150)

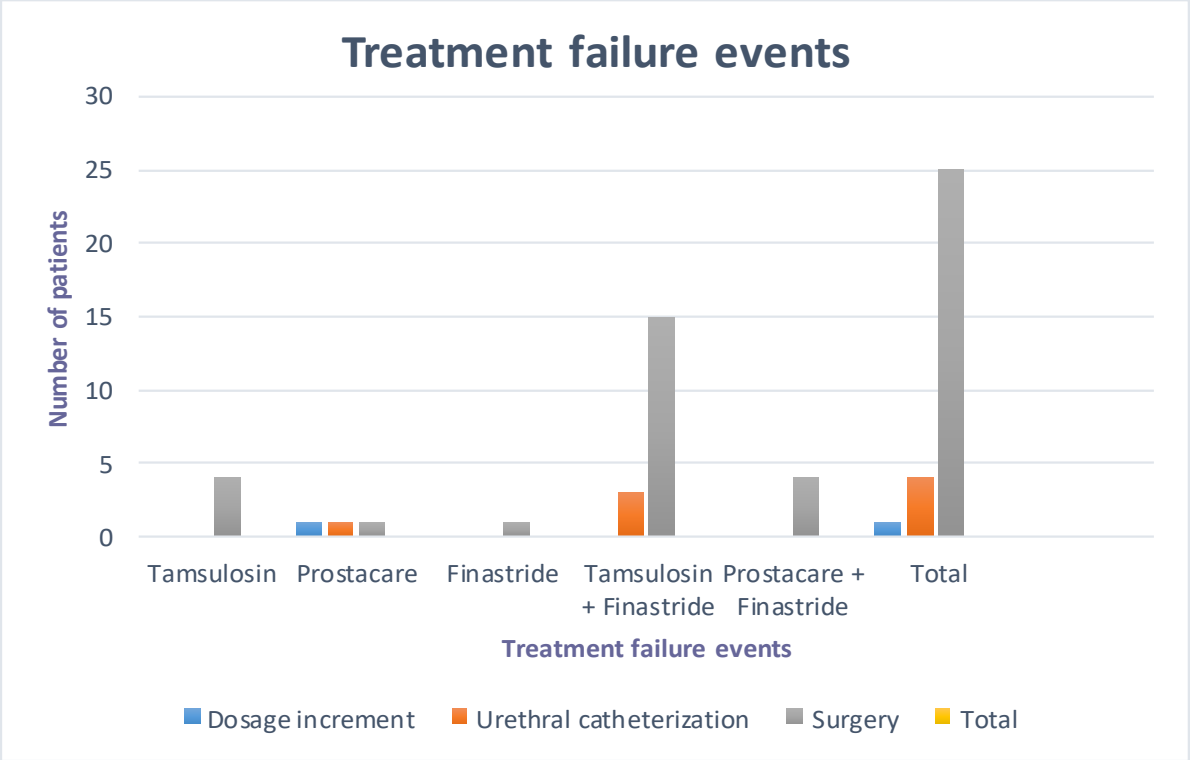
		Before			After		
Medication	**Total patient**	**Mild**	**Moderate**	**Severe**	**Mild**	**Moderate**	**Severe**
Tamsulosin	44	3 (6.8)	24 (54.5)	17 (38.7)	31 (70.5)	13 (29.5)	0 (0.0)
Prostacare	5	0 (0.0)	4 (80.0)	1 (20.0)	1 (20.0)	4 (80.0)	0 (0.0)
Finasteride	1	0 (0.0)	0 (0.0)	1 (100)	1 (100)	0 (0.0)	0 (0.0)
Tamsulosin + Finasteride	94	2 (2.1)	44 (46.8)	48 (51.1)	61 (64.9)	31 (33.0)	2 (2.1)
Prostacare + Finasteride	6	0 (0.0)	0 (0.0)	6 (100)	1 (16.7)	5 (83.3)	0 (0.0)
Total	150	5	72	73	95	53	2

4.5: Treatment failure events for specific medical therapy

Figure 2; Majority of patients their management was converted to surgery and this was mostly observed among patients on tasulosin + finasteride combination therapy.

The second most observed treatment failure event was urethral catheter use within three months of medical therapy, which was mostly seen in same group of tamsulosin finasteride (Figure 2).

Figure 2: shows treatment failure events during three months of therapy



4.6: General HRQL (Q8 on IPS chart) among patients with BPO

Table 2: The overall mean change in quality of life before and after undergoing treatment with medical therapy was statistically significant ($p<0.001$).

Comparison between mean quality of life at baseline and at third month of therapy for men undergoing treatment with Tamsulosin and tamsulosin + finasteride was made. The other treatment groups were excluded from this comparison due to small number of individuals using the medication(s).

The mean difference from baseline in the group who used tamsulosin was larger compared to those on a combination of tamsulosin+finasteride but for both groups the mean change in quality of life from baseline was statistically significant $p<0.001$ and $p=0.003$ for tamsulosin and tamsulosin+finasteride respectively (Table 2).

Table 2: Paired samples t test for mean QoL between men undergoing treatment with two different medication(s)

Medication	Total (n)	Quality of life Mean (SD)		Mean difference	P-value
		Before	After		
Tamsulosin	44	4.56 (0.7)	1.55 (0.8)	3.01	<0.001
Tamsulosin + Finasteride	94	4.35 (0.7)	1.46 (0.8)	1.89	0.003

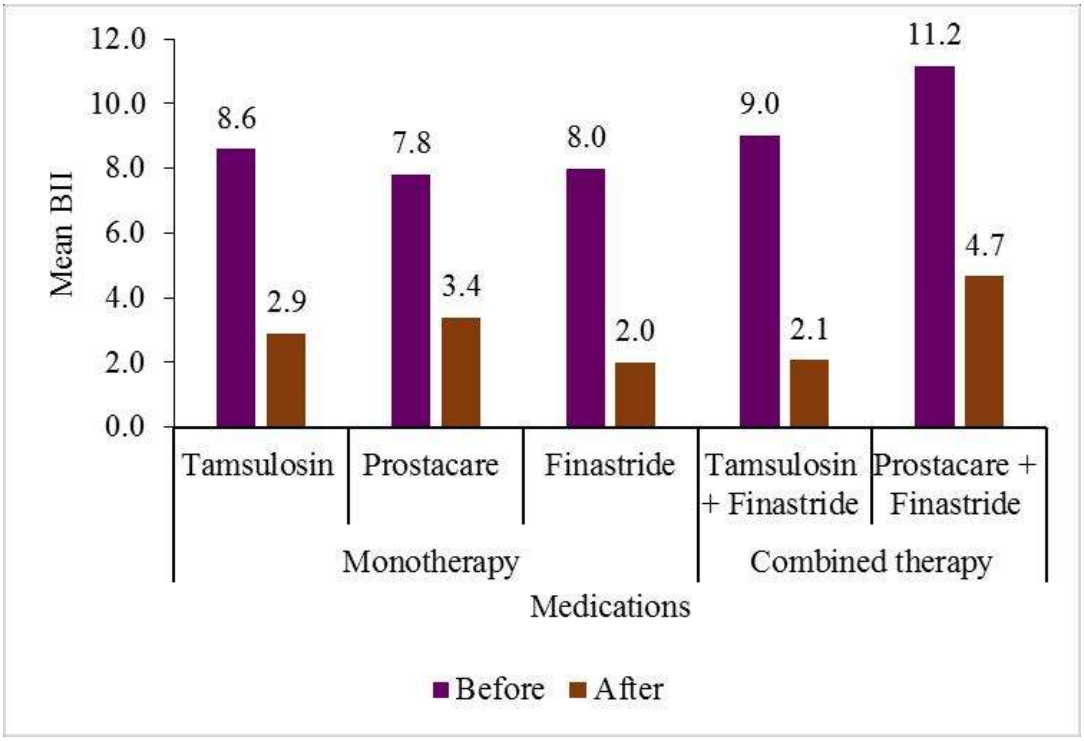
4.7: General HRQL using BPH impact index (BII) score for BPO patients

Figures 3 shows BII (BPH impact index score) mean scores at baseline and at third month of therapy for BPO patients.

Patients receiving combination therapy had higher mean baseline BII than those treated with monotherapy. All medical treatment showed a relevant improvement in BII score ($p<0.001$) at third month of therapy.

The smallest improvement of BII from baseline was observed in the Prostacare group, with a mean change 4.4 points while the largest change in BII was in tamsulosin + finasteride, with mean change 6.9 points (Figure 3).

Figure 3: Baseline and end of study mean BII by treatment groups.



4.8. Adverse effects of various medical therapies

Table 3; shows the overall incidences of adverse effects (AE) with use of medications was reported by 23(15.3%) men. A combination therapy of tamsulosin+finastride was associated with majority of AEs which was reported by 17 men. In terms of absolute numbers, the most frequent AE were poor erection, poor ejaculation and dizziness (Table 3).

Table 3: Adverse effects of various medical therapies (N=150).

Side effects	Tamsulosin	Prostacare	Finasteride	Tamsulosin + Finasteride	Prostacare + Finasteride	Total
Dizziness	2	0	0	4	0	6
Erectile dysfunction	0	0	0	5	0	6
Loss of libido	0	0	0	4	1	5
Poor ejaculation	2	0	0	4	0	6
None	40	5	1	76	5	127
Total	44	5	1	94	6	150

CHAPTER FIVE

5.1 DISCUSSION

This study has evaluated changes in symptoms and QoL among patients with BPO managed by medications based on what is currently practiced at a tertiary hospital in Tanzania. We observed the overall significant improvements LUTS and quality of life in patients who were on medical therapy for BPO. The majority of participants of this study had baseline moderate and severe symptoms. This finding was similar to a Ghanaian study where similar proportions of symptoms were dominant(20). At third month of therapy six out ten men of the studied population had mild symptoms proving evidence of overall good outcome of available medical therapies in treating BPO at MNH.

In the current study the majority of patients were given combination therapy of tamsulosin and finasteride or monotherapy of tamsulosin and few were given phytotherapeutic drug (*S. repens*) either alone or in combination. The reason for these clinicians' preferences of other drugs over pytotherapeutic drug was not established but could be lack of hospital treatment protocol. In the AUA BPH Guideline, pytothrapeutic medications are considered as a treatment option(5) , and it has been recommend that general conclusion about *S. repens* should not be made because these products potency needs to be assessed individually as may differ depending on extraction procedure(44–46).Our study findings gives a clue that further research is needed on the available and approved *S. repens* drug product which is currently used in Tanzania.

There was marked improvement of both symptoms and QoL before and after therapy between the most prescribed monotherapy and combination therapy was nearly the same. These findings were different from other studies which have proved combination therapy to be superior to monotherapy(24,40). The tendency to have equivalent symptom and QoL improvement between combination of tamsulosin and finasteride and tamsulosin alone was also observed in QUALIPROST study(42). These results could be explained by short duration of treatment in these two studies and differ from others in which significant differences was observed after long term therapy which was above nine months.

In this study three out of ten men had outcome events related to failure of medical therapy. The rate of conversion to surgery was high among those on combination therapy of tamsulosin and finasteride group in comparison to any other groups. This finding was different from what has been reported by other studies proving combination therapy of tamsulosin and finastride tends to reduce the rate of conversion to surgery and incidences of AUR(40). The only explanation for these differences could be, the current study had most patients with moderate and severe symptoms prescribed combination therapy with short study duration of treatment while severe symptoms have been associated with high chances of symptom progression and treatment failure(22,23).

All of the medical treatments studied were associated with improvements in both symptoms and QoL using both IPS and BII score tools, this observed improvement was similar to that observed in previous studies of different drug therapies using similar tools(41,42). The trend of change of QoL with change in symptom was observed also in one study done in four European countries, where QoL was less affected in Germany than other countries and the study concluded that the change in QoL may also differ basing on geographical discrepancies and cultural habits or merely organizational differences(43).

In the current study the overall reported treatment side effect incidences were more in the combined therapy group. Tamsulosin +Finasteride was associated with high reported incidences of adverse side effects among users which was similar to another study comparing side effects in group of therapies which reported less adverse effects with use of monotherapy(40).Explanation for this observation could be due to combined effect of medications on a combination therapy group. The most reported side effects in the current study were dizziness, poor ejaculation and poor erectile function.

5.2 LIMITATIONS

Data were obtained under conditions of real-life practice with no randomization or blinding; patients were therefore allocated to a specific management approach based on clinician judgment, which could lead to a selection bias.

The relatively short follow-up period of three months could also be considered a limitation when studying a chronic disease and use of medications like 5 alpha-reductase inhibitors which have been proved to have maximum effect with use for six months.

Like any other study of medical therapy, drug adherence is a factor which can affect results. In this study there was no use of any designed tool for adherence monitoring.
Unavailability of uroflometry machine for monitoring treatment progress among patients was also one of the limiting factors.

Despite such limitations, studies like this can contribute useful information on the outcomes associated with day-to-day patient management strategies.

5.3 CONCLUSION

Majority of patients receive a combination therapy of Tamsulosin and finastride and monotherapy of tamsulosin for LUTs. Pytothrerapeutic drug either alone or in combination were the least preferred by clinicians.

In general medical therapy for LUTS for BPE at MNH was associated with considerably significant improvements in QoL and symptoms. Tamsulosin and a combination of tamsulosin and finasteride had equivalent efficacy in improving both symptoms and QoL. Adverse effects were more reported to those who received a combination of tamsulosin and finasteride.

The results of this study add evidence on current treatments for LUTS due to BPE at MNH and should help to further inform decision-making regarding treatment.

5.4 RECOMMENDATIONS

1. Need for hospital treatment protocol for management of BPO.
2. Need for further similar research with long duration and large sample size
3. Need for further research with larger sample size about quality of life with use of the available phytotherapeutic agent.

5.5 DISSEMINATION PLAN

The results of this study were submitted for partial fulfillment of requirements for degree masters of medicine in Urology. Research report was disseminated to teaching, research and consultancy unit of MNH and was presented at department of surgery and thereafter dissemination to dean school of medicine and director of post graduate studies. MUHAS and principal author hold copyright of the research findings

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APPENDICES

Appendix I: INFORMED CONSENT FORM (ENGLISH VERSION)

ID-NO. ____

Greetings! Sir
My name is Dr. HERRY KIBONA, I am doing research on determining the impact of medical therapy on health-related quality of life among patients on treatment for lower urinary tract symptoms due to benign prostatic enlargement at Muhimbili National hospital.

Purpose of the Study is to determine the impact of various medications on health-related quality of life among patients on treatment for lower urinary tract symptoms due to benign prostatic enlargement at Muhimbili national hospital.

What participation involves; if you agree to join the study, you will be interviewed to answer of questionsin the questionnaires and some of your information will be taken from your hospital file and your treatment will be followed up to 90 days.

Confidentiality; Confidentiality will be observed and unauthorized persons will have noaccess to the data collected.

Benefits; This study will help in knowing the impact on HRQL of various available medical treatment options for treating LUTS due BPE in the current practice at MNH. This study will attempt to provide evidence for met or unmet medical needs for a number BPE patients with LUTS treated with various medications.

Risks; we do not expect that any harm will happen to you because of participating in this study.

Right to withdraw: You can stop participating in this study at any time, even if you have already given your consent and refusal to participate or withdrawal from the study will involve no penalty.

Contact persons; if you have questions about this study, you should contact the Principal investigator:

Dr. Herry Kibona , hopkdr@gmail.com of Muhimbili University of Health and Allied Sciences, P.O.BOX 65001, DAR ES SALAAM and if you ever have questions about your rights as a participant, you may call DR.JOYCE MASALU, Chairperson of Senate Research and Publications Committee, P. O. BOX 65001, Dar es Salaam. Telephone: + 255 22 2152489.

Signature

I …….have read and understood the contents in this form and my questions have been answered.

I agree /do not agree to participate in this study.

Signature/thumb of the participant…….

Signature/thumb of the witness ……

Signature of the Investigator ……...

Date of signed Consent ……

Appendix 2; INFORMED CONSENT (SWAHILI VERSION)

FOMU YA RIDHAA KWA WAGONJWA

Namba ya utambulisho _____

Habari yako, Jina langu ni Dr. HERRY KIBONA, mwanafunzi wa uzamili chuo kikuu cha tiba Muhimbili.

Lengo la utafiti

Kubaini matokeo ya matibabu kwa kutumia dawa tofauti kutibu dalili za mkojo kutokana na ukubwa wa tezi la kiume.

Ushiriki wa utafiti;

Ukikubali kushiriki katika utafiti huu,utasailiwa ili kuweza kujibu maswali toka kwenye dodoso la utafiti huu napia taarifa nyingine zinazokuhusu zitachukuliwa kutoka katika jalada lako la hospitali na matibabu yako yatafuatiliwa hadi siku 90.

Usiri; Kutakuwa na usiri na hakuna mtu yeyote asiyehusika atakayepata taarifa zilizokusanywa katika utafiti.

Faida: Kama utakubali kushiriki kwenye utafiti itasaidia kujua matokeo ya matibabu kwa dawa tofauti kwa ajili ya kutibu dalili za mkojo zinazosababishwa na tezi la kiume.Utafiti utasaidia kupata taarifa ya matokeo ya matibabu kwa kutumia dawa tofauti kutoka kwa wagonjwa ili kuboresha tiba ya tezi la kiume kwa kutumia dawa.

Madhara: Hatutegemei madhara yoyote kukutokea kwa kushiriki kwako kwenye utafiti huu.

Haki ya kujitoa;Unaweza kujitoa kushiriki katika utafiti huu muda wowote hata kama umekwishatoa idhini ya kuwa mshiriki. Kukataa kushiriki au kujitoa kwenye utafiti hakuta husisha adhabu yoyote.

Nani wa kuwasiliana naye ;kama una maswali kuhusiana na utafiti huu, wasiliana na mtafiti mkuu Dr. HERRY KIBONA(0717066909,baruapepe : hopkdr@gmail.com) wa Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili , P. O. Box 65001,DSM.

Kama unaswali kuhusu haki zako kama mshiriki unaweza kumpigia simu **DR. JOYCE MASALU**

Mwenyekiti wa Kamati ya Utafiti na Uchapishajiwa Chuo Kikuu cha Afya na Sayansi shirikishi Muhimbili, P.O.BOX 65001, DAR ES SALAAM. Simu+255 22 2152489.

Sahihi

Mimi ……..… nimesoma maelezo ya fomu hii na kuyaelewa napia maswali yangu yamejibiwa

Nakubali/Ninakataa kushiriki katika utafiti huu…….

Sahihi/alama ya kidole gumba cha mshiriki ……

Sahihi/alama ya kidole gumba cha shahidi ……

Sahihi ya Mtafiti ……

Tarehe ya kutia sahihi ya idhini ya kushiriki ……

Appendix 3; QESTIONAIRRE (ENGLISH VERSION)

SECTION ONE

Phone number……....

prescribed……

Medication(s)

ID number.....

Date of start……

1. Age (years)

    1) 30 – 49
    2) 50 –69
    3) 70-89
    4) 90- and above

2. Level of education
    1) No formal education
    2) Primary education level
    3) Secondary education level
    4) Higher education level

3. Occupation

    1) Peasant
    2) Formal employment
    3) Petty trader
    4) Unemployed
    5) Others (specify)……

SECTION TWO

4. Main complains

a. ……

b. ……

c. ……

d. …….

e. ……

5. Duration……..

6. Reported side effects of medication

1) Dizziness ……

2) Headache……..

3) Poor ejaculation……..

4) Nausea …….

5) Others (specify) ……..

7. Abdominal pelvic ultrasound

a) Residual volume before……and after 3 months……

b) Prostate volume before……...and after 3months……

8. Adverse outcome related occurring during 3 months of therapy

a) Urethral catheterization

b) Urine retention

c) Dose increment

d) BPE surgery

TOTAL IPS SCORE BEFORE TREATMENT ……..

TOTAL IPS SCORE AFTER THREE MONTHS OF TREATMENT……

QUALITY OF LIFE SCORE BEFORE TREATMENT ……..

QUALITY OF LIFE AFTER TREATMENT……

International Prostate Symptom Score (IPSS) chart

In the past month:	Not at All	Less than 1 in 5 Times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	**1 Time**	**2 Times**	**3 Times**	**4 Times**	**5 Times**	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							

Score: 1-7: *Mild* 8-19: *Moderate* 20-35: *Severe*

Quality of Life Due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

BPH Impact index score chart

	None	Only a little	Same	A lot	
1. Over the past month, how much physical discomfort did any urinary problems cause you?	0	1	2	3	
2. Over the past month, how much did you worry about your health because of any urinary problems?	0	1	2	3	
	Not at all bothersome	Bothers me a little	Bothers me some	Bothers me a lot	
3. Overall, how bothersome has any trouble with urination been during the past month?	0	1	2	3	
	None of the time	A little of the time	Some of the time	Most of the time	All of the time
4. Over the past month, how much of the time has any urinary problem kept you from doing the kinds of things you would usually do?	0	1	2	3	4

Appendix 4; QESTIONAIRRE (SWAHILI VERSION)

DODOSO NAMBA…….

SEHEMU YA KWANZA

Namba ya simu…….

Dawa alizoandikiwa……..

Tarehe ya kuanza Tiba ……. Namba ya utambulisho…….

1. Umri (miaka)
   1)30-49
   2)50-69
   3)70-89
   4)90 nakuendelea
2. Kiwango cha elimu
   1) sijasoma
   2) Elimu ya msingi
   3) Elimu ya sekondari
   4) Elimu ya chuo
3. Kazi
   1) mkulima
   2) kazi ya kuajiriwa
   3) biashara ndogo
   4) sinakazi
   5) nyinginezo…….

4. Shida za kiafya zinazokusumbua
   a……
   b……
   c……..
   d……..
   e……..

5. Muda wa shida kiafya……
6. Kuna madhara yoyote uliopata baada ya kutumia dawa unazotumia kwa shida ya mkojo(baada ya miezi mitatu)
   1) kizunguzungu
   2) kichwa kuuma
   3) kupata mshindo mdogo au hakuna kwenye tendo la ndoa
   4) kichefuchefu
   5) Nyinginezo……

7. Vipimo vilivyofanyika (Ultrasound)
   a)Mkojo unaobaki baada ya kukojoa(kabla ya dawa)…..(baada ya miezi 3)……(jaza asilimia)
   b) Ukubwa wa tezi(kabla ya dawa)……(baada ya miezi mitatu)……
   c) PSA ……..

8. Matokeo mabaya kutokea wakti wa matumizi ya dawa
   a) Kuwekewa mpira wa mkojo
   b) Mkojo kugoma kabisa kutoka
   c) Dozi ya dawa kuongezwa
   d) Kufanyiwa upasuaji

JUMLA YA ALAMA ZA DALILI ZA MKOJO KABLA YA DAWA…….

JUMLA YA ALAMA ZA DALILI ZA MKOJO BAADA YA MIEZI MITATU YA TIBA……..

ALAMA ZA UBORA WA MAISHA KABLA YA DAWA ……,……

ALAMA ZA UBORA WA MAISHA BAADA YA MIEZI MITATU YA TIBA…….

JEDWALI LA KUPIMA KIWANGO CHA DALILI ZA MKOJO KWA MGONJWA

	Katika kipindi cha mwezi mmoja uliopita?	**Haijatokea hata mara moja** **0**	**Chini ya mara moja katika kila mara tano** **1**	**Mara chache sana chini ya nusu ya nyakati zote** **2**	**Karibu nusu ya wakati wote** **3**	**Mara kwa mara Zaidi ya nusu ya wakati wote** **4**	**Karibu mara zote** **5**
1.	Ni mara ngapi baada ya kukojoa unajiskia kama mkojo haukumalizika?						
2.	Ni mara ngapi ulilazimika kwenda kukojoa tena kabla ya masaa mawili baada ya kukojoa awali?						

3.	Ni mara ngapi ilitoke kukatika kwa mkojo na kuanza tena wakati ukikojoa?						
4.	Ni mara ngapi umeshindwa kujizuia kabisa kukojoa?						
5.	Ni mara ngapi umekojoa kwa shida na mkojo kutiririka bila nguvu?						
6.	Ni mara ngapi imebidi usukume mkojo kwa nguvu ili utoke unapoanza kukojoa?						
7.	Ni mara ngapi ilikubidi uamke usiku kwenda kukojoa baada ya saa yako ya kulala mpaka saa yako ya kawaida ya kuamka?	Hakuna 0	Mara moja 1	Mara mbili 2	Mara tatu 3	Mara nne 4	Mara tano au Zaidi 5

Score; 1-7; Mild **8-19; Moderate** **20-35; Severe**

Swali la kupima adha na ubora wa maisha kwa wenye dalili za mkojo	**Ningefurahi Sana**	**Ningefurahi**	**Ningeridhika**	**Ningeona sawa tu**	**Nisingeridhika**	**Ningekuwa na majonzi**	**Maisha hayawezekani**
Je katika maisha yako yote ungeendelea kuishi na dalili hizi za kukojoa utajiskiaje?	0	1	2	3	4	5	6

JEDWALI LA KUPIMA ADHA NA UBORA WA MAISHA KWA MGONJWA MWENYE DALILI ZA MKOJO ZITOKANAZO NA KUVIMBA TEZI LA KIUME

	Sijapata	**Nimepata kidogo sana**	**Wastani**	**Nimepata sana**	
1. Katika mwezi mmoja uliopita ni kwa kiasi gani umepata adha kiafy kutokana na shida ya mkojo uliyonayo?	0	1	2	3	
2. Katika mwezi mmoja uliopita ni kwa kiasi gani umepata wasiwasi kwa afya yako kutokana na shida ya mkojo uliyonayo?	0	1	2	3	
3. Kwa ujumla,shida ya kukojoa imekusababishia adha kiasi gani katika mwezi mmoja uliopita?	Sikupata adha	Nilipata adha kidogo sana	Nipata adha kidogo	Nilipata adha sana	
	0	1	2	3	
4. katika mwezi mmoja uliopita je ni kwa muda gani shida ya mkojo imekuzidia kufanya shughuli ambazo ulizoea kufanya	Hakuna	Muda kidogo sana	Muda kiasi	Muda mwingi	Muda wote
	0	1	2	3	4

JUMLA YA ALAMA KABLA……

JUMLA YA ALAMA BAADA……..