



**Comparing The Efficacy And Safety Of
Treatment With Fixed Dose Of Tadalafil Or
Tamsulosin And Their Combination Therapy
In Patients With Benign Prostatic
Hyperplasia And Erectile Dysfunction**

Thesis

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Urology*

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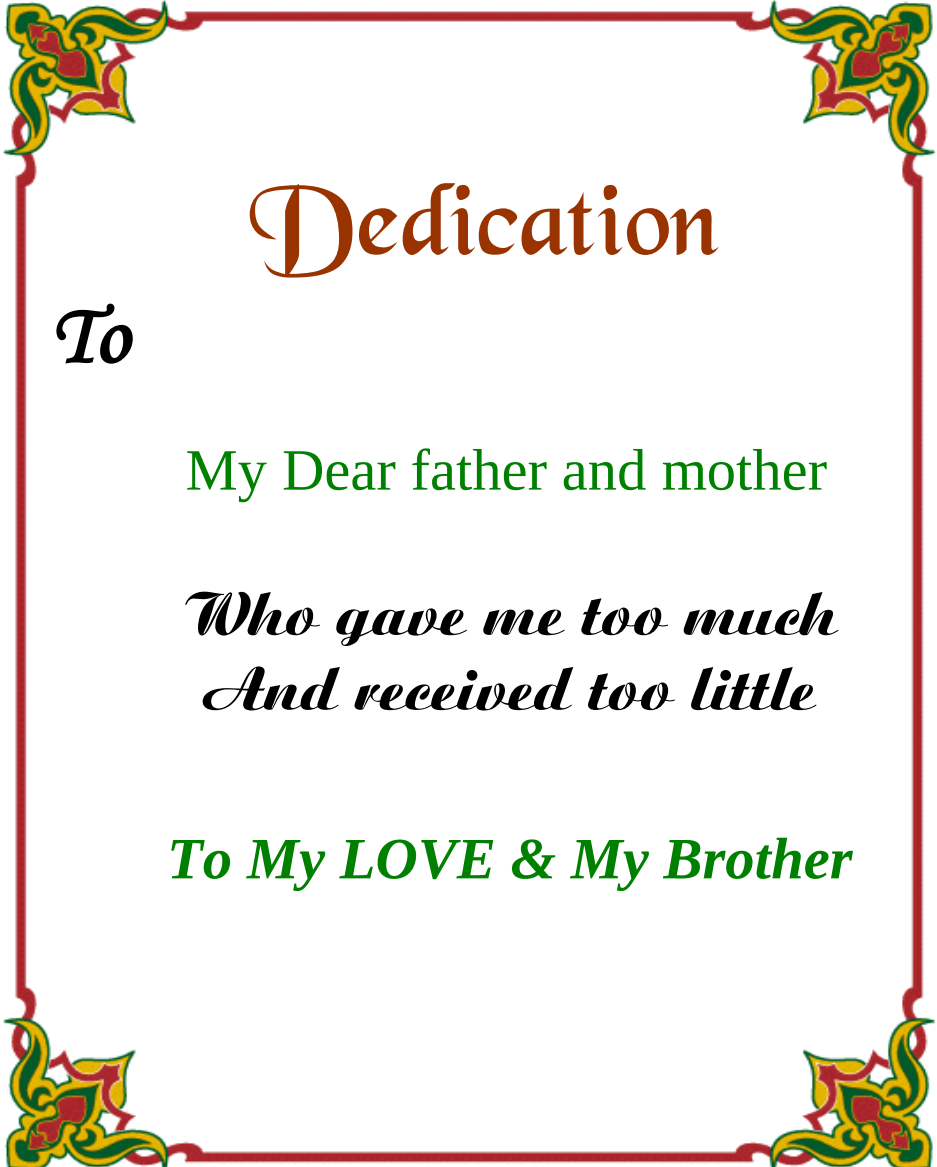
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Kirollos nabil



Dedication

To

My Dear father and mother

*Who gave me too much
And received too little*

To My LOVE & My Brother

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List of Abbreviations

Abb.	Full term
<i>ACP</i>	<i>American College of Physicians</i>
<i>AR</i>	<i>Adrenergic Receptor</i>
<i>ATP</i>	<i>Adenosine Triphosphate</i>
<i>AUA</i>	<i>American Urological Association</i>
<i>AUR</i>	<i>Acute Urinary Retention</i>
<i>BOO</i>	<i>Bladder Outlet Obstruction</i>
<i>BPE</i>	<i>Benign Prostatic Enlargement</i>
<i>BPH</i>	<i>Benign Prostatic Hyperplasia</i>
<i>BUN</i>	<i>Blood Urea Nitrogen</i>
<i>cAMP</i>	<i>Cyclic Adenosine Monophosphate</i>
<i>CCs</i>	<i>Corpora Cavernosa</i>
<i>cGMP</i>	<i>Cyclic Guanosine Monophosphate</i>
<i>DHT</i>	<i>Dihydrotestosterone</i>
<i>DRE</i>	<i>Digital Rectal Examination</i>
<i>ED</i>	<i>Erectile Dysfunction</i>
<i>eGFR</i>	<i>Estimated Glomerular Filtration Rate</i>
<i>eNOS</i>	<i>Endothelial Nitric Oxide Synthase</i>
<i>FDA</i>	<i>Food and Drug Administration</i>
<i>GTP</i>	<i>Guanosine-50-Triphosphate</i>
<i>H&E</i>	<i>Hematoxylin and Eosin</i>
<i>IIEF-5</i>	<i>International Index of Erectile Function</i>
<i>IP3</i>	<i>Inositol Trisphosphate</i>
<i>IPSS</i>	<i>International Prostate Symptom Score</i>
<i>IQR</i>	<i>Inter-Quartile Range</i>
<i>LH</i>	<i>Luteinizing Hormone</i>
<i>LUTS</i>	<i>Lower Urinary Tract Symptoms</i>
<i>MMAS</i>	<i>Massachusetts Male Aging Study</i>
<i>MUSE</i>	<i>Medicated Urethral System for Erections</i>
<i>NH2</i>	<i>Amino Terminus</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>NIH</i>	<i>National Institutes of Health</i>
<i>NO</i>	<i>Nitric Oxide</i>
<i>NOS</i>	<i>Nitric Oxide Synthase</i>
<i>P</i>	<i>Phosphate</i>
<i>PAH</i>	<i>Pulmonary Arterial Hypertension</i>
<i>PDE</i>	<i>Phosphodiesterase</i>
<i>PDE5</i>	<i>Phosphodiesterase Type 5</i>
<i>PGE1</i>	<i>Prostaglandin E1.</i>
<i>PSA</i>	<i>Prostate-Specific Antigen</i>
<i>PVR</i>	<i>Postvoid Residual</i>
<i>PVRU</i>	<i>Postvoid Residual Urine</i>
<i>PZ</i>	<i>Peripheral Zone</i>
<i>QOL</i>	<i>Quality of Life</i>
<i>S</i>	<i>Serine</i>
<i>sGC</i>	<i>Soluble Guanylate Cyclase</i>
<i>SHBG</i>	<i>Sex Hormone-Binding Globulin</i>
<i>SPSS</i>	<i>Statistical Package for Social Science</i>
<i>TGF</i>	<i>Transforming Growth Factor</i>
<i>TSH</i>	<i>Thyroid-Stimulating Hormone</i>
<i>TUIP</i>	<i>Transurethral Incision of the Prostate</i>
<i>TUMT</i>	<i>Transurethral Microwave Therapy</i>
<i>TUNA</i>	<i>Transurethral Needle Ablation of the Prostate</i>
<i>TURP</i>	<i>Transurethral Resection of the Prostate</i>
<i>TZ</i>	<i>Transitional Zone</i>
<i>UGS</i>	<i>Urogenital Sinus</i>

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a disorder characterized by a proliferation of both stromal and epithelial cells of the prostate in the transitional zone surrounding the urethra (*Roehrborn, 2008; Chughtai et al., 2016*).

BPH is a common diagnosis among the ageing male population with increasing prevalence (*Chughtai et al., 2016*).

BPH can be defined as a histopathological change consisting of both glandular and fibromuscular hyperplasia. It is estimated that 10% of men in their 50s and almost 90% of men over 80 have BPH (*Vuichoud and Loughlin, 2015*).

BPH is a frequent cause of lower urinary tract symptoms (LUTS) in men and is a common histological finding — particularly in ageing men. Although ‘normal’ prostates in adult men are typically 15–30 ml in volume, and glands >30 ml are commonly deemed ‘enlarged’, no strict cutoff value has been defined and, for many physicians, enlarged prostate volume is a subjective finding on examination. Furthermore, the extent of prostatic enlargement varies considerably because the extent of hyperplasia is variable (*Lepor, 2005*).

LUTS affect one-third of men over 55 and half of men over 65 and while LUTS due to BPH (LUTS/BPH) are generally thought of as a disease of older men the costs of

treating this disease start accruing when patients are in their 40s (*Sterling et al., 2019*).

Many risks factors, both modifiable and non-modifiable, can increase the risk of development and progression of BPH and (lower urinary tract symptoms) LUTS. The symptoms can be obstructive (resulting in urinary hesitancy, weak stream, straining or prolonged voiding) or irritative (resulting in increased urinary frequency and urgency, nocturia, urge incontinence and reduced voiding volumes), or can affect the patient after micturition (for example, postvoid dribble or incomplete emptying) (*Chughtai et al., 2016*).

About half of men with BPH develop an enlarged prostate gland, called benign prostatic enlargement (BPE) among these, about half develop some degree of bladder outlet obstruction (BOO). BOO and/or changes in smooth muscle tone and resistance that can accompany BPH may result in LUTS (*Liu et al., 2017*).

BPH results in compression of the urethra, causing resistance to urine flow known as bladder outlet obstruction (BOO). This resistance can also result in obstruction-induced changes of bladder function, such as overactivity of the detrusor muscle or, conversely, reduced contractility of the detrusor muscle. BOO can present as LUTS, infections or retention, as well as other conditions. BPH and BOO impose

considerable burden on the health of older men and on health care costs (*Chughtai et al., 2016*).

The relationship between LUTS and erectile dysfunction (ED) have received increased attention recently because both diseases are highly prevalent, frequently co-associate in the same aging male group, and contribute significantly to the overall quality of life. The link between ED and LUTS has biologic plausibility given the four leading theories of how these diseases interrelate. These explanations fall into four theories each with a variable amount of supporting data. These include: (1) NOS/NO levels decreased or altered in the prostate and penile smooth muscle, (2) Autonomic hyperactivity effects on LUTS, prostate growth and ED., (3) increased Rho-kinase activation/endothelin activity, and (4) prostate and penile ischemia (*McVary, 2005*).

LUTS associated with BPH is a highly impactful condition that is often undertreated and can be bothersome and negatively impact on a patient's quality of life (QoL). LUTS/BPH have a major impact on men, their families, health services and society (*Speakman and Cheng, 2014*).

Treatment for LUTS/BPH remains largely driven by patient symptomatology with medical therapy or watchful waiting as the first-line management strategies (*Sterling et al., 2019*).

Lifestyle interventions such as modifying fluid intake or toileting behavior are typically the first-line treatments to reduce symptoms in patients with LUTS/BPH. When necessary, pharmacological treatment also may be initiated to reduce symptoms and prevent or delay disease progression (*Strittmatter et al., 2013*).

Many medical and surgical treatment options exist. Surgery should be reserved for patients who either have failed medical management or have complications from BPH, such as recurrent urinary tract infections, refractory urinary retention, bladder stones, or renal insufficiency as a result of obstructive uropathy (*Kim et al., 2016*).

Apart from medications, one important strategy is advice on exercise and diet, encouraging the patient to self-manage his disease. This may help to reduce the need for surgery with its many possible side effects and long term recurrence (*Lim, 2017*).

The current standard of care for LUTS/BPH includes α -adrenergic blockers, 5 α -reductase inhibitors, used alone or in combination. These therapies are associated with bothersome sexual side effects. The primary goals of LUTS attributed to BPH treatment are to reduce LUTS, improve prostate-related quality of life, and prevent or delay disease progression (*Strittmatter et al., 2013*).