بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

MONA MAGHRABY

Comparative Study Between α-Blockers and Combination of α-blockers and Phosphodiestrase 5-Inhibitors in Treatment of Benign Prostatic Hyperplasia

Thesis

Submitted for Partial Fulfilment of M.D degree in Urology

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2020

سورة البقرة الآية: ٣٢

Acknowledgment

First of all, thanks to **Allah** *whose magnificent help was the main factor in completing this work.*

I would like to express my special thanks to ***Prof. Dr. Hany Mostafa Abdallah,*** *Professor of Urology, Faculty of Medicine, Ain Shams University, who had expressed so much sincere care and devoted much of his time. I'm deeply obligated for his kind supervision, constructive criticism, unlimited help, keen interest and great encouragement during the progress of this work.*

My deepest appreciation and profound gratitude to ***Dr. Ahmed Farouk Mahmoud,*** *Lecturer of Urology, Faculty of Medicine, Ain Shams University. I appreciated and enjoyed his valuable advice, generous cooperation and great support.*

Lastly but not the least I would like to express my great thanks to ***All members of the Urology Department,*** *Ain Shams University, for their valuable continuous guidance and kind attitude during this study has made its completion possible.*

Mamdouh Kartabeh

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List of Abbreviations

Abb.	Full term

5-ARs ..... *: 5-α-reductases*
ACS ..... *: American cancer society*
AR ..... *: Androgen receptor*
AUA ..... *: American urological association*
AUR ..... *: Acute urine retention*
BOO ..... *: Bladder outlet obstruction*
BPH ..... *: Benign prostatic Hyper-plasia*
cAMP ..... *: Cyclic adenosine monophosphate*
cGMP ..... *: Cyclic guanosine*
DHT ..... *: Dihydrotestosterone*
DRE ..... *: Digital rectal examination*
ED ..... *: Erectile dysfunction*
FB ..... *: Foreign body*
FDA ..... *: Food drug administration*
GF ..... *: Growth factor*
IPSS ..... *: International prostate symptom score*
KTP ..... *: Potassium – Titanyl phosphate*
LUTS ..... *: Lower urinary tract system symptoms*
MTOPS ..... *: Medical therapy of prostatic symptoms*
NO ..... *: Nitrous oxide*
PAE ..... *: Prostatic artery embolization*
PDE-5 ..... *: Phosphodiestrase-5*
PDE5-IS ..... *: Phosphodiestrase type 5 inhibitors*
PSA ..... *: Prostatic specific antigen*
QOL ..... *: Quality of life*
RE ..... *: Retrograde ejaculation*

List of Abbreviations (Cont...)

Abb.	Full term

TRUS ..... *: Trans-rectal ultrasound*

TUIP ..... *: Transurethral incision of prostate*

TUMT ..... *: Trans-urethral microwave therapy*

TUNA ..... *: Transurethral needle ablation of prostate*

TURP ..... *: Transurethral resection of prostate*

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common conditions affecting middle-aged men. This condition can be symptomatic or asymptomatic. Up to 15-25% of men aged 50-65 years have lower urinary tract symptoms (LUTS) ***(Abram et al., 2002).***

BPH Development is under hormonal, genetic, and environmental control. There is evidence indicates that metabolic disorders and lifestyle factors are important in the etiology of BPH and LUTS, including obesity, diabetes, diet and exercise ***(Mongiu and McVary, 2009)***.

Androgens have a key role in the development and growth of the prostate as well as in the pathogenesis of BPH. Testosterone is converted to dihydrotestosterone (DHT) by 5-α-reductases (5-ARs) predominantly in the stromal tissue. The higher affinity for the androgen receptor (AR) to DHT allowing it to accumulate in the prostate even when circulating testosterone levels are low ***(Hoclement and Habib, 2011)***.

The evaluation and treatment of BPH depends on the symptoms that affect the patient's quality of life. The symptoms score most commonly used to evaluate prostatic patients is the International Prostate Symptom Score (IPSS) ***(Chapple et al., 2015)***.

Treatment options can be based on degree of IPSS symptoms without need to specialized tests such as Qmax and postvoid residual urine (PVR) measurement, the first-line treatments to reduce symptoms in patients with LUTS/BPH is to modify lifestyle such as fluid intake or toileting behavior. pharmacological treatments to reduce LUTS/BPH are α-adrenergic blockers and 5α-reductase inhibitors, used alone or in combination ***(Strittmatter et al., 2013).***

α-adrenergic blockers and 5-α reductase inhibitors are two classes of medications used as medical therapy for voiding symptoms due to BPH, anticholinergic agents or new β_3-agonist therapy may also be used in the patients with predominantly storage symptoms ***(Minutoli et al., 2016)***.

By relaxing the prostatic smooth muscles during the act of voiding the α-adrenergic blockers serve as an effective treatment of BPH. Doxazosin, terazosin, tamsulosin, alfuzosin and silodosin are all appropriate therapies for patients with BPH causing LUTS, Patients respond differently to each alpha blocker but they are generally considered to be equally effective in relieving LUTS ***(Gacci et al., 2014)***.

One of common side effect in patients using tamsulosin or silodosin is the retrograde ejaculation (RE); some patients will find RE troublesome; however, and some patient not ***(Bird et al., 2014)***.

Recently, phosphodiestrase type 5 inhibitors (PDE5-Is) sildenafil, vardenafil and tadalafil which are widely used as first-line oral treatment for erectile dysfunction, are effective in the treatment of LUTS ***(Singh et al., 2014)***.

In human tissues, 11 phosphodiestrase (PDE) families have been distinguished, and there is significant variation in distribution and function in different tissues. It is known that isoenzymes 1, 2, 3, 4, 5, 7, 8, 9 and 10 are expressed in the human prostate, whereas isoenzymes 1, 3, 4 and 5 are present in the human destrusor. PDE-5 inhibitors inhibit degradation of cyclic guanosine monophosphate (cGMP) which is an intracellular second messenger that mediates several pharmacologic effects Therefore, PDE-5 inhibitors, by increasing cGMP in the lower urinary tract, can potentially modulate sensory signals, microvasculature dilation and smooth muscle cell relaxation in the prostate, urethra and bladder ***(Azevedo et al., 2014)***.

Several studies conclude that nitric oxide (NO)/cGMP system and related key proteins, including the cGMP-degrading PDE-5, are important factors in the control of the normal function of the prostate. This may affect the contractile activity of the smooth musculature, secretory granular function, as well as the regulation of proliferation of smooth muscle, granular epithelial cells and stromal connective tissue ***(Azevedo et al., 2014)***.

Several clinical trials on the effect of PDE-5 inhibitors on male LUTS have been published. In these studies, different PDE-5 inhibitors (sildenafil, vardenafil, tadalafil) and combinations of an α-blocker (alfuzosin or tamsulosin). According to a recent meta-analysis, the use of PDE-5 inhibitor alone was associated with a significant improvement of IPSS at the end of studies compared with placebo. The combination of an alpha blocker and PDE-5 inhibitor significantly improved IPSS and Qmax at the end of the studies compared with alpha blockers alone ***(Gacci et al., 2012)***.