SAFETY AND EFFICACY OF SILDOSIN FOR THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA

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بسم الله الرحمن الرحيم

قَالُوا سُبْحَانكَ لاَ علِمَ لَنَا إِلاّ مَا عَلّمْتَنَا

إِنَّكَ أَنتَالْعَلِيمُ الْحَكِيمُ

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LIST OF ABBREVIATIONS

ATP:	Adenosine triphosphate
BOO:	Bladder outlet obstruction BPH: Benign prostatic hyperplasia BWT: Bladder wall thickness
C/S:	Culture and sensitivity
CBC:	Complete blood count
CI:	Confidence interval
ED:	Erectile dysfunction
EjD:	Ejaculatory dysfunction
DRE:	Digital rectal examination
ECG:	Electrocardiogram
IBM:	International business machine
IPPS:	International Prostate Symptom Score
IPSS-QoL:	Quality of life related to urinary symptoms
LUTs:	Lower urinary tract symptoms
LUTs/BPH:	Lower urinary tract symptoms associated with benign prostatic hyperplasia
MSAM-7:	Multinational Survey of the Aging Male-7
NANC:	Non-adrenergic non-cholinergic
NO:	Nitric oxide
PSA:	Prostatic specific antigen
PVR:	Post void residue
Qmax:	Maximum urinary flow rate
QoL:	Quality of life
SMCs:	Smooth muscle cells
SPSS:	Statistical package for social science
St.D:	Standard deviation

TEAEs:	Treatment-emergent adverse events
TOWC:	Trial without catheter TRUS: Trans rectal ultra-sound U/S: Ultra-sound
UT:	Urinary tract

Abstract

Background:α1 adrenergic receptor antagonists are commonly used as the first-line treatments for LUTS associated with BPH**.** Silodosin is a novel α_1-adrenergic receptor antagonist whose affinity for the α_{1A}-adrenergic receptor is 162 times higher than that for the α_{1B}-adrenergic receptor, and 55 times higher than that for the α_{1D}-adrenergic receptor, Therefore, silodosin does not increase the incidence of blood pressure-related side effects, which are mainly result from the inhibition of the α_{1B}-adrenergic receptor.

Objective: To test the hypothesis that the efficacy of silodosin(in dose of 8 mg once daily) would not be inferior to tamsulosin (in dose of 0.4 mg once daily) in treating patients with LUTS associated with BPH, with lesser cardiovascular side effects (as judged by the minimal changes of blood pressure and heart rate after treatment).

Design, setting, and participants: A randomized, double-blind, placebo- and active-controlled, parallel-group study assessed men ≥ 50 yrs. of age with LUTS/BPH, InternationalProstate Symptom Score (IPSS) ≥ 13,Post Voiding Residue(PVR) ≤ 150ml and maximum urinary flow rate (Qmax) between4 and 15 ml/s. Following screening, subjects completed a 24-wk silodosin 8 mg once daily, tamsulosin 0.4 mg once daily and placebo.

Measurements: Outcomes were assessed by change from baseline in IPSS, quality of life (QoL), Qmax, PVR, systolic blood pressure (S.BP), diastolic blood pressure (D.BP) and heart rate (HR) to endpoint of the study. Responders to the treatments on the basis of IPSS decrease of ≥ 25% and Qmax increase of ≥ 30% were calculated.

Results: Silodosin and tamsulosin significantly improved IPSS total score in comparison with placebo (p=0.005) and(p=0.007), respectively.Silodosin and tamsulosin significantly improved QoL (p<0.0001) and (p<0.0001),respectively.Silodosinandtamsulosin significantly improved Qmax (p<0.0001) and (p<0.0001),respectively.Silodosin and tamsulosin significantly improved PVR (p<0.0001) and(p=0.022), respectively, with highly statistically significant difference between both (p<0.0001).However, regardingsystolic blood pressure, a minor but statistically significant change versus placebo was observed with tamsulosin (p=0.026) and for a lesser extent with silodosin but non-significant (p = 0.177). Similarly, diastolic blood pressure had hardly statistically significant change with tamsulosin (p = 0.058), while statistically non-significant changein diastolic blood pressure occurred with silodosin (p=0.387).While both silodosin and tamsulosin did not affect heart rate significantly (p = 0.204) and (p = 0.515), respectively, with statistically significant difference between both of them (p = 0.025). In silodosin group, a retrograde ejaculation was reported in 10 patients from 35 patients were sexually active (28.6%) andonly one subject reported headache. While in tamsulosin group, a retrograde ejaculation was reported in 1patients from 36 patients were sexually active (2.8%), three subjects reported headache and three reported postural hypotention.

Conclusions: Silodosin is not only comparable to tamsulosin in treatment of LUTS/BPH, but alsosuperior numerically, with higher safety profile. However, retrograde ejaculation is considered troublesome for sexually active patients.

Keywords: Silodosin, tamsulosin, benign prostatic hyperplasia, Lower urinary tract symptoms, quality of life, α-1A adrenergic receptors.

INTRODUCTION

Benign Prostatic Hyperplasia (BPH) is a non-malignant enlargement of the prostate caused by cellular hyperplasia of both glandular and stromal elements ***(Chapple, 1992)***.

Benign prostatic hyperplasia (BPH) is a common progressive disease among men, with an incidence that is age-dependent. Histological BPH, which typically develop after the age of 40 years, ranges in prevalence from >50% at 60 years to as high as 90% by 85 years of age. BPH contribute to, but is not the single cause of, bothersome lower urinary tract symptoms (LUTS) that may affect quality of life. The prevalence of troublesome symptoms increases with age, with symptoms typically occurring in men aged ≥50 years. Approximately 50% of patients with histological BPH report moderate to severe LUTS, consisting of storage and voiding symptoms. Although bothersome LUTS may affect quality of life by altering normal daily activities and sleep patterns, mortality associated with BPH is rare. Although uncommon, serious complications of BPH may occur, including acute urinary retention, renal insufficiency, urinary tract infection, hematuria, bladder stone, and renal failure ***(Yoshida et al., 2011)***.

These complications may be triggered or worsened by inadequate management of BPH. The incidence of acute urinary retention in untreated patients ranges from 0.3%to3.5% per year; the risk of developing other long-term complication is unclear ***(O΄Leary, 2003)***.

The management of patients with BPH includes non-pharmacological, pharmacological, and surgical option, with the choice of therapy typically depending on the presence and severity of symptoms. Watchful waiting is the preferred management strategy for patients with