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PROSTATIC DISORDERS
ORIGINAL ARTICLE

Sildenafil citrate in combination with tamsulosin versus tamsulosin monotherapy for management of male lower urinary tract symptoms due to benign prostatic hyperplasia: A randomised, double-blind, placebo-controlled trial

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KEYWORDS

Tamsulosin;
Sildenafil;
Lower urinary tract symptoms (LUTS);
Benign prostatic hyperplasia (BPH)

ABBREVIATIONS

BMI, body mass index;
CONSORT, Consolidated Standards of Reporting Trials;
ED, erectile dysfunction;

Abstract ***Objective:*** To assess the additive effect of sildenafil citrate to tamsulosin in the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia (LUTS/BPH) in men with or without erectile dysfunction (ED).

Patients and methods: In all, 150 men with untreated LUTS/BPH with or without ED were randomised to receive sildenafil 25 mg once daily (OD) or placebo OD (night time) combined with tamsulosin 0.4 mg OD (day time) for 6 months. Changes from pre-treatment scores in International Prostate Symptom Score (IPSS), IPSS-quality of life (QoL) score, maximum urinary flow rate (Q_{max}), and the five-item version of the International Index of Erectile Function questionnaire (IIEF-5) were assessed at 3 and 6 months. Safety profiles were assessed by physical examination and monitoring clinical adverse events.

Results: Group A comprised of men who received tamsulosin and sildenafil (75 men), whilst those in Group B received tamsulosin and placebo (75). The IPSS was significantly improved in Group A compared to Group B, at −29.3% vs −13.7% ($P = 0.039$) at 3 months and −37% vs −19.6% ($P = 0.043$) at 6 months

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after treatment. Q_{max} significantly improved in both groups compared with before treatment ($P < 0.001$). The IIEF-5 scores improved more in Group A than in Group B, at 58.7% vs 11.7% at 3 months and 62.4% vs 12.4% at 6 months after treatment (both $P < 0.001$).

Conclusion: Sildenafil citrate combined with tamsulosin improved LUTS, erectile function, and patient QoL more than tamsulosin monotherapy with the merit of a comparable safety profile in patients with LUTS/BPH.

IIEF-5, five-item version of the International Index of Erectile Function questionnaire;
NO, nitric oxide;
OD, once daily;
PDE5-I, phosphodiesterase type 5 inhibitor;
Q_{max}, maximum urinary flow rate;
QoL, quality of life;
RCT, randomised controlled trial;
SMD, standardised mean difference

Introduction

BPH is the most common and important pathology that contributes to male LUTS [1]. There is a direct relationship between LUTS and age, with an overall prevalence of >50% in men aged ⩾50 years [2,3]. The prevalence of erectile dysfunction (ED) is also similarly high and increases with age. About 35% of men aged 40–70 years have moderate to complete ED, which is strongly related to age and other co-morbidities such as cardiovascular disease, diabetes, and depression [4]. LUTS due to BPH (LUTS/BPH) and ED are common disorders among ageing men, with a striking relationship. In addition, both have a significant negative impact on quality of life (QoL) [5]. In their meta-analysis of 12 randomised controlled trials (RCTs), Gacci et al. [6] reported that the combination of phosphodiesterase type 5 inhibitors (PDE5-Is) and α_1-adrenergic receptor blockers significantly improved the IPSS [standardised mean difference (SMD) −1.8, 95% CI −3.7 to 0.0; $P = 0.05$] and International Erectile Function score (SMD +3.6, 95% CI +3.1 to +4.1; $P < 0.001$), as well as Q_{max} (SMD +1.5 mL/s, 95% CI +0.9 to +2.2; $P < 0.001$) when compared with the use of α_1-adrenergic receptor blockers alone.

Our aim in the present study was to assess the additive effect of sildenafil citrate to tamsulosin in the treatment of LUTS/BPH in men with or without ED in a prospective, randomised, placebo-controlled, double-blind study.

Patients and methods

Patient enrolment

This study was conducted between May 2013 and May 2014. Approval from our ethics committee was obtained and a written consent was signed by each patient before the study. In all, 150 patients who were diagnosed with LUTS/BPH were enrolled. The inclusion criteria were: (i) patients who were recently diagnosed LUTS/BPH without any history of medical or surgical intervention for BPH, (ii) no absolute indication for surgical intervention, (iii) patients with or without ED, (4) a PSA level of <4 ng/dL, and (v) a body mass index (BMI) of ⩽30 kg/m^2, as obesity is a risk factor for both ED and male LUTS. The exclusion criteria were: (i) patients with significant cardiovascular disease, neurological, and psychiatric disorders, (ii) history of hypersensitivity and contraindication to one of the study drugs, (iii) patients with confirmed prostatic malignancy or any other active urinary tract disease, (iv) participation in another clinical trial in the 3 months prior to the study.

Study design

This study was a prospective, two-armed, randomised, double-blind (was carried out by relevant outpatient clinic pharmacist who provided us with a sealed randomisation list that was unblinded at the end of follow-up), placebo-controlled (placebo prepared by the Pharmaceutics Department in a tablet formulation similar to the original drug but without any active ingredients), comparative study between tamsulosin 0.4 mg once daily (OD) at day time plus sildenafil 25 mg OD at night and tamsulosin 0.4 mg OD at day time plus placebo at night in the treatment of patients with LUTS/BPH. Patients who fulfilled the entry criteria at selection were randomised into the two groups. Patients were randomly assigned blinded medication (placebo or sildenafil, plus tamsulosin) using a computer generated pseudorandom code in a 1:1 ratio by the study centre with a fixed block size of four.

Main outcome measures

The primary endpoint was clinical efficacy assessments for LUTS/BPH, which were evaluated by the IPSS and QoL score. The secondary endpoints were maximum urinary flow rate (Q_{max}); erectile function evalu-