

Silodosin versus tamsulosin in symptomatic benign prostatic hyperplasia-Our experience

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Abstract : *Aim:* Benign prostatic hyperplasia (BPH) is the most common cause of lower urinary tract symptoms in elderly men. Selective α_1 -adrenergic antagonists are now first-line drugs in the medical management of BPH. We conducted randomized, controlled trial to compare the effectiveness and safety of the new α_1 -blocker silodosin versus the established drug tamsulosin in symptomatic BPH.

Materials and Methods: Ambulatory male BPH patients, aged above 50 years, were recruited on the basis of International Prostate Symptom Score (IPSS). Subjects were randomized in 1:1 ratio to receive either tamsulosin 0.4 mg controlled release or silodosin 8 mg once daily after dinner for 12-week. Primary outcome measure was reduction in IPSS. Proportion of subjects who achieved IPSS <8, change in prostate size as assessed by ultrasonography and changes in peak urine flow rate and allied uroflowmetry parameters, were secondary effectiveness variables. Treatment emergent adverse events were recorded.

Results: Data of 57 subjects - 28 on silodosin and 29 on tamsulosin were analyzed. Final IPSS at 12-week was significantly less than baseline for both groups. However, groups remained comparable in terms of IPSS at all visits. There was a significant impact on sexual function (assessed by IPSS sexual function score) in silodosin arm compared with tamsulosin. Prostate size and uroflowmetry parameters did not change. Both treatments were well-tolerated. Retrograde ejaculation was encountered only with silodosin and postural hypotension only with tamsulosin.

Conclusions: Silodosin is comparable to tamsulosin in the treatment of BPH in Indian men. However, retrograde ejaculation may be troublesome for sexually active patients.

Keywords – BPH-benign prostatic hyperplasia, IPSS-international prostate symptom score, QoL-quality of life

I. INTRODUCTION

Lower urinary tract symptoms (LUTS) are a common problem of aging males. Benign prostatic hyperplasia (BPH) is the most common cause of LUTS in elderly men over 70 years of age. BPH, usually, starts in men in their 50s; by the age of 60 years, 50% of men have histological evidence of BPH and 80% of men in their 70s suffer from BPH-related LUTS. The clinical manifestations of BPH include LUTS, poor bladder emptying, urinary retention, an overactive bladder, UTI, hematuria, and renal insufficiency. Historically, the pathophysiology of clinical BPH was attributed to BOO secondary to macroscopic enlargement of the prostate gland. The International Prostate Symptom Score (IPSS) is recommended as the symptom scoring instrument to be used for the baseline assessment of symptom severity in men presenting with LUTS. However, the IPSS cannot be used to establish the diagnosis of BPH. IPSS is the ideal instrument to grade baseline symptom severity, assess the response to therapy, and detect symptom progression in those men managed by watchful waiting. Additional testing should be considered after the initial evaluation if there is a significant chance the patient's LUTS may not be due to BPH. Urinary flow rate, post void residual (PVR) urine volume, and pressure-flow urodynamic studies are appropriate tests to consider in the evaluation of men with moderate to severe symptoms (IPSS 8 to 35). The value of pressure-flow studies is debated. The definitive management of symptomatic BPH is surgery to relieve the obstruction imposed by the enlarged portion of the prostate. However, apart from invasiveness, there are potential complications of surgery, including the unfortunate development of permanent urinary incontinence, TUR syndrome. Thus, there is a need for continued research on drug treatment for symptomatic BPH. Medical therapies extensively investigated for BPH include α -adrenergic blockers, 5 α -reductase inhibitors, aromatase inhibitors, and numerous plant extracts. Newer therapies include antimuscarinic drugs and phosphodiesterase inhibitors (PDEIs) and several combinations of these agents. α_1 -blockers are now considered as first-line drugs in the medical management of BPH. Silodosin, an α_{1A} -adrenoceptor blocker introduced into the Indian market recently, is said to be highly selective for this receptor subtype. Our objective was to compare the effectiveness and safety of silodosin in elderly Indian men with BPH, in comparison to the older established α_1 -blocker tamsulosin, through a randomized controlled trial (RCT).

II. MATERIAL AND METHODS

The study was conducted in the department of urology at a tertiary hospital in Tamil Nadu. A total of 57 ambulatory, treatment naive, male patients over 50 years of age with bothersome LUTS from BPH and International Prostate Symptom Score (IPSS) >7 were recruited during the period from August 2013 to April 2015. Those patients with history of LUTS but not BPH, acute retention of urine in past 6 months, raised prostate specific antigen (PSA) level at baseline, serious co-morbidity of vital organs, use of concomitant medication having anticholinergic, androgenic or estrogenic influence, on other α -adrenergic antagonists or diuretics or with a history of prostatic or per urethral surgery or substance abuse were excluded. Subjects were randomised in two groups. They took either tamsulosin 0.4 mg controlled-release capsule or silodosin 8 mg capsule once daily after dinner for 12-week. 28 patients were assigned to silodosin group and 29 patients to tamsulosin group.

The primary effectiveness variable for this study was symptom relief as assessed by IPSS scoring. The total score was taken as the sum of seven individual symptom scores. In addition, the quality of life (QoL) assessment was done on a 7-point scale and quality of sexual life assessed by a 6-item questionnaire that form part of the broader symptom scoring. The secondary effectiveness variables were: (a) Proportion of subjects who became completely or relatively symptom free (IPSS <8) after 12-week of treatment (b) change in prostate size, in terms of volume, as assessed at ultrasonography (USG) by a radiologist unaware of treatment allocation and (c) changes in peak urine flow rate and allied parameters assessed at uroflowmetry by a blinded operator.

Subjects underwent standard laboratory investigations (complete blood count, fasting plasma glucose, routine liver function tests and creatinine level) at baseline and study end. Vital signs were recorded at each study visit and all treatment-emergent adverse events, either reported spontaneously by trial subjects or noted by the attending investigator, were recorded in the structured case report form. History suggestive of postural hypotension and retrograde ejaculation (in sexually active patients) was specifically sought at each visit. Patients were followed up at 4 and 8-week from the start of the treatment, with the final study visit being at 12-week. The null hypothesis was that test drug (silodosin) is equivalent to an active comparator (tamsulosin) in the treatment of symptomatic BPH. IPSS and allied scores had skewed distribution, and therefore were compared between groups by Mann-Whitney U-test and within group by Friedman's analysis of variance, followed by Dunn's test for post-hoc comparison between two individual time points. Chi-square test or Fisher's exact test was employed for intergroup comparison of categorical variables, as appropriate. GraphPad Prism version 5 (San Diego, California: GraphPad Software Inc., 2007) software were used for the statistical analysis.

III. RESULTS

Mean age of the patients was 61-62 years in both the groups. Mean weight around 60 kg and mean symptom duration around 9 to 10 months. Change in the total IPSS from baseline in the silodosin, tamsulosin, groups was -8.3, -6.8, respectively. Silodosin showed a significant decrease in IPSS versus tamsulosin at 2 weeks. The change in quality of life score from baseline was -1.7, -1.4. There was not much change in prostatic size of the patients as assessed by ultrasonography in both the groups. Adverse effects were seen in 13 patients out of total 57 patients included in study (22.8%). Drug related adverse effects seen in 10 patients in silodosin group out of total 28 patients (35.7%) and in 8 patients of tamsulosin group out of total 29 patients (27.5%). Maximum no of complaints were dyspepsia in silodosin group (n=4), and headache and postural hypotension in tamsulosin group (n=3). Out of 18 sexually active male patients in silodosin group, 4 patients had retrograde ejaculation (22.2%). There were no cases of postural hypotension in silodosin group. There were no cases of retrograde ejaculation in tamsulosin group. None of the patients required hospitalization following adverse effects. Compliance of the patients was excellent and none of the patients discontinued the treatment.

IV. CONCLUSION

Silodosin is comparable to tamsulosin in the treatment of BPH in Indian men. However, retrograde ejaculation may be troublesome for sexually active patients.

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