Original Research Article

The Study of Tadalafil and Tamsulosin as Monotherapy for Lower Urinary Tract Symptoms Due to Benign Hyperplasia of Prostate

R.Vinoth Kumar[1], K. Senthilnathan[2*]

[1]Assistant Professor, Department of Urology, Aarupadai Veedu Medical College and Hospital, Puducherry,India
[2]Senior Assistant Professor, Department of Urology, Thanjavur Medical College, Thanjavur,India

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Abstract

Introduction: Benign prostatic hyperplasia (BPH) is highly prevalent in elderly men and often results in lower urinary tract symptoms (LUTS), including urinary frequency, urgency, nocturia, intermittency, straining, incomplete emptying, and a weak urinary stream. LUTS secondary to BPH (LUTS/BPH) increases with age and negatively impacts patients' quality of life. In addition to surgical interventions, the current standard treatments for LUTS/BPH consist of α1-adrenergic blockers, 5α-reductase inhibitors and phytotherapies (used alone or in combination). Although efficacious, these therapies have the potential for side effects related to sexual dysfunction.**Materials and Methods:** This is a prospective study conducted by Department of Urology, Arupadai Veedu Medical College, Puducherry from January 2020 to December 2020. After obtaining written informed consent, patients were registered and divided into the following two groups randomally by card method: Tamsulosin group (group T), receiving 0.4 mg of tamsulosin hydrochloride once daily in the evening, and tadalafil group (group D), receiving 5 mg of tadalafil in the evening after meal.**Results:** A total of 120 patients were included in the study. They were compared in terms of age, prostate size, postvoid residual urine, uroflow parameters IPSS and IIEF score. Mean age of patients was comparable 68.4+/-12.3 for tamsulosin group and 67.2+/-11.8 in tadalafil group. Mean prostate size was 56 and 52 respectively. Datas for Prostate size, postvoid residue uroflow parameters and IPSS scores **Conclusion:** Symptoms of erectile dysfunction and LUTS frequently occurs together. These could well be treated with monotherapy of tadalafil. It is still not clear significance of treating subclinical erectile dysfunction.

Keywords: Benign prostatic hyperplasia, nocturia, IPSS and IIEF score.

Introduction

Benign prostatic hyperplasia (BPH) is highly prevalent in elderly men and often results in lower urinary tract symptoms (LUTS), including urinary frequency, urgency, nocturia, intermittency, straining, incomplete emptying, and a weak urinary stream. LUTS secondary to BPH (LUTS/BPH) increases with age and negatively impacts patients' quality of life. In addition to surgical interventions, the current standard treatments for LUTS/BPH consist of α1-adrenergic blockers, 5α-reductase inhibitors and phytotherapies (used alone or in combination). Although efficacious, these therapies have the potential for side effects related to sexual dysfunction[1].Alpha blockers like prazosin, alfuzosin, tamsulosin and silodosin had been approved for use in patients of LUTS due to BPH and had been found to improve symptoms of LUTS. However Tadalafil is most recent addition this armantarium and only recently been approved by FDA for use in LUTS due to BPH[2].Mechanism of action of tadalafil is that it inhibit PDE 5 inhibtion and improve erectile function by increasing the amount of cyclic guanosine monophosphate in the smooth muscle of the corpus cavernosa [3].This action increases penile blood flow, resulting in penile erection during sexual stimulation. PDE5 inhibition also affects concentration of cyclic guanosine monophosphate in the smooth muscle of the prostate, the bladder, and their vascular supply, but the precise mechanism for reducing BPH symptoms has not been determined[4].Aging is a key risk factor for the development of male ED. Kinsey showed that the prevalence of ED increased with age from 0.1% at 20 yr to 75% at 80 yr. A half century later, the MMAS largest known survey on sexual dysfunction showed that the prevalence of ED increased from 39% in men in their 40s to 67% for men in their 70s[5]. Using the same question-aire as the MMAS study, the Cross-National Epidemiological Study was conducted in four different countries with varying cultures: Brazil, Italy, Japan, and Malaysia. The results confirmed the findings of the MMAS in these different countries.

**Correspondence*
Dr. K. Senthilnathan
Senior Assistant Professor, Department of Urology, Thanjavur Medical College, Thanjavur, India.
E-mail: docvksen@yahoo.co.in

Materials and Methods

This is a prospective study conducted by Department of Urology, Arupadai Veedu Medical College, Puducherry from January 2020 to December 2020. After obtaining written informed consent, patients were registered and divided into the following two groups randomally by card method: Tamsulosin group (group T), receiving 0.4 mg of tamsulosin hydrochloride once daily in the evening, and tadalafil group (group D), receiving 5 mg of tadalafil in the evening after meal. A total of 120 consenting male patients with LUTS with BPH who visited outpatient department of Surgery and Urology and satisfied the followings condition: Men age more than 45 years, storage symptoms (increased day time frequency, urgency and nocturia and or voiding symptoms (hesitancy, incomplete voiding, impaired stream or interruption of stream), nocturia >2, maximum flow rate <15 ml/sec with a voided volume of at least 150 ml, postvoid residual urine less than 100 ml by transabdominal ultrasound, IPSS >13 points, international prostatic symptom bother score >3 points were enrolled in this study. Patients who had previous prostate surgery, severe visceral disease, postural hypotension, neurogenic bladder dysfunction, suspected prostate cancer, urethral stricture disease, history of pelvic irradiation, bladder

neck disease, acute bacterial prostatitis, acute urinary tract infection, urolithiasis, concomitant medication that may alter the voiding pattern before inclusion (calcium antagonists like monoamineoxidase inhibitors or anticholinergic drugs), active hematuria, renal insufficiency (serum creatinine >2.0mg/dl), severe hepatic impairment (transaminases >2 times the upper normal limit and total bilirubin >1.5 mg/dl), patients on antipsychotic medications, insulin dependant diabetes mellitus, history of severe heart disease were excluded. Evaluation included clinical determination of IPPS, QoL, IIEF, maximum flow rate (ml/s), time to maximum flow, average flow rate, average flow time by uroflometry performed on Laborie Urocap III uroflowmeter with Bluetooth technology, postvoid residual urine volume and prostate size by ultrasonographically at inclusion, 1 month and 3 month respectively. Student's t test is used for statistical analyses.Prevalence of erectile dysfunction and LUTS due to BPH increases with old age. Tadalafil is marketed to improve both these symptoms. This drug has been used for erectile dysfunction but effect on LUTS is found in post marketing surveillence. Now we want to compare effectiveness of tadalafil with a established drug tamsulosin for the indication of LUTS due to BPH.

Results

Table 1: Prostate size

	Baseline	1 Month	3 Month	P Value
Group1:Tamsulosin	56.00 ±6.29	54.00 ± 6.47	54.00 ± 7.16	0.15
Group 2: Tadalafil	52.00±7.18	52.00±7.01	52.00±7.17	0.17

Table 2: Post void residual volumes

	Baseline	1 Month	3 Month	P Value
Group1:Tamsulosin	86.00 ±11.20	30.00 ± 10.97	10.00 ± 6.55	≤0.001
Group 2: Tadalafil	80.00±15.06	73.00±10.74	67.00±6.17	0.065

Table 3: Flow rates in both groups

	Tamsulosin				Tamsulosin			
	Inclusion	Month 1	Month 3	P value	Inclusion	Month 1	Month 3	P value
Maximum flow rate (ml/s)	9.4±0.82	12.06±1.35	12.23±1.22	≤0.001	9.2±1.47	10.8±2.13	10.5 ± 1.79	0.08
Average flow rate (ml/s)	5.4±0.77	6.8±0.64	6.9±0.61	≤0.001	5.2±0.79	5.3±0.66	5.4±0.74	0.06
Time to Maximum flow	38.0±4.87	32.1±3.35	30.2±2.78	≤0.001	47.35±6.57	35.7±4.47	33.60±4.39	0.045
Average flow time	12.0±2.89	8.4±2.00	7.65±1.79	≤0.001	12.4±3.26	11.34 ± 2.03	10.2±2.10	0.038

Table 4: IPSS and IIEF Scores of both groups

Scores	Inclusion	Month 1	Month 3	p value	Inclusion	Month 1	Month 3	p value
IPSS	20.5 ± 3.38	14.0 ± 2.74	12.00 ± 1.94	≤0.001	18.0 ± 2.79	12.0 ± 1.9	10.0± 1.25	≤0.001
IIEF-5	11.4 ± 0.48	12.0 ± 0.55	12.2 ± 0.48	0.525	12.3 ± 0.62	16.5 ± 0.58	17.2± 0.48	≤0.001

A total of 120 patients were included in the study. They were compared in terms of age, prostate size, postvoid residual urine, uroflow parameters IPSS and IIEF score.

Mean age of patients was comparable 68.4+/-12.3 for tamsulosin group and 67.2+/-11.8 in tadalafil group. Mean prostate size was 56 and 52 respectively. Datas for Prostate size, postvoid residue uroflow parameters and IPSS scores are shown in Tables 1,2,3 and 4.Both drugs does not decrease prostate size however tamsulosin improve post void residual while tadalafil did not. Both drugs do improve LUTS symptoms and uroflow parameters but only tadalafil improve erectile dysfunction.Out of 120 patients only 86 patients were sexually active. Out of 86, fourty two were in tamsulosin group and 44 were in tadalafil group. Both drugs were well tolerated no patient were needed to stop drug due to side effects. Both the drugs well tolerated. In tadalfil group except for 2 patient complained of mild headache, one of patients had nasal cogestion and one other body pain. None of patients stopped drugs. No major side effect was reported by patient on tamsulosin group except for two patient reporting weakness and one had mild headache.

Discussion

LUTS and Erectile dysfunction are highly related diseases as both had increased incidence and prevalence with increasing age[6,7]. For a long time both were considered as two different diseases and were treated separately. Many times erectile dysfunction part is neglected both by patient and physician as it is considered normal part of ageing and untreatable. Treatment used for LUTS also has negative impact on sexual function of male patient and worsen the disease[8].

The Multinational Survey of the Ageing Male (MSAM7), one of the largest population based studies of ageing men conducted, evaluated the associations between age, LUTS, concomitant comorbidities and male sexual dysfunction in > 12,000 men in the United States and Europe. In MSAM7, the overall prevalence of LUTS was 90%, while the overall prevalence of ED (erectile dysfunction) and EjD (ejaculatory dysfunction) was 49% and 46%, respectively. The rate of both ED and EjD was significantly dependent on age and correlated highly with the severity of LUTS[9].Selective α1-blockers are most polular first line treatment. It is considered the standard of care16 and the most effective medical therapy for LUTS due to benign prostate enlargement.. Their use is based on the presence of contractile tissue in the prostate mediated via α1-adrenergic receptors abundant in the bladder neck, prostate capsule, and stroma. This dynamic component demonstrated to contribute approximately 40% of outflow obstruction.In an open-label tamsulosin study, 30% of subjects reported abnormal ejaculation and 6% reported impotence.

McVary and Roehrborn on the double-blind, placebo-controlled study and dose finding study respectively reported no change in PVR (post voidal residual volume) in the tadalafil group. Our study also demonstrated no change in PVR even at end of 3 months.Porst and colleagues reported improvement in IPSS but changes in peak urinary flow (Qmax) and PVR were small and not clinically meaningful. In this context, Brock and colleagues reported on another paper based on the same database of patients that changes in BPH–LUTS after 12 weeks of treatment with placebo or various doses of once-daily tadalafil were similar in men with or without comorbid ED. After 12 weeks, changes in IPSS in men with ED and without ED were not significantly different (subgroup/interaction p values: 0.352/0.644). It shows that effect on LUTS is independant of the effect on ED. Our study also shows similar findings[9].All of these studies reported that tadalafil is not only efficacious but also a safe treatment. As in the classic ED trials, the most common side effects were headache, dyspepsia, nasal congestion, flushing and back pain[10].Recently, data on the combination of tadalafil with finasteride (a 5α-reductase inhibitor) have been published. IPSS improvement is significantly higher in the combination group compared with the finasteride only group at the. As expected, IIEF improved significantly in the combination group ($p < 0.001$). Combination therapy was well tolerated and most adverse events were mild/moderate.

Conclusion

Symptoms of erectile dysfunction and LUTS frequently occurs together. These could well be treated with monotherapy of tadalafil. It is still not clear significance of treating subclinical erectile dysfunction.

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