International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 7, July 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.7.2024.3

ORIGINAL RESEARCH

Study to assess the safety and effectiveness of Tamsulosin for treating non neurogenic lower urinary tract symptoms in post-menopausal women

[1]Dr. Pushpendra Kumar Shukla, [2]Dr. Ravi Patel, [3]Dr. Padma Shukla, [4]Dr. Atul Kumar Singh, [5]Dr. Vijay Kumar Shukla, [6]Dr. Vivek Sharma, [7]Dr. Varsha Shukla

[1,6]Associate Professor, [5]Assistant Professor, Department of Urology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India
[2]Resident Surgical Officer, [4]Associate Professor, [7]Assistant Professor, Department of Surgery, Shyam Shah Medical College, Rewa, Madhya Pradesh, India
[3]Associate Professor, Department of Obstetrics and Gynaecology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

Corresponding Author
Dr. Atul Kumar Singh
Associate Professor, Department of Surgery, Shyam Shah Medical College, Rewa, Madhya Pradesh, India
E mail: atulksp28@gmail.com

Received Date: 23 May, 2024 Acceptance Date: 25 June, 2024

ABSTRACT

Background: Females have a high prevalence of lower urinary tract symptoms (LUTS), ranging from 64% to 76%. The prevalence and severity of LUTS are higher in postmenopausal women due to low estrogen levels affecting genitourinary tissue. Tamsulosin is an uroselective α1A adrenergic receptor antagonist used for the treatment of benign prostatic hyperplasia, with proven efficacy and safety. It is also used off-label for the treatment of lower urinary tract symptoms in females. The present study aims to assess the safety and efficacy of Tamsulosin in the treatment of non-neurogenic lower urinary tract voiding symptoms in post-menopausal women. **Methods:** The present study is a prospective observational study conducted from February 2020 to July 2021 in the Department of Surgery and Urology at Shyam Shah Medical College, Rewa (M.P). After applying inclusion and exclusion criteria, 163 patients were selected for the study. Comprehensive clinical history, physical examinations, and relevant investigations were done. The International Prostate Symptom Score (IPSS) and IPSS Quality of Life index (IPSS-QOL) were also evaluated. After categorizing the patients into voiding and storage symptoms, including urinary incontinence, those with voiding dysfunction were prescribed 0.4 mg of Tamsulosin for 30 days and follow-up was planned on day 15 and day 30. During these follow-up visits, the response to the treatment was monitored by uroflowmetry, ultrasonography for post-void residual volume (PVR), IPSS score, and IPSS-QOL index. **Results:** The average age of postmenopausal females with LUTS in this study was 55.84 ± 9.37 years. The prevalence of LUTS was 44.15%. There was a significant change in International Prostate Symptom Score (IPSS) from 11.70±3.87 to 6.91±1.91, IPSS-Quality of Life (QOL) from 3.90±0.87 to 2.23±0.7, maximum flow rate (Qmax) from 12.73±3.79 to 14.66±2.86, and post-void residual (PVR) from 67.04±25.5 to 46.56±14.75 at the last follow-up. Adverse reactions were noted in 5.14% of patients, which resolved after discontinuation of medication. **Conclusion:** The study conclusively demonstrates that Tamsulosineffectively alleviates LUTS in post-menopausal women, significantly improving both objective measures and patient-reported outcomes. Overall, Tamsulosin was shown to be an effective therapy with a good safety profile for managing LUTS in post-menopausal women, contributing to improved urinary function and quality of life

Key words: Lower urinary tract symptoms, Post-menopausal, International prostatic symptom score, Tamsulosin

INTRODUCTION

Lower urinary tract symptoms (LUTS) are defined by the International Continence Society (ICS) as symptoms related to the lower urinary tract. These symptoms may originate from the bladder, urethra, prostate (in men), and/or adjacent pelvic floor or pelvic organs, or at times may be referred from similarly innervated anatomy such as the lower ureter. Normal lower urinary tract function relies on the ability to store urine in the bladder and the ability to

DOI: 10.69605/ijlbpr_13.7.2024.3

void urine at a time that suits the individual. LUTS are categorized according to the time at which they are experienced in relation to the micturition cycle [1].There are three types of urinary symptoms: storage symptoms, which include overactive bladder symptoms such as urgency, urgency incontinence, frequency, and nocturia, as well as dysuria and stress incontinence ,voiding symptoms, which include a poor and/or interrupted stream, terminal dribble, hesitancy, and straining and post-micturition symptoms, which include post-micturition dribbling and the sensation of incomplete emptying.

Females have a high prevalence of LUTS, ranging from 64% to 76% according to the EPIC study conducted in 2006[2]. The prevalence and severity of LUTS are higher in postmenopausal women due to low estrogen levels affecting genitourinary tissue [3]. LUTS is a significant cause of morbidity in postmenopausal women and has a negative impact on their quality of life, with many patients reporting depression and anxiety [4]. The average age of menopause in Indian females is 46 years, with a life expectancy of 72.2 years in 2019 [5]. According to trends, 76% of the postmenopausal population will live in developing countries like India by 2030, making LUTS a major health problem[6].

The adrenergic receptors found at the bladder neck are mainly α1-adrenergic, with three subtypes identified: α1A, α1B, and α1D. The bladder predominantly contains α1A and α1D receptors[7]. It's thought that the α1D receptor may cause the symptoms of an overactive bladder, while the α1A receptor subtype may cause obstructive symptoms. Alpha-adrenergic receptor antagonists used in men with LUTShave proven to be effective. It's suggested that a selective α1 adrenoceptor antagonist, with greater specificity for α1A and α1D receptors, could be beneficial in managing LUTS in women. Tamsulosin is an uroselective α1A adrenergic receptor antagonist used for the treatment of benign prostatic hyperplasia, with proven efficacy and safety. It is also used off-label for the treatment of lower urinary tract symptoms in females[8].

The present study aims to assess the safety and efficacy of Tamsulosin in the treatment of non-neurogenic lower urinary tract voiding symptoms in post-menopausal women."

METHODS

The present study is a prospective observational study conducted from February 2020 to July 2021 (18 months) in the Department of Surgery and Urology at Shyam Shah Medical College, Rewa (M.P). The study included postmenopausal women up to 70 years of age, with an IPSS≥8, normal urine analysis, and willing to provide written consent. Patients with urinary tract infections, neurological diseases, diabetic neuropathy, bladder cancer, IPSS<8, predominant storage, and bothersome incontinence symptoms were excluded from the study. Ethical approval was obtained from the institutional ethics committee.

The study focused on postmenopausal women with LUTS who visited the surgery outpatient department (OPD) and met the inclusion criteria. Out of 1087 postmenopausal women with LUTS who visited the surgery and urology OPD, 201 patients with predominant voiding dysfunctionwere chosen for the study. Nine of them stopped treatment due to side effects, and others were lost to follow-up. Ultimately, 163 patients attended the second follow-up on the 30th day, selected for the final evaluation.

Informed consent was obtained from all participants, who were then briefed about the nature of the study. The selected patients underwent thorough clinical history-taking, physical examinations including abdominal and perineal examinations, as well as neurological assessments. Additionally, objective and subjective evaluations were done using routine investigations, ultrasonography, uroflowmetry, IPSS, and IPSS-QOL index. After categorizing the patients into voiding and storage symptoms, including urinary incontinence, those with voiding dysfunction were prescribed 0.4 mg of Tamsulosin for 30 days and were advised to revisit the hospital on day 15 and day 30. During these follow-up visits, patients were interviewed regarding their IPSS and IPSS-QOL index. Uroflowmetry and ultrasonography for post-void residual volume were used for treatment assessment. Patients who failed to attend the follow-up visits were excluded from the study. Statistical analyses were conducted using IBM SPSS version 22.0, located in Chicago, IL, USA. The Student's t-test was utilized to determine the level of significance, with p-values < 0.05 considered as significant

RESULTS

The study collected data from 2462 patients, among whom 1087 were identified as having LUTS, indicating a prevalence rate of 44.15%. This suggests that almost half of the post-menopausal women in the study experienced symptoms related to LUTS. The highest prevalence of LUTS was found in the 56-60 age group, comprising 31.77% of the patients, followed by the 51-55 age group at 26.21%, the 45-50 age group at 15.91%, and the 61-65 age group at 18.21%. The average age of postmenopausal females with LUTS in this study was 55.84 ± 9.37 years.

Table 1: Presenting Lower Urinary Tract Symptoms (n = 1087)

Presenting Symptom	No. of Patients	Percentage
Storage	814	74.88
Voiding	336	30.19
Urinary Incontinence	128	11.77

DOI: 10.69605/ijlbpr_13.7.2024.3

Nocturia(≥ 2 times)	684	62.92
Frequency	303	27.84
Urgency	195	18.44
Intermittency	248	22.18
Slow stream	208	19.13
Straining	99	9.1
Incomplete voiding	120	11.03
Post micturition dribbling	104	9.56

In Table 1, the most commonly reported symptom was urinary nocturia occurring ≥ 2 times/night during sleep, which affected 62.92% of the patients. The second most prevalent symptom was frequency, experienced by 27.84% of the patients, followed by intermittency (22.18%) and poor stream (19.13%). Urgency was reported by 18.44% of the women, while incomplete voiding and post-micturition dribbling were less common, reported by 11.03% and 9.56% of the patients, respectively. These findings highlight the diverse nature of LUTS in post-menopausal women, with a significant proportion experiencing multiple symptoms simultaneously.

Table 2: Baseline IPSS and Uroflometry parameters and change at 15th day and 30th day after treatment with Tamsulosin 0.4 mg OD (n =163)

Period	Baseline(Day 0)	Post Treatment Day 15	Post Treatment Day 30
Mean IPSS Score	11.70±3.87	8.72±2.24	6.91±1.91
Range	8 to 22	4 to 17	3 to 12
P value	-	**<0.0001**	**<0.0001**
Mean IPSS QoL Index	3.90±0.87	3.38±0.70	2.23±0.70
Range	3 to 5	2 to 5	1 to 4
P value	-	**<0.0001**	**<0.0001**
Mean MFR(ml/s)	12.73±3.79	13.39±3.14	14.66±2.86
Range	6 to 24	6 to 22	8 to 24
P value	-	**0.0014**	**<0.0001**
Mean AFR(ml/s)	6.11±2.33	6.51±1.91	7.41±1.68
Range	2 to 11	3 to 11	5 to12
P value	-	**0.0012**	**<0.0001**
Mean PVR(ml)	67.04±25.50	57.96±17.00	46.56±14.75
Range	25 -118	20-95	20-92
P value	-	**<0.0001**	**<0.0001**
Mean day time frequency	9.8±2.48	8.20±2.14	7.24±2.01
Range	7 to 14	5 to 13	4 to 12
P value	-	**<0.0001**	**<0.0001**
Mean episodes of nocturia	2.52±2.00	1.65±1.23	1.60±1.32
Range	0 to 7	0 to 4	0 to 5
P value	-	<0.0001	<0.0001

Table 2 evaluated the effectiveness of a treatment by measuring various clinical parameters at baseline (Day 0), Day 15, and Day 30. The average IPSS significantly decreased from 11.70±3.87 at baseline to 6.91±1.91 by Day 30 ($p<0.0001$), indicating a significant improvement in urinary symptoms. Similarly, the mean IPSS-QOL index improved from 3.90±0.87 to 2.23±0.70 ($p<0.0001$), reflecting enhanced patient satisfaction. The mean QmaxanAFR showed significant increases, from 12.73±3.79 ml/s to 14.66±2.86 ml/s ($p<0.0001$) and 6.11±2.33 ml/s to 7.41±1.68 ml/s ($p<0.0001$), respectively, indicating improved urinary flow. The mean PVR volume decreased from 67.04±25.50 ml to 46.56±14.75 ml ($p<0.0001$), suggesting improved bladder emptying. Mean daytime frequency and episodes of nocturia also reduced significantly, from 9.8±2.48 to 7.24±2.01 ($p<0.0001$) and 2.52±2.00 to 1.60±1.32 ($p<0.0001$), respectively. Overall, these results demonstrate significant improvements in urinary symptoms, quality of life, and bladder function after treatment.Out of 177 patients, 5 (2.82%) reported headache and dizziness, 3 (1.69%) reported cough, and 1 had worsening stress urinary incontinence during their 15th-day visit. All reactions resolved after medication was stopped.

DISCUSSION

In the present study, the prevalence of LUTS in postmenopausal women was 44.15%. The average age was 55.84 ± 9.37 years, and the highest prevalence of LUTS was found in the 56-60 age group, comprising 31.77% of the patients, followed by the 51-55 age group at 26.21 %. In a large population cross-

DOI: 10.69605/ijlbpr_13.7.2024.3

sectional EpiLUTS study, out of 15681 women, the mean age was 56.7 ± 10.5 years. The prevalence of at least one LUTS "sometimes" was 76.3%, and least “often” was 52.5% in women [4]. The most commonly reported symptom in the present study was nocturia(62.29%), followed by frequency (27.84 %), intermittency (22.81 %), and poor stream (19.13%). Zhang et al (2014) conducted a population-based cross-sectional survey that involved a total of 18992 respondents. The study found that the prevalence of lower urinary tract symptoms (LUTS) was 55.5% and increased with age. Storage symptoms were more prevalent than voiding symptoms (53.9% vs. 12.9%). The most common symptoms reported were nocturia (23.4%), urgency (23.3%), and stress urinary incontinence (SUI) (18.9%)[9]. In the EPILUTS study, frequency was the most common LUTS found in 24.6% of participants, followed by nocturia (15%), terminal dribbling (14.5%), and urgency (11.1%) [4].

In the present study, based on predominant presenting symptoms, storage dysfunction (74.88%) was more common than voiding dysfunction (30.19%) or urine incontinence (11.77%). Moreira et al. (2013) conducted a cross-sectional population-based survey that included 1500 women of ≥ 30 years and found predominant storage symptoms in 76.4% of the patients, while predominant storage symptoms were present in 39.7% of the patients, and 5.8% had incontinence as the predominant symptoms [10].

Our study shows that Tamsulosin statistically affects IPSS scores, IPSS-QOL Index, Qmax, and AFR in women with non-neurogenic voiding dysfunction. This study also indicates that the patient’s quality of life improved by treatment and that most patients felt a benefit. Tamsulosin demonstrated effectiveness in female patients with voiding dysfunction. Most patients showed subjective and objective improvements and were satisfied with treatment. Our findings and other significant studies suggest that Tamsulosin offers an initial treatment option for female non-neurogenic voiding dysfunction (Table 3) [11,12,13,14].

Table 3: Summary of comparison with other studies

Author (Year)	Description of study	Tamsulosin dose and duration	IPSS	IPSS-QOL index	MFR (ml/s)	PVR (ml)
Costantini E (2009) [11]	Prospective, Longitudinal open-label n= 63 Mean age 60.2±16 years	0.4 mg 30 days	NA	NA	Increased from 14.8 ± 5.7 to 18.28 ±7.2 (P<0.0001)	Decreased from 50.6 ± 64.7 to 29.6 ± 37.7 (P <0.001)
Lee K S (2010) [12]	Open-label, n= 106 Mean age 52.9 years	0.2 mg 8 weeks	Decreased from 23.9±6.09 to 16.1±8.17 (P<0.0001)	Decreased From 4.79±0.96 3.73±1.40 (P<0.0001)	Increased from 10.2±2.79 to 13.5±5.65 (P<0.001)	Decreased from 69.13±85.45 to 39.88±48.39 (P<0.001)
Kim S O (2014) [14]	Prospective observation n= 324 mean age 58.3 ± 11.2 years	0.2 mg 4Weeks	Decreased from 15.2 ± 8.9 to 13.6 ± 3.4 (P<0.03)	Decreased from 3.4 ± 1.2 to 2.9 ± 1.6 (P<0.001)	Increased 13.3±7.8 to 20.4±8.2 (P<0.001)	Decreased from 75.3 ± 23.7 to 54.8 ± 27.5 (P<0.01)
Tripathi N K (2021)	Comparative study(Tamsulosin/Estrogen) n=80 each	0.4 mg	Tamsulosin group increased	NA	Increased from 6.9 ± 1.3 ml/s to 17.8 ± 1.6	Decreased from 122 ± 13 to 33 ±7
Present Study (2024)	Prospective observation IPSS>7 n= 163 mean age 55.84 ± 9.37 years	0.4 mg 30 days	Decreased from 11.70±3.87 to 6.91±1.91 (P<0.001)	Decreased from 3.90±0.87 to 2.23±0.70 (P<0.001)	Increased from 12.73±3.79 to 14.66±2.86 (P<0.001)	Decreased from 67.04±25.50 to 46.56±14.75 (P<0.001)

NA: Not assessed

In the present study, 5.14% of patients reported adverse effects, which resolved after discontinuation of the medication. Similar observations were also reported by Costantini et al and Lee et al [11,12]. Many studies in male and female patients suggest that Tamsulosin is well-tolerated as a once-daily oral medication with a good safety profile. Limitations of the present study include being an open-label study with no control group for comparison, being a single-center study, and having a shorter follow-up period.

DOI: 10.69605/ijlbpr_13.7.2024.3

CONCLUSION

The study conclusively demonstrates that Tamsulosin effectively alleviates LUTS in post-menopausal women. It significantly improves both objective measures and patient-reported outcomes. Over the 30-day treatment period, patients showed noticeable reductions in the IPSS, IPSS-QOL index, PVR volume, and frequency of daytime and nocturnal urination. Overall, Tamsulosin was shown to be an effective therapy with a good safety profile for managing LUTS in post-menopausal women, contributing to improved urinary function and quality of life.

ABREBIATIONS

LUTS: Lower urinary tract symptoms
IPSS: International Prostate Symptom Score
IPSS-QOL: International Prostate Symptom Score, Quality Of Life
PVR: Post-void Residual
Qmax: Maximum Flow rate
AFR: Average Flow Rate

REFERENCES

1. Drake MJ. Fundamentals of terminology in lower urinary tract function. *NeurourolUrodyn*. 2018;37(S6):S13-S19. doi:10.1002/nau.23768.
2. Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: Results of the EPIC study. Eur Urol 2006;50(6):1306–1314.
3. Varella LR, Bezerra da Silva R, Eugênia de Oliveira MC, MeloPH,Maranhão TM, Micussi MT. Assessment of lower urinary tract symptoms in different stages of menopause. J PhysTherSci 2016;28(11):3116–3121.
4. Coyne KS, Wein AJ, Tubaro A, et al. The burden of lower urinary tractsymptoms: Evaluating the effect of LUTS on health-related quality of life,anxiety and depression: EpiLUTS. BJU Int 2009;103(suppl 3):4–11.
5. MeetaM, Digumarti L, Agarwal N, Vaze N, Shah R,Malik S. Clinical practice guidelines on menopause: *An executive summary and recommendations:Indian Menopause Society 2019–2020. J Midlife Health 2020;11(2):55–95.
6. Kriplani A, Banerjee K. An overview of age of onset of menopause innorthern India.Maturitas 2005;52(3–4):199–204.
7. Schwinn D. Novel role for α1-adrenergic receptor subtypes in lower urinary tractsymptoms. BJU Int 2000; 86: 11–22.
8. Boyd K, Hilas O. alpha-adrenergic blockers for the treatment of lower-urinary-tractsymptoms and dysfunction in women. Ann Pharmacother 2014; 48: 711–722.
9. Zhang L, Zhu L, Xu T, et al. A Population-based Survey of the Prevalence, Potential Risk Factors, and Symptom-specific Bother of Lower Urinary Tract Symptoms in Adult Chinese Women. *Eur Urol*. 2015;68(1):97-112. doi:10.1016/j.eururo.2014.12.012
10. Moreira ED Jr, Neves RC, Neto AF, et al. A population-based survey of lower urinary tract symptoms (LUTS) and symptom-specific bother: results from the Brazilian LUTS epidemiology study (BLUES). *World J Urol*. 2013;31(6):1451-1458. doi:10.1007/s00345-013-1057-8
11. Costantini E, Lazzeri M, Bini V, et al. Open-label, longitudinal study of tamsulosin for functional bladder outlet obstruction in women. *Urol Int*. 2009;83(3):311-315. doi:10.1159/000241674
12. Lee KS, Han DH, Lee YS, et al. Efficacy and safety of tamsulosin for the treatment of non-neurogenic voiding dysfunction in females: a 8-week prospective study. *J Korean Med Sci*. 2010;25(1):117-122. doi:10.3346/jkms.2010.25.1.117
13. Kim, S.-O., Choi, H. S., & Kwon, D. (2014). The alpha-1 Adrenoceptor Antagonist Tamsulosin for the Treatment of Voiding Symptoms Improves Nocturia and Sleep Quality in Women. *Urology Journal*, *11*(3), 1636–1641. https://doi.org/10.22037/uj.v11i3.1941.
14. Tripathi N K et al 2021 The Treatment of Lower Urinary Tract Symptoms (LUTS) in Perimenopausal Females Using Alpha-1A Blockers (Tamsulosin) and Estrogen's: A Comparative Study. Intnational journal of toxicological and pharmacological research 2021;11(2);67-71.