ORIGINAL RESEARCH PAPER

Pharma

A COMPARATIVE STUDY OF ALPHA-1A BLOCKERS (TAMSULOSIN) VERSUS ESTROGENS IN THE TREATMENT OF LOWER URINARY TRACT SYMPTOMS IN PERIMENOPAUSAL FEMALES

KEY WORDS: Urinary Tract Infection, Alpha- 1a Blockers, tamsulosin, Estrogen, Perimenopausal, Post residual volume, Qmax.

Mahesh Jain Assistant professor, Department of Pharmacology, Sri Aurobindo medical college and post graduate institute Indore (M.P).

Rimjhim Sahu* Associate Professor Department of Pharmacology, People's College of Medical Sciences & Research Centre Bhopal (M.P) *Corresponding Author

ABSTRACT

Background: Lower urinary tract symptoms (LUTS) in perimenopausal females are one of the major urological issues which lead them to considerable inconvenience and comorbidities. The present study was performed to compare alpha-1a blockers (tamsulosin) versus estrogens in the treatment of lower urinary tract symptoms in perimenopausal females. **Material and methods:** All perimenopausal females between the age group of 45 and 60 years were part of the study. The first group was given alpha-1a blocker (tablet tamsulosin 0.4 mg OD HS (Urimax, CIPLA) and other group was given estrogen in the topical form (Evalon Cream, Organon (India) Ltd) (0.5% to 1% twice daily) for application topically in the periurethral region. Improvements in the flow of urine as estimated by uroflowmetry and decrease in Post-void residual (PVR) urine as estimated by ultrasound sonography (USG). After that, data analysis was done. The statistical test used to analyze the results was unpaired t-test. **Results:** Patients were followed up with uroflowmetry and PVR urine assessment with USG. In the alpha-1a blocker group, pretreatment mean maximum flow rate (Qmax) of patients was 7.31±1.5ml/s and posttreatment Qmax was 17.56±1.7. In the estrogen group, pretreatment Qmax was 7.42±1.3ml/s and posttreatment Qmax was 11.2±1.2. This difference was statistically significant ($P \leq 0.0001$). In the alpha-1a blocker group, pretreatment PVR urine was significant (121±13), which became insignificant (35±7) after the treatment, whereas in the estrogen group, PVR was significant posttreatment (115±10) also. **Conclusion:** The present study concluded that Alpha blockers are effective in the treatment of LUTS female patients as there was improvement in Qmax, decrease in PVR. The effect of alpha blockers on LUTS in females should be assessed and treated according to the underlying cause.

Lower urinary tract symptoms (LUTS) are a common health problem among women in the younger as well as older age group. Around 15.5%–53.7% of the women are affected by LUTS. Lower urinary tract symptoms (LUTS) in perime nopausal female are mainly due to urethral stenosis. There are problems of bladder outlet obstruction (BOO) and impaired contraction of the detrusor in patients of chronic urinary retention.[1] LUTS include both the storage and voiding symptoms including the quality of life bothersome. The alpha receptors in the bladder - 1D and in the urethra - 1A in the females appear to mediate the LUTS similar to the male counterparts.[2] LUTS may be categorized into irritative and obstructive symptoms. There are changes in the bladder due to aging such as the decreased capacity of the bladder and estrogen loss, which further develops in LUTS.[3] The treatment of the female LUTS includes lifestyle modifications, behavioural therapy, pelvic floor muscle and bladder training and pharmacological therapy. The pharmacological therapy includes the use of alpha blockers and the antimuscarinics. Among the alpha blockers tamsulosin is most commonly used.

Tamsulosin is potent, specific and selective alpha blocker having good specificity for α1D and α1A receptors located in the bladder and the urethra respectively. It has also been shown to increase the flow, decrease the detrusor pressure and concomitant improvement in LUTS.[4] Topical estrogens are also used in the management of LUTS in perimenopausal females. Estrogen works by acting on estrogen receptors in urethral mucosal cells by aborting atrophy of mucosal cells due to a lack of estrogen in perimenopausal females. Alpha-1a blockers act by selective blockage of alpha-1a receptors present in the bladder neck and relieve obstruction.[1] The present study was performed to compare alpha-1a blockers (tamsulosin) versus estrogens in the treatment of lower urinary tract symptoms in perime nopausal females.

MATERIAL AND METHODS:

The present study was performed among 120 perime nopausal females to compare alpha-1a blockers (tamsulosin) versus estrogens in the treatment of lower urinary tract symptoms in perimenopausal females over a period of 1 year. All perimenopausal females between the age group of 45 and 60 years were part of the study. Before the commencement of the study ethical clearance was obtained and written consent was obtained from the patients. All perimenopausal females between the age group of 45 and 60 years presented with the retention, past history of urethral dilatation, or having urinary infection were excluded from the study. The first group was given alpha-1a blocker (tablet tamsulosin 0.4 mg OD HS) and other group was given estrogen in the topical form (0.5% to 1% twice daily) for application topically in the periurethral region.

Patients were followed up with clinical features of the International Prostate Symptom Score (IPSS) and objectively by uroflowmetry and postvoid residual urine (PVR) estimation (ultrasonography [USG]). Improvements in the flow of urine as estimated by uroflowmetry and decrease in PVR urine as estimated by USG. After that, data analysis was done. The statistical test used to analyze the results was unpaired *t*-test.

RESULTS:

Perimenopausal women were divided into two groups and the first group was given alpha-1a blocker (tablet tamsulosin 0.4 mg OD HS) (n=60) and other group was given estrogen in the topical form (0.5% to 1% twice daily) for application topically in the periurethral region) (n=60).

Patients were followed up with uroflowmetry and PVR urine assessment with USG. In the alpha-1a blocker group, pretreatment mean Qmax (maximum flow rate) of patients was 7.31±1.5ml/s and posttreatment Qmax was 17.56±1.7. In the estrogen group, pretreatment Qmax was 7.42±1.3ml/s and posttreatment Qmax was 11.2±1.2.

This difference was statistically significant ($P \leq 0.0001$). In the alpha-1a blocker group, pretreatment PVR urine was significant(121±13), which became insignificant(35±7) after the treatment, whereas in the estrogen group, PVR was significant posttreatment (115±10) also.

Table 1: Table showing comparision of both groups with respect to Qmax and PVR

	alpha-1a blocker group	Estrogen Group	p-value
Qmax (ml/s)			
Pretreatment	7.31±1.5	7.42±1.3	<0.0001
Posttreatment	17.56±1.7	11.2±1.2	
PVR (ml)			
Pretreatment	121±13	125±14	<0.0001
Posttreatment	35±7	115±10	

DISCUSSION:

LUTS include both storage and voiding symptoms. The lower urinary tract function is maintained and coordinated by the balance between the parasympathetic and the sympathetic nervous systems. The continence is maintained during the storage phase by relaxation of bladder muscles by Beta 2 adrenergic receptors and inhibition of the parasympathetic system causing the contraction of the external sphincter. During the voiding phase, reverse happens. The sympathetic system is inhibited by the pontine micturition center, which also activates the parasympathetic system. This causes stimulation of the muscarinic receptors on the detrusor muscle to cause sustained bladder contraction and urethral relaxation.[4]

Patients were followed up with uroflowmetry and PVR urine assessment with USG. In the alpha-1a blocker group, pretreatment mean Qmax (maximum flow rate) of patients was 7.31±1.5ml/s and posttreatment Qmax was 17.56±1.7. In the estrogen group, pretreatment Qmax was 7.42±1.3ml/s and posttreatment Qmax was 11.2±1.2. This difference was statistically significant ($P \leq 0.0001$). In the alpha-1a blocker group, pretreatment PVR urine was significant(121±13), which became insignificant(35±7) after the treatment, whereas in the estrogen group, PVR was significant posttreatment (115±10) also.

Lee *et al*. conducted a study on female patients who presented with symptoms of LUTS. They used tamsulosin (alpha-1a blocker) to know about the potential effects of alpha1-blocker in female patients with voiding LUTS. They observed that 33.0% of the patients showed an elevation of more than 50% in Qmax with very few side effects after 8 weeks of treatment.[5]

Krishnendu Maiti et al did a study and found that in the Alpha-blocker group, pretreatment mean Qmax (maximum flow rate) of patients was 7.2 ml/s and posttreatment Qmax was 18.4. In the topical estrogen group, the values were 7.4 ml/s and 10.2, respectively. This difference was statistically significant ($P < 0.0001$). In the Alpha-blocker group, pretreatment PVR urine was significant, which became insignificant after the treatment, whereas in the topical estrogen group, PVR was significant posttreatment also.[1]

Amrapali D Gosavi et al did a prospective double-blind placebo-controlled study and found that there was statistically significant difference in the baseline IPSS between the two groups and there was a very weak correlation between baseline IPSS and mean change from baseline in IPSS in both groups. Three patients lost to follow up in the tamsulosin group (6%), one patient due to no improvement in the symptoms and two due to adverse effect of the drug. In the placebo group, two patients (4%) lost to follow up due to no improvement in the symptoms. Significant improvements were noted in the storage and voiding symptoms in the tamsulosin group as compared to the placebo group.[4]

Pischedda A, et al concluded that the use of α_1-blockers may be an initial treatment option for female functional bladder neck obstruction, as this therapeutic option proved to be effective in more than 50% of our patients suffering from this voiding dysfunction.[6] Ahmad T et al found that Tamsulosin significantly decrease IPSS, PVR and improve Qmax, so they should be used as first line treatment for moderate to severe LUTS in women.[7] Kessler TM et al found that Terazosin had a significant symptomatic and urodynamic effect in two-thirds of patients. These results suggest that terazosin may be an effective treatment option in women with voiding dysfunction due to functional bladder outlet obstruction.[8]

CONCLUSION:

The present study concluded that Alpha blockers are effective in the treatment of LUTS female patients as there was improvement in Qmax, decrease in PVR. The effect of alpha blockers on LUTS in females should be assessed and treated according to the underlying cause.

REFERENCES:

1. Maiti K, Jaiswal A, and Pal DK. A comparative study of alpha-1a blockers (tamsulosin) versus estrogens in the treatment of lower urinary tract symptoms in perimenopausal females. Indian J Pharmacol. 2020 Jan-Feb; 52(1):6–9
2. Schwinn DA, Michelotti GA. Alpha1-adrenergic receptors in the lower urinary tract and vascular bed: potential role for the alpha1d subtype in filling symptoms and effects of ageing on vascular expression. BJU Int 2000; 2(Suppl 85):6–11.
3. Moreno E, Andreu A, Pérez T, Sabaté M, Johnson JR, Prats G. Relationship between *Escherichia coli* strains causing urinary tract infection in women and the dominant faecal flora of the same hosts. *Epidemiol Infect.* 2006; 134: 1015–23.
4. Amrapali D Gosavi et al (2020) 'Role of tamsulosin in Female Lower Urinary Tract Symptoms ', International Journal of Current Medical and Pharmaceutical Research, 06(11), pp 5379-5382.
5. Lee KS, Han DH, Lee YS, Choo MS, Yoo TK, Park HJ, 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;25:117–22.
6. Pischedda A, Pirozzi Farina F, Madonia M, Cimino S, Morgia G. Use of alpha1-blockers in female functional bladder neck obstruction. *Urol Int.* 2005;74:256–61.
7. Ahmad T, Rahman AU, Khan MA. Efficacy of tamsulosin therapy in females with non-neurogenic lower urinary tract symptoms. *J Postgrad Med Inst.* 2014;28:288–91.
8. Kessler TM, Studer UE, Burkhard FC. The effect of terazosin on functional bladder outlet obstruction in women: A pilot study. *J Urol.* 2006;176:1487–92.