

The Treatment of Lower Urinary Tract Symptoms (LUTS) in Perimenopausal Females Using Alpha-1A Blockers (Tamsulosin) and Estrogen's: A Comparative Study

Dr. Narendra Kumar Tripathi

Assistant Professor, Department of Pharmacology, ICARE Institute of Medical Sciences and Research & Dr. Bidhan Chandra Roy, Hospital, Haldia, West Bengal, India.

Received: 17-02-2021 / Revised: 25-03-2021 / Accepted: 10-04-2021

Corresponding author: Dr. Narendra Kumar Tripathi

Conflict of interest: Nil

Abstract

Aim: The aim of the present study to compare the alpha-1a blockers (Tamsulosin) with Estrogen's in the treatment of lower urinary tract symptoms in perimenopausal females.

Methods: A comparative study was conducted in the Department of Pharmacology, ICARE Institute of Medical Sciences and Research & Dr. Bidhan Chandra Roy, Hospital, Haldia, West Bengal, India, for 13 months. All 80 perimenopausal females between the age group of 40 and 58 years presented with the retention, past history of urethral dilatation, or having urinary infection were excluded from the study. All 80 other patients between the age group of 40 and 58 years having LUTS were included in 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.

Results: Perimenopausal women were divided into two groups and females of each group were given either alpha-1a blocker or topical estrogen. The mean age group of patients was 50.50 years (45–55 years). Alpha-1a blocker group had 80 females and topical estrogen had 80 females. Patients were followed up with uroflowmetry and PVR urine assessment with USG. In the first group, pre-treatment mean Qmax (maximum flow rate) of patients was 6.9 ± 1.3 ml/s and post treatment Qmax was 17.8 ± 1.6 . In the second group, pre-treatment Qmax was 7.6 ± 1.2 ml/s and post treatment Qmax was 9.8 ± 2.1 . This difference was statistically significant ($P \leq 0.0001$). In the first group, pre-treatment PVR urine was significant, which became insignificant after the treatment, whereas in the second group, PVR was significant post treatment also.

Conclusion: The conclusion of this study is that alpha-1a blockers should be used as a first-line medical management in perimenopausal females with symptoms of LUTS, as they have a clear advantage over topical estrogens in improvement in symptoms of LUTS.

Keywords: Estrogen, perimenopausal, Tamsulosin, uroflowmetry

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Lower urinary tract symptoms (LUTS) include storage, voiding, and post-micturition

symptoms, whereas overactive bladder (OAB) syndrome is a subgroup of storage symptoms

that includes urinary urgency, urge urinary incontinence, frequency, and nocturia[1]. Several large epidemiological studies have evaluated the prevalence and bother of LUTS, including OAB, in population-based analyses[2] These studies reported that LUTS were highly prevalent and bothersome, LUTS affected over 60% of men and women, with some variability depending on study population, age, survey methodology, data collection, definition of LUTS, and culture or ethnicity. However, data for LUTS are lacking for Central and Eastern Europe. Even in large-scale European epidemiological studies conducted to ascertain the prevalence of LUTS, countries from Central and Eastern Europe have not been included[3]. To date, no large population-representative study in any country of this region has reliably evaluated the prevalence of all LUTS and OAB using the definitions approved by the International Continence Society (ICS)[4] These data are necessary to promote health, increase awareness, and reduce the burden of disease. Population estimates attract interdisciplinary frameworks for national health improvement programs instituted with appropriate allocation of resources by governments and healthcare systems. In some recent reports, some encouraging results are found with the use of oral alpha-1a blockers (Tamsulosin 0.4 mg). The existing literature says that alpha-1a blockers have good results in improving LUTS in perimenopausal females as well as estrogen also acts as a good agent in relieving LUTS. There is a knowledge gap between the efficacy of results between these two agents. Hence, in this study, our research question will be to compare the treatment options by alpha-1a blockers and topical estrogen in the treatment of LUTS in perimenopausal females and also to strengthen the existing literature about the efficacy of both the agents in the treatment of LUTS in perimenopausal females. The aim of the study was to compare the outcome of

alpha-1a blockers and topical estrogen in the treatment of LUTS in perimenopausal females.

Materials and Methods

A comparative study was conducted in the Department of Pharmacology, ICARE Institute of Medical Sciences and Research & Dr. Bidhan Chandra Roy, Hospital, Haldia, West Bengal, India, for 13 months, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

All 80 perimenopausal females between the age group of 40 and 58 years, were included in this study. More than 85% of the patients presented were from low socioeconomic status and 15% of the patients were from low middle-class society. All of them were housewives by occupation. All 80 perimenopausal females between the age group of 40 and 58 years presented with the retention, past history of urethral dilatation, or having urinary infection were excluded from the study. All 80 other patients between the age group of 40 and 58 years having LUTS were included in 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) (i.e., poor stream, intermittency, straining, and incomplete voiding) and objectively by uroflowmetry and post void residual urine (PVR) estimation [ultrasonography (USG)].

Primary endpoints included improvements in the flow of urine as estimated by uroflowmetry and decrease in PVR urine as estimated by USG. Secondary endpoints included clinical improvements of voiding symptoms (i.e., poor stream, intermittency, incomplete voiding). 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 females of each group were given either alpha-1a blocker or topical estrogen. The mean age group of patients was 50.50 years (45–55 years). Alpha-1a blocker group had 80 females and topical estrogen had 80 females. Patients were followed up with uroflowmetry and PVR urine assessment with

USG. In the first group, pre-treatment mean Qmax (maximum flow rate) of patients was

6.9 ± 1.3 ml/s and post treatment Qmax was 17.8 ± 1.6 . In the second group, pre-treatment Qmax was 7.6 ± 1.2 ml/s and post treatment Qmax was 9.8 ± 2.1 . This difference was statistically significant ($P \leq 0.0001$). In the first group, pre-treatment PVR urine was significant, which became insignificant after the treatment, whereas in the second group, PVR was significant post treatment also (table.1)

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

	Group 1 (alpha blocker)	Group 2 (topical estrogen)	P-value
Qmax (ml/s)			
Pre-treatment	6.9 ± 1.3	7.6 ± 1.2	<0.0001
Post-treatment	17.8 ± 1.6	9.8 ± 2.1	
PVR (ml)			
Pre-treatment	122 ± 13	126 ± 15	<0.0001
Post-treatment	33 ± 7	110 ± 12	

Secondary outcome measures have also been compared such as clinical improvements in the LUTS symptoms of the patients. In the first group, 70% of the patients had an improvement in clinical symptoms, whereas in the second group, only 10% had an improvement of symptoms. This difference was clinically significant.

Discussion

LUTS in perimenopausal females are one of the major urological issues among them. This leads to considerable inconvenience and comorbidities to females. Several studies revealed that LUTS are common among females. About 15.5%–53.7% of the adult women are affected by LUTS and it can affect their social life very badly[5]. 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[6]. However, nowadays, it

is also a common health problem among women in the younger age group[7].

The treatment of perimenopausal LUTS includes conservative management and pharmacological management such as alpha-blockers and anticholinergics. Topical estrogens are also used in the management of LUTS in perimenopausal females. There are many evidence in trials which prove the efficacy of alpha-adrenoceptor antagonists in female patients with LUTS[8]. Recent studies show that alpha1-adrenoceptor antagonists are useful in improving voiding symptoms in women with nonneurogenic bladder with outlet obstruction or underactive detrusor[9]. 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[10].

There are few literatures which showed the effect of topical estrogen in improving LUTS in perimenopausal females. However, in majority of studies, there were less number of women participants, diversity in clinical and urodynamical outcomes, and short duration of treatment.

However, in our study, we got major clinical improvements in the first group, i.e., alpha-blocker group. Pre and post-treatment difference in Qmax in alpha-blocker group was significant because of its relaxing effect on the bladder neck and urethra, whereas in the second group (estrogen group), this difference was very minute as compared to alpha-blocker group. Various studies have been done which showed the superiority of alpha-blockers in the management of LUTS symptoms in perimenopausal females[11]. According to the literature, topical estrogen has the advantage over alpha-blockers in having less side effects as compared to alpha-blockers, but there are some studies which contradict this statement, such as Lee **et al.** conducted a study on female patients who presented with symptoms of LUTS[8] They used Tamsulosin (alpha-1a blocker) to know about the potential effects of alpha-1-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. They concluded that Tamsulosin is an efficacious drug in female patients with obstructive urinary symptoms regardless of its grade. There is a significant reduction in mean and maximal urethral pressure over the entire urethra after using tamsulosin 0.4 mg orally. In a study conducted by Kessler **et al**[9]. nonselective alpha-blockers were used in the treatment of functional urinary obstructive symptoms in 15 women. The assessment of symptoms and urodynamic parameters was done before and 4 weeks after the initiation of alpha-blocker therapy. The

result was that there was a significant increase from 9 s to 20 s in the median maximum flow rate. They concluded that alpha-blockers had a significant role in the improvement of symptoms and urodynamics in two-third of the patients. Ahmad **et al.** also concluded in their study that tamsulosin significantly decreases IPSS and PVR and improves Qmax, so they should be used as the first-line pharmacological agent for moderate to severe LUTS in women[11] According to our study, there is a major decrease in PVR urine in alpha-blocker group, whereas in the topical estrogen group, a decrease in PVR urine was minimal. This finding was supported by many studies which shows the superiority of alpha-blocker in the management of LUTS in perimenopausal females[11] Lee **et al.** reported a decline of PVR from 69.13 + 85.45 of baseline to 39.88 + 48.39 after 8 weeks of treatment ($P < 0.01$)[8] The present study concludes that there was a significant improvement in IPSS, Qmax, and PVR after tamsulosin treatment in female patients.

Conclusion

The conclusion of this study is that alpha-1a blockers should be used as a first-line medical management in perimenopausal females with symptoms of LUTS, as they have a clear advantage over topical estrogens in improvement in symptoms of LUTS (improvement in Qmax, decrease in PVR, and clinical improvement).

Reference

1. Abrams, P. et al. Te standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol. Urodyn.* 21, 167–178 (2002).
2. Coyne, K. S. et al. Te prevalence of lower urinary tract symptoms (LUTS) in the USA, the UK and Sweden: results

- from the Epidemiology of LUTS (EpiLUTS) study. *BJU Int.* 104, 352–360 (2009).
3. Irwin, D. E. 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.* 50, 1306–1314 (2006) (discussion 1314–1305).
 4. Irwin, D. E., Kopp, Z. S., Agatep, B., Milsom, I. & Abrams, P. Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. *BJU Int.* 108, 1132–1138 (2011).
 5. Boyle P, Robertson C, Mazzetta C, Keech M, Hobbs FD, Fourcade R, et al. The prevalence of lower urinary tract symptoms in men and women in four centres. The UrEpik study. *BJU Int.* 2003;92:409–14.
 6. Pinnock C, Marshall VR. Troublesome lower urinary tract symptoms in the community: A prevalence study. *Med J Aust.* 1997;167:72–5.
 7. 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.
 8. 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.
 9. 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.
 10. 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.
 11. 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.