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Research Article

ROLE OF TAMSULOSIN IN FEMALE LOWER URINARY TRACT SYMPTOMS

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ABSTRACT

Introduction: 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. Voiding dysfunction in women is defined by the International Continence Society and International Urogynecological Association as abnormally slow and/or incomplete urination diagnosed based on symptoms and urodynamic studies. But presently there is a lack of standardized diagnostic criteria and clinical guidelines. So, female LUTS is overlooked and underestimated. Moreover, the pathophysiological mechanism of female LUTS is unknown.

Methods: This study was a prospective double-blind placebo-controlled study. It was carried out in the Department of Urology at Tambe Hospital, Sangamner, Ahmednagar, Maharashtra, India. A total of 100 patients were enrolled in the study and were randomly allocated to either tamsulosin group or the placebo group in double blind fashion. The study was conducted for six weeks period. The primary outcome was symptomatic and subjective improvement and improvement of IPSS and quality of life score at the end of the study. The secondary outcomes were improvements in the urinary flow rates and changes in the post void residual urine. The mean changes from baseline and at six weeks between the two groups were noted and compared. Following collection of data, it was analysed by computer software Statistical Package for the Social Sciences (SPSS version 19).

Results: The baseline characteristics of each patient in both the groups were measured and were comparable regarding the age, weight, duration of symptoms and the IPSS. 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 (p value <0.01) as compared to the placebo group.

Conclusion: Alpha blockers are effective in the treatment of LUTS female patients. The effect of alpha blockers on LUTS in females should be assessed and treated according to the underlying cause. Apart from this, the role of alpha blockers in combination therapy with other drugs like antimuscarinics should also be investigated.

INTRODUCTION

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 (1).LUTS looks more of a social problem and affects the quality of life in around half of affected females (2). LUTS include both the storage and voiding symptoms including the quality of life bothersome. The alpha receptors in the bladder - α1D and in the urethra - α1A in the females appear to mediate the LUTS similar to the male counterparts (3). The severity of urinary symptoms and the degree of bothersome associated with LUTS are quantified using the International Prostate Symptom Score (IPSS) similar to the males (4, 5, 6, 7). 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. We here explain how tamsulosin matters in the life a female and how the symptoms improve with the use of tamsulosin.

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METHODS

This study was a prospective double-blind placebo-controlled study. It was carried out in the Department of Urology at Tambe Hospital, Sangamner, Ahmednagar, Maharashtra, India. The inclusion criteria included new cases of LUTS, age more than 25 years, IPSS more than or equal to 8, normal urine analysis and willingness to give written informed consent. The exclusion criteria included active urinary tract infection, pregnancy, stress urinary incontinence, history of radiation therapy to pelvic region, neuropathic bladder conditions, bladder malignancy and all contraindications for alpha blockers. This study was reviewed and approved by the ethical committee of Tambe Hospital, Sangamner, Ahmednagar, Maharashtra, India.

A total of 100 patients were enrolled in the study and were randomly allocated to either tamsulosin group or the placebo group in double blind fashion. The block randomisation size of four was carried out by computer generated random number before the participants received any treatment. Each group consisted of 50 participants. In the tamsulosin group three patients lost to follow up – one due to symptoms not improved and two due to adverse effect of the drug and in the placebo group two patients lost to follow up due to no improvement in the symptoms. All one hundred patients were included in the analysis.

The study was conducted for six weeks period. This included three visits – first during the start of the study, second after three weeks and last visit at the completion of the study. Patients were randomised to either groups. Medicines were packed in a concealed packet to maintain the blinding. Patients had to take medicine i.e. tamsulosin 0.4 mg or placebo daily in the evening after the food. IPSS form was filled by the patients themselves in their own language i.e. Hindi, English or Marathi. Uroflowmetry was carried using the same machine of sigma company. The parameters measured were maximum flow rate in ml/sec, voided volume in ml, flow time in ml/sec and mean flow rate in ml/sec. Minimum volume required for correct measurement was 150 ml. If the voided volume was insufficient then the patients were asked to drink 300-400 ml of fluid and a second uroflowmetry was done in next 1-2 hours. All the adverse events were noted during the visits of the patients. The regularity of the treatment was confirmed by asking the patients and counting of the remaining medicines, if any. Patients were advised not to take any other medication for their LUTS.

The primary outcome was symptomatic and subjective improvement and improvement of IPSS and quality of life score at the end of the study. The mean change in the symptoms and the IPSS were noted and compared between the two groups. The secondary outcomes were improvements in the urinary flow rates and changes in the post void residual urine. The mean changes from baseline and at six weeks between the two groups were noted and compared.

Following collection of data, it was analysed by computer software Statistical Package for the Social Sciences (SPSS version 19).All the participants who took even a single dose of medicine after the randomisation were included in the study. Adverse events were reported in numbers and percentages.

RESULTS

A total of 100 patients with LUTS were included in the study. Fifty patients were assigned randomly to each tamsulosin and placebo group.

The baseline characteristics of each patient in both the groups were measured and were comparable regarding the age, weight, duration of symptoms and the IPSS.

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. In the tamsulosin group, the Spearman's coefficient was 0.38 and p value was 0.7 while the Spearman's coefficient was 0.30 and the p value was 0.2in the placebo group. So, it was assumed that the difference in the baseline IPSS in the two groups had no significant effect on the difference in the mean change from baseline the two 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.

Table 1 Demographic characteristics and baseline data

	Tamsulosin		Placebo	
Age (years)	Mean	Range	Mean	Range
	44.2	25-76	46.5	25-73
Weight (kgs)	49.6	40-72	51.3	40-74
Duration of Symptoms (months)	37	15-45	35	16-50
IPSS	17.4	11-28	18.2	10-30

Table 2 Baseline IPSS and other parameters

	Tamsulosin group		Placebo group	
	Before (Mean)	After (Mean)	Before (Mean)	After (Mean)
IPSS	17.4	11.4	18.2	15.6
Frequency	3.5	2.3	3.6	3.0
Urgency	3.1	2.4	3.4	3.1
Nocturia	3.2	2.2	3.5	2.9
Straining	3.7	2.7	3.6	3.1
Intermittency	4.0	2.8	3.9	3.3
Stream	3.4	2.3	3.5	3.0
Incomplete emptying	3.3	2.1	3.4	3.1
Urgency incontinence	4.0	2.2	3.9	3.2
Terminal dribble	3.3	2.6	3.4	2.8
Maximum flow rate (ml/sec)	18.1	19.2	18.4	19
Mean flow rate (ml/sec)	7.2	7.7	7.4	7.5
Voided volume	252.3	300.5	260.4	270.7
Postvoid residual urine	125.4	60.2	131.6	110.5
Quality of life score	4.5	2.5	4.5	3.5

Table 2 shows the IPSS and other parameters before and after treatment and the differences in each treatment group. The mean change in the IPSS was higher and statistically significant in the tamsulosin group as compared to the placebo group. Similar was the mean change from baseline of mean flow rate and the post void residual urine in both the groups. But for the maximum flow rate the changes from baseline were not significant in both the groups.

Significant improvements were noted in the storage and voiding symptoms in the tamsulosin group (p value <0.01) as compared to the placebo group.

Two patients (4%) in the tamsulosin group experienced side effects of the drug like dizziness, rhinitis and asthenia. They were lost to follow up due to the side effects. There were no side effects in the placebo group.

DISCUSSION

The prevalence of female LUTS is reported to be as high as 19 % (8). LUTS include both storage and voiding symptoms. The lower urinary tract function is maintained and co-ordinated 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-3 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.
Many drugs are used to treat LUTS in females like antimuscarinics and alpha 1 adrenergic receptor antagonists. The rationale for using alpha 1 adrenergic receptor antagonists is based on the facts that the alpha receptors in the bladder - α1D and in the urethra - α1A in the females appear to mediate the LUTS similar to the male counterparts (3).In animal studies on the rabbit, it is shown that the female urethra has a similar density and affinity of a1-adrenergic receptors (9), compared to the male counterpart, and in healthy females tamsulosin has been shown to cause relaxation of the urethra (10).

Only few studies have reported usefulness of alpha blockers in female LUTS (8, 11, 12, 13). In our study, most of the patients in the tamsulosin group perceived moderate to marked improvement in their storage as well as voiding symptoms. Patients exhibited statistically significant symptom relief in the study done by Do Kyung Kim *et al* (13).

Our study is among one of those randomised controlled study that investigated the therapeutic benefit of alpha blockers tamsulosin in females with LUTS. We did this study over 100 patients with 50 patients in each tamsulosin and placebo group respectively. The demographic and baseline characteristics of patients in each group were not statistically significant except for the IPSS, which was higher in the placebo group. To prove this whether this difference is significant or not we did Spearman's correlation and found that there is a weak correlation between baseline IPSS and mean change in IPSS in both the groups. Also we reached the power of 80% to detect the clinical significance.

We did separate analysis for the voiding and storage symptoms and found statistically significant difference. Shang-Jen Chang *et al* also found statistically significant difference in the voiding and storage symptoms in their study on the effectiveness of tamsulosin in treating women with voiding difficulty.

In our study, there was statistically significant difference in the mean flow rate and the maximum flow rate in the tamsulosin but not in the placebo group. Therefore, the changes in the IPSS may be due to changes in the flow rates and the level of changes in the urinary symptoms could be due to these changes. Do Kyung Kim *et al* (13) in their study indicated that α1-blockers are effective in reducing urinary symptom scores, increasing Qmax, and decreasing PVR urine volume.

All the findings in our study were different from other studies as our study is more detailed, we used tamsulosin not terazosin like others (11), and tamsulosin is more efficacious than terazosin.

One more important finding in our study was the mean change in the quality of life score from 4.5 to 2.4 in the tamsulosin group. This was statistically significant in the tamsulosin group as compared to the placebo group. This indicates that most of the patients were satisfied with treatment in the tamsulosin arm.

We used tamsulosin in the dose of 0.4 mg. It was well tolerated at this dose daily. Dizziness, rhinitis and asthenia were the noted side effects in two patients in the tamsulosin group. Because of the side effects, these two patients lost to follow up and resulted in premature withdrawal from the study. Do Kyung Kim *et al* (13) also recorded the similar side effects of tamsulosin in their study.

The deficiency in the study was subjectiveness of the IPSS and the quality of life score. We tried a lot to minimize the bias when patients filled the IPSS form, but there were few misunderstandings among the patients that reflected the reliability of the IPSS and the quality of life score. Another deficiency was that we should have included antimuscarinics in our study as they are more commonly used to treat LUTS in females. This would have made three arms in the study to compare the results more efficaciously.

CONCLUSIONS

Alpha blockers are effective in the treatment of LUTS female patients. The effect of alpha blockers on LUTS in females should be assessed and treated according to the underlying cause. Apart from this, the role of alpha blockers in combination therapy with other drugs like antimuscarinics should also be investigated.

Conflicts of interest: None
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