203

Lee Y[1], Lee K[2], Lee H S[2], Kim J C[3], Seo J T[4], Choo M[5], Lee J G[6], Lee J Y[7], Lee J Z[8], Oh S[9], Na Y G[10]

1. *Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, Korea,* ***2.*** *Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea,* ***3.*** *Holy Family Hospital, The Catholic University of Korea College of Medicine, Bucheon, Korea,* ***4.*** *Cheil General Hospital & Women's Healthcare Center, Kwandong University College of Medicine, Seoul, Korea,* ***5.*** *Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea,* ***6.*** *Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea,* ***7.*** *Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea.,* ***8.*** *Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea,* ***9.*** *Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea,* ***10.*** *Chungnam National University Hospital, Chungnam National University College of Medicine, Daejeon, Korea*

EFFICACY OF ALPHA-BLOCKER FOR THE TREATMENT OF VOIDING DYSFUNCTION IN WOMEN: 8 WEEK, RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY (PHASE Ⅱ)

Hypothesis / aims of study

Several studies suggest that women with voiding phase dysfunction may have a benefit from alpha-blockers. However, there is a lack of evidence based on the randomized placebo controlled trials. This study was conducted to compare the efficacy of alpha-blocker to placebo for the treatment of voiding phase dysfunction in women.

Study design, materials and methods

Women aged ≥ 18 years with voiding symptoms over 3 months were screened by physical exam, pressure-flow study, urethral calibration (for women diagnosed as bladder outlet obstruction (BOO) in pressure-flow study) and international prostate symptom score (IPSS). Women with IPSS ≥ 15 and a maximum flow rate (MFR) <15 mL/sec with a minimum voided volume of 100 mL and/or a postvoid residual (PVR) >150 mL were randomly allocated to either alfuzosin (Handok Pharma's XATRAL XL Tab. 10mg) or placebo group. Exclusion criteria included anatomical BOO, surgery for incontinence or cystocele, significant pelvic organ prolapse (POPQ ≥ III), positive cough test, and neurologic diseases. After 8 weeks of medication, changes in the IPSS, Bristol female lower urinary tract symptoms (BFLUTS) questionnaire, MFR/PVR, and voiding diary parameters were compared between alfuzosin and placebo groups. Treatment satisfaction was also evaluated. For subgroup analysis, patients were categorized into 3 groups according to the Blaivas-Groutz BOO nomogram (no; mild; moderate or severe) [1]. To look for a difference of 2.0 between the two groups for the change in the total IPSS, 122 patients per group was required with a significance level of 5%, and power of 80%, assuming standard deviation of 5.533.

Results

A total of 154 (alfusozin; 79, placebo; 75) women were included in the analysis as an intention-to-treat set. A median age was 59.0 years and a median IPSS was 23.0 (voiding; 14.0, storage; 9.0). Median MFR and PVR were 10.9ml/sec and 23.0ml with a median voided volume of 177.2ml. According to the pressure-flow study, 26 (alfuzosin 17, placebo 9) had no BOO, 90 had mild BOO (alfuzosin 43, placebo 47) and 27 (alfuzosin 15, placebo 12) had moderate or severe BOO. Baseline patient demographics and clinical data were comparable between groups except MFR (alfuzosin; 9.9ml/sec vs placebo; 11.3ml/sec, p=0.0411). After 8 weeks of treatment, IPSS total score was decreased by 7.0 in alfuzosin and by 8.0 in placebo group without significant difference (p=0.7875). Changes in IPSS subscores, MFR/PVR, and voiding diary parameters were also not significantly different between groups (Table). Approximately 54% in alfuzosin and 62% in placebo group were satisfied with the treatment (p=0.3102). In the results of the subgroup analysis according to the BOO grade, no difference was observed between alfuzosin and placebo group.

Interpretation of results

For the treatment of female voiding dysfunction, alfuzosin was not significantly beneficial over placebo. BOO grade did not affect the treatment results.

Concluding message

Alpha-blocker was not effective for the treatment of voiding dysfunction in female patients regardless of BOO grade. Female patients might have a variety of pathophysiology for the voiding symptoms. Further study is needed to find the pathogenesis of the female voiding dysfunction and to find the value of urodynamic study in this field.

Table. Changes in questionnaires, uroflow parameters and bladder diary

Variables	Alfuzosin		Placebo		p value
	Baseline	8 weeks	Baseline	8 weeks	
IPSS					
Total	23.0 (18.0,28.0)	14.0 (9.0,21.0)	22.0 (18.0,27.0)	14.0 (9.0,22.0)	0.7875‡
Voiding	15.0 (11.0,17.0)	8.0 (5.0,12.0)	14.0 (11.0,18.0)	9.0 (5.0,13.0)	0.8367‡

Storage	9.0 (7.0,12.0)	6.0 (3.0,9.0)	9.0 (6.0,11.0)	6.0 (3.0,9.0)	0.9318‡
QoL score	5.0 (4.0,6.0)	4.0 (3.0,5.0)	5.0 (4.0,5.0)	3.0 (3.0,5.0)	0.9677‡
BFLUTS					
Filling sum	6.0 (5.0,8.0)	5.0 (4.0,7.0)	6.0 (5.0,8.0)	5.0 (4.0,7.0)	0.7227‡
Voiding sum	6.0 (4.0,8.0)	3.0 (2.0,6.0)	6.0 (4.0,9.0)	4.0 (2.0,6.0)	0.7511†
Incontinence sum	1.0 (0.0,4.0)	1.5 (0.0,3.0)	1.0 (0.0,5.0)	1.0 (0.0,4.0)	0.0429‡
Sexual sum	0.0 (0.0,1.0)	0.0 (0.0,1.0)	0.0 (0.0,1.0)	0.0 (0.0,1.0)	0.8907‡
QoL sum	4.0 (2.0,8.0)	3.0 (1.0,6.0)	4.0 (2.0,8.0)	3.0 (1.0,6.0)	0.5626‡
Bladder diary parameters					
Frequency/24hr	10.0 (8.3,14.0)	9.7 (7.7,11.7)	10.0 (8.0,12.3)	9.5 (7.7,10.7)	0.6520‡
Urgency episode/24hr	4.7 (0.3,9.5)	1.7 (0.0,7.7)	2.0 (0.3,7.3)	0.7 (0.0,3.7)	0.7497‡
Urgency severity /micturition	2.4 (1.6,3.0)	2.1 (1.6,2.9)	2.1 (1.8,2.8)	2.0 (1.4,2.4)	0.4563‡
Uroflow parameters					
MFR (ml/sec)	9.9 (8.3,12.3)	13.8 (9.5,17.8)	11.3 (9.6,12.8)	15.9 (10.4,22.1)	0.4348‡
PVR (ml)	24.0 (2.0,95.0)	4.0 (0.0,46.0)	21.5 (8.0,100.0)	10.0 (0.0,30.0)	0.7867‡
Voiding volume (ml)	181.0 (128.5,262.0)	194.8 (108.7,293.8)	169.0 (129.1,242.8)	183.9 (123.0,280.5)	0.6016‡

Data; median (interquantile range), † : T-test, ‡ : Mann-Whitney test

References

1. Blaivas JG, Groutz A. Bladder outlet obstruction nomogram for women with lower urinary tract symptomatology. Neurourol Urodyn 2000; 19: 553-64.

Specify source of funding or grant	**Handok Pharma**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**ClinicalTrials.gov; NCT00679315**
Is this a Randomised Controlled Trial (RCT)?	**Yes**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**IRB of Samsung Medical Center**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**