438

Han J[1], Kim K S[2], Park S[3], Kim S J[4], Park W H[5], Choo M[2]

1. *Pusan National University Yangsan Hospital,* ***2.*** *University of Ulsan College of Medicine, Asan Medical Center,* ***3.*** *Ulsan University Hospital, University of Ulsan College of Medicine,* ***4.*** *Seoul St. Mary's Hospital, The Catholic University of Korea College of Medicine,* ***5.*** *Inha University College of Medicine*

EFFECTS OF ALPHA 1-ADRENERGIC BLOCKER AND/ OR PHOSPHODIESTERASE TYPE-5 INHIBITOR ON DETRUSOR FUNCTION AFTER BLADDER OUTLET OBSTRUCTION IN RAT

Hypothesis / aims of study

There is recent several studies that PDE-5 inhibitors might be useful as a treatment for bothersome LUTS associated with BPE [1,2]. However, whether PDE-5 inhibition ameliorates LUTS by acting on the prostatic urethra or on the bladder is not clear.

This study was undertaken to assess the efficacy of the α_1-blocker silodosin, PDE-5 inhibitor mirodenafil, and the combination of both on lower urinary tract symptoms suggestive of benign prostatic hyperplasia.

Study design, materials and methods

Six weeks old male Spraque-Dawley rats were dived into five groups (n=10 in each group) of sham control, bladder outlet obstruction (BOO, experimental control), silodosin, mirodenafil and the combination of both-treated. BOO group and drug-treated groups were partially obstructed for 6 weeks. Concurrently, silodosin (3mg/kg/day), mirodenafil (10mg/kg/day) and combination were administrated orally for drug-treated groups for 6 weeks. After 6 weeks, the effect of drugs was determined using urodynamic study and contractile response to field stimulation and drug stimulation.

Results

The bladder weights of the BOO group were significantly increased compared with the control and drug-treated groups. In drug-treated groups, especially in combination group, cystometric parameters including number of voids per minute (NVM), peak pressure (PP), nonvoiding contraction (NVC) decreased compared to BOO group (Table). Intercontraction interval (ICI) increased significantly in drug-treated groups, especially in combination group than BOO group. The contractile response to all frequency of stimulation, bethanechol and KCl were decreased in obstruction group and the contractile response in the α_1-blocker treated group and the combination group were higher than that in the BOO group. In the contractile response to ATP, the contractile responses in obstruction group significantly increased. But there is no significant difference in the contractile response of PDE-5 treated group compared with BOO group. In all the contractile response to field and drug stimulation, however, there is no significant difference in the contractile response of PDE-5 treated group compared with BOO group (Figure).

Interpretation of results

These findings suggest that the combination of silodosin and mirodenafil is more effective than silodosin monotherapy to improve detrusor overactivity related BPH without affecting detrusor contractility.

Concluding message

These findings suggest that the combination of silodosin and mirodenafil is more effective than silodosin monotherapy to improve detrusor overactivity related BPH without affecting detrusor contractility.

Table. Urodynamic parameters in each group

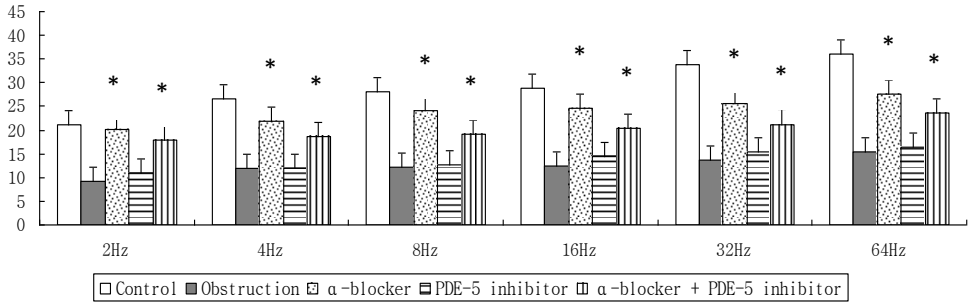
Group	NVM (voids/min)	ICI (min)	PP	NVC (/min)
Sham control	0.10 ± 0.02	10.20 ± 2.84	19.83 ± 4.46	0.26 ± 0.10
Experimental control	0.25 ± 0.78	4.29 ± 1.12	26.07 ± 6.69	0.85± 0.49
α-blocker	0.12 ± 0.03*	8.49 ± 1.90*	23.01 ± 3.17*	0.40 ± 0.28*

PDE-5 inhibitor	0.13 ± 0.02*	7.80 ± 1.02*	23.44 ± 4.97*	0.57 ± 0.17*
α-blocker + PDE-5 inhibitor	0.11 ± 0.03*	9.96 ± 1.94*	19.90 ± 4.05*	0.30 ± 0.12*

ICI; intercontraction interval, NVC; non-voiding contraction, NVM; number of voids per minute, PP; peak pressure

; The data are expressed as the means ± SD. *: significant difference compared to experimental control (obstruction) group ($p < 0.05$)

Figure. The contractile response to field stimulation in each group



; The data are expressed as the means ± SD. *: significant difference compared to experimental control (obstruction) group ($p < 0.05$)

References
1. Kaplan SA, Gonzalez RR, Te AE. Combination of alfuzosin and sildenafil is superior to monotherapy in treating lower urinary tract symptoms and erectile dysfunction. Eur Urol 2007;51:1717-23.
2. Dmochowski R, Roehrborn C, Klise S, Xu L, Kaminetsky J, Kraus S. Urodynamic effects of once daily tadalafil in men with lower urinary tract symptoms secondary to clinical benign prostatic hyperplasia: a randomized, placebo controlled 12-week clinical trial. J Urol 2010;183:1092-7.

Disclosures
Funding: none **Clinical Trial:** No **Subjects:** ANIMAL **Species:** rat **Ethics Committee:** Asan Medical Center Institutional Review Board