201

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THE EFFICACY OF FESOTERODINE FOR THE TREATMENT OF NEUROGENIC DETRUSOR OVERACTIVITY AND/OR LOW COMPLIANCE BLADDER.

Hypothesis / aims of study
The aim of this study is to evaluate the efficacy of fesoterodine for neurogenic detrusor overactivity (NDO) and/or low compliance bladder by urodynamic study (UDS).

Study design, materials and methods
This research is a 12-week single-arm study. Inclusion criteria were patients older than 16 years old with a known neurogenic disorder in a stable condition for more than 6 months, and with storage dysfunction due to neurogenic detrusor overactivity (NDO) and/or low compliance bladder. Exclusion criteria included patients having an indwelling catheter, acute infection of the genitourinary tract, genitourinary tract anomalies or clinical relevant diseases of the kidneys; and any condition that in the opinion of the investigator made the patient unsuitable for the study. The participants enroll in this study are required to be off all previous treatments that might influence voiding function for 2 weeks, and to maintain a frequency volume chart (FVC) for 3 days after 1 week of washout. Following the 2 weeks washout period, the participants receive fesoterodine 4mg/day for 12 weeks.

A video-urodynamic study was performed before and at three months following treatment. The primary end point is the amount of change in maximum cystometric capacity (MCC) following treatment. The secondary end points are the changes in the following urodynamic parameters between pre- and post-treatment: bladder capacity at first desire to void, bladder volume at first involuntary contraction (FIC), amplitude of DO, bladder compliance, maximum flow rate (Qmax), detrusor pressure at Qmax, detrusor opening pressure, maximum Watt factor, Watt factor at Qmax, BOO index and disappearance rate of DO in NDO patients. Changes in overactive bladder symptom score (OABSS), international consultation on incontinence questionnaire-short form (ICIQ-SF), international prostate symptom score (IPSS), King's health questionnaire (KHQ) and the 36-item short form health survey (SF-36) as well as changes in number of void, amount of each void and number of leak in 24 hours by FVC for 3 days are also evaluated before treatment, at 4 weeks and 12 weeks following treatment.

Sample size calculation is based on the ability to detect 40 ml difference in MCC following 12 weeks treatment. In total, 60 patients would yield 80% power to detect such a defference, assuming standard deviation of 100 ml and alpha error of 0.05. Considering an approximate 20% patient dropout rate, a total of 77 patients are required.

Table 1 Results of UDS before and at 12 weeks of treatment.

Cystometry	Before	12 weeks	P-value
All patients (n= 60)			
Bladder capacity at first desire to void (ml)	154.1±84.9	187.0±109.3	0.0255
Maximum cystometric capacity (ml)	247.0±127.4	326.0±127.6	<0.0001
Bladder compliance (ml/cmH_2O)	28.1±30.6	50.2±87.1	<0.0001
Patients with detrusor overactivity (DO) (n= 51)			
Bladder capacity at first desire to void (ml)	157.3±73.4	187.6±111.3	0.0383
Maximum cystometric capacity (ml)	257.0±121.9	330.5±123.6	<0.0001
Bladder compliance (ml/cmH_2O)	31.7±31.3	57.8±92.5	0.0160
Bladder capacity at first involuntary contraction (ml)	204.5±124.7	289.4±131.8	<0.0001
Amplitude of detrusor overactivity (cmH_2O)	49.1±23.5	33.0±26.6	0.0003
Patients with low-compliance bladder without DO (n= 9)			
Bladder capacity at first desire to void (ml)	132.8±143.7	183.6±103.0	0.3846
Maximum cystometric capacity (ml)	179.8±149.4	300.3±154.0	0.0034
Bladder compliance (ml/cmH_2O)	4.1±2.4	7.0±3.8	0.0058
Pressure-flow study in patients with DO (n=32)			
Maximum flow rate (Qmax) (cmH_2O)	10.3±7.5	13.8±9.7	0.0334
Detrusor pressure at maximum flow (PdetQmax) (cmH_2O)	43.5±23.2	36.6±20.7	0.2988
Detrusor opening pressure (PdetOP) (cmH_2O)	50.7±29.5	39.4±25.1	0.1276
Watt factor max	11.7±9.9	13.5±12.1	0.7010
Watt factor Qmax	8.5±4.3	10.0±7.7	0.3870
Bladder outlet obstruction index	25.4±24.4	15.9±20.4	0.1602

Results
Seventy seven patients with NDO and/or low compliance bladder were studied. The median age was 67 years old. Fifty two patients were male. The underlying neurological diseases were brain-related diseases in 19 patients, spinal cord-related diseases in 49 patients and others in 9 patients (post-hysterectomy in 4, post-abdominal aortic aneurysm surgery in 1 and diabetes mellitus

in 4). Adverse events were noted in 40 patients (51.9%); the most frequent adverse event was dry mouth in 20 patients, followed by constipation in 7 patients. Moreover, 13 patients (16.9%) were dropped out by adverse events.
Urodynamic study could be performed both before and after the treatment in 60 patients. The results are summarized in Table 1. In 51 patients with DO, DO was disappeared in 12 patients (23.5%).

Pressure flow study could be performed both before and after that in 35 patients (DO in 32 and low compliance bladder in 3). Since the number was small, it was not evaluated in low compliance bladder.

Fifty seven patients could answer OABSS, ICIQ-SF, IPSS and KHQ both before and after the treatment. Furthermore, fifty four patients could answer SF-36 (Table 2, Figure 1).

Table 2 Results of various questionnaires before, at 4 weeks and at 12 weeks of treatment.

		Before	4weeks	P value at 4weeks		12 weeks	P value at 12 weeks
OABSS total score		7.1±4.1	6.0±4.2	0.0500		5.3±4.1	0.0041
ICIQ-SF total score		9.2±5.7	7.7±5.9	0.0823		7.2±5.7	0.0004
IPSS total score		11.0±8.7	10.0±8.2	0.2535		9.1±8.7	0.4134

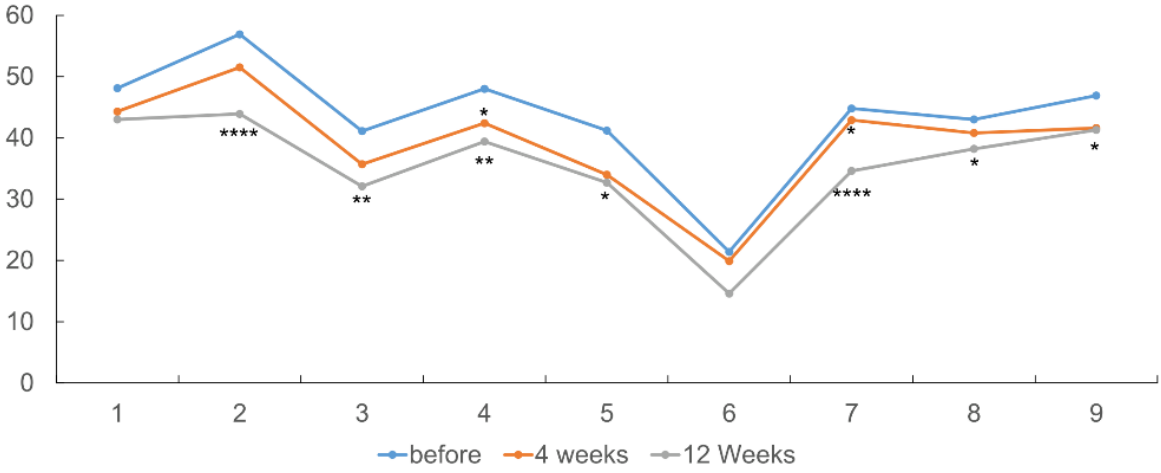

Fig. 1 Results of King's Health Questionnaire before, 4 weeks (n= 66) and 12 weeks (n= 57). Numbers on the x-axis indicate the following domains: (1) General Health Perceptions; (2) Incontinence Impact; (3) Role Limitations; (4) Physical Limitations; (5) Social Limitations; (6) Personal Relationships; (7) Emotions; (8) Sleep and Energy; and (9) Severity Measures. *P < 0.05; **P < 0.005; ***P < 0.0005; and ****P < 0.0001 compared with baseline (Wilcoxon matched-pairs signed ranks test).

Interpretation of results
It has been reported that anticholinergicsare effective in decreasing bladder filling pressure, increasing bladder compliance and increasing bladder capacity in patients NDO or low compliance. All cystometric parameters during filling phase improved significantly after fesoterodine therapy, except for bladder volume at first desire to void in patients with low compliance bladder without DO. Fesoterodine was effective in increasing bladder capacity and compliance in the patients with NDO and/or low compliance bladder.

Concluding message
Fesoterodine appeared to be effective for the therapy of NDO and/or low compliance bladder.

References
1. M. Watanabe, et al. Efficacy of extended-release tolterodine for the treatment of neurogenic detrusor overactivity and/or low-compliance bladder. Int. J. Urol. 2010; 17: 931-936.

Disclosures
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