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EFFICACY OF TOLTERODINE ER FOR THE TREATMENT OF NEUROGENIC DETRUSOR OVERACTIVITY OR LOW COMPLIANCE BLADDER – ASSESSMENT BY URODYNAMIC STUDY-

Hypothesis / aims of study
Tolterodine is widely used for the treatment of overactive bladder. Although anticholinergics are useful for the treatment of overactive bladder (OAB), they have also showed some effects for the treatment of neurogenic detrusor overactivity.
The efficacy of anticholinergics are usually evaluated by patients' subjective symptoms questionnaire (e.g. OABSS, ICI-Q or OAB-Q) and voiding diary [1]. However, these parameters do not always reflect voiding dysfunction. Some patients with neurogenic detrusor overactivity lack bladder sensation. Some have both storage and voiding dysfunctions, and perform clean intermittent catheterization with anticholinergics. In neurogenic bladder patients with detrusor overactivity or low compliance bladder, and in those who are performing clean intermittent catheterization, an increase in bladder capacity with anticholinergics is important in order to decrease the frequency of catheterization and to prevent the upper urinary tract deterioration. The evaluation of only lower urinary tract symptom may not be useful in these patients, and evaluation with urodynamic study is useful for assessing the efficacy of tolterodine on neurogenic bladder. The aims of the present study is to evaluate the efficacy of tolterodine ER 4mg/day for the treatment of neurogenic detrusor overactivity (NDO) or low compliance bladder through assessing urodynamic parameters.
Study design, materials and methods
This is a one arm, single centre study to evaluate the efficacy of tolterodine on neurogenic detrusor overactivity through urodynamic assessment. Patients enrolled in this study are required to be off all previous medication which may influence voiding function, e.g. anticholinergics, antihistamines, alpha and beta- adrenoceptor agonists and antagonists for 2 weeks, and to maintain a 3 days diary after one week washout. After the two week washout period, the patients are given tolterodine ER 4mg/day for 12 weeks. Video urodynamics or ambulatory urodynamics are performed with the same method before and after the treatment.
The efficacy on OAB symptoms through OABSS and voiding diary and safety of tolterodine are also assessed.
47 patients (22 males, 27 females), with a mean age of 58±20 (18-84) years, with neurogenic bladder, who suffer from brain lesions, spinal cord lesions, Multiple sclerosis, Parkinson's disease, multiple system atrophy, etc, were included in the study. 19 patients (40%) were on clean intermittent catheterization (CIC) and other patients could void by their own. 40patients had NDO and 7 had low compliance bladder.
Primary endpoint was change in the urodynamic parameter of maximum cystometric capacity (MCC) between pre- and post-treatment, and number (percent) of patients whose maximum cystometric capacities were increased by >50ml after the treatment. Secondary endpoint was changes in the following urodynamic parameters between pre- and post-treatment: bladder capacity at first desire to void, bladder capacity at first involuntary detrusor contraction (FIC), amplitude of DO, bladder compliance, maximum flow rate (Qmax), maximum detrusor pressure, maximum detrusor pressure at Qmax. Changes in OAB symptoms and QOL scores (changes in overactive bladder symptom score: OABSS, ICIQ-SF and KHQ), and changes in number of voids, amount of each void, and number of leaks in 24 hours by voiding diary were also evaluated before, and at weeks 4 and 12 after treatment.
For safety, changes in postvoid residual urine volume before and after treatment through ultrasound, and incidence and severity of all reported adverse events were evaluated.
Results
43 patients completed the study. Urodynamic study could be performed both before and after the treatment in 38 patients. MCC increased significantly by 49ml ($P<0.0001$), and MCC was increased by >50ml after the treatment in 18 (47%) of patients. In patients with DO (n=29), bladder capacity at FIC increased significantly ($p=0.051$), amplitude of DO decreased significantly ($p=0.0009$) after the treatment. In patients with low compliance bladder (n=6), bladder compliance did not change significantly, but MCC increased by >50ml after the treatment in 4 (67%) of patients. In patients who could void, Qmax, postvoid residual, and maximum detrusor pressure and maximum detrusor pressure at Qmax did not change significantly.
In OABSS, scores of daytime frequency, urgency and urgency incontinence significantly decreased after the treatment (all $p<0.05$), but those of nocturia and total score did not. In ICIQ-SF, scores of frequency of leaks, amount of leaks, QOL score and the sum of these scores significantly decreased after the treatment. In KHQ, scores of role limitations domain and emotions domain decreased significantly ($p<0.05$). In voiding diary, number of voids (day and night), number of urgency in 24 hours, amount of each void, and number and amount of leaks in 24 hours were all significantly decreased ($p<0.05$).
Interpretation of results
In patients with NDO, all urodynamic parameters improved significantly after tolterodine treatment. OAB symptoms including daytime frequency, urgency and urgency incontinence, and QOL score significantly improved significantly. Tolterodine appeared to be tolerable because no serious side effect was observed and only 4 patients withdrew with unknown reasons. In patients with low compliance bladder, MCC increased in 67% of patients, and thus could decrease the frequency of catheterization.
Concluding message
Tolterodine seemed to be effective for the treatment of DO and low compliance bladder in neurogenic bladder.

References

1. Symptom assessment tool for overactive bladder syndrome-overactive bladder symptom score. Urology 68:318-23, 2006

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Is this study registered in a public clinical trials registry?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Ethics Committee of Dokkyo Medical University**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**