355

Zhang Z[1], Zheng J[1], Pan Z[1], Sun Z[1]
1. *Department of urology,huadong hospital affiliated to Fudan University*

THE EFFICACY OF TOLTERODINE ER WAS ENHANCED BY COMBINING LOW-DOSE VAGINAL ESTROGEN TREATMENT AND BLADDER TRAINING FOR POSTMENOPAUSAL WOMEN WITH OVERACTIVE BLADDER （OAB）

Hypothesis / aims of study
Anti-muscarinic agent is currently the front-line pharmacotherapy in relieving major symptoms of overactive bladder (OAB) with an efficacy of 65-75% (1). Other conservative therapies include bladder training (BT) (2) and low-dose vaginal estrogen treatment (ET) for postmenopausal women with OAB (3). The aim of this study is to investigate whether the efficacy of Tolterodine ER could be further improved in postmenopausal women if combined with other conservative therapies such as low-dose vaginal (ET) and BT.

Study design, materials and methods
This is an unblinded study without placebo. Between March 2011 and February 2012, 165 postmenopausal women aged 62 year-old (range: 48-82) presenting with symptoms of urgency and frequency, with or without urge incontinence, were prospectively enrolled in this study. After the one week run-in period, they were randomly grouped to be Tolterodine ER alone (Group To, n=41), Toltrodine ER + vaginal ET (Group To+E, n=43), Toltrodine ER + bladder training (BT) (Group To+B, n=47) and Toltrodine ER+BT+ VET (Group To+E+B, n=34). During 12 weeks, Tolterodine ER was orally administrated 4 mg once per day, Vaginal conjugated equine estrogen 0.625 mg was locally applied twice a week. Patients underwent BT were educated by a nurse specialist provided with a written sheet that informs training techniques. All patients had a baseline and 12th week post-treatment evaluation, The patient perception of bladder condition (PPBC) were used for subjective outcome measure while the following validated measures were used to evaluate objective outcomes: the mean numbers of day-time micturition, urgency episodes, nocturia and pads usage.

Results
All patients were evaluated according to the protocol at 12 weeks without withdrawal from the treatment. At the end of the study, the improvements of both subjective and objective outcome measures were seen in all groups. As compared with baseline, the median percentage(%) reductions in four groups (To vs To+E vs To+B vs To+E+B) were as followings: day-time micturition (33 vs 41 vs 54 vs 66), urgency episodes (58 vs 60 vs 71 vs 87), nocturia (36 vs 33 vs 42 vs 49) and pads usage (56 vs 60 vs 71 vs 78); whereas the median percentage(%) increases of PPBC was (53 vs 50 vs 66 vs 82). Comparisons of Group To+E+B and Group To in all above evaluation measures were statistically significant ($P < 0.001$). The administration of Tolterodine ER was in general well tolerated; the most common adverse event was mild dry mouth.

Interpretation of results
For postmenopausal women with OAB, the efficacy of Toltrodine ER could be enhanced by combining with other conservative therapies. In this study, the combination of To+E+B was superior to either To alone or To+E and To+B. However, no synergistic effect was found in Group To+E compared with To alone (P=0.667).

Concluding message
The combination of Tolterodine ER plus low-dose vaginal ET and BT is a safe and effective therapy for postmenopausal women with OAB.

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