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RESPONSE TO FESOTERODINE IN OVERACTIVE BLADDER (OAB) PATIENTS IS INDEPENDENT OF THE URODYNAMIC FINDING OF DETRUSOR OVERACTIVITY.

Hypothesis / aims of study
The efficacy and safety of fesoterodine, a non-selective muscarinic antagonist were investigated in non-neurogenic urge-incontinent patients to determine if the finding of baseline detrusor overactivity correlates with treatment outcomes. A second goal was to determine the accuracy of urodynamic evaluation by the investigators and concordance among three central readers who were not investigators.

Study design, materials and methods
Adults of either gender entering a phase 2 multicenter randomized double-blind placebo-controlled study investigating fesoterodine in urinary urge incontinence with increased frequency and urgency of ≥ 6 months and urge incontinence ≥ 1 month duration underwent baseline urodynamic examination according to the International Continence Society urodynamic standards. Three urologists, blinded to investigator and treatment identities, independently reviewed urodynamic tracings. Subjects assigned to Stratum A had ≥ 1 symptom-associated involuntary detrusor contraction whereas Stratum B patients had normal filling cystometry. Although the investigators at each center assigned a stratum to individual subjects, the final analysis was performed on the final stratum assignment made by the principal reader. Efficacy evaluation relied on changes in number of micturitions/24 hours and urge incontinence episodes/week.

A total of 173 patients were randomized to the 8-week double blind treatment segment; of these, 99 were finally assigned as Stratum A and 74 as Stratum B. The randomized allocation for Stratum A was 24 cases on placebo, 25 on fesoterodine 4mg, 28 on 8mg, and 22 on 12mg. The allocation for Stratum B was 19, 19, 19, and 17 to placebo, and fesoterodine 4 mg, 8 mg, and 12 mg, respectively. Two subjects were not treated due to randomization error and consent withdrawal.

Results
There was a high degree of concordance among investigators and the reviewing urodynamic readers. In 14% of cases assigned to stratum A by investigators at different centers, the urodynamic readers reassigned the subjects to stratum B. Only 6% of subjects assigned to stratum B by investigators were reassigned by the readers.

After two weeks of treatment fesoterodine consistently improved the number of micturitions/24 hours versus placebo, $p = 0.0499$ in both strata of patients. Multiple regression analysis estimated the slope at –0.16, $p=0.0001$, indicating linear dose-response relationship.
Similar improvement in mean number of urge incontinence episodes/week occurred with fesoterodine for which the multiple regression analysis estimated a slope of –0.72, $p=0.0022$, denoting a linear dose-response relationship. There was no significant difference between the two strata:

Analysis of covariance analysis of number of micturitions/24 hours based on the difference between strata A&B

Measured criteria	Estimate for difference from placebo	Standard error for the difference	95% confidence interval of the difference	p-value (2-sided)
Micturition frequency/24 hours	0.191	0.360	– 0.52, 0.90	0.5961
Urge incontinence episodes/week	0.697	2.059	– 3.37, 4.76	0.7355

Interpretation of results

These results suggest that treatment response to antimuscarinic agents in urge incontinent patients is independent of the finding of urodynamic detrusor overactivity.

The methodology of the central urodynamic reading committee proved to be highly concordant, reliable, and reproducible; it can be a model for future trials involving urodynamic studies.

Concluding message

Fesoterodine fumarate efficacy and tolerability in patients with OAB is not influenced by urodynamic characterization.

Perhaps, using urodynamic data as entry criteria in studies of antimuscarinic agents in patients with urge incontinence may be of little value. However, further research is needed to determine if urodynamic studies would predict response to antimuscarinic therapy in patients with symptoms of overactive bladder without incontinence.

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