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PROPIVERINE HYDROCHLORIDE REDUCED FREQUENCY AND PERCEPTION OF URGENCY IN TREATMENT OF OVERACTIVE BLADDER: A 12 WEEK PROSPECTIVE, RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED STUDY

Hypothesis / aims of study

A recent meta-analysis of randomised controlled trials on antimuscarinic treatment of overactive bladder (OAB) concluded that the drugs produce significant improvements in OAB symptoms compared with placebo but that the benefits are of limited clinical significance (1). A possible reason for this was the lack of data based on urinary urgency and the use of sensitive patient driven criteria. Urgency is the central symptom of OAB and is very bothersome to patients, therefore, any effective treatment for OAB must reduce this symptom. However, the subjective nature of urgency makes it difficult to measure. The aim of this study is to explore the efficacy of propiverine (20 mg, qd) in reducing the urgency and the patient's perception from baseline to 12 weeks of treatment in OAB patients.

Study design, materials and methods

Eligible male and female patients over 18 years old were randomized 1:2 to placebo or 20 mg propiverine hydrochloride once daily in this 12-week, multicenter, parallel, double-blind, placebo controlled trial. Subjects were required to have an average frequency of ≥10 voids/24 h and have experienced at least three episodes of urgency during the 3-day voiding diary period. Patients recorded micturition frequency, voided volume, frequency of urgency, severity of urgency using a voiding diary during run-in period, weeks 4 and 12 (directly preceding clinic visits). In the voiding diary patients recorded every voluntary micturition and marked the level of urgency associated with it for each event. The Indevus Urgency Severity Scale (IUSS) (2) was used to measure urgency, and urgency was defined as ≥2 point. Overall patient's perception of urgency was assessed by Urgency Perception Score (UPS) (3). Primary end point was change from baseline in average number of urgency per 24 hours at 12 weeks. Secondary efficacy variables were change in average urgency severity per micturition, frequency of micturition during day and night, and patient's perception of urgency and treatment benefit.

Results

A total of 264 patients (mean 52.2 years, 74% female) were enrolled, 176 on propiverine and 88 on placebo. The efficacy analysis included all randomized patients who received at least one dose of the study drug, had efficacy data available from the baseline and at least one on-treatment visit, and were compliant with study medication more than 75% (221 patients). Baseline characteristics were comparable between the two treatment groups. Propiverine significantly decreased frequency of urgency, micturition frequency/24 hours, and daytime frequency (Table). Improvement of nocturia and urgency severity per voiding was not significantly different between the two groups. The proportion of patients able to finish tasks before voiding in response to urgency was more significantly increased in the propiverine group (4.93% to 45.07%) than in the placebo group (3.80% to 26.58%) (P<0.005). The proportion of patients unable to hold urine upon experiencing urgency was decreased by 60.53% with propiverine, compared with 21.05% with placebo (P<0 .005). The proportion of patients reporting "much benefit" from treatment was greater for propiverine than for placebo (38.7% vs 15.2%; P<0 .005).

Interpretation of results

Propiverine significantly decreased mean frequency of urgency and improved patient's perception of urgency compared to placebo. Perception of treatment benefit was more pronounced in propiverine than placebo group. But, propiverine was not superior to placebo for improvement in urgency severity per micturition. This discrepancy pointed to the need to develop more reliable patient-reported subjective assessment of urinary urgency in clinical studies of OAB treatments. The improvement rate with regard to nocturia was similar in both groups. This discrepancy in terms of daytime and night time improvement may be due to the multifarious etiology of nocturia.

Concluding message

Propiverine 20 mg once daily produced significant improvement in the major symptoms of OAB and patient's perception compared with placebo. Discrepancy between urgency severity score and patient's perception to treatment benefit requires the development of a clinically sensitive tool for the assessment of urgency severity.

Wk	Placebo (n=79)	Propiverine (n=142)	P value*

No. voids/24 hrs			
Baseline	12.99	12.77	
Change from baseline			
Week 4	-2.55	-2.84	0.6321
Week 12	-2.58	-3.56	0.0015
No. diurnal voids			
Baseline	11.13	11.02	
Change from baseline			
Week 4	-2.19	-2.49	0.7125
Week 12	-2.16	-3.04	0.0019
No. nocturnal voids			
Baseline	1.86	1.74	
Change from baseline			
Week 4	-0.36	-0.35	1.0000
Week 12	-0.42	-0.52	0.3314
No. urgency voids/24 hrs			
Baseline	7.62	7.41	
Change from baseline			
Week 4	-2.26	-2.64	0.8138
Week 12	-2.97	-3.78	0.0147
Urgency severity score /void			
Baseline	1.67	1.63	
Change from baseline			
Week 4	-0.15	-0.18	1.0000
Week 12	-0.26	-0.41	0.0844

* Difference assessed by t-test or Wilcoxon Two Sample Test.

References:
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HUMAN SUBJECTS: This study was approved by the Samsung Medical Center and followed the Declaration of Helsinki Informed consent was obtained from the patients.