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COMBINATION TREATMENT WITH PROPIVERINE HYDROCHLORIDE PLUS DOXAZOSIN GITS IN MEN WITH OVERACTIVE BLADDER COEXISTING BENIGN PROSTATIC OBSTRUCTION: A PROSPECTIVE, RANDOMIZED, CONTROLLED, MULTICENTER STUDY

Hypothesis / aims of study

Treatment of overactive bladder (OAB) symptoms in men with benign prostatic obstruction (BPO) is a therapeutic challenge. Combining the current α1-adrenoceptor antagonists with antimuscarinic might theoretically provide improved symptom relief. Antimuscarinic therapy can be expected to lead to a deteriorated voiding up to complete retention in these patients. Recent study reported the safety of antimuscarinic in terms of the post-void residuals and acute urinary retention in BPO(1, 2). We evaluated the efficacy and safety of propiverine hydrochloride combined with doxazosin GITS in patients with overactive bladder coexisting benign prostatic obstruction.

Study design, materials and methods

In a multicenter, double-blind study, men aged ≥50 years with urgency and frequency (> 8 times/24hours) and urodynamically proven BOO (Abrams/Griffith score >20) were randomised (1:2) to group 1- doxazosin GITS (4 mg once daily) only and, group 2 - propiverine hydrochloride (20mg once daily) plus doxazosin GITS. Before commencing treatment patients were evaluated by digital rectal examination, PSA, voiding-frequency chart, International Prostatic Symptom Score (IPSS), and urodynamic study. Patients were excluded if they had a baseline post void residual (PVR) exceeded 30% of maximum cystometric capacity. Reevaluation with voiding-frequency chart, IPSS, uroflowmetry, and PVR was performed after 8 weeks of treatment. Patient's Global Satisfaction Questionnaire was performed after 8 weeks of treatment. Tolerability was evaluated from adverse event reports and withdrawal rates.

Results

A total of 228 (group 1: 76, group 2: 152) men were randomized into the study and 198 (86.8%) completed the 8-weeks of treatment. Baseline parameters were comparable in both groups. A significant difference was noted in both groups after treatment for urinary frequency, maximum flow rate (Qmax), average micturition volume, and IPSS. Compared with group 1, the changes from baseline in the daytime frequency and total voiding frequency were statistically significantly higher in group 2 (Table). Changes from baseline in maximum flow rate (Qmax) were statistically equivalent in both groups. PVR was significantly increased in group 2, but not in group 1. Statistically significant Increase of PVR in group 2 (+ 20.7 ml) was not accompanied by urinary retention and therefore, not considered to be clinically significant. Change of total IPSS from baseline was not significantly different between two groups, but urgency symptom (item 4) and storage symptoms (sum of item 2, 4, 7) were significantly lower in group 2 (p=0.032, 0.044 respectively). Change of voiding symptoms (sum of item 1, 3, 5, 6) was similar in both groups. In Patient's Global Satisfaction Questionnaire, satisfaction rate was significantly higher in group 2 than group 1 (p=0.014). Propiverine was safe and well tolerated as measured with adverse events and treatment withdrawals. A total of 9 (11.8%) in group 1 and 21 (13.8%) in group 2 patients discontinued prematurely primarily due to adverse events. Overall adverse event rate was higher in group 2 (p=0.0024). Dry mouth was significantly higher in group 2 than group 1 (19.1% vs. 11.8%) but did not result in increased treatment discontinuation. Other adverse events were similar in both groups. Acute urinary retention was not reported in each treatment group.

Table. Voiding-frequency and uroflow parameters at baseline and 8 weeks after treatment.

	Group 1 (n=67)		Group 2 (n=131)		p-value*
	Baseline	Week 8	Baseline	Week 8	
Day time frequency	8.47 ± 2.10	7.56 ± 1.68	8.80 ± 3.20	6.94 ± 2.27	0.01099
Nocturia	2.19 ± 1.15	1.63 ± 0.89	2.24 ± 1.15	1.50 ± 1.03	0.32929
Total voiding frequency	10.66 ± 2.85	9.14 ± 2.15	11.01 ± 3.71	8.42 ± 2.74	0.00613
Average Micturition volume (ml)	163.97 ± 51.64	195.52 ± 72.70	169.61 ± 57.10	224.42 ± 94.73	0.01294
Qmax (ml/sec)	10.46 ± 4.23	12.24 ± 7.17	10.39 ± 4.28	11.40 ± 5.06	0.41715
PVR (ml)	30.77 ± 31.00	26.06 ± 29.61	28.83 ± 31.21	49.56 ± 69.17	0.00651

* Changes from baseline to 8 weeks between group 1 and group 2.

Concluding message

Combination treatment with propiverine plus doxazosin improves storage symptoms including voiding frequency and urgency and increased patient's satisfaction to treatment. Propiverine did not affect the urinary flow rate and no acute urinary retention was observed. This study revealed combination therapy of α1-adrenoceptor antagonists with antimuscarinic is an effective and relatively safe first line treatment modality in selected patients with overactive bladder coexisting benign prostatic obstruction.

References

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