

COMBINATION THERAPY USING ALPHA-BLOCKER AND ANTIMUSCARINIC DRUGS IN MEN WITH LOWER URINARY TRACT SYMPTOMS SUGGESTIVE OF BLADDER OUTLET OBSTRUCTION AND AN OVERACTIVE BLADDER: IS IT SAFE AND EFFICACIOUS?

Hypothesis / aims of study

Combination therapy with an alpha-blocker plus an antimuscarinic has been shown to improve quality of life and symptomatic improvement in men with urodynamically proven bladder outlet obstruction (BOO) and overactive bladder (OAB) (1 and 2). However, the clinical utility of this regimen remains to be defined, as there is a theoretical danger of impairment of obstructive symptoms and acute urinary retention. Hence, we assessed the efficacy and safety of treating men with both lower urinary tract symptoms (LUTS) suggestive of BOO and OAB syndrome with combination therapy of an alpha-blocker and an antimuscarinic drug.

Study design, materials and methods

The study included 89 men diagnosed with LUTS suggestive of BOO and concomitant OAB syndrome at one tertiary urological institution who met the inclusion and exclusion criteria. Included were men with LUTS suggestive of BOO with normal urine analysis and a benign digital rectal examination (DRE). Exclusion criteria included previous urological surgery or current pharmacological therapy including an alpha-blocker, finasteride or antimuscarinic agents. In addition, men with neurological diseases (stroke, diabetes, multiple sclerosis, Parkinson's disease) were excluded. Patients with a history of malignancies of the genitourinary tract were also excluded. Initial clinic visit included a urological history, physical exam and digital rectal examination. Routine laboratory tests were taken, including PSA and urinary analysis. All men had standard uroflow and post-void residual urine (PVR) measured by transabdominal ultrasound, and completed the International Prostate Symptom Score (IPSS).

They were started on terazosin 1mg at bedtime and titrated to 2mg for 6 weeks. If the flow was suboptimal, 5mg was given at bedtime as the maximal dose. On follow-up, they continued to have storage symptoms and were then started on a trial of tolterodine 2mg BD or oxybutynin 5mg BD. Their symptoms, uroflow and post-void residual urine, International Prostate Symptom Score (IPSS) and side-effects were recorded subsequently. Results were assessed statistically using Wilcoxon Signed Ranks Test and values are presented as the mean with $P < 0.05$ considered to indicate significant differences. The study was approved by the hospital's ethics committee.

Results

The median age of patients was 64.3. The median length of follow-up was 7.8 months (range 6-36 months). 21 out of 89 men (23.6%) stopped antimuscarinic therapy because they defaulted or were excluded because of diagnosis of other pathology. 68 men continued with the combination therapy and subsequent clinic visits showed that 60 out of 68 men (88.2%) showed improvement in their storage symptoms, with statistical improvement in uroflow (Qmax), IPSS, quality of life and the number of episodes of nocturia (*Table 1*). 8 out of 68 men (11.8%) showed improvement in their uroflow but not storage symptoms. There was no acute urinary retention observed and no statistical difference in post-void residual urine ($p=0.586$). Side effects were minimal with 1 patient complaining of dry eyes of which moisturizing eye-drops helped. Combination therapy was well tolerated.

Table 1 – Results before and after combination treatment.

	Before Treatment Mean	After Treatment Mean	P
IPSS	22.4	10.4	0.001
QOL	4.3	2.1	0.003
Nocturia	4.2	2.1	0.007
Qmax, mL/s	8.4	13.2	0.05
PVR, ml	46	48	0.856

Interpretation of results

Combination therapy using alpha-blockers and antimuscarinic agents in men with LUTS suggestive of BOO and OAB syndrome showed improvement in storage symptoms, uroflow, IPSS, quality of life and number of episodes of nocturia in 88.2% of men. This is comparable to a previous study where 73% of men with urodynamically proven BOO and detrusor overactivity showed improvement after adding tolterodine to an alpha-blocker (2).

Combination therapy of alpha-blocker and antimuscarinic drugs appear to be effective, safe and well tolerated in clinical practice, with low risk of acute urinary retention. This concurred with previous studies (1, 2, and 3). The theoretical fear of impairment of obstructive symptoms also appears unfounded as Qmax was increased with no statistical increase in post-void residual urine.

Concluding message

Combination therapy of alpha-blocker and antimuscarinic in men with LUTS suggestive of BOO and OAB appears to be effective, safe and well tolerated in clinical practice, with low risk of acute urinary retention or impairment of obstructive symptoms. The low risk of acute urinary retention concurred with previous studies. Future randomized studies should be done to address this.

References

- (1) Combination treatment with an alpha-blocker plus an anticholinergic for bladder outlet obstruction: a prospective, randomized, controlled study. J Urol 2003; 169: 2253-6.
- (2) Comparison of doxazosin with or without tolterodine in men with symptomatic bladder outlet obstruction and an overactive bladder. BJU Int 2004; 94: 817-820.
- (3) Tolterodine therapy in men with bladder outlet obstruction and symptomatic detrusor overactivity is not associated with urinary safety concerns. J Urol 2002; 167 (Suppl): 1048.