

RATE AND PREDICTIVE FACTORS OF THE ANTICHOLINERGIC ADD-ON THERAPY IN MEN WITH RESIDUAL OVERACTIVE BLADDER SYMPTOM AFTER 4 WEEKS OF α -BLOCKER MONOTHERAPY

Hypothesis / aims of study

Overactive bladder (OAB) occurs in approximately 50% to 75% of men with benign prostatic obstruction (BPO) and up to 38% of men with BPO continue to suffer from OAB after relief the obstruction [1,2]. Results from several recent studies of men with OAB symptoms and other lower urinary tract symptoms (LUTS) (with or without some degree of BPO) suggest that anticholinergic and α -AR antagonist combination therapy improves OAB symptoms effectively without increasing the incidence of acute urinary retention [3]. In our knowledge, there was no published data about the proportion and predictive factor of combination therapy among the patients treated with α -blocker. The aim of this study was to investigate the proportion of patients and predictive factor for the solifenacin add-on treatment in men with persistent OAB symptoms after tamsulosin monotherapy for 4 weeks.

Study design, materials and methods

This was phase IV, prospective, open-label, observational, multicenter study. Primary objective was to explore the rate of add-on therapy with solifenacin in men with OAB symptoms after 4 weeks of tamsulosin monotherapy. Secondary objective was to explore the predictive factors of determining the solifenacin add-on therapy. Inclusion criteria of tamsulosin monotherapy were men aged ≥ 45 yr with IPSS ≥ 12 , symptoms of OAB as verified by the score of OAB screener V8 ≥ 8 , 3-day bladder diary (mean urinary frequency ≥ 8 , urgency episodes ≥ 2 episode/24hr). Subjects were treated with tamsulosin 0.2mg once daily for 4 weeks. After that, the patients who have persistent OAB symptoms were received solifenacin 5mg once daily. The criteria of solifenacin add-on therapy after tamsulosin monotherapy included that symptoms of OAB as verified by the the score of OAB screener V8 ≥ 8 , a rating of the tamsulosin treatment satisfaction as "Dissatisfied" or "A little satisfied" on the Patient-Rated Global Assessments of Treatment Satisfaction, and 3-day bladder diary (frequency ≥ 8 times/24 hours, urgency episodes ≥ 1 episode/24 hours. At baseline and week 4, subjects completed the International Prostate Symptom Score (IPSS), Quality of life (QoL) index, OAB screener V8, International Consultation of Incontinence Questionnaire-Male LUTS (ICIQ-MLUTS), patient's perception of bladder condition (PPBC), and 3-day bladder diaries. The proportion and predictive factor for add-on therapy were evaluated.

Results

Of total 303 patients, 261 patients completed 4 weeks of tamsulosin treatment. The patients who added solifenacin were 181 and the proportion of add-on therapy among tamsulosin monotherapy was 69.4% (181/261, 95% CI 0.693-0.749). The predictive factors of the solifenacin add-on therapy were duration of LUTS, total and storage scores of IPSS, item 4 score related to urgency, number of micturitions for 24 hours, nocturnal micturitions, urgency episode for 24 hours, urgency severity score in bladder diary, and OAB V8 score by the univariate analysis. When the multivariate analysis were performed, LUTS durations could be the predictive factor of add-on therapy (OR=1.008, 95% CI 1.000-1.016, $p=0.048$). Serum PSA (OR=1.706, 95% CI 1.180-2.468, $p=0.0045$), prostate size (OR=0.973, 95% CI 0.948-0.998, $p=0.0364$) could be the predictive factor of solifenacin add-on therapy. The change of total, storage, voiding score and item 4 score of IPSS, QoL score was statistically significant after 4-week tamsulosin monotherapy ($p<0.0001$). The parameters of bladder diaries such as number of micturitions per 24 hr, nocturnal micturitions, daytime micturitions and urgency episodes were changed significantly after tamsulosin therapy for 4-weeks. The sum of OAB V8 questionnaires, ICIQ-voiding subscores, ICIQ-incontinence subscores, PPBC were improved after tamsulosin monotherapy ($p<0.05$).

Interpretation of results

The current study showed that 69.4% of men with OAB and LUTS suggestive BPH received the anticholinergic add-on therapy after 4 weeks of α -blocker because of residual OAB symptoms. By univariate analysis, several predictive factors of anticholinergic add-on treatment was founded. The severity of symptom at baseline may be one of the factors deciding the add-on therapy with an anticholinergic agent to previous α -blocker treatment. Patients with a longer duration of symptoms and more severe symptoms, the add-on rate of anticholinergic was higher. However, we could not obtain the clinically valuable predictive factor with significant odds ratio by multivariate analysis.

Concluding message

In the patients with BPO and OAB symptoms, 70% of the patients needed anticholinergic treatment after α -blocker treatment. Results of this study may help communication between the patient and physician, and patients with a risk factor may be notified the possibility of anticholinergic add-on.

Table . The analysis of risk factor on the anticholinergic add-on therapy by univariate analysis

Univariate analysis		
OR	95% CI	p-value

Age (year)	1.004	0.972-1.036	0.814
LUTS duration(months)	1.009	1.001-1.016	0.020*
PSA (ng/ml)	1.296	0.983-1.711	0.066
Prostate volume (cc)	0.989	0.970-1.009	0.292
PVR (ml)	1.002	0.995-1.008	0.646
IPSS			
Total index score	1.060	1.007-1.117	0.027*
Storage subscale	1.159	1.046-1.284	0.005*
Voiding subscale	1.034	0.970-1.102	0.310
Item 4			0.022*
0	0.343	0.060-1.967	0.572
1	0.490	0.109-2.201	1.000
2	0.232	0.070-0.767	0.008
3	0.779	0.214-2.831	1.000
4	0.579	0.151-2.217	1.000
QoL item	1.324	0.977-1.793	0.070
Bladder diary variables			
Micturations per 24h	1.137	1.014-1.275	0.027*
Nocturnal micturations	1.422	1.126-1.795	0.003*
Daytime micturations	1.050	0.943-1.170	0.369
Urgency episodes per 24h	1.106	1.016-1.204	0.019*
Urgency severity score	1.041	1.009-1.074	0.011*
Urgency severity score per voiding	1.447	0.969-2.161	0.071
OAB screener V8 score	1.084	1.036-1.135	0.001*
ICIQ-Male LUTS			
Voiding subscore(VS)	1.015	0.951-1.084	0.649
Incontinence subscore(IS)	1.145	1.038-1.263	0.007*
Most bothersome symptom	0.545	0.276-1.078	0.0813

LUTS ; Lower Urinary Tract Symptoms, PVR ; post-void residual urine, IPSS ; International Prostate Symptom Score, QoL ; Quality of Life, ICIQ-MLUTS ; international consultation of incontinence modular questionnaire-Male Lower Urinary Tract Symptoms

* P<0.05, Logistic Regression analysis.

LUTS, IPSS, nocturia, frequency, urgency in bladder diary, and OAB V8 score

References

1. Br J Urol (1994) 74:50-56.
2. Neurourol Urodynm (2001) 20:237-247
3. Curr Opin Urol (2008) 18:11-15.

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What were the subjects in the study?	HUMAN
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Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes