

## DO PATIENTS WITH NEUROGENIC LOWER URINARY TRACT DYSFUNCTION (NLUTD) BENEFIT FROM TREATMENT WITH ALPHA-BLOCKERS? A RETROSPECTIVE STUDY OF MEN AND WOMEN WITH MULTIPLE SCLEROSIS (MS) AND MIXED LUTS

### Hypothesis / aims of study

Few published data exist concerning the efficacy and safety of the use of alpha-blockers in neurogenic lower urinary tract dysfunction (NLUTD). Tamsulosin has been shown to improve bladder storage and emptying in MS and SCI. In a randomized, controlled trial followed by an open-label 1-year study using alpha-blockers in patients with suprasacral spinal cord lesions, urodynamic, bladder diary and IPSS parameters were significantly improved only in the open-label phase but not in the controlled study. Furthermore, while alpha-blockers currently remain an off label treatment in women with either NLUTD or non neurogenic primary bladder neck obstruction, only sparse published data exist with regard to the use of alpha-blockers in women with MS and they concern limited number of patients. Consequently, the most recent report of the ICI neurogenic bladder committee could only propose the use of alpha-blockers as an alternative second line therapy in NLUTD with increased PVR, with caution.

We conducted a retrospective analysis of data associated with the efficacy and safety of the use of alpha-blockers in male and female patients with MS. subjective symptom changes and objective uroflow parameters were studied.

### Study design, materials and methods

We retrospectively studied 100 patients with MS and mixed voiding and storage neurogenic LUTS, who had available follow-up data from a 3-month scheduled follow-up visit. We analyzed data from patients who received alpha-blocker monotherapy (Group I), or received an initial combination of an alpha-blocker with an antimuscarinic or an alpha-blocker in addition to a previously administered treatment with an antimuscarinic (Group II). Objective clinical outcomes of efficacy included uroflow parameters (maximum urinary flow – Qmax, voided volume – VV, post-void residual – PVR and Bladder Voiding Efficacy index - BVE%). Subjective improvement was assessed with the Patient Perception of Bladder Condition questionnaire, and patients were considered to have improved if they reported at least 50% subjective improvement in their symptoms.

Discontinuation of alpha-blockers due to symptomatic orthostatic hypotension or worsening of preexisting urinary incontinence (UI) was also recorded.

For statistical analysis purposes we used the paired t test and the Fisher's exact test.

### Results

Forty-nine out of the 100 consecutive MS patients (49%) had received treatment with an alpha-blocker, 21 of them (n=21, Group I) as monotherapy, 18 as a combination start treatment with an antimuscarinic and 10 as an addition to a pre-existing treatment with antimuscarinics (n=28, Group II).

In the overall study group, mean PVR (163.4 ml versus 98.6 ml, p=0.026) and mean BVE% (59.43±22.33% vs 68.83±23.00%, p=0.049) significantly improved, while mean Qmax (11.82 ml/sec versus 15.67ml/sec, p=0.056) showed a tendency to improve after treatment. Voided Volume (212.6 ml versus 253.5 ml, p=0.11), and total Bladder Capacity (BC) (377.6 ml versus 351.6 ml, p=0.46) showed no significant changes. A per group analysis showed statistically significant improvement in PVR reduction in Group I patients (241.5ml versus 112.9 ml, p=0.017) and in BVE% (52.38±19.72 vs 69.32±25.25, p=0.025), but Qmax (13.08±6.65 vs 16.85±10.88, p=0.114) and BC changes (508.08±222.91 vs 403.66±142.93, p=0.076) did not reach significance. In Group II, a significant increase in VV (162.57±92.19 vs 219.57±116.89, p=0.033) was observed. Improvements were noted in mean values of the remaining uroflow parameters, but they did not reach significance (Table 1).

Table 1. Changes in uroflow parameters following treatment in both study groups.

	Group I			Group II		
	Before	Follow up	P value	Before	Follow up	P value
Qmax	13.08±6.65	16.85±10.88	0.114	10.66±5.85	14.57±9.14	0.105
VV	266.54±176.00	290.77±187.55	0.609	162.57±92.19	219.57±116.89	0.033
PVR	241.54±156.60	112.89±107.32	0.017	90.81±94.68	85.26±59.47	0.807
BC	508.08±222.91	403.66±142.93	0.076	256.38±143.46	303.19±100.89	0.212
BVE%	52.38±19.72	69.32±25.25	0.025	65.97±23.30	68.38±21.66	0.689

Subjective improvement of urinary symptoms greater than 50% was reported in 55.1% (n=27/49). Discontinuation of alpha-blocker treatment due to clinically symptomatic hypotension or due to worsening of incontinence was recorded in 10.2% (n=5/49) and 16.3% (n=8/49) of the study sample, respectively. Symptomatic hypotension, worsening of UI and overall symptoms improvement were not found to be statistically significant different among females (n=26) and males (n=23) (Table 2).

Table 2. Discontinuation of alpha-blocker treatment according to gender and cause

	Hypotension	Worsening of UI	Subjective improvement of LUTS ≥50%
Men (n=23)	8.7% (n=2)	17.4%(n=4)	60.9%(n=14)
Women (n=26)	11.5% (n=3)	15.4%(n=4)	50%(n=13)
Fisher's exact test	P=1.0	P=1.0	P=0.77

### Interpretation of results

According to our findings, alpha-blockers alone or in combination with an antimuscarinic may be beneficial in NLUTD in almost half of MS patients, irrespective of the gender, by improving post-void residua and bladder voiding efficiency. Satisfaction from treatment, adverse effects and discontinuation of alpha-blockers seem to be comparable between men and women with MS. Results need to be interpreted with caution, due to the lack of a control arm in the study. Other limitations of our study are the small number of patients and its retrospective nature.

### Concluding message

In this small-sized retrospective study, results suggest that the use of alpha-blockers as monotherapy or in combination with an antimuscarinic may improve clinical parameters in patients with MS and mixed NLUTD symptoms. Objective and subjective clinical outcomes as well as adverse events leading to treatment discontinuation were comparable between men and women. Based on evidence that both the incidence and prevalence of MS will increase in the future, larger randomized controlled studies would be of interest, to determine whether alpha-blockers could be a viable alternative to the use of clean intermittent catheterizations.

### Disclosures

**Funding:** None **Clinical Trial:** No **Subjects:** HUMAN **Ethics not Req'd:** It is retrospective analysis of routinely applied diagnostic test data **Helsinki:** Yes **Informed Consent:** No