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Title: TAMSULOSIN: EFFICACY AND SAFETY IN NEUROGENIC LOWER URINARY TRACT DYSFUNCTION (NLUTD)

Aims of the study:

Many trials have evaluated the use of α_1-blockers in NLUTD indicating that they may have a small but useful effect in facilitating bladder storage and emptying and in reducing autonomic dysreflexia. Most of these trials were however small, non-randomised, uncontrolled and/or of short duration. We report on a large, randomised, placebo-controlled study with long-term follow-up involving the α_{1A}/α_{1D}-blocker tamsulosin.

Methods:

Patients with NLUTD secondary to supra-sacral spinal cord lesions (with maximum urethral pressure (MUP) $\geq$ 60 cm H_2O and detrusor hyperreflexia or a voiding contraction) were randomised to 4-week double-blind therapy with placebo, tamsulosin 0.4 mg or tamsulosin 0.8 mg (after 2 weeks on 0.4 mg) once daily. After completion of the study, patients could continue open-label tamsulosin therapy (0.4 mg with possible dose increase to 0.8 mg in case of insufficient response and lack of side effects) for up to 1 year. The primary efficacy parameter was MUP.

Results:

263 patients were randomised in the placebo-controlled study. Although the mean reduction in MUP at 4 weeks did not reach statistical significance over placebo, it was larger with tamsulosin (-12.2 and -9.6 cm H_2O for 0.4 and 0.8 mg) than placebo (-6.5 cm H_2O). 186 patients continued long-term open-label therapy of whom 134 completed 1 year with a more pronounced reduction in mean MUP (by -18.0 cm H_2O or -15% at endpoint, $p<0.001$). At endpoint in the long-term study, tamsulosin also reduced maximum urethral closure pressure and improved cystometry parameters related to bladder storage (bladder volume at first phasic detrusor contraction and at maximum cystometric capacity) and emptying (voiding time, voided volume, residual urine) and increased mean voided volume based on the micturition diary statistically significantly versus baseline (table 1). The I-PSS-QoL score, several questions about symptoms related to urinary leakage and 1 question related to bladder emptying were also significantly improved (table 1). In addition, the frequency, bothersomeness and severity of symptoms diagnosed as autonomic dysreflexia decreased statistically significantly versus baseline (table 1) and 14 of the 36 patients that suffered from symptoms of autonomic dysreflexia at baseline were symptom-free at endpoint. Finally, 71% of patients were slightly (44%) or much (27%) improved according to the investigators. Both doses were effective and well tolerated.

Conclusions:

Long-term tamsulosin treatment produces a positive effect on bladder storage and emptying in patients with NLUTD. It also reduces symptoms of autonomic dysreflexia. Both doses (0.4 and 0.8 mg) are effective and well tolerated.

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Table 1.
Statistically significant mean changes from baseline to endpoint during long-term tamsulosin therapy

Parameter		Baseline		Change	p-value
	N*	Mean (SD)	N**	Mean (SE)	
Urethral Pressure Profilometry					
Maximum urethral pressure: cm H_2O	147	89.3 (31.5)	147	-18.0 (2.8)	<0.001
Maxiumum urethral closure pressure: cm H_2O	147	79.6 (30.8)	147	-15.7 (2.8)	<0.001
Cystometry (filling rate 20 mL/min)					
Bladder volume at 1st phasic detrusor contraction: mL	141	206.6 (112.8)	141	18.7 (9.3)	0.046
Bladder volume at maximum cystometric capacity: mL	141	255.3 (121.3)	140	29.9 (10.1)	0.004
Voiding time: s	110	94.5 (111.4)	94	33.0 (12.1)	0.008
Voided volume: mL	128	117.9 (99.6)	122	46.8 (9.9)	<0.001
Residual urine volume: mL (filling rate 100 mL/min)	91	158.7 (145.2)	78	-30.1 (12.6)	0.019
Micturition Diary					
Mean voided volume per micturition: mL	109	188.1 (112.8)	101	17.7 (8.4)	<0.001
Urinary Symptom Questionnaire					
IPSS-QoL	146	4.2 (1.5)	146	-0.4 (0.1)	<0.001
Score on incomplete bladder emptying	146	1.2 (1.4)	145	-0.2 (0.1)	0.013
Score on frequency urinary leakage	146	2.3 (1.5)	145	-0.2 (0.1)	0.036
Score on severity urinary leakage	145	2.3 (1.6)	144	-0.3 (0.1)	0.006
Score on frequency underwear change due to leakage	146	1.2 (1.2)	143	-0.2 (0.1)	0.028
Score on frequency pad usage	146	1.1 (1.6)	145	-0.2 (0.1)	0.019
Score on leakage during sexual intercourse	74	0.6 (0.8)	57	-0.2 (0.1)	0.040
Score on bother due to leakage during sexual intercourse	65	0.7 (1.1)	47	-0.3 (0.1)	0.021
Score on frequency autonomic dysreflexia	141	0.6 (1.3)	141	-0.2 (0.1)	0.035
Score on bothersomeness autonomic dysreflexia	141	0.7 (1.3)	141	-0.3 (0.1)	0.007
Score on severity autonomic dysreflexia	140	0.7 (1.4)	140	-0.2 (0.1)	0.043

* number of patients with baseline value; ** number of patients with both baseline and endpoint value