

THE EFFECT OF ANTICHOLINERGIC THERAPY ON URGENCY SEVERITY IN PATIENTS WITH OVERACTIVE BLADDER: CLINICAL ASSESSMENT OF A NEWLY VALIDATED TOOL

Aims of Study

Most epidemiological studies of overactive bladder (OAB) have focused on urge urinary incontinence and its prevalence, often overlooking 24-hour frequency and urgency, the more common symptoms of the disorder. 16,000 surveyed subjects indicated that urgency and 24-hour frequency are more prevalent in individuals between the ages of 35 and 55 years. Specifically, 17% of respondents reported having OAB symptoms with 14% reporting 24-hour frequency, 9% urgency and 6% urge urinary incontinence.¹ While treatments are available for the indication of OAB, few trials have looked at the impact of treatment on the prevalence of urgency, largely due to the lack of a validated metric for urgency severity quantification.

Trospium chloride, a quaternary amine, is an antimuscarinic agent that has been a leading treatment for OAB in Europe over 20 years. The objective of this study was to determine the effects of trospium vs. placebo on the severity of urgency associated with OAB in patients with predominant urge urinary incontinence as part of a 12 week efficacy and safety study.

Methods

This was a parallel, randomized, double-blind, placebo-controlled trial in patients with OAB. Symptoms of urgency, ≥ 10 voids per day and ≥ 1 urge urinary incontinence episode per day were required for inclusion. Participants received either trospium chloride 20 mg bid or placebo for 12 weeks following a 3week washout and completion of a 7-day baseline bladder diary to record each void, urgency severity, and urge urinary incontinence episode per day. The 7-day bladder diary included the validated Urgency Severity Scale (IUSS)² which asks patients to rate the urgency severity prior to toileting where:

0: NONE - no urgency

1: MILD - awareness of urgency, but *easily tolerated*

2: MODERATE - enough urgency discomfort that it *interferes with* usual activity/ tasks

3: SEVERE - extreme urgency discomfort that abruptly *stops all* activity/tasks

Treatment effects were measured at weeks 1, 4 and 12. Change in urgency severity, urge frequency per 24 hours, urinary frequency per 24 hours, and number of urge urinary incontinence episodes per 24 hours from baseline, were our outcomes of interest. Efficacy analyses were done using the intent-to-treat sample and the last observation carried forward data set. ANOVA models or where appropriate, rank ANOVA were used.

Results

523 patients were studied at 51 sites (262 trospium /261 placebo). The mean age was 62 years and 74% were female. The most frequently reported adverse events were dry mouth and constipation. 24-hour frequency and urge urinary incontinence episodes per day were significantly reduced starting at week 1 and persisted through week 12.³

Mean Change from Baseline*	Urgency Severity Score Associated with Voids		Urge Frequency per 24 Hours	
	trospium (n=253)	placebo (n=256)	trospium (n=253)	placebo (n=256)
Baseline	1.77	1.77	11.29	11.72
	p=0.88		p=0.11	
*Week 1	-0.11	-0.01	-1.13	-0.71
	p=0.003		p=0.06	
*Week 4	-0.18	-0.06	-2.10	-1.00
	p=0.004		p<0.0001	

*Week 12	-0.22	-0.04	-2.30	-1.08
	p=0.0001		p<0.0001	

Conclusions

Trospium-treated patients moved from having, on average, a moderate degree of urgency with each toilet void toward experiencing a mild sensation of urgency with each void, whereas, placebo-treated patients had no notable change. In addition, trospium was found to be effective in reducing the average urge frequency, 24-hour frequency and urge urinary incontinence episodes per 24 hours in patients with OAB in comparison to placebo. Trospium was also well tolerated.

References

¹Milsom I, Abrams P, Cardozo L, et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. Br J Urol Int 2001 Jun; 87(9):760-6.

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³Zinner N, Gittelman M, et al. Trospium Chloride Improves Overactive Bladder Symptoms: A Multicenter Phase III Trial (Abstract). Annual American Urological Association Meeting, Chicago, IL, April 26, 2003.