

A STUDY OF THE SIGNIFICANCE OF IDENTIFYING DETRUSOR INSTABILITY IN THE TREATMENT OF OVERACTIVE BLADDER SYMPTOMS

Aims of Study

To assess the outcome of treatment in patients with symptoms of frequency, urgency and/or urge incontinence, comparing (1) Those with demonstrable unstable bladders, as shown by a positive urodynamic assessment, against (2) Those without instability on urodynamics. By these means to test the clinical relevance of diagnosing detrusor instability.

Methods

The study was designed as a multi-centre, double-blind, parallel group experiment, with patients randomised to receive placebo or Tolterodine for 12 weeks. Patients were classified as having positive or negative findings from a urodynamic assessment and treatment allocation was balanced within each of these strata. It was anticipated that the ratio of the numbers of patients would be approximately 70:30 (positive: negative) and the study was powered on this.

Suitable patients aged 18 or over, suffering from urinary frequency (an average of at least 8 micturitions per 24 hours) and urinary urgency, with or without urinary urge incontinence, for at least 6 months were identified and screened at visit 1. Patients were examined and issued with a diary card to be completed for seven days prior to their next visit. They were also completed a quality of life questionnaire the King's Health Questionnaire (KHQ). A urodynamic assessment was arranged and the patients were classified as having unstable bladder (positive urodynamics) or not (negative urodynamics). If patients satisfied the entry criteria and had given informed consent, they were randomised to receive treatment for twelve weeks with either tolterodine (4mg capsules, once daily) or placebo. They were issued with a further diary to be completed seven days before the next visit.

Patients were reviewed after four weeks, twelve weeks at which visits outcome data were collected.

Analysis of covariance (ANCOVA) was used to compare the effects of treatment and urodynamic diagnosis on the change in primary outcome measure, average voided volume. This was tested at the 5% level of significance.

Results

419 patients were screened, 308 patients were randomised and 307 patients took medication and were analysed on intention to treat. 154 patients had positive urodynamics and 153 had negative urodynamics. Of the patients with a positive assessment, 81 patients were randomised to receive Tolterodine and 73 to receive placebo. The corresponding figures for those with a negative assessment were 84 and 69 respectively. The treatment groups were very evenly matched with respect to age, sex and race. 80% of patients were female, and 96% of patients were white. The mean age of the patients was 56, ranging from 22 to 89. The treatment groups were well matched with respect to weight and height. The primary efficacy variable was the mean volume voided per micturition. The analysis of the data showed that there was no statistically significant interaction between urodynamic status and treatment. The estimated mean changes, averaged across all patients, seen for each treatment are shown in the Table below:

Estimated overall mean changes in voided volume at end of study

Full Analysis Set

Treatment Mean (95% Confidence Interval) p-value for difference

Tolterodine	Placebo	Difference
26.17 (18.23, 34.10)	15.91 (7.25, 24.57)	10.25 (-0.01, 20.52)
		$p=0.05$

The change in the mean number of voids per day was significantly greater in the Tolterodine group than in the placebo group. The difference was similar for both positive and negative urodynamics. There was no evidence of any difference between treatments in the change in incidence of incontinence, regardless of urodynamic status. The King's Questionnaire was seen to relate well to the subjects' perception of bladder condition. The incidence of treatment-emergent adverse events was similar in the two treatment groups, with around 50% of the patients in the study reporting events. The most frequent events seen in the Tolterodine group were those anticipated, namely dry mouth, dyspepsia and headache. The incidence of other events was low.

Conclusions

In this study Tolterodine was more effective than placebo in treating urinary urge and frequency, regardless of whether or not patients had positive evidence of unstable bladder as determined by a urodynamic assessment. These data therefore support the proposition that patients with symptoms of an overactive bladder should be treated with an antimuscarinic on the basis of symptoms alone. They contradict the proposition that urodynamics are necessary in the treatment of the overactive bladder and leave the onus on the requirement to furnish data in support of a role.

(1) Urodynamic variables cannot be used to classify the severity of detrusor instability. *Br J Urol* 1998; 82(4):499-502.

(2) Ambulatory urodynamics. [*Current Opinion in Obstetrics & Gynecology* 1995; 7(5):378-381.

Tolterodine: a safe and effective treatment for older patients with overactive bladder. *J Am Geriatr Soc* 2001; 49(6):700-705.