

## ALPHA LITHIC AGENTS FOR WOMEN WITH LOWER URINARY TRACT SYMPTOMS

### Hypothesis / aims of study

Urethral obstruction, a relatively frequent pathology in women, is often difficult to diagnose. It is associated with major symptoms which lower quality of life. Once anatomy- and function-related pathologies such as urethral stenosis, urogenital prolapse, neurological abnormalities and systemic disorders which interfere with bladder emptying have been excluded, a group of patients remain with lower urinary tract obstruction that could benefit from pharmacological therapy. This study assessed the role of alpha lithic agents in therapy for women with lower urinary tract obstructive symptoms.

### Study design, materials and methods

This prospective study consecutively recruited 59 women (mean age  $61.2 \pm 15$  years; range: 21-84 years) with severe obstructive symptoms which were isolated in 13 (22%) and associated with irritative symptoms in the other 46 (78%); 24 of these 46 referred recurrent infections. Before starting therapy, all women provided a detailed case history, answered a symptoms questionnaire and underwent free flowmetry with ultrasound imaging of residual urine. Urodynamics were performed in 43 patients, 3 of whom resulted normal, 17 obstructed, 14 hypocontractile, 8 were obstructed and unstable and 1 was obstructed and hypocontractile. Methods, definitions and units conform to the standards recommended by the International Continence Society. Patients were fully informed about Tamsulosine and its side effects and all gave informed consent. Tamsulosine was prescribed in a single daily dose of 0.4 mg for at least 30 days. Follow-up included clinical check-ups and uroflowmetry after 1, 3, 6, 12 months and then annually. Efficacy was assessed clinically i.e. subjective improvement of symptoms and agreement to continue therapy and urodynamically i.e. increased maximum flow (Q max) and /or reduction or disappearance of post-micturitional residue. The Wilcoxon test and McNemar test were used for the statistical analyses.

### Results

Obstructive symptoms improved significantly in 44/59 patients (74.45%;  $p < 0.0001$ ). Associated irritative symptoms also improved significantly in 17/46 women (37%;  $p < 0.0001$ ). Flowmetry results significantly improved in 32/59 women (54%) (before therapy Qmax  $14.1 \pm 5.7$  ml/sec vs  $18 \pm 7$  ml/sec afterwards;  $p < 0.01$ ). Post micturitional residue was reduced in 33/59 women (56%) and disappeared in 11/59 (19%) (post void residue before therapy  $53.8 \pm 20.3$  ml vs  $31.3 \pm 38.3$  afterwards;  $p < 0.01$ ). Volume of voided urine did not modify significantly (before therapy  $302 \pm 165$  ml vs  $319 \pm 145$  ml after;  $p = \text{NS}$ ).

Pre-operative urodynamic diagnosis did not impact on response to therapy. Tamsulosine therapy was well tolerated by most patients but was suspended in 3 who referred low blood pressure and in 1 complaining of urgency.

### Interpretation of results

The role of alpha lithic agents in therapy for women with lower urinary tract obstructive symptoms has not yet been established. The few data available from studies and experimental models in males agree on the rationale for such an approach which is the presence of a high concentration of alpha 1 adrenergic receptors in the bladder neck, urethra and periurethral tissue while beta adrenergic receptors prevail in the rest of the detrusor surface. Consequently stimulation by the sympathetic nervous system causes bladder relaxation to ensure filling and contraction of the continence structures to prevent leaking. Little is known about the mechanism in women. In the present study we attempted to act selectively through the alpha 1 adrenergic receptors to reduce the obstructive micturitional disturbances in the lower urinary tract without interfering with the detrusor bladder filling mechanism. We observed significant clinical and urodynamic improvements in 74.45% and 54% of our patients respectively and an improvement in associated irritative symptoms in 37% of cases. Our improvement in Qmax in 54% of patients confirms the few data available in this field. Kumar et al (1) and Sivkov et al (2) report Qmax improved in respectively in 50%

and 55.4% of patients. Our clinical results with a 77% success rate fall between the two experience of 50% in the Kumar series and 100% reported by Sikov.

#### Concluding message

Tamsulosine administration to women with lower urinary tract obstructive symptoms can be justified by the severity of symptoms and lack of therapeutic options except for self-catheterism or surgery which are invasive, less well accepted by patients and not without risks. In our view alpha lithic agents might be considered first-line therapy as they are safe, efficacious and have few side effects. Invasive approaches should be reserved as a later option.

#### References

1. Use of alpha1-adrenergic blockaders in voiding disorders in women – Urologia 2002 sep-Oct (5 Suppl): 52-63
2. Management of functional bladder neck obstruction in women: use of alpha –blockers and pediatric resectoscope for bladder neck incision - J.Urol. 1999 Dec 162 :2061-5
3. Ruolo dell'alfuzosina nei disturbi di vuotamento funzionali nella donna - Università di Napoli – SUICMI 1997