

## **COMPARISON OF THE EFFICACY OF TOLTERODINE AND OXYBUTYNYN IN DIFFERENT URODYNAMIC SEVERITY GRADES OF IDIOPATHIC DETRUSOR OVERACTIVITY .**

### **Hypothesis / aims of study**

The hypothesis that was evaluated in this trial, was that tolterodine and oxybutynin have different efficacies in specific, according to the urodynamic grade of severity, groups of patients with idiopathic detrusor overactivity . If this hypothesis was proven, the urodynamic grade of severity could be used as a prognosticator of responsiveness to one or the other of the evaluated medications. A secondary aim was to examine the association of clinical severity of overactivity with urodynamic parameters and especially the overactivity index.

### **Study design, materials and methods**

In this open, randomized, two-way crossover study, 128 women with urodynamically confirmed, idiopathic detrusor overactivity were recruited. After diagnosis, they were categorized in 4 groups-grades of severity, according to the characteristics of the first overactive detrusor contraction during filling cystometrogram: high volume-low pressure (grade-group I), high volume-high pressure (grade-group II), low volume-low pressure (grade-group III) and low volume-high pressure (grade-group IV). Patients in each group were randomized as far as which drug to receive first: oxybutynin 15mg (divided in three doses) or tolterodine 4mg (divided in two doses) orally per day for six weeks. At the end of this period a new voiding diary was completed and urodynamic assessment repeated. After a wash out period of 3-4 weeks, patients switched to the alternate preparation and the same cycle of evaluation was repeated after 6 weeks.

After collection of urodynamic data, the overactivity index was calculated as the sum of pressures generated by all overactive detrusor contractions during filling cystometry divided by cystometric capacity (and multiplied by 100 for practicality reasons).

The primary outcome measure for the comparison of the two drugs was average volume of voided urine per micturition which was calculated by dividing the total voided volume in a three-day voiding diary by the total number of voids. The analyses for the comparison of efficacy were performed on a per protocol basis.

### **Results**

Out of 128 patients, twenty-one were excluded from analyses: thirteen withdrew due to side effects and 8 were excluded due to protocol violations. The remaining 107, successfully completed the study protocol: 40 in group IV, 36 in III, 25 in II and 6 in group I.

In the total study population the average volume voided per micturition was significantly increased with both drugs in comparison to baseline, but there was no difference in the efficacy of the two drugs.

In groups IV and III both oxybutynin and tolterodine significantly increased the average volume of voided urine per micturition but the differences between the drugs were not significant ( $p>0,05$ ).

In group II neither of the drugs achieved significant changes in the outcome measure ( $p>0,05$ ).

The association of urodynamic and clinical parameters was evaluated in the total study population: overactivity index was strongly associated to average urine volume voided per micturition and to a lesser extent to average number of voids per day (correlation coefficients 0, 72 and 0, 62 respectively). None of the other urodynamic parameters (bladder volume at first overactive contraction, pressure of first overactive contraction, maximum detrusor

pressure, cystometric capacity) was well correlated to the abovementioned clinical parameters.

#### **Interpretation of results**

Despite comparable efficacy for the two drugs in the literature and the characterization of urodynamic severity of overactivity being arbitrary, it is not uncommon to hypothesize that oxybutynin is the most potent and thus the medication of choice in severe detrusor overactivity. This hypothesis was evaluated but not proven in this trial as tolterodine and oxybutynin were clinically equipotent when average volume of voided urine per micturition was the primary outcome measure for their comparison.

Oxybutynin and tolterodine were also clinically equipotent in groups with other grades of overactivity.

Despite clinical equivalence, there are differences in their actions on specific urodynamic parameters. In patients with low volume- high pressure overactivity (group IV), for example, oxybutynin was superior to tolterodine in reducing the overactivity index, decreasing the bladder volume at first desire to void and increasing the cystometric capacity. The significance of these differences needs to be examined in further studies.

#### **Concluding message**

Tolterodine and oxybutynin are clinically equipotent in treating idiopathic detrusor overactivity in specific severity groups of patients. Urodynamic effects are somewhat different.

Overactivity index is a useful formula for the description of urodynamic severity of overactivity as it correlates well to clinical parameters but its validity especially as a prognostic tool needs further investigation.