

## **INTRAVESICAL RESINIFERATOXIN FOR THE TREATMENT OF IDIOPATHIC DETRUSOR OVERACTIVITY IN WOMEN: A RANDOMIZED PLACEBO CONTROLLED STUDY**

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

Idiopathic detrusor overactivity (IDO) is a highly prevalent condition, which may cause profound impact in the quality of life (QoL), of affected patients. The primary therapeutic approach to IDO is usually treatment with anticholinergic drugs, bladder retraining and physical therapy either alone or in combination. Unfortunately, those therapies are many times unsatisfactory in terms of clinical benefits or limited by troublesome side effects. Recently intravesical instillation of capsaicin and resiniferatoxin for the treatment of overactive bladder has been proposed. These substances, collectively referred as vanilloids, share a common functional ability to desensitize C-fibers that results in blocking of presumed abnormal afferent input from the bladder to the spinal cord.<sup>1,2</sup> RTX is an ultrapotent analogue of capsaicin naturally occurring in the latex of a cactus-like plant named *Euphorbia resinifera*. Unlike capsaicin RTX has the advantage of being less painful when instilled in the bladder making the treatment easily feasible under topical analgesia.<sup>2</sup> We present the results of a randomised, double blind, placebo controlled study on women suffering from idiopathic detrusor overactivity submitted to intravesical treatment with RTX 50 nM in saline and 10% ethanol or to saline and 10% ethanol only (placebo).

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

We prospectively randomised 60 women into 2 groups to receive a single dose of 50 nM resiniferatoxin in 10% ethanol and saline (group 1) or a 10% ethanol and saline solution (group2) intravesically for 30 minutes. All patients had at least 6-month history of frequency, urgency, nocturia, with or without urge-incontinence, idiopathic detrusor overactivity and no history of neurologic disease, infra-vesical obstruction, recent or present urinary tract infection, stone disease, radiation therapy or severe pelvic organ prolapse. We used voiding questionnaire, bladder diary, QoL questionnaire, and pad-tests to evaluate pre-treatment voiding patterns. Biochemical and haematological profiles were obtained pre- and 30 days post-treatment to check the safety of the drug. Patients were clinically evaluated 7 days after instillation and the complete pre-treatment work-up was repeated at 30 days after treatment.. The study was approved by the ethical committee of both institutions. Statistical analysis was made with chi-square test for proportions, ANOVA for longitudinal repetitive data, "t" test for independent groups and Mann-Whitney and Wilcoxon tests for scores. The results are expressed as means plus or minus standard deviation.

### **Results**

The two groups were homogeneous regarding age, race, clinical, surgical, obstetric and gynaecologic antecedents. There were four patients lost to follow-up in group 2 and one patient in group 1 who were excluded from further analysis. The voiding symptom profile and the urodynamic patterns were also homogeneous between the two groups except for the number of incontinence episodes (lower in group 1). The daytime frequency decreased from a median of 9,67  $\pm$  2,89 voids to 8,94  $\pm$  2,77 in the RTX group and from 10,03  $\pm$  2,72 to 8,90  $\pm$  2,76 ( $p=0,027$ ) in the placebo group; the number of incontinence episodes decreased from a median of 3,01  $\pm$  2,51 episodes to 2,59  $\pm$  3,06 in the RTX group and from 5,47  $\pm$  3,54 to 4,27  $\pm$  3,86 in the placebo group ( $p=0,014$ ); the number of night voidings decreased from a median of 2,18  $\pm$  1,02 voids to 1,68  $\pm$  1,15 in the RTX group and from 2,32  $\pm$  1,23 to 1,82  $\pm$  1,12 in the placebo group ( $p=0,001$ ). The patient self-reported sensation of improvement was not different between groups I and II as well ( $p=0,43$ ). The functional cystometric capacity increased from 111,4  $\pm$  67,8 ml to 149,36  $\pm$  95,7 in group I and from 125,4  $\pm$  74,3 to 179,5  $\pm$  118,9 in group II ( $p=0,06$ ); the maximal cystometric capacity increased from 281,6  $\pm$  182,1 ml to 301  $\pm$  159,9 in group I and from 244,3  $\pm$  91 ml to 272,6  $\pm$  107,2 in group II ( $p=0,13$ ). Although significant differences were found in the parameters

daytime frequency, number of incontinence episodes, night-time voidings and functional cystometric capacity when comparing pre and post treatment status in both groups, there were no statistically significant differences between patients from group I (RTX) when compared to group II (placebo) in any of those parameters ( $p = 0,80$ ;  $p = 0,22$ ;  $p = 0,61$  and  $p = 0,24$  respectively). There were no statistically significant differences between the haematological and biochemical profile before and after treatment in any of the groups.

#### **Interpretation of results**

Curiously both RTX and placebo equally improved parameters such as daytime frequency, number of incontinence episodes, nocturia, patient perception of improvement, functional and maximal cystometric capacity. Although both treatments promote statistically significant improvement in the clinical and urodynamic parameters studied the instillation of RTX 50 nM showed no advantage over the placebo in women with idiopathic detrusor overactivity.

#### **Concluding message**

The use of resiniferatoxin for the treatment of women with IDO was not better than placebo in this randomised, double-blind, placebo-controlled study.

#### **References**

- 1-The effect of intravesical resiniferatoxin in patients with idiopathic detrusor instability suggests that involuntary contractions are triggered by C-fiber input. J Urol 168, 575-579, 2002
- 2- Bladder afferents and their role in the overactive bladder. Urology 59 (Suppl 5<sup>a</sup>): 37-42, 2002