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# THE EFFECT OF INTRAVESICAL RESINIFERATOXIN IN NEUROGENIC FORMS OF BLADDER OVERACTIVITY. PRELIMINARY RESULTS OF A RANDOMISED PLACEBO CONTROLLED CLINICAL TRIAL

## Aims of Study

Several clinical trials have suggested in the recent years that desensitisation of bladder type C sensory fibres by intravesical administration of vanilloids, capsaicin [1,2] or its ultrapotent analogue resiniferatoxin (RTX) [3], represent a new therapeutic approach to bladder overactivity of spinal origin. Unfortunately most of them were open studies which do not guarantee the superiority of the active compound over the vehicle solution used for bladder instillation. As a matter of fact, up to now only one placebo controlled trial with capsaicin was undertaken [4]. Therefore, the present study was delineated to compare, under controlled conditions, the effect of intravesical resiniferatoxin in patients with bladder overactivity of spinal origin.

## Methods

Twenty patients with bladder overactivity of spinal origin (7 cases with multiple sclerosis, 7 cases with spinal cord injury, 4 cases with transverse myelitis and 2 cases of myelomeningocele, with a mean age of 37 years) gave written informed consent approved by the Ethics Committee of our institution to enter in the study. Patients had normal biochemical blood tests, sterile urine (except those performing clean intermittent catheterization of the bladder) and a normal ultrasound examination of the entire urinary tract. Two cystometrograms were thereafter obtained at two different occasions and the volume to first detrusor contraction (FDC) and maximal cystometric capacity (MCC) were recorded. Patients were then blindly randomised to be instilled during 30 minutes with 100ml (or half of MCC) of a 50nM RTX solution (RTX group) or its vehicle, 10% ethanol in saline (ethanol group). During instillation patients were asked to score the discomfort in a 0-10 visual analogue scale. Cystometrograms were repeated at 1 and 3 months after instillation to determine post-treatment FDC and MCC. In addition, patients that were able to fill accurately a micturition chart were asked to document micturition and incontinence episodes during at least three days before and after instillation. For statistical purposes the average of the two FDC and MCC determined in each patient before and after bladder instillation were used. A *t*-test for means was applied to compare mean FDC, MCC, urinary frequency and incontinence episodes in the RTX and ethanol before and after treatment.

## Results

Before treatment the RTX group had a mean FDC and MCC of 143±105 ml and 186±109 ml, respectively, whereas the ethanol group mean FDC and MCC were 104±68 ml and 159±124 ml, respectively. These differences had no statistical significance. The mean discomfort score induced by RTX was 2.0± 2 and by ethanol was 0.7±3 (*ns*). After treatment, in the RTX group FDC and MCC rose to 187±109 ml (*p=0.03*) and 332±142 ml (*p=0,0001*), respectively. In the ethanol group FDC and MCC rose to 116±107 ml (*ns*) and 175±83 ml (*ns*), respectively. The mean FDC and MCC of the RTX and ethanol group after treatment were statistically different (*p=0.04* and *p=0.003*), respectively. Urodynamic data are summarised in the Table below. Eight patients in the RTX group and four patients in the ethanol group filled micturitions charts before and after treatment. The decrease of the urinary frequency in the RTX group from 9.3±2 to 7.4±1.4 was significantly greater (*p=0.05*) than that of the ethanol group, from 10.5±2 to 9.3±2 (*ns*). The decrease of the daily number of incontinence episodes in the RTX group (3.0±3 to 1.3±1.5) and in the ethanol group (2.3±3 to 0.7±1.1) were not statistically significant.

| | **FDC** | **FDC** | **MCC** | **MCC** |
|---|---|---|---|---|
| | *Before* | *After* | *Before* | *After* |
| **RTX** (n=11) | 143±105 | 187±105 | 186±109 | 332±142 |
| **Ethanol** (n=9) | 104±68 *(NS)* | 116±67 *(p=0.04)* | 159±124 *(NS)* | 175±83 *(p=0.003)* |

## Conclusions

The preliminary results of this controlled trial confirm that RTX is superior to 10% ethanol, the vehicle solution, to increase bladder capacity and decrease urinary frequency in patients with neurogenic forms of bladder overactivity. In addition, RTX instillation did not evoke more discomfort than 10% ethanol. These findings further support the role of intravesical RTX in the treatment of bladder overactivity of spinal origin.

**References**

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