

## DOSE/EFFECT CURVES OF INTRAVESICAL INFUSION OF NOCICEPTIN/ORPHANIN N/OEQ BY URODYNAMIC ASSESSMENT IN PATIENTS WITH NEUROGENIC DETRUSOR OVERACTIVITY

### Aims of Study

Nociceptin/Orphanin EQ (N/OEQ), a recently discovered heptadecapeptide, which exerts several physiological actions by activating a specific Gprotein coupled receptor named OP<sub>4</sub>, is able to elicit a robust acute inhibitory effect on micturition reflex in animals. A preliminary pilot study and a successive randomized, placebo-controlled, double-blind study showed that N/OEQ produced a clear inhibitory effect on micturition reflex in patients suffering from neurogenic incontinence. So far all these findings have been obtained using the same N/OEQ concentration: 1 $\mu$ M.

The aim of this study is to test the acute urodynamic effects according to a dose/effect curve in patients suffering from neurogenic detrusor overactivity.

### Methods

The study involved 5 patients who presented a neurogenic detrusor overactivity, due to spinal cord injury, refractory to oral and/or intravesical oxibutynin chloride. All patients displayed high voiding pressure and/or severe bladder overactivity associated with frequent urine leakage. All subjects gave their written consent. The study has been previously approved by a local Ethical Committee.

For the testing cystometrograms, which were recorded in two different stages, the bladder was filled, at a flow rate of 25 ml/min, with a solution containing 1  $\mu$ M N/OEQ and 100 nM N/OEQ. We measured the following urodynamic parameters: bladder capacity (BC), volume threshold for the appearance of detrusor overactivity (VT-DO), and maximum bladder pressure (MBP), measured during the involuntary bladder contraction. *Statistical analysis.* Data were expressed as mean  $\pm$  SD of 7 determinations. Data were statistically analyzed using the Student t test for paired or unpaired data as specified in table legends. P < 0.05 was set as the criterion for a significant difference.

### Results

The intravesical infusion of the solution containing 1  $\mu$ M N/OEQ produced the following changes: BC (ml) and VT-DO (ml) significantly increased from 175  $\pm$  38.98 to 263  $\pm$  53.09, and from 107  $\pm$  27.74 to 208  $\pm$  66.76, respectively. MBP (cm H<sub>2</sub>O) decreased from 77.2  $\pm$  11.90 to 71  $\pm$  10.83 without statistically significant value.

The intravesical infusion of the solution containing 100 nM N/OEQ produced the following changes: BC (ml) and VT-DO (ml) increased from 175  $\pm$  38.98 to 201  $\pm$  33.49, and from 107  $\pm$  27.74 to 144  $\pm$  29.02, respectively. MBP (cm H<sub>2</sub>O) increased from 77.2  $\pm$  11.90 to 76  $\pm$  10.83 without statistically significant value.

During the infusion of 1  $\mu$ M N/OEQ or 100 nM N/OEQ no symptomatic reaction was observed.

### Conclusions

The present study seems to confirm the previously reported effects of N/OEQ in a selected group of patients suffering from neurogenic overactive bladder and it shows that the efficacy of N/OEQ is dose dependent.