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**Title:** URODYNAMIC AND CLINICAL EVIDENCE OF ACUTE INHIBITORY EFFECTS OF INTRAVESICAL NOCICEPTIN/ORPHANIN FQ IN PATIENTS SUFFERING FROM DETRUSOR OVERACTIVITY.

**Purpose:**

Management of patients suffering from neurogenic incontinence is complex and available treatments are not satisfactory. Nociceptin/orphanin FQ (NC), a recently discovered neuropeptide, has been reported to inhibit the micturition reflex in the rat. These experimental results prompted us to investigate the urodynamic and clinical effects of intravesical instillation of NC in humans.

**Material & Methods:**

The study involved 5 normal subjects (mean age 40.4 ys., range 21 - 54) and 9 patients (mean age 40.4 ys., range 24-54). All patients presented a detrusor hyperreflexia refractory to standard therapies. They were invited to undergo a filling cystometrogram with saline solution and after 30 minutes a new cystometrogram with a solution containing 1  $\mu$ M NC. The following urodynamic parameters were recorded: bladder capacity (BC), volume threshold for the appearance of detrusor hyperreflexia (VT-DH) and maximum bladder pressure (MBP). A clinical and urodynamic follow-up was performed after 15 days. The data were statistically analyzed using one way analysis of variance followed by the Dunnett test for multiple comparison.  $P < 0.05$  was set as the criterion for a significant difference.

**Results:**

Intravesical instillation of 1  $\mu$ M NC in subjects with a normal cystometrogram did not produce significant functional changes. The intravesical infusion of the solution containing 1  $\mu$ M NC in patients with detrusor hyperreflexia produced a statistically significant increase of BC and VT-DH from 164 ml  $\pm$  84 to 301 ml  $\pm$  118 ( $p < 0.05$ ), and from 93 ml  $\pm$  41 to 231 ml  $\pm$  104 ( $p < 0.05$ ), respectively. MBP decreased from 79 cmH<sub>2</sub>O  $\pm$  25 to 54 cmH<sub>2</sub>O  $\pm$  44, but it was not statistically significant ( $p = 0.19$ ). After 15 days, all the patients reported absence of clinical improvement and the urodynamic control did not show any significant changes compared to the pre-NC-treatment values. During the infusion of 1  $\mu$ M NC, no severe symptomatic reactions were observed.

**Conclusion:**

Our results demonstrate that NC is able to elicit a robust inhibitory effect on micturition reflex in patient with

neurogenic bladder but not in normal subjects. The ideal dosage, the route of administration of NC and the treatment interval are not yet established.