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INTRAVESICAL INSTILLATION OF NOCICEPTIN/ORPHANIN FQ (N/OFQ) IN PATIENTS WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS): RESULTS FROM A PILOT STUDY

Hypothesis / aims of study

To study the safety, the tolerability and the efficacy of intravesical instillation of the natural occurring peptide nociceptin/orphanin FQ (N/OFQ) for the treatment of interstitial cystitis/painful bladder/Chronic Pelvic Pain Syndrome (IC/PBS).

Study design, materials and methods

23 (21/2 f/m) subjects (mean age 55.8 ± 17.78 years – median 55) with IC/PBS consented to receive twice a week, for 4 weeks, intravesical instillation of the natural occurring peptide N/OFQ (1mg/10ml saline). Inclusion criteria were: age from 18 to 75 inclusive, IC/PBS that meets disease diagnostic criteria as defined by ICS, refractory to previous therapies, which did not target un-myelinated C fibres, to have at least one voided volume ≥ 100 cc in a 24 hour period, confirmed by the bladder diary and provide signed informed consent. Exclusion criteria were: currently pregnant or breastfeeding, Hunner's ulcers on cystoscopy, intravesical therapy or bladder hydrodistention within the previous 60 days, routine use of narcotics other than codeine or propoxyphene for the previous 30 days, previous bladder surgery, evidence of clinically significant co-morbidities and any condition that in the judgment of the investigator would place the subject at increased risk. Primary outcome consist in changes of O'Leary-Sant questionnaire and a pain VAS scale (0= no pain, 10=worst pain) which were recorded at baseline (t_0), the day of last instillation (t_{4w}) and after 12 weeks (t_{12w}).

Results

All the patients completed the treatment. A statistically significant decrease of IC problem index and O'Leary-Sant total score was recorded at t_{4w}: 6.25 ± 3.61 vs. 8.45 ± 3.32 (p =0.036) and 13.62 ± 6.89 vs. 17.91 ± 6.72 (p=0.005) respectively. No statistically significant decrease was observed for IC symptom index: 7.37 ± 3.60 vs. 9.45 ± 3.79 (p=0.063). An impressive decrease of VAS scale was observed at t_{4w}: 4.54 ± 2.48 vs. 7.29 ± 1.60 (p=0.001). After 12 weeks 15 over 23 were satisfied with the results of treatment and they had not received any further drug or therapy. A decrease of O'Leary-Sant total score was maintained at $t12_w$: 14.33 ± 5.23 (p=0.05). VAS scale remained statistically significant lower after 12 weeks: 5.2 ± 2.64 (p=0.002). No significant adverse event was recorded in all the patients during the treatment and after 3 months.

Interpretation of results

In a previous pilot non controlled, non randomized study Lazeri et al. demonstrated that intravesical instillation of N/OFQ at 1 μM inhbits the micturition reflex in spinally lesioned patients but not in normal subjects (1). This observation prompted Authors to re-investigate the effect of N/OFQ under more controlled conditions: a randomized, placebo-controlled, double-blind study. They demonstrated that the intravesical instillation of N/OFQ produces a robust inhibitory effect on micturition reflex in patients with neurogenic overactive bladder (2). The lack of effect of the analog [desPhe^1]N/OFQ, strongly suggested that the effects of the natural peptide are due to activation of NOP receptors. These studies indicated that NOP receptor agonists could represent a novel approach for the treatment of the LUTS. In the present paper our preliminary results seem to suggest that N/OFQ is able to elicit an inhibitory effect on LUTS and pain in patients with IC/PBS.

Concluding message

For our best knowledge it is the first evidence of such effect, however, further randomised placebo controlled trials are mandatory to confirm our data.

References

1. Lazzeri M, Calò G, Spinelli M, Guerrini R, Beneforti P, Sandri S, Zanollo A, Regoli D, Turini D. Urodynamic and clinical evidence of acute inhibitory effects of intravesical nociceptin/orphanin FQ on detrusor overactivity in humans: a pilot study. J Urol. 2001 Dec;166(6):2237-40
2. Lazzeri M, Calò G, Spinelli M, Guerrini R, Salvadori S, Beneforti P, Sandri S, Regoli D, Turini D. Urodynamic effects of intravesical nociceptin/orphanin FQ in neurogenic detrusor overactivity: a randomized, placebo-controlled, double-blind study. Urology. 2003 May;61(5):946-50

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