

18

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BLADDER NERVE GROWTH FACTOR (NGF)-EXPRESSION PREDICTS OUTCOME IN PATIENTS TREATED BY INTRAVESICAL CAPSAICIN FOR REFRACTORY DETRUSOR HYPERREFLEXIA

Aim of Study. We investigated the bladder expression of NGF in patients with a chronic spinal pathology and prospectively performed a correlation between the peripheral intensity of NGF and the outcome to therapy by intravesical capsaicin, used in order to treat refractory urinary incontinence.

Methods. 12 patients, 7 women and 5 men (mean age 40.8 yr., range 24 to 62), suffering from chronic spinal myelopathy, were enrolled. Three patients showed a detrusor acontractility (areflexia) and nine a detrusor hyperreflexia. They were offered to undergo intravesical infusion of high dosage of capsaicin to treat their refractory urinary incontinence. Cystoscopy and bladder biopsy, to detect bladder NGF expression by monoclonal antibody Nerve Growth Factor-2.5S Sigma, were performed before starting the therapy. Clinical follow-up, simple voiding patten and a filling cystometrogram were recorded after 3 and 6 months.

Results. In 5 over 9 patients with detrusor hyperreflexia, a strongly positive NGF immunohistochemical staining was recorded. It was localized in the basal layer of urothelium, in lymphocytic inflammatory cells, in nerve fibers and in the nerve bundles. Some positivity was observed in the smooth muscle cells. A low-moderate or absent NGF immunohistochemical staining was recorded in the patients with a diagnosis of detrusor areflexia. The patients with intense NFG immunohistochemical staining reported a significant clinical improvement after intravesical capsaicin (4 were dry after six months and one occasionally showed incontinence). In the five patients with an intense NGF staining (+++), a highly significant increase of bladder capacity was observed after 3 (basal vs three months: 186±016 vs 382±26 ml, P<0.01) or 6 (380±25, P<0.01 vs basal) months. In contrast, the bladder capacity of the three patients with detrusor overactivity but a lower NGF staining (+, ++) increased less markedly after capsaicin instillation at the intermediate end point (basal vs three months: 163±15 vs 247±32, P<0.05) and this effect was no longer significant at the 6th month (220±12, ns vs basal).

Conclusion. Our findings show high bladder NGF immunohistochemical staining in patients suffering from spinal cord lesion and that its density could be related to intravesical capsaicin outcome used in order to treat detrusor hyperreflexia. The results support the soundness of a new approach in the treatment of neurogenic incontinence and show that it is worthwhile to continue to explore the physiopathology of sensory innervation in voiding pathology.

19

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NERVE GROWTH FACTOR (NGF) GENE THERAPY USING REPLICATION DEFECTIVE HERPES SIMPLEX VIRUS (HSV) VECTORS FOR DIABETIC BLADDER DYSFUNCTION

Aims of Study

Diabetic cystopathy resulting from sensory neuropathy may potentially be treated by direct gene therapy. We investigated NGF gene transfer to the