

NERVE GROWTH FACTOR AND THE NEUROGENIC BLADDER

Hypothesis / aims of study

Nerve growth factor (NGF), has been implicated in the regulation of bladder sensory function, as well as neurogenic detrusor overactivity (NDO). The urothelium has been suggested to play an active role in the modulation of afferent activity in the bladder by releasing several paracrine modulators including ATP and nitric oxide. Although several studies have demonstrated the presence of NGF immunoreactivity in the urothelium of experimental animals, possible release of NGF from the human urothelium has not yet been studied. Therefore, we have explored NGF presence in human urothelium and measured the levels in the urine of patients with multiple sclerosis and neurogenic bladder dysfunction.

Study design, materials and methods

Immunohistochemistry: We obtained bladder biopsies from patients with NDO with flexible cystoscopy. We examined NGF expression using commercially available antibodies. Samples were embedded in OCT medium and stored at -60°C until 12 µm sections were serially cut. Sections were stained manually and using the Leica microsystems Bondmax automated immunostainer in the Department of Neuropathology. **Urine ELISA:** Urinary NGF levels were measured by enzyme-linked immunosorbent assay method and normalized by urinary creatinine levels (NGF/Cr) from urine samples from patients with MS and healthy volunteers. The urinary NGF/Cr levels and Urinary Symptom Profile (USP) were compared.

Results

Positive NGF immunostaining was found in urothelium of healthy human bladder sections and from biopsies with neurogenic detrusor overactivity. Early data from 15 patients shows a positive correlation between high USP scores and higher urinary NGF/Cr ratio. The mean urinary NGF/Cr levels in patients with MS and symptoms of overactive bladder and healthy controls were 20.96 and 5.29, respectively ($p=0.028$).

Interpretation of results

Urothelium could represent an important cellular source of NGF in healthy, as well as in inflamed and overactive bladder. Mean urinary concentrations of NGF/Cr are raised in patients with MS and neurogenic bladder when compared with healthy controls.

Concluding message

Future targeting of the urothelial receptors or signalling pathways modulating NGF release may provide a novel strategy in the treatment of detrusor overactivity.

Disclosures

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