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HIGHER LEVELS OF DETRUSORIAL NGF AND OF ITS HIGH AFFINITY RECEPTOR IN OVERACTIVE BLADDER PATIENTS: WHAT IS THE SIGNIFICANCE?

Aims of Study

Many experimental evidences suggest a possible correlation between the bladder NGF expression and chronic outlet obstruction (BOO), bladder inflammation and /or detrusor overactivity (DO). The increase of NGF levels in varying models of inflammation in the bladder has been showed by Dupont in 2001. In the same year Chuang showed the possible involvement of NGF in bladder hyperactivity pathogenesis after inducing hyperreflexia in experimental animals by the intravesical administration of NGF. More recently, Steers and Tanner, by experimental researches performed respectively in the animals and in the humans, demonstrated the increase of NGF expression in BOO and DO. The higher levels of NGF showed in these subjects have been indicated as the consequence of the neuro and myoplasticity secondary to the bladder muscle hypertrophy which is the main hystological finding in the BOO and DO. Basing on these experimental evidences, the aim of our study was to evaluate the detrusorial and urinay NGF expression in patients affected by BOO with or without DO.

Methods

47 pts eligible, after urodynamic assessment, for prostatic open surgery for BOO secondary to BPH were enrolled in the study after informed consent was signed. The pts were divided in two groups according to the presence (19/47) or not (28/47) of DO associated. Preoperatory urinary sample and intraoperatory detrusor (anterior bladder wall) and bladder mucosa samples were taken in all the patients enrolled. All the specimens were stored in polipropilene tubes at –80°C until the NGF determination. The urinary samples were centrifugated (1500 rpm at 4° C), neutralized by NaOH 0.1 N solution, then treated with proteasis inhibitor before the refrigeration. Urinary, detrusorial and mucosal NGF assessment were performed by immunoenzymatic assay (ELISA method). High affinity NGF receptor (TrkA) presence and its quantitative evaluation were detected respectively by immunochemistry and optical density (OD). Quantitative Reverse Transcriptase-Polymerase Chain Reaction (RT _PCR) was used to analyze the TrkA RNA messanger.

Results

NGF was found in all the urinary, detrusorial and mucosa samples stored. Patients with BOO+DO presented significant higher detrusorial levels of the neurotrophin (0,769±0,453 pg//?g) than patients without DO (0,166±0,11 pg/?g) [p <0,1]. No significant difference was otherwise observed in the urinary NGF concentration between the two groups of patients (0,02+/-0,1 pg/mcl in BOO+DO and 0,02+/-0,4 pg/mcl in BOO). TrkA receptor was revealed in all the detrusorial (8 specimens) samples tested, with higher OD levels in the 4 patients with BOO+DO (0,62±0,28) than the 4 patients with BOO (0,47±0,12). TrkA receptor was also found in the 2 mucosa specimens tested. TrkA RNA messanger was found in the two samples tested.

Conclusions

Our data confirms the previous experimental evidences reported in Literature about the presence of NGF in the human detrusor, mucosa and urine, enhancing their significance due to the associated finding of its high affinity receptor in detrusor and mucosa samples showed in our series. This fact should indicate that the neurotrophin is produced and utilized in situ both in the bladder muscle and mucosa. Moreover, the higher levels of NGF protein and TrkA found in the patients with BOO+DO, although the variability of the results can not allow a conclusion, prompt us to better investigate the possible correlation between DO and NGF, and to better understand its role in the neuro and myoplasticity related to the hystopathological changes associated to the BPH, BOO and DO. It is also of great interest the chance of dosing NGF protein in urine, whose expression seems not to be associated to

BOO or DO and whose origin is still under investigation. Surely future investigations on a larger number of patients also pertaining to different pathologic cathegories could allow a better comprehension of the physiopathologic mechanisms of some voiding dysfunctions such as DO, whose etiopathogenesis is still not completely understood.

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