

DOSE URINARY NGF LEVEL PREDICT SYMPTOMATIC SEVERITY IN PATIENTS WITH INTERSTITIAL CYSTITIS?

Hypothesis / aims of study

Nerve growth factor (NGF) has critical roles in development and maintenance of peripheral nervous system. It has attracted attention as a biomarker of overactive bladder (OAB); urinary NGF level is known to increase in OAB and suppressed after an efficacious treatment for OAB. We investigated urinary NGF levels in interstitial cystitis (IC) to explore the possibility of NGF as an objective marker of IC.

Study design, materials and methods

We measured NGF levels in urine specimens derived from 35 patients with IC (3 men and 32 women, median age of 67 years). The diagnosis of IC was made based on the guideline for IC and hypersensitive bladder syndrome [1], which comprises 1) lower urinary tract symptoms such as bladder hypersensitivity, urinary frequency, bladder discomfort and bladder pain; 2) bladder pathology such as Hunner's ulcer and mucosal bleeding after over-distension; 3) exclusions of confusable diseases such as infection, malignancy and calculi of the urinary tract. The patients were also compatible with National Institute of Diabetes and Digestive Kidney Diseases (NIDDK) consensus inclusion and exclusion criteria for clinical trials. Urine was collected before the hydrodistension, and cystoscopic findings during the hydrodistension procedure were recorded. All patients responded to Core Lower Urinary Tract Symptom Score (CLSS), an assessment tool that can evaluate symptoms in a non-disease-specific manner (range: 0 to 30) [2]. Quality of Life (QoL) was measured by QoL Index (QoLI) of International Prostate Symptom Score (range: 0 to 6). Urinary NGF levels were measured using ELISA kit, Emax ImmunoAssay System (Promega, USA). The NGF levels were standardized by creatinine concentrations and expressed as NGF/Cr ratio. Statistical analysis was performed with JMP software using chi-square test considering p-values of less than 0.05 as significant.

Results

Hunner's ulcers and glomerulations on hydrodistension were found in 23 (65.7%) and 33 (94.3%), respectively. Median urinary NGF level was 9.24 pg/ml (range: 1.06 – 389.9), with median NGF/Cr ratio of 0.16. NGF/Cr ratios were divided into 3 grades as low (below 0.1, n=14), intermediate (0.1-1.0, n=11), and high (above 1.0, n=10). The NGF/Cr ratios were significantly high in patients with nocturia of four or more times (p=0.04), with urgency incontinence (p=0.04), with bladder pain (p=0.02) and with affected QoL (p=0.04) (Table.1). No statistical significant relation with NGF/Cr ratio were found for age, presence of ulcer and LUTS including voiding frequency, urgency, week urinary stream, straining on urination, residual urinary sensation.

Interpretation of results

Urinary NGF level was associated with symptom severity of nocturia, urgency incontinence and bladder pain as well as QoL impairment in this study population.

Concluding message

Urine NGF level could be used as a biomarker of diagnosis and outcome evaluation in IC.

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References

1. Int J Urol. 2009; 16(7):597-615.

2. Int J Urol. 2008;15(9):816-20.

Specify source of funding or grant	There are no external funding of the study nor grants.
Is this a clinical trial?	Yes
Is this study registered in a public clinical trials registry?	No
Is this a Randomised Controlled Trial (RCT)?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	the Ethics Committee of the University of Tokyo
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes