

## THE CORRELATION OF URINE NERVE GROWTH FACTOR LEVELS WITH BLADDER NERVE STAINING CONCENTRATION AND SYMPTOM SCORE SEVERITY IN INTERSTITIAL CYSTITIS PATIENTS

### Hypothesis / aims of study

Interstitial cystitis (IC) is a challenging disease effects millions of people around the world especially women. It presents with suprapubic pain, frequency, urgency and dysuria but there are not any definitive diagnoses and treatment modalities yet. IC may have unfavorable affects on daily activities, business life, social and family relations as well as it causes an economic burden. In this original study, we aim to assess the role of nerve fibers and nerve growth factor (NGF) in IC etiopathology and to demonstrate if there is a correlation between bladder nerve staining concentration, NGF and symptom severity. Thus, there might be no reason for unnecessary, expensive and troublesome tests and treatments.

### Study design, materials and methods

A prospective clinical study was conducted between March 2014 and February 2015 with 15 IC patients and 18 controls after local ethics committee approval. Informed consent was obtained from patients and control subjects. Bladder biopsies were obtained from 15 IC patients and 9 controls. Midstream clean-catch urine specimens were collected from all patients and controls for urine NGF and creatinine measurements. O'Leary Sant Interstitial Cystitis symptom and problem index was used to asses symptom severity and affects of the disease on patient life. Biopsies fixed in formalin were sectioned to 5- $\mu$  thicknesses and stained with S-100 immune histochemical dye. Patients and controls were classified into 3 groups as no staining, mild staining and obvious staining by an experienced urologic pathologist according to bladder nerve fiber staining concentration.

### Results

The mean age of the IC patients was 52 years, while that of the control group was 46.9. S-100 staining was negative 7 (%29.2) of 24 patients of those 1 of them was IC patient and the remaining 6 were controls. Mild staining was demonstrated in 10 IC patients as well as obvious staining was shown in 4 IC patients. Mean urine NGF level normalized to the urine Cr level (NGF/Cr) in IC patients was  $0,34726 \pm 0,225$  and  $0,09434 \pm 0,0813$  in controls. The mean symptom score in IC patients was  $12.27 \pm 2.4$  as well as the mean problem score was  $10.9 \pm 2.3$ .

### Interpretation of results

There was no significant difference between the age of two groups ( $p > 0.5$ ). Mean urine NGF level normalized to the urine Cr level (NGF/Cr) in IC patients was significantly higher than that in controls ( $p < 0.001$ ). The nerve fiber staining concentration and NGF/Cr level in IC patients were significantly correlated with O'Leary Sant IC symptom ( $p = 0.024$  and  $p = 0.001$ , respectively) and problem index ( $p = 0.010$  and  $p = 0.028$ , respectively) scores independently. But no correlation was found between nerve staining concentration and NGF/Cr levels. This may be due to low patient volume in each group.

### Concluding message

This is the first study in the literature, showing the importance of nerve fiber staining and urine NGF levels in IC patients and their effects on symptom and problem index scores. The role of nerve system and related neuropeptides and neurotrophins in IC pathogenesis cannot be ruled out. NGF could be use as a useful biomarker both for the diagnosis and assessment of symptom and problem severity. Because of the low patient number and limited current evidence more large, controlled and randomized trials are mandatory.

### Disclosures

**Funding:** This work was supported by Research Fund of Hacettepe University. **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Hacettepe University Non-interventional Clinical Research Ethics Board **Helsinki:** Yes **Informed Consent:** Yes