

## INDICATION OF NEURO-SELECTIVE PATHOGENESIS IN INDIVIDUAL PATIENTS WITH OVERACTIVE BLADDER OR PAINFUL BLADDER SYNDROME BY MEASURE OF CURRENT PERCEPTION THRESHOLD OF THE BLADDER AFFERENT FIBERS

### Hypothesis / aims of study

The Neurometer® (Neuron, Baltimore, MD, USA) is an electro-diagnostic device to measure the current perception threshold (CPT) on small myelinated (A-delta) and unmyelinated (C) afferent nerve fibers (1). Recently we described the first application of this device for quantitative neuro-selective measurement of the CPT (i.e. vesical sensory threshold) values of the A-delta and C fibers in the human bladder mucosa, allowing the detection of hyper-esthetic (abnormally low) or hypo-esthetic (abnormally high) vesical sensory threshold (2). Diagnosing of the quantitative dysfunction on such specific subpopulation of bladder afferent fibers in patient with overactive bladder (OAB) or painful bladder syndrome (PBS) could improve understanding of the pathogenesis in the individual patient, potentially guiding appropriate therapeutic intervention for each patient. The aim of this study is to analyze the relationship between the CPT values of the bladder afferent fibers and the clinical characteristics in the patients with OAB and PBS, in whom previous therapeutic interventions were ineffective.

### Study design, materials and methods

Thirty-eight selected patients (8 male, 30 females) with OAB (n=25, age ranged from 43 to 80) and PBS (n=13, age ranged from 22 to 70), in whom previous therapeutic interventions were ineffective, were enrolled in this study. The CPT values (1=0.01mA) were measured at frequencies including 250 Hz and 5 Hz by Neurometer® using an intravesical electrophysiology catheter (6Fr in diameter) on the posterior bladder body wall and skin dispersion electrode. The continuous sinusoidal stimuli at frequencies of 250 Hz and 5 Hz could reflect functions of the small myelinated (A-delta) and the unmyelinated (C) fibers, respectively. In all patients, bladder diary was reported. In the patients with PBS, the Interstitial Cystitis Symptom Score (O'Leary-Sant symptom index) were reported. Morbidity time of the patients with OAB (3 months to 10 years) or PBS (12 months to 10 years) was determined from the patient reported time interval with complaining of definitive symptom, referring the first time of cystoscopic diagnosis for PBS. Cystoscopically, the glomerulation was found in 9 out of the 13. Statistical analysis was performed using Mann-Whitney U test and single linear regression analysis.

### Results

In the patient with refractory PBS, significant linear correlations were found between the morbidity time and the bladder CPT value of A-delta fiber ( $r=0.83$ ,  $p=0.002$ ) as well as C-fiber ( $r=0.61$ ,  $p=0.049$ ). In the patient with refractory OAB, significant linear correlation was found between the morbidity time and the bladder CPT value of C-fiber ( $r=0.47$ ,  $p=0.031$ ), but not of A-delta fiber ( $r=0.26$ ,  $p=0.2$ ). The overall mean CPT value of C-fiber was significantly ( $p=0.040$ ) lower in the patients with refractory OAB (mean 31.9, range from 2.4 to 173) than in the patients with refractory PBS (mean 61.6, range from 3.5 to 173). The overall mean CPT value of A-delta fiber seemed quite similar between the patients with refractory OAB (mean 85.2, range from 5 to 220) and with refractory PBS (mean 82.3, range from 5.9 to 216). Among the patient reported symptoms in the patient with refractory PBS, the bladder CPT value of C-fiber had significant linear correlation to the severity in 24-hour frequency ( $r=0.65$ ,  $p=0.03$ ) as well as in maximum voided volume ( $r=0.67$ ,  $p=0.02$ ), although no clear correlation between the CPT values and the patient reported symptoms was found in the patients with refractory OAB. In the patients with refractory PBS, the cystoscopic finding of the glomerulations was associated with the higher CPT values of C-fiber ( $p=0.031$ ) and A-delta fibers ( $p=0.073$ ).

### Interpretation of results

The measurement of neuro-selective CPT values could identify dysfunction of the subpopulations of bladder sensory afferent fibres, associated with the clinical characteristics. The CPT values of the 250Hz (A-delta fiber) and 5Hz (C-fiber) in the patients with either refractory OAB or PBS were found to become higher according to the prolonged morbidity time. Patient reported symptoms such as the 24-hour frequency and maximum voided volume had greater correlation with CPT values of C-fiber in the patients with refractory PBS than in patients with refractory OAB. These results suggested possible differences in neuro-pathogenesis between refractory OAB and PBS. The neuro-selective quantitative measurement of CPT value of the bladder afferent fibers in the patients with OAB and PBS potentially contribute to select appropriate therapeutic intervention. Further study based on the increased number of patients and monitored outcomes by various treatment arms seems necessary to clarify the role of CPT value measure on clinical setting.

### Concluding message

The neuro-selective quantitative assessment of CPT values of the bladder afferent fibers could improve understanding of neuro-pathogenesis in the individual patients with OAB and PBS.

### References

1. Arch Phys Med Rehabil 68: 210, 1987.
2. Eur Urol 45:70, 2004.

**FUNDING: NONE**

**CLINICAL TRIAL REGISTRATION:**

**This clinical trial has not yet been registered in a public clinical trials registry.**

**HUMAN SUBJECTS:** This study was approved by the Committee for Clinical Research on Human Subjects in Kyoto Prefectural University of Medicine and followed the Declaration of Helsinki. Informed consent was obtained from the patients.