

## THE NEUROMETER AS AN INSTRUMENT FOR APPROPRIATE SELECTION AND MONITORING OF INTRAVESICAL RESINIFERATOXIN THERAPY FOR PATIENTS WITH DETRUSOR HYPERREFLEXIA

### Aims of Study

The Neurometer is a portable constant current sine wave stimulator, which has recently been advocated for the quantification of peripheral nerve dysfunction by the measurement of detection thresholds for constant current stimulation (1). Stimuli are applied through surface electrodes at three frequencies and a forced choice method is used to determine the minimum amplitude of detection. Neurometer devices are reported to assess independently the functional integrity of the large myelinated, small myelinated and unmyelinated sensory nerve fibers at any cutaneous site. Recently we first applied this device for the human bladder (2). We reported that quantitative measurement of current perception threshold (CPT) values could be successfully assessed using an intravesical electrode on the human bladder wall in the physiological condition. A $\delta$  fiber is reported to have a significant function for ordinary urinary sensory, connected to a tension receptor in the bladder wall. Capsaicin-sensitive afferent nerves (C-fiber) exist in the human bladder and become functionally significant in the detrusor hyperreflexia (3). Additionally, intravesical resiniferatoxin was reported to be over 1000 times more effective than intravesical capsaicin for detrusor hyperreflexia (4). In our previous study, the quantitative selective measurement of the CPT of the bladder afferent fibers could be successfully assessed in hyper-sensitive and hypo-sensitive dysfunction. The aim of this study is to determine whether the new test for the CPT values of C-fiber could contribute to the appropriate selection of intravesical resiniferatoxin as well as to the monitoring of the therapeutic effects.

### Methods

In 8 volunteers and 8 patients with detrusor hyperreflexia due to incomplete cervical and/or thoracic spinal diseases who were diagnosed by the presence of uninhibited contraction as well as by a positive ice-water test, the measurement of CPT values in the bladder was performed. CPT values were measured using a neurometer (Neuroton, Baltimore, MD), which emits graded alternating current stimuli at 2000, 250, and 5 Hz at digitally calibrated levels from 0 to 10 mA. CPT values at frequencies of 2000, 250, and 5Hz were determined on the bladder wall using an intravesical electrophysiology catheter (5 French size, fixed curve) (Cordis Webster Inc, Baldwin Park, CA). At each frequency the current was increased until the patient could perceive a sensation. The measurement of the minimum threshold for perception was performed at at least three points, of which the average was determined as the CPT value in the bladder. Intravesical resiniferatoxin instillation therapy was performed using 1microM 100ml for 30 min. in patients with detrusor hyperreflexia due to spinal cord injury. The examination procedures using the Neurometer as well as intravesical resiniferatoxin instillation therapy were permitted by the Committee for clinical research on human subjects in our institution.

### Results

The mean CPT values of the 8 volunteers (mean age 39 years) are considered to be a control for normal sensitivity (A $\beta$ , 83.0 $\pm$ 34.5 ; A $\delta$ , 50.5 $\pm$ 28.7 ; and C fibers, 26.2 $\pm$ 17.7). In the 8 patients the bladder CPT value (4.0 $\pm$ 1.9) at 5Hz was significantly lower ( $p < 0.01$ ) than that in the controls (26.2 $\pm$ 17.7), which could suggest hyper-sensitivity by abundant C-afferent fiber causing hyper-reflexia.

A case report; A 27 year old male, who had suffered from severe reflex incontinence because of cervical spinal cord injury caused by a traffic accident when he was 19 years of age, underwent intravesical resiniferatoxin instillation therapy. Incontinence improved significantly from a total of 600 ml a day to almost dry between pre- and post-treatment using 5-6 times a day of intermittent self-catheterization. Water-filling cystometry demonstrated approximately 150% increase of bladder capacity at uninhibited contraction on the 3rd day after treatment. The Neurometer demonstrated that the CPT value of C-fiber changed from 5.1 to 14 by the 3rd day after treatment, and then increased to 75 by the 21 day after treatment, which suggested the treatment could bring about a change from hyper- to hypo-sensitivity of the afferent C-fiber. The CPT values of A $\delta$  fiber as well as A $\beta$  fiber showed no significant change from the treatment.

### **Conclusions**

Using the Neurometer, intravesical resiniferatoxin has improved the clinical symptom of reflex incontinence, accompanied with increase of bladder capacity as well as a change into hypo-sensitivity of C-fiber, in a patient with detrusor hyperreflexia who was determined to have hyper-sensitivity of C-fiber in the bladder wall. Neurometer may contribute to appropriate selection as well as the monitoring of intravesical instillation therapy for patients with detrusor hyper-reflexia.

### **References**

- (1) Arch Phys Med Rehabil 68: 210-213, 1987
- (2) Neurol Urodyn 20:573-574, 2001
- (3) Lancet 229,1239, 1992
- (4) Lancet 350, 640, 1997