

## **INFLUENCE OF STRESS URINARY INCONTINENCE ON DETRUSOR CONTRACTILITY: AN IN VITRO STUDY**

### **Hypothesis / aims of study**

After surgery for stress urinary incontinence (SUI) voiding difficulties are not uncommon. Although they can be due to increased urethral resistance by the surgery technique, detrusor hypocontractility has been suggested as another cause. Since studies investigating detrusor contractility in SUI are lacking, we investigated such effects on detrusor strips contractility in a rat model for SUI.

### **Study design, materials and methods**

With permission of the local ethics committee SUI was created in female virgin wistar rats (n=9) by dilating the vagina (1) under ketamine/xylazine anaesthesia. In order to obtain a prolonged period of 8 weeks of SUI we repeated this procedure five times. Stress incontinence was objectivated by the sneeze test using a rat whisker inserting into the nostril to induce sneezing. To evaluate the influence of SUI a control group (n=9) was anaesthetised with the same doses of drugs at equal intervals. In this group the vagina was not dilated.

After 8 weeks the rats were sacrificed. The bladder was weighted and separated into 4 longitudinal strips of bladder corpus (ventral left, ventral right, dorsal left, dorsal right) and one transverse strip of bladder dome. The ventral left strip was prepared for morphometric analysis: the paraffin embedded formalin fixed sections were stained with Trichrome Masson. Bladder contractility was investigated in vitro in tissue baths by studying the effect of electrical field stimulation (EFS) (4Hz, 800 mA). Different contraction mechanisms were further studied with KCl ( $10^{-2}$  mol/l), betanechol ( $10^{-3}$  mol/l) and ATP ( $10^{-2}$  mol/l),

Changes in smooth muscle density were investigated by the Chalkley method (2), which evaluates differences in amount of smooth muscle area and connective tissue area.

Contraction strength to KCl is expressed in newton (N). Results are expressed as mean +/- s.e.m. Smooth muscle density is expressed as relation (amount of smooth muscle area/ amount of connective tissue area).

### **Results**

In the study group the sneeze test was positive in all rats up to 8 weeks, in the control group non of the rats showed SUI.

The total bladder weight (SUI: 0.136 g +/- 0.0087), control group: 0.116 g +/- 0.0153,  $p > 0.05$ ), weight and length of the separate bladder strips were not statistically different between the two groups. Detrusor contraction to KCl was similar in the two groups (SUI: 0.033 N +/- 0.0029, control group: 0.028 N +/- 0.0020,  $p > 0.05$ ) with no influence of the localisation of the strips. Muscular reaction to all other stimuli was normalised to KCl response. In the study group nerve-mediated contractions towards EFS were significantly smaller than in the control group (SUI: 38 +/- 4.7%, control group : 63 +/- 5.0%,  $p = 0.000293$ ). This effect was seen in both bladder corpus and bladder dome separately. Bladder strip contractility to betanechol was not different in study group and control group (SUI: 128 +/- 4.3%, control group: 132 +/- 4.2%,  $p > 0.05$ ) in all regions. However detrusor contractility towards ATP was significantly reduced in the study group (SUI: 38 +/- 2.5%, control group: 47 +/- 3.7%,  $p = 0.0223$ ).

The smooth muscle density was not different between the two groups (SUI: 1.61 +/- 0.0600, control group: 1.68 +/- 0.0665,  $p > 0.05$ ). This effect was seen in both bladder corpus and bladder dome separately.

### **Interpretation of results**

Our data show that detrusor contractility is affected in SUI in rats. Neurogenic contractions to EFS and smooth muscle contractions to ATP were reduced in SUI in rats while contractions to betanechol were normal. Since detrusor contraction is initiated by ATP and would be maintained by acetylcholine (3), our results suggest that after 8 weeks of SUI in rats, primarily the initiation but not the maintenance of the detrusor contraction would be affected.

Based on these results it needs to be determined if similar mechanism could be responsible in voiding difficulties in women with SUI.

### **Concluding message**

Our in vitro study in rats brings arguments for reduced bladder contractility in SUI. This would be due primarily to ATP related mechanism which is involved in initiating detrusor contraction. Such mechanism, if applicable in women, might explain voiding difficulties as seen after incontinence surgery.

### **References**

- (1) Effect of simulated birth trauma on the urinary continence mechanism in the rat. *Urology*, 52(1): 143-151, 1998.
- (2) Method for the quantitative morphologic analysis of tissues. *J Natl Cancer Inst* 1943, 4: 47-53.
- (3) Purinergic and cholinergic components of bladder contractility. *Life Sci* 1995, 56(6): 445-454.