

## **NON-NEURONAL ACETYLCHOLINE AND ATP RELEASES FROM ISOLATED NORMAL AND NEUROGENIC HUMAN BLADDER**

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

The main neurotransmitter in bladder contraction is acetylcholine released from cholinergic nerve endings. However, non-adrenergic and non-cholinergic neurotransmitters may contribute to contractions in human bladder with pathological conditions or aged bladder. It has been reported that adenosine triphosphate (ATP) is the most important NANC neurotransmitter in bladder contraction. Furthermore, several reports suggest the releases of ACh and ATP from the non-neuronal origin, especially from urothelium (1, 2). Bladder stretch may cause the increases in non-neuronal ACh and ATP releases, which may be the stimulating factors for afferent nerves resulting to increase in micturition reflex. The present study was designed to evaluate the differences in non-neuronal ACh and ATP releases from isolated normal and neurogenic human bladder.

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

Human bladders were obtained from 10 patients (control group), who were undergoing cystectomy due to bladder carcinoma, and 8 patients (neurogenic bladder group: 3 cases: spina bifida; 5 cases: spinal cord injury) who had undergoing bladder augmentation. Bladder strips with or without urothelium were suspended in organ bath filled with Krebs-Henseleit solution, and tension developments were recorded in both groups. Microdialysis probe was inserted into the strip, and Ringer solution was perfused into the probe at a constant flow rate. The effects of elevation of the resting tension (0 to 4 g) induced by strip stretching on non-neuronal ACh and ATP releases were also evaluated. The amount of ACh and ATP in the dialysate fraction by HPLC with ECD, and luciferine-luciferase assay, respectively.

### **Results**

In the control and neurogenic human bladders strips, there were non-neuronal ACh and ATP releases, which were not inhibited by treatment with tetrodotoxin. The non-neuronal ACh (table 1) and ATP (table 2) releases from strips with urothelium were significantly higher than that from strips without urothelium in both groups. In the neurogenic group, basal ACh and ATP release with urothelium was about 4.6 and 14.7 times higher than that without urothelium, respectively. Stretch of the strips without urothelium did not cause any significant increases in non-neuronal ACh and ATP releases in both groups. However, in strips with urothelium, stretch of bladder strips caused significant increase in ACh and ATP releases. In the neurogenic group, ACh and ATP releases in the stretch condition were about 5.6 and 11.2 times higher than that in the basal condition, respectively.

### **Interpretation of results**

The present data showed that there are ACh and ATP releases from non-neuronal origin in the control and neurogenic human bladder. Urothelium may partly contribute to non-neuronal ACh and ATP releases, and bladder stretch caused increase in both non-neuronal ACh and ATP releases. In the neurogenic bladder, the basal and stretch-induced release in non-neuronal ATP release was more prominent, as compared with ACh release.

### **Concluding message**

The present study suggests that the non-neuronal ACh and ATP are partially released from urothelium in the control and neurogenic human bladders. Both non-neuronal ACh and ATP may have an important role on the regulation of bladder function. ATP may have a relative contribution to detrusor dysfunction in the neurogenic bladder.

### **References**

- 1) Urology 63 (Suppl 3A) 17-23, 2004.
- 2) J. Neurosci. 21: 5670-5677, 2001.

Table 1 Non-neuronal ACh releases (fmol/g tissue) from control and neurogenic human bladder

Group	Urothelium	Basal release (Resting tension 0 g)	Release in stretch (Resting tension 4 g)
Control (n=10)	With	43.5 ± 5.9#	198.7 ± 20.3*#
	Without	15.6 ± 3.8	23.2 ± 6.8
Neurogenic (n=8)	With	105.8 ± 12.5#	588.7 ± 66.5*#
	Without	23.2 ± 5.2	33.7 ± 6.0

\* Significantly different from the comparable value for resting tension 0 g (P<0.05)

# Significantly different from the comparable value without urothelium (P<0.05)

Table 2 Non-neuronal ATP releases (fmol/g tissue) from control and neurogenic human bladder

Group	Urothelium	Basal release (Resting tension 0 g)	Release in stretch (Resting tension 4 g)
Control (n=10)	With	18.7 ± 3.2#	32.4 ± 5.3*#
	Without	4.5 ± 0.5	6.8 ± 1.1
Neurogenic (n=8)	With	85.5 ± 11.5#	957.9 ± 115.4*#
	Without	5.8 ± 1.8	9.5 ± 2.0

\* Significantly different from the comparable value for resting tension 0 g (P<0.05)

# Significantly different from the comparable value without urothelium (P<0.05)