

EFFECTS OF AGE AND MUSCLE STRETCHING ON ACETYHLCHOLINE RELEASE IN ISOLATED HUMAN BLADDER SMOOTH MUSCLES

Aims of Study

It has been reported that bladder smooth muscle function changes with age. The main neurotransmitter in bladder contraction is acetylcholine (ACh) released from cholinergic nerve endings. Furthermore, several reports suggest that the non-neurogenic ACh release may contribute to bladder function. The present study was designed to evaluate the effects of age on ACh release in the isolated human bladder smooth muscles strips with or without epithelium. Furthermore, the effects of muscle stretching on ACh release were also studied.

Methods

Human bladders were obtained from 29 patients, who were undergoing cystectomy due to bladder carcinoma. Smooth muscle strips with or without epithelium were suspended in organ bath filled with Krebs-Henseleit solution, and tension developments were recorded. Microdialysis probe was inserted into the strip, and Ringer solution was perfused into the probe. The effects of age and elevation of the resting tension (0 to 4 g) induced by muscle strip stretching on ACh releases were evaluated. Furthermore, the dialysate during electrical field stimulation (EFS: supramaximum voltage, 0.5 ms duration, 60 Hz and 3 s train) was collected, and the effect of age on EFS-induced ACh releases is also evaluated. The amount of ACh released in the dialysate was measured by HPLC coupled with electro-chemical detection.

Results

In human bladder trips before EFS, there were basal ACh releases, which were not inhibited by treatment with tetrodotoxin. The basal ACh releases from muscle strips with epithelium were not significantly different from that of strips without epithelium. However, the basal releases from smooth muscle strips with epithelium in older (over 65 years) patients were significantly higher than that in younger patients (under 65 years). In the smooth muscle strips with epithelium, the elevation of the resting tension by stretching caused increase in basal ACh release (table 1), and the increased basal ACh release was not inhibited by treatment with tetrodotoxin. The % increase in basal ACh release induced by smooth muscle stretching was significantly higher in the older patients than in the younger patients (table 2). EFS caused significant increases in ACh releases in both human bladder smooth muscles strips with and without epithelium, which were significantly inhibited by treatment with tetrodotoxin. ACh releases induced by EFS decreased with age, and there was a significant negative correlation between age and EFS-induced ACh release.

The data demonstrate that there is age-related increase in basal ACh release, and age-related decrease in EFS-induced ACh release in human bladder smooth muscles. Smooth muscle stretching also increased basal ACh releases. It is suggested that bladder epithelium may play an important role on basal ACh releases, and that the age-related changes in basal and EFS-induced ACh releases may contribute to changes in bladder function.

Table 1. Effects of epithelium and resting tension on ACh release from human bladder strips

	Basal ACh release; pmol/g tissue (Resting tension 0)	% Increase in ACh release			
		Resting tension; g			
		1	2	3	4
With epithelium (n=15)	0.028±0.02	91.6±14.2*	148.5±25.7*	171.3±37.0*	197.8±36.2*
Without epithelium (n=14)	0.029±0.03	29.2±7.8	62.0±12.5	32.0±9.8	59.6±9.9

P < 0.01; Significantly different from comparable values without epithelium.

Table 2. Effects of age on ACh release from human bladder strips with epithelium

Age	Basal ACh release; pmol/g tissue (Resting tension 0)	Maximum % Increase in ACh release
Over 65 years (n=8)	0.033±0.01*	277.4±53.8*
Under 65 years (n=7)	0.024±0.01	106.9±9.8

P < 0.02; Significantly different from comparable values under 65 years.

Conclusions

The data demonstrate that there is age-related increase in basal ACh release, and age-related decrease in EFS-induced ACh release in human bladder strips. Smooth muscle stretching also increased basal ACh releases. It is suggested that bladder epithelium may play an important role on basal ACh releases, and that the age-related changes in basal and EFS-induced ACh releases may contribute to changes in bladder function.