

Authors: Kageyama S, Shinbo H, Hayami S, Watanabe T, Ushiyama T, Suzuki K, Fujita K
Institution: Department of Urology, Hamamatsu University School of Medicine
Title: AGE RELATED CHANGES IN CARBACHOL-INDUCED CONTRACTION AND WASHOUT RELAXATION IN HUMAN URINARY BLADDER DETRUSOR MUSCLE

Aim of study:

To investigate the affinity differences of muscarinic receptor to carbachol by measuring the contraction and relaxation of human detrusor muscle strips *in vitro*.

Materials and methods:

Specimens of human urinary bladder were obtained from 16 patients who underwent total cystectomy for bladder cancer. Bladders muscle strips 10x2 mm in size were cut from non-cancerous area in the anterior wall or dome and the mucosa and serosa were removed. Changes in the force of contractions were measured isometrically in the organ bath containing Krebs-Henseleit (K-H) solutions.

Results:

Carbachol (CCh; 10nM-10µM) caused concentration dependent contractions, however, the magnitude of contraction was decreased with age [1]. After CCh stimulation, muscle strips were washed for 1 minute using K-H solutions. The muscle strip contraction did not return to base line, but showed slight sustained contraction. Twenty minutes after first washout, the muscle strips were washed again for another 1 minute, and the muscle strips returned to base line with recovering the rhythmic contraction (Figure 1). This sustained contraction was not observed in rat urinary bladder muscle strips. The ratios of relaxing by first washout to total relaxation (%1stWR) were changed by patients age (Figure 2).

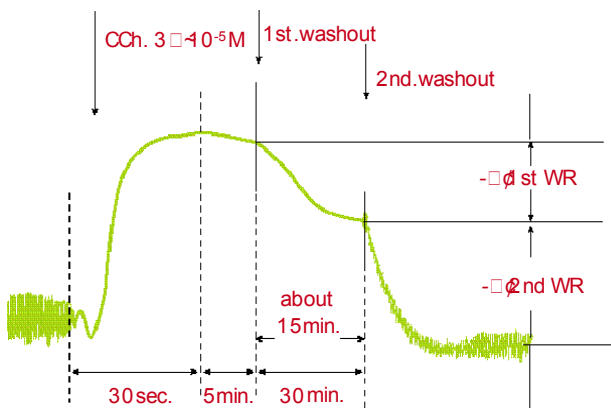


Figure 1

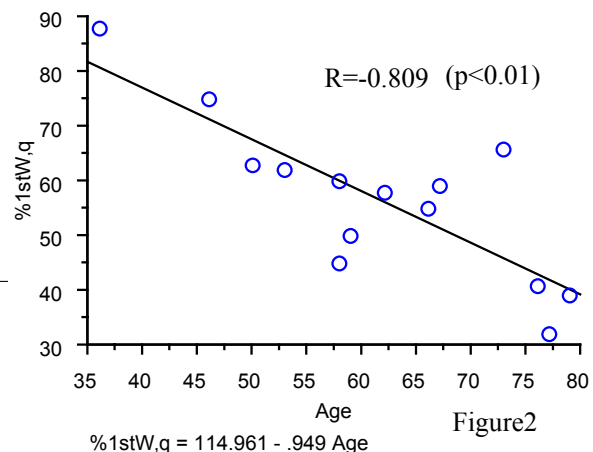


Figure2

Conclusions:

First washout may abolish the binding of detrusor muscle membranous muscarinic receptor combined with CCh. Age-related decrease of both phasic contraction and %1stWR after CCh-induced contraction were observed. Our results suggest that muscarinic receptors in human urinary bladder membrane may decrease with age. It will be one of a key evidence that senile patients are refractory to the treatment for overactive bladder using anti-cholinergic agents. We are going to the radioligand binding study to confirm this evidence.

References:

1) Br. J. Pharmacol. 131: 1482-1488, 2000. 2) Br. J. Urol., 84: 343-349, 1999.