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THE EFFECTS OF ATEROSCLEROSIS-INDUCED CHRONIC ISCHEMIA ON BLADDER FUNCTION IN WATANABE HERITABLE HYPERLIPIDEMIC (WHHL) RABBITS

Hypothesis / aims of study

Arteriosclerosis induced ischemia has been shown to produce smooth muscle dysfunction in various organs. Several studies have suggested that ligation or balloon injury of bladder arteries caused the detrusor overactivity and/or impairment of detrusor contractility. The present experiment was designed to evaluate the effects of chronic bladder ischemia on bladder function using Watanabe heritable hyperlipidemic (WHHL) rabbits. The rabbits have hyperlipidemic state and atherosclerotic lesions, which are similar to that of human. It has been reported that WHHL rabbits are good model to study the development and progression of atherosclerosis and the related pathological conditions.

Study design, materials and methods

20-24 months old male WHHL rabbits (n=6: WHHL group) and the age and sex-matched Japanese white rabbits (n=10: control group) were used in this experiment. After one week of control period, each rabbit was maintained in the metabolic cage, and was continuously measured the number of micturition and each micturition volume for 3 days. After pentobarbital anesthesia, catheters were inserted into bladder dome for filling cystometry. Micturition volume, micturition frequency, post-void residual urine were evaluated. After sacrifice, bladder and common and internal iliac artery were obtained for histological evaluation. In addition, bladder smooth muscle strip was suspended in an organ bath, and tension development was recorded. The contractions induced by carbachol, KCl (80 mM) and electrical field stimulation (EFS; supramaximum voltage, 0.3 msec duration, 2.5 - 40 Hz and 3 sec train) were evaluated.

Results

The daily number of micturition and micturition volume are presented in Table 1. Although the daily urine volumes were not different between groups, the number of micturition in WHHL group was significantly higher than that in the control. The micturition volume of WHHL group was significantly lower than that of the control. Cystometric findings in WHHL group showed the premicturition contractions, shorter interval and lower micturition volume, as compared to the control group. However, the micturition pressures were not significantly different between groups. The residual urines were not observed in both groups. In the functional study using muscle bath technique, the contractile responses induced by carbachol and EFS in WHHL groups tended to be lower than that in the control group. Histological examination of bladder demonstrated that urothelium was thicker in WHHL group than in the control. The internal iliac artery in WHHL group showed significant atherosclerosis lesions, thickening of media and narrowing arterial lumen size.

Table 1. Micturition pattern of WHHL rabbits

	WHHL rabbit (n=6)	Control (n=10)
Daily urine volume (ml/day)	72.56 ± 2.31	75.75 ± 9.03
No. of micturition (No./day)	5.79 ± 1.30*	2.48 ± 1.12

Average voided volume (ml)	16.10 ± 3.76*	30.1 ± 4.56
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* Significantly different from comparable value of the control (P<0.05)

Interpretation of results

The histological findings of the iliac artery and bladder in WHHL rabbit suggest poor blood supply to the bladder, and pathophysiological change in bladder smooth muscle and urothelium. Furthermore, the present data demonstrate that bladder condition of WHHL rabbits is detrusor overactivity state, which may be caused by arteriosclerosis-induced bladder ischemia.

Concluding message

This chronically hyperlipidemic (WHHL) rabbit shows detrusor overactivity, and bladder ischemia may contribute to the pathological conditions. This rabbit may be a useful animal model for evaluation of pathophysiology of overactive bladder.