229

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PROGRESSION OF VASCULAR DAMAGE AND BLADDER DYSFUNCTION IN RATS

Hypothesis / aims of study

Vascular endothelial dysfunction and atherosclerosis increase with age, and pelvic arterial occlusive disease may lead to impaired lower urinary tract perfusion and play an important role in the development of bladder dysfunction. The abdominal aorta and its branches, especially the bifurcation of the iliac arteries, are particularly vulnerable to atherosclerotic lesion. An experimental study in rat has shown that chronic treatment of NG-nitro-L-arginine methyl ester (L-NAME), an inhibitor of endothelial nitric oxide synthase, together with a high cholesterol diet, leads to detrusor hyperactivity (1). However, whether the severity of bladder dysfunction, ranging from detrusor hyperactivity to detrusor underactivity, depends on the degree of vascular damage remains to be fully elucidated. Therefore, the present study investigated whether arterial endothelial injury (AI) with L-NAME and a high cholesterol diet produces detrusor underactivity in the rats.

Study design, materials and methods

Adult (16-week old) male Sprague-Dawley rats were divided into control, L-NAME, and AI/L-NAME groups. The L-NAME group (N=5) received L-NAME (3mg/ml) dissolved in drinking water and a 2% cholesterol diet for 8 weeks. The AI/L-NAME group (N=7) underwent balloon endothelial injury of the bilateral iliac arteries and were given L-NAME and cholesterol diet for 8 weeks after AI. The third group, receiving a regular diet for 8 weeks, was used as an age-matched control group (N=9). After cystometrogram (CMG) recording in conscious animals, rats from each group were euthanized, and the bladders and common iliac arteries were harvested for pharmacological studies and histological examination.

Results

The body weight in the L-NAME and AI/L-NAME groups was significantly lower than in controls. The bladder weight was not significantly different among the three groups. The H&E staining of the iliac arteries from AI/L-NAME group showed obvious arterial wall thickening with a neo-intimal formation, but the iliac arteries in the L-NAME group did not change. The mean arterial wall thickness in the AI/L-NAME group was significantly greater than that of the other groups. Bladder capacity and voided volume in the L-NAME group were less than in controls, while these cystometric parameters in the AI/L-NAME group were significantly larger than in controls without affecting maximum pressure. The post-void residual volume in the AI/L-NAME group tended to increase compared with the other groups. In the organ bath study, contractile responses of bladder strips to KCL, electrical field stimulation, carbachol and ATP in the L-NAME and AI/L-NAME groups were significantly less than in controls. The contractile responses to the stimuli in the AI/L-NAME group were the lowest among the three groups.

Interpretation of results

Bladder blood flow could not be investigated in this study. However, it is reasonable to assume that bladder microcirculation may be more reduced by vascular endothelial dysfunction plus arterial occlusive disease than by vascular endothelial dysfunction alone. Furthermore, continued urine storage and bladder distension under ischemic condition may increase bladder damage. Although a decrease in maximum bladder pressure was not observed in the AI/L-NAME group, the increase in bladder capacity and the development of residual urine, and impaired detrusor contractility to various stimuli in in-vitro study, might reflect the beginning of detrusor underactivity.

Concluding message

Our findings suggest that progressive vascular damage might cause bladder dysfunction, developing from detrusor hyperactivity to detrusor underactivity.

Figure1.H&E staining of cross section of common iliac arteries (x40, upper panel, x400, lower panel) in animals of control, L-NAME and AI/L-NAME groups. Bar graph shows arterial wall thickness.

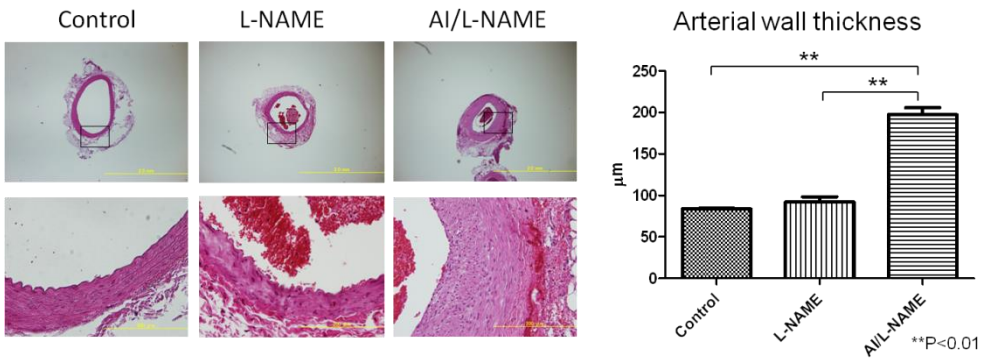


Figure 2. Typical cystometrogram recordings.

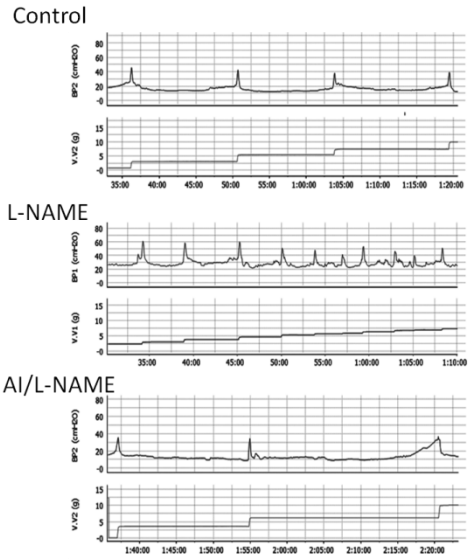
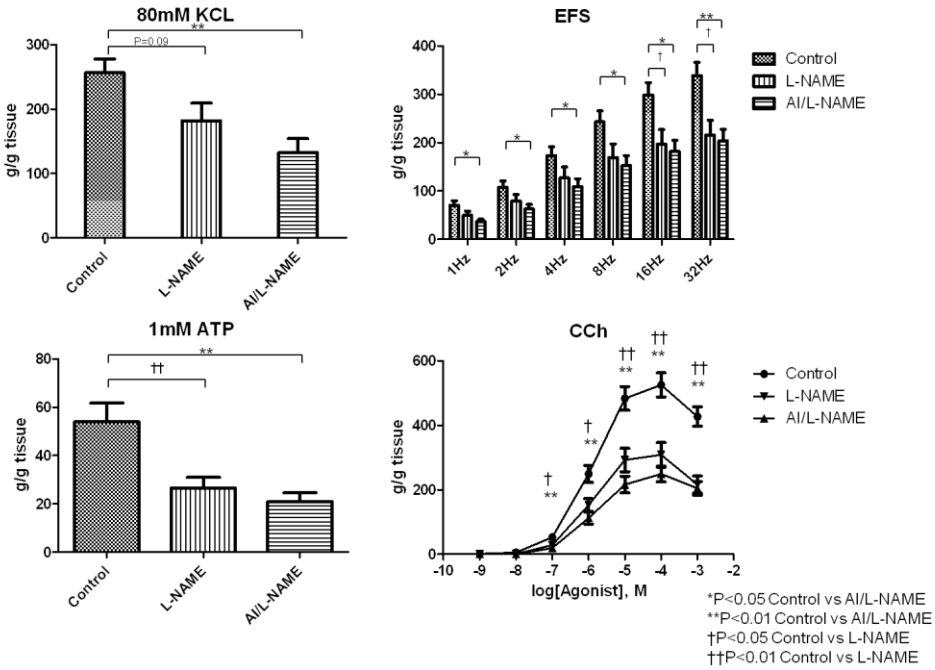


Table1. Animal and bladder weight, cystometric parameters.

	Control	L-NAME	AI/L-NAME
Body weight (g)	575.5±6.3	468.0±8.6	480.0±10.2
Bladder weight (g)	0.24±0.01	0.24±0.01	0.23±0.01
Bcap (ml)	2.0±0.14	1.5±0.33	3.2±0.24
V.V (ml)	1.9±0.15	1.5±0.36	3.0±0.21
R.V (ml)	0.10±0.06	0.06±0.03	0.24±0.06
BP (H_2O mmHg)	15.6±0.6	17.6±2.1	15.1±0.8
TP (H_2O mmHg)	26.3±0.9	27.5±3.6	28.7±1.6
MP (H_2O mmHg)	45.8±2.1	45.1±2.3	46.7±5.3

Bcap: bladder capacity, V.V: voided volume, R.V: residual volume
BP: baseline pressure, TP: threshold pressure, MP: maximum pressure
**P<0.01

Figure 3. Contractile responses to KCL, electrical field stimulation (EFS), ATP and carbachol (CCh)



References

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Disclosures

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