225

Lee T[1], Kwon Y H [2], Park C S[2], Suh J K[1]
1. Dept of Urology, Inha University Hospital , 2. Dept of Pharmacology, Inha University

ALTERATIONS OF NITRIC OXIDE SYNTHASE ISOFORMS IN THE PROXIMAL URETHRA OF DIABETIC RAT WITH AGING: PROTEIN EXPRESSION

Hypothesis / aims of study

Nitric oxide synthase (NOS) activity is known to be essential for opening of normal urethra during voiding(1). and NOS expression has been shown to be altered with diabetes(2). We characterized the distribution and expression of NOS isoforms in urethral tissues of diabetic rats comparing to those of controls and explored how they are altered with aging.

Study design, materials and methods

A total of 17 male Sprague-Dawley rats weighing 200 to 500 g were divided into 2 groups, including 8 into the control and 9 in the experimental group (Table 1). Diabetes was induced in the two day-old neonates by intraperitoneal administration of streptozotocin (100 mg/kg), which was the Non-insulin dependent diabetes mellitus (NIDDM) model. Rats detected as high serum glucose level greater than 200 mg/dl. 12 weeks after injection were considered diabetic. The proximal urethra was obtained under anesthesia at 12, 24 and 36 weeks. Immunohistochemical analysis and Western blot for neuronal (n), endothelial (e), and inducible (i) NOS were done in the proximal part of proximal urethra, respectively.

Results

1**. Immunohistochemical analysis.** a) **nNOS:** The quantity and intensity of n-NOS immunoreactivity in diabetic rats were significantly less than those in control rats, which findings were prominent with aging. b) **eNOS:** At 12 weeks of age, The quantity and intensity of e-NOS immunoreactivity in diabetic rats were significantly less than those in age-matched controls, but no difference between them in 24 and 36 weeks of age. c) **iNOS:** There was no difference between immunoreactivities of diabetic and control rats in all three age groups.
2. Protein expression. a) **nNOS:** In all age groups, the n-NOS expressions in diabetic rats were less than those in controls. Especially, the decreasing tendency of protein expression with the increasing blood glucose level was revealed by a simple regression graph. b) **eNOS:** At 12 weeks of age, the e-NOS expressions in diabetic rats were higher than those in controls. In other age group**s**, there was no difference between expressions in diabetic and control rats. c) **iNOS:** In all age group**s**, there was no difference between expressions in diabetic and control rats.

Interpretation of results

These results indicate that the urethral constitutive NOS isoforms in diabetes of NIDDM changed with aging.

Concluding message

These changes of proximal urethral NOS in diabetics may have an important role in the pathogenesis of the diabetic cystopathy, which might be related to development of dynamic obstruction in patients with diabetes mellitus.

Table 1. Detailed information of diabetic and control rats.

	12 week			24 week			*36 week*		
	DM	Control		DM	Control		DM	*Control*	
Number	5	2		2	3		2	*3*	
Blood Sugar	265.50 ± 92.63	84.50 ± 2.12		322.00 ± 33.94	84.33 ± 2.52		475.00 ± 35.00	*87.67 ± 4.73*	
Body Weight	*289.67 ± 38.45*	*260.00 ± 14.14*		*555.00 ± 7.07*	*383.33 ± 28.87*		*345.00 ± 7.00*	*466.67 ± 14.43*	

References

(1) Neural control of urethral outlet activity in vivo: Role of nitric oxide. J Urol 1995; 153:2004-9. (2) Urethral resistance and nitric oxide containing nerve in rats of Non-insulin dependent diabetes mellitus model. Neurourol Urodyn 19:412, 2000