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Title (type in CAPITAL LETTERS): PREJUNCTIONAL ALPHA-1 ADRENERGIC RECEPTORS INHIBIT NITRERGIC NEUROTRANSMISSION IN RABBIT URETHRA

Aims of Study

It has been confirmed that nitric oxide (NO) released from nitrergic nerve relaxes urethral smooth muscles (1, 2). Recent studies have shown that the release of NO from vasodilator nerve can be inhibited through prejunctional either muscarinic or alpha adrenergic receptors in several vascular vessels (3, 4). However no evidence is available about prejunctional modulation of nitrergic neurotransmission in urethral smooth muscles. The purpose of the present study was to investigate whether prejunctional alpha adrenergic receptors influence neurogenic relaxation of rabbit urethral smooth muscle.

Methods

Female New Zealand white rabbits weighing 2.5 kg were killed by exanguination after intravenous injection of sodium pentobarbital. The urethra were removed out through an abdominal midline incision. The urethral strip was suspended in a 20 ml muscle bath filled with Krebs-Henseleit solution, was connected to an isometric force displacement transducer, and an isometric tension development was recorded. Electrical field stimulation (EFS) (0.5 msec pulse duration, 0.1-15 Hz and 3 sec train) was applied to urethral preparations precontracted with 0.1 μM endothelin-1. The microdialysis probe (O-P-100-10, Eikom, Kyoto, Japan) was inserted into the strip. Krebs-Henseleit solution was perfused into the probe at a rate of 2 μl/min. The dialysate during EFS (0.5 msec pulse duration, 7 Hz, 3 sec train and 1 min interval for 10 min) was collected. A volume of 10 μl of the each sample was injected into the NO_x analyzer, and the amount of NO_2^-/NO_3^- released in the dialysate was measured based on the Greiss method, as reported previously (5). The effects of alpha adrenergic antagonists (prazosin and yohimbine) on the relaxation responses and NO_2^-/NO_3^- releases induced by EFS were eveluated.

Results

In the presence of guanethidine (10 μM) and atropine (1 μM), EFS caused relaxation responses and NO_2^-/NO_3^- releases in the rabbit urethral strips precontracted with endothelin-1. The relaxation responses and NO_2^-/NO_3^- releases were significantly inhibited in the presence of L-NNA (100 μM) or tetrodotoxin (1 μM). Pretreatment with

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prazosin (0.01 - 1 μM) and yohimbine (0.1 - 10 μM) did not cause significant effect on endothelin-1-induced contractions in the rabbit urethral strips. Pretreatment with prazosin caused dose-dependent increases in the relaxation responses and NO_2^-/NO_3^- releases induced by EFS in the rabbit urethral strips. While, pretreatment with yohimbine decreased the relaxation responses and NO_2^-/NO_3^- releases induced by EFS (Table 1).

Table 1 Effects of prazosin (1 μM) and yohimbine (10 μM) on EFS-induced relaxation responses and NO_2^-/NO_3^- (NOx) releases in the rabbit urethra

	Maximum relaxation (%)		NOx release (pmol/g urethra)	
	Control	Treatment	Control	Treatment
Prazosin	65.8±2.3	87.5±1.42*	28.2±3.5	42.5±5.6*
Yohimbine	68.5±3.0	45.2±1.23*	32.1±2.9	24.5±2.2*

* Significantly different from the comparable value for control ($p < 0.05$).

Conclusions

The present data suggest that the relaxation responses mediated by NO released from nitrergic nerve in the rabbit urethra are enhanced and inhibited by blockade of prejunctional alpha-1 and alpha-2 adrenergic receptors, respectively.

References

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