

THE RELAXING EFFECT OF ACETYLCHOLINE ON PHENYLEPHRINE-INDUCED CONTRACTION OF ISOLATED RABBIT PROSTATE STRIPS IS MEDIATED BY NEURONAL NITRIC OXIDE SYNTHASE (NITRERGIC NERVE)

Hypothesis / aims of study

The colocalization of nitrergic nerves with cholinergic nerves, and the cotransmission of nitric oxide with acetylcholine in cholinergic nerves, have been demonstrated in prostate glands of various species. These findings suggest that nitric oxide may act both as a cholinergic transmitter and as a modulator of neurotransmission in prostate stroma. Thus, in this study we investigated the correlation between cholinergic transmission and nitric oxide synthase in isolated rabbit prostate strips.

Study design, materials and methods

Prostates isolated from male rabbits weighing approximately 4-6 kg were used in organ bath studies. We investigated the relaxation effect of acetylcholine on phenylephrine-induced contraction of isolated strips. Changes in acetylcholine-induced relaxation after preincubation with L-NAME (nonspecific nitric oxide synthase inhibitor), 7-nitroindazole (selective neuronal nitric oxide synthase inhibitor), and aminoguanidine (irreversible inducible nitric oxide synthase inhibitor) were measured in these preparations. The effects of cholinergic antagonists (hexamethonium, atropine), and selective muscarinic receptor antagonists (pirenzepine, AF-DX116, 4-DAMP, and tropicamide) were also evaluated.

Results

. Acetylcholine dose-dependent treatment did not elicit any marked response in the resting states of the experimental strips, but evoked considerable relaxation in the phenylephrine-contracted state. Acetylcholine-induced relaxation was inhibited not only by nitric oxide synthase inhibitors (10 μ M L-NAME or 10 μ M 7-nitroindazole) but also by 10 μ M atropine and some selective muscarinic receptor antagonists (10⁻⁶ M AF-DX116 and 10⁻⁸ M 4-DAMP). By contrast, relaxation was significantly increased by pretreatment of strips with 10 mM L-arginine.

Interpretation of results

The involvement of NO in Ach-induced relaxation in the present study appears apparent. NO may act directly as a transmitter to cause relaxation of smooth muscle, or indirectly as a modulator by facilitating the release of other transmitters that cause relaxation. We identified two of four selective muscarinic receptor antagonists, M₂ and M₃, that inhibited acetylcholine-induced relaxation.

Concluding message

Acetylcholine relaxes the phenylephrine-induced contraction of isolated rabbit prostate strips. This relaxation may be mediated by both muscarinic cholinergic and neuronal nitric oxide synthase pathways. M₂ and M₃ receptors are thought to play key roles in this mechanism.

References

1. Dixon JS, Jen PY and Gosling JA: The distribution of vesicular acetylcholine transporter in the human male genitourinary organs and its co-localization with neuropeptide Y and nitric oxide synthase. *NeuroUrol Urodyn.* 19: 185-94, 2000.

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