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Title: THE ROLE OF PREJUNCTIONAL BETA-ADRENERGIC RECEPTORS ON ACETYLCHOLINE RELEASE IN ISOLATED HUMAN BLADDER

Aims of Study:

It has been confirmed that norepinephrine released from sympathetic nerve endings play an important role in relaxation of bladder smooth muscle throgh β-adrenoceptors. However, there is no information available on the role of β-adrenergic receptor in prejunctional site of cholinergic nerve ending. Therefore, in the present study, we evaluated the effects of β-adrenergic receptors on ACh release and contractile response induced by electrical field stimulation (EFS) in human isolated bladder smooth muscles, using microdialysis procedure and high-performance liquid chromatography (HPLC) with electrochemical detection (ECD) (1).

Methods:

Bladder smooth muscle strips obtained from patients who undergo radical cystectomy for bladder carcinoma mounted in the 20 ml thermostatically controlled organ baths filled with modified Krebs-Henseleit solution. Each muscle strip was connected to a force displacement transducer, and isometric tension was recorded. The microdialysis probe (O-P 100-10, Eicom, Kyoto, Japan) was inserted through the muscle strip, and the inlet cannula of the prove was connected to a microinfusion syringe pump. Ringer (pH 7.4) containing 100 μM physostigmine sulfate was continuously perfused at a rate of 2 μl/min. EFS (supramaximun voltage, pulse duration 0.5 ms, frequency 20 Hz, train of pulse 2 s and stimulation interval 2 min) was applied to muscle strips, and tension developments were recorded.

The dialysate from microdialysis probe during EFS was collected, and a volume of 10 μl was injected into the ACh assay system. The amount of ACh in the dialysate fraction was mesured by HPLC with ECD as proviously reported (1). The effects of pretreatment with isoproterenol (non-selective β-agonist; 0.1 - 100 μM) and propranolol (non-selective β-antagonist; 0.1 - 100 μM) on the contractile responses and ACh releases induced by EFS were evaluated.

Results:

EFS caused contractile response and ACh release in human detrusor smooth muscle. Pretreatment with tetrodotoxin almost completely suppressed EFS-induced contractile response and ACh release. Pretreatment with isoproterenol caused cocentration dependent decrease in EFS-induced ACh releases and contractile responses. The maximum decrease rates were about 40% and 15% of the control, respectively. On the other hand, the pretreatment with propranolol increased the ACh releases dose dependently, but did not have effects on the contractile responses.

Conclusions:

The data suggest that there are prejunctional β-adrenoceptors and that the stimulation of prejunctional β-adrenoceptor may inhibit EFS-induced ACh release from cholinergic nerve endings in human isolated bladder smooth muscles.

References,

1. Life Sci., 62, PL 393-399, 1998.