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CONTRACTILE ROLE OF ENDOTHELIN ETA AND ETB RECEPTOR IN THE GUINEA-PIG URINARY BLADDER

Aims of Study

The endothelins (ETs) have a variety of biological activities both in cardiovascular and non-cardiovascular tissues including the urinary tract [1]. The action of ETs is mediated through at least two distinct subtypes of receptors, termed the endothelin ET_A and the endothelin ET_B receptors. Radioligand binding experiments showed the presence of the endothelin ET_A and ET_B receptors in the rabbit and the rat urinary bladder. But the functional role of endothelin ET_B receptor in the urinary bladder is unclear. There are conflicting observation about the contractile effect of endothelin-1 (ET-1) in the guinea-pig urinary bladder, showing the weak contractile response induced by ET-1 [2] and no effect on the basal muscle tone and the response to transmural nerve stimulation [3]. The present study was designed to clarify the distribution and the function of the endothelin receptors in the guinea-pig urinary bladder.

Methods

Male guinea-pigs (450-600g) were killed by cervical dislocation. Detrusor strips (2×10mm) were prepared from the dome of the urinary bladder.
The concentration of ET-1 in the muscle layer and the mucosa was determined using ET-1 ELISA kit.
The tissue was immediately frozen in isopentane. 20μm-thick sections were cut in a cryostat, thaw-mounted onto gelatin-coated slides. And the distribution of [^{125}I]ET-1 binding sites was examined by in vitro receptor autoradiography.
The preparations removed mocosa were placed in 20ml organ baths containing Kebs-Ringer solution. Mechanical responses were recorded by means of an isometric transducer. The effects of ET-1 and sarafotoxin S6c on the basal tension and on the twitch contractions evoked by electrical field stimulation (EFS) were examined in the absence and presence of antagonists for endothelin receptors.

Results

The concentration of ET-1 in the muscle layer and the mucosa was 707.5±67.5 pg/g wet weight and 1367.7±95.0 pg/g wet weight, respectively.
[^{125}I]ET-1 binding sites were distributed in the muscle layer. BQ123 at 2×10^{-7} M, a selective endothelin ET_A receptor antagonist diminished the number of the binding sites of [^{125}I]ET-1 in the muscle layer by about 25%, and BQ788 at 2×10^{-7} M, a selective endothelin ET_B receptor antagonist reduced it in the muscle layer by about 61%. Additon of both the antagonists almost abolished the [^{125}I]ET-1 binding.
ET-1 caused a concentration dependent tonic contraction and potentiated the amplitude of twitch contractions induced by EFS. BQ123 at 10^{-6} M significantly reduced the ET-1-induced response. BQ788 at 10^{-6} M little reduced the response to ET-1. Combined treatment with BQ123 and BQ788 reduced more strongly the response to ET-1 than the case of the treatment with BQ123 alone. Sarafotoxin S6c, a selective agonist of endothelin ET_B receptor produced a little but significant contraction and potentiated the amplitude of twitch contraction induced by EFS. The responses to sarafotoxin S6c were completely inhibited by BQ788 at 10^{-6} M.

Conclusions

ET-1 and both the endothelin ET_A and ET_B receptors exist in the detrusor smooth muscle of guinea-pig urinary bladder. ET-1 plays a role in the regulation of the muscle tension of guinea-pig urinary bladder through autocrinal system via not only the endothelin ET_A but also the endothelin ET_B receptor.

References

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