MUSCARINIC AND PURINERGIC RECEPTORS ARE ALTERED IN THE BLADDER OF RAT MODELS WITH INTERSTITIAL CYSTITIS

Study design, materials and methods

The rat models with interstitial cystitis were induced by the intravesical instillation of 0.4 N HCl (0.2 ml) and by the intraperitoneal injection of CYP (75 mg/kg) every third day for a total of four injections. The mechanical responses of bladder in these rats were monitored by the cystometric method under anaesthesia. Then, rats were sacrificed by the exsanguination from descending aorta, and the bladder was excised. Muscarinic and purinergic (ATP) receptors in the bladder homogenates were measured by measuring specific binding of [3H]NMS and [3H]-methylene ATP ([3H]-MeATP), respectively, using specific radioligands, [N-methyl-3H]scopolamine ([3H]NMS) and [3H] -methylene ATP ([3H]-MeATP), respectively.

Results

Compared with that of control rats, the body weight of HCl-pretreated rats was similar and that of CYP-pretreated rats was significantly increased. In addition, the bladder weights of both HCl- and CYP-pretreated rats were significantly increased. In the cystometry of HCl-pretreated rats, there were significant decreases of micturition intervals and micturition volumes and also marked increase in the frequency of micturition. Similarly, the cystometry of CYP-pretreated rats showed significant decreases of micturition intervals and micturition volumes with a marked increase in the frequency of micturition. The Bmax values for specific [3H]NMS binding were significantly (55% and 43%, respectively) decreased in the bladder of both HCl- and CYP-pretreated rats compared with control rats (Fig. 1). Similarly, there were significant decreases (72% and 31%, respectively) of Bmax for specific [3H] -MeATP binding in the bladder of both HCl- and CYP-pretreated rats compared with control rats. On the other hand, Kd values for specific binding of [3H]NMS and [3H] -MeATP in the bladder were not significantly altered by the treatment with HCl and CYP (Fig. 1). Furthermore, The identification of subtypes of muscarinic and ATP receptors and measurement of ATP release in the bladder of these control and cystitis-induced rats are under way.

Interpretation of results

These data suggest that pretreatment with HCl and CYP in rats causes significant increase in the bladder weight and significant decrease in the density of ligand binding sites of not only muscarinic receptors but also ATP receptors in this tissue, accompanied by the decreases of micturition intervals and micturition volumes and by the increase in the frequency of micturition.
Fig. 1. Muscarinic (upper panel) and ATP (lower panel) receptor densities (Bmax) in the bladder of sham rats and HCl- or CYP-induced cystitis rats.

Concluding message
The present study has provided the first evidence to suggest that muscarinic and ATP receptors in the bladder may be at least partly involved in the pathophysiology of interstitial cystitis.

References:

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