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EFFECT OF ESTROGEN ON CYCLIC AMP CONTENTS IN CULTURED HUMAN BLADDER SMOOTH MUSCLE CELLS

AIMS OF STUDY

Estrogen has been shown to influence morphology and function of the lower urinary tract smooth muscles In female rabbit detrusor smooth muscles, our previous studies demonstrated that estrogen treatment caused the increased relaxant responses mediated by ß2- and ß3- adrenergic receptor subtypes, which might be related to the increased cAMP content induced by change in the biochemical property of the catalytic unit of adenylate cyclase (Urol Res., in press) Although the presence of estrogen receptors has been demonstrated in the human lower urinary tract, there is few information about the effect of estrogen on ß-adrenergic receptor-adenylate cyclase system in human urinary bladder Therefore, the present study was undertaken to determine the effect of estrogen on intracellular cyclic AMP (cAMP) contents in cultured human bladder smooth muscle cells.

METHODS

Specimens of human urinary bladder were obtained from 8 postmenopausal women who underwent total cystectomy due to malignant bladder tumor Human bladder smooth muscle cells were isolated by collagenase dissociation and cultured in serum-free D-MEM/F-12 medium with or without 17ß-estradiol (0 1 nM-0 1 μM) for 72 hours Intracellular cAMP contents in human bladder smooth muscle cells cultured in each medium during incubation with isoproterenol (non-selective ß-adrenergic receptor agonist), dobutamine (ß1-adrenergic receptor selective agonist), procaterol (ß2-adrenergic receptor selective agonist) or GS-332 (ß3-adrenergic receptor selective agonist) were measured by radioimmunoassay The effects of forskolin, which increases cAMP contents by interaction at the catalytic unit of adenylate cyclase without stimulating ß-adrenergic receptors, on the intracellular cAMP contents were also evaluated

RESULTS

Isoproterenol (0 1 nM-1 μM), procaterol (0 1 nM-1 μM), GS-332 (0 1 nM-1 μM) and forskolin (0 1-30 μM) caused concentration-dependent increases in cAMP contents, and dobutamine (0 1 nM-1 μM) did not caused in human bladder smooth muscle cells cultured in medium without 17ß-estradiol When cells were cultured in medium with 17ß-estradiol, isoproterenol, procaterol, GS-332 and forskolin caused increases in cAMP contents, which were significantly greater as compared with cells cultured in medium without 17ß-estradiol Furthermore, 17ß-estradiol in the medium increased cAMP contents in human bladder smooth muscle cells in a concentration dependent manner

CONCLUSIONS

The present study demonstrated that ß2- and ß3- adrenergic receptor stimulation activated adenylate cyclase and increased cAMP contents, and that estrogen treatment enhanced the cAMP production in bladder smooth muscle cells isolated from postmenopausal women These results suggest that estrogen treatment may promote cAMP-dependent relaxations in postmenopausal human bladder.

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