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Abstract Reproduction Form B-1

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Title (type in CAPITAL LETTERS): **EFFECTS OF OVARIAN HORMONES ON ß-ADRENERGIC RECEPTOR-MEDIATED RELAXATIONS IN THE FEMALE RABBIT BLADDER**

AIMS OF STUDY

Ovarian hormones have been shown to influence morphology and function of the lower urinary tract smooth muscles. Although an increase in ß-adrenergic receptor responsiveness with estrogen treatment has been reported in several tissues including myometrium and blood vessels, there is few information about the effects of ovarian hormones on ß-adrenergic receptor-mediated relaxations of urinary bladder. ß-Adrenergic receptors have now been classified by pharmacological and molecular biological studies into 3 subtypes: ß1, ß2 and ß3, and several reports have demonstrated the presence of ß-adrenergic receptor subtypes in the lower urinary tract smooth muscles. Therefore, the present study was undertaken to determine the effects of ovarian hormones on the relaxations induced by various ß-adrenergic receptor selective agonists in female rabbit detrusor smooth muscles.

METHODS

Ovariectomized mature female New Zealand white rabbits were untreated or treated with estrogen (0.1 mg/kg/day) and/or progesterone (1 mg/kg/day) for 2 weeks. The sham operated rabbits were prepared as control. Using muscle bath technique, the relaxations to isoproterenol (non-selective ß-adrenergic receptor agonist), dobutamine (ß1-adrenergic receptor selective agonist), procaterol (ß2-adrenergic receptor selective agonist) and GS-332 (ß3-adrenergic receptor selective agonist) on 80 mM KCl-induced tonic contractions were measured in the detrusor strips from all groups. The effects of forskolin, which increases cyclic AMP (cAMP) content by interaction at the catalytic unit of adenylyl cyclase, and dibutyryl cyclic AMP (DBcAMP), which is a cell permeable cAMP analogue, on KCl-induced tonic contractions were also evaluated. Furthermore, the cAMP content increased by various ß-adrenergic receptor selective agonists were measured by RIA in the detrusor strips from all groups.

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RESULTS

The contractile responses to carbachol and KCl in the detrusor strips were not significantly different in all groups. Isoproterenol (0.1 nM-1 μM) and procaterol (0.1 nM-1 μM) significantly relaxed the detrusor strips from all groups on KCl-induced tonic contractions, as compared with dobutamine (0.1 nM-1 μM) and GS-332 (0.1 nM-1 μM). Ovariectomy caused a significant decrease in the relaxations to isoproterenol, procaterol, GS-332 and forskolin (0.1-30 μM), and the cAMP production induced by isoproterenol (10 μM), procaterol (10 μM) and GS-332 (10 μM). Estrogen treatment after ovariectomy returned these parameters to the control values. However, ovariectomy and estrogen treatment did not affect the relaxations to DBcAMP (0.1-3 mM). Progesterone treatment after ovariectomy did not affect ß-adrenergic receptor-mediated responses.

CONCLUSIONS

The present study 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 adenylyl cyclase in female rabbit detrusor smooth muscles. These results may support the usefulness of estrogen for the therapy of urinary incontinence in postmenopausal women. On the other hand, progesterone treatment did not affect ß-adrenergic receptor responsiveness in female rabbit detrusor smooth muscles. Since progesterone reduces estrogen-induced endometrial proliferation, a combination of progesterone with estrogen would seem fevorable on the therapy.

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