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RELAXANT EFFECTS OF ACUTE ADMINISTRATION OF ESTRADIOL THROUGH NON-ESTROGEN RECEPTOR MECHANISMS ON MALE AND FEMALE URINARY BLADDER CONTRACTILITY

Hypothesis / aims of study

The precise effect of estrogen levels on urinary bladder contractility remains controversial [1]. Furthermore, it is not clear whether the effect of 17-beta-estradiol on bladder smooth muscle contraction is mediated by the nuclear estrogen receptor [2]. Thus, the present study was designed to analyse the effect of acute administration of 17-beta-estradiol in bladder smooth muscle and the involvement of specific estrogen receptor stimulation in this effect.

Study design, materials and methods

Male and female pig detrusor strips were mounted for tension recording in an organ bath, super fused with Krebs solution at 37°C and stimulated electrically and pharmacologically. Mechanical responses were recorded using an isometric force transducer. Responses to cumulative concentrations of 17-beta-estradiol (1, 10, 30 µM) were obtained in strips pre contracted with 100 mM potassium chloride, 10-µM acetylcholine chloride and electro-stimulation. For comparison, the effect of the DMSO at the same concentrations was evaluated (the cumulative concentration was, at the most, 0,1% of total). The involvement of estrogen receptor in the effects of 17-beta-estradiol was assessed by incubating some strips with the selective estrogen receptor antagonist ICI 182.780 before estradiol to be placed (in equimolar doses). Data were expressed as the mean ± standard error of the mean. Student's t-test was used to determine the statistical significance at the 0.05 levels.

Results

Estradiol at dose of 30 µM elicited significant relaxation of electrically and pharmacologically contracted female and male strips. Pretreatment with the pure estrogen receptor antagonist had no effect on 17-beta-estradiol-induced relaxations.

Table: Mean force in seven male and female pig detrusor strips after different stimuli.

	Maximum force (microNewton)					
	Ach		*ES*		*KCl*	
	Female	*Male*	*Female*	*Male*	*Female*	*Male*
Control	650	634	979	973	430	378
Estradiol 30µM	264*	261*	143*	172*	43**	38**
Antagonist estradiol 30µM + Estradiol 30 µM	182*	223*	290*	189*	39**	41**

* *p* value less than 0,05 vs control ** *p* value less than 0,05 vs control and Ach stimulus

Interpretation of results

We have demonstrated that 17-beta-estradiol induces muscle relaxation of female as well as male pig detrusor which is not mediated by the classic estrogen receptor. In the light of these results, we can say that estradiol has a stronger inhibitory effect on the depolarization of muscle cell membrane compared to the muscarinic receptor-operated contraction. Estradiol might therefore have a direct effect on depolarization operated calcium channels.

Concluding message

In conclusion, we speculate that under our conditions estrogen may act through a non-genomic pathway, most likely via cell membrane receptors which are not inhibited by ICI 182.780. Furthermore, the possible role of K(+) channel deactivation in the inhibition of contraction induced by 17-β-estradiol in pig bladder provides a new approach to further research into the treatment of detrusor overactivity.

Reference

1. The effect of ovariectomy and estradiol on rabbit bladder smooth muscle contraction and morphology. J Urol 2003, 170:634-637.
2. Sequence and expression of human estrogen receptor complementary DNA. Science 1986, 231:1150-1154.