

## RELAXANT EFFECTS OF ESTRADIOL THROUGH NON-GENOMIC PATHWAYS IN MALE AND FEMALE PIG BLADDER SMOOTH MUSCLE: INSIGHTS INTO THE TREATMENT OF THE OVERACTIVE BLADDER SYNDROME

### Hypothesis / aims of study

Estrogen has a multitude of biological effects that may account for its apparent benefits on the urinary tract (which remain to be proved in randomized clinical trials) including favorable effects on smooth muscle of both bladder and urethral vasculature [1, 2]. However, there are considerable contradictory data published in the literature on the specific effects of estrogen administration on bladder contractility [1, 3].

The present study was designed to analyse the effect of 17- $\beta$ -estradiol in bladder smooth muscle contractility and the involvement of specific estrogen receptor stimulation in this effect.

### Study design, materials and methods

Castrated male and female pig detrusor strips were mounted for tension recording in an organ bath, superfused with Krebs solution at 37°C and stimulated electrically and pharmacologically. In order to verify the acute effect of 17- $\beta$ -estradiol on muscle contractility the strips were incubated with different concentrations of the hormone. Muscle contractions were induced by potassium chloride, acetylcholine chloride and electrical field-stimulation. The involvement of the estrogen receptor in the effects of 17- $\beta$ -estradiol was assessed by incubation of some strips with the selective estrogen receptor antagonist ICI 182.780 before estradiol was applied.

Data are expressed as means  $\pm$  standard error of the mean, when appropriate. Differences of maximal force and time constant between pre and post-treatment were evaluated with SPSS 8.0 for Windows using Student's paired *t*-test. The level of significance chosen was 95% ( $p < 0.05$ ).

### Results

Estradiol at a dose of 30  $\mu$ mol/l elicited a lower amplitude of contractions induced by EFS, Ach and KCl in female as well as in castrated male pig bladder smooth muscle strips. The effects of 17- $\beta$ -estradiol were stronger in contractions induced by potassium chloride than those induced by other forms of stimulation. Pre-treatment with the pure estrogen receptor antagonist had no effect on 17- $\beta$ -estradiol-induced inhibition of muscle contractility.

### Interpretation of results

These observations suggest that 17- $\beta$ -estradiol induces lower amplitude of contraction of female as well as castrated male pig detrusor which is not mediated by the classic estrogen receptor. Furthermore, we can conclude that estradiol has a stronger inhibitory effect on the depolarisation of muscle cell membrane compared to a muscarinic receptor-induced contraction. Furthermore, the possible role of potassium channel deactivation in the inhibition of contraction induced by 17 beta estradiol in pig bladder provides a new approach to further research into the treatment of detrusor overactivity.

### 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- $\beta$ -estradiol in pig bladder provides a new approach to further research into the treatment of detrusor overactivity.

### References

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