Flutamide-induced alterations in CYP17A1 gene expression and local testosterone synthesis in porcine luteal tissue - a new insight into androgens action during pregnancy

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INTRODUCTION

BACKGROUND: The corpus luteum (CL) is an ephemeral endocrine gland, which primary function is secretion of progesterone (P4). The pig is a particularly interesting model, because porcine CL is required to support pregnancy throughout the entire gestational period and it is the major source of P4. The cytochrome P450 17α-hydroxylase/17,20-lyase (CYP17A1) was found in small luteal cells from day 50 of gestation, indicating the potential sites of androgen synthesis. To date, it was established that androgens are able to modulate luteal function during pregnancy by stimulation of CL to P4 release.

HYPOTHESIS: Androgens are a new important factor, which might be involved directly or indirectly in the CL functioning and maintenance of pregnancy in pigs.

AIM OF THE STUDY: To determine whether mid- and late gestational exposure to the anti-androgen flutamide influences CYP17A1 gene expression in the luteal tissue and the local testosterone (T) synthesis in pigs.

RATIONALE: Our strong motivation to undertake this endeavor is explained by negative effects of environmental compounds, such as anti-androgens (fungicides, herbicides), which interfere with the action of endogenous hormones and disrupt animal fertility.

METHODS

Real-time PCR: analysis of CYP17A1 mRNA expression with TaqMan Gene Expression Assay (Applied Biosystems)

Immunohistochemistry: CYP17A1 localization using anti-CYP17A1 antibody (1:100; gift from prof. Dale B. Hales from Southern Illinois University, Carbondale, USA)

Radioimmunoassay (RIA): testosterone (T) concentration in homogenates from CLs

RESULTS

Analysis of CYP17A1 mRNA expression by real-time PCR

Radioimmunological analysis of T level

Immunohistochemical localization of CYP17A1

CONCLUSIONS

In conclusion, androgen deficiency during mid- and late pregnancy in pigs following antiandrogen flutamide administration affects luteal T synthesis in CLs. The observed changes in T production are probably the consequences of altered CYP17A1 gene expression. However, we found different regulation depending on the day of pregnancy. Because T undergoes further conversion to estradiol, a steroid hormone important before parturition, the altered T level might subsequently affect estradiol concentration.

Obtained results confirm our hypothesis that androgens are important factors regulating the maintenance of pregnancy in pigs.

Supported by the National Science Center a grant No. (2011/03/D/NZ4/00303).