ANDROGEN AND ESTROGEN IMBALANCE AFFECTS FOLLICULOGENESIS IN THE NEONATAL PORCINE OVARY INFLUENCING CELL PROLIFERATION AND APOPTOSIS

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Objective: Disruption of signalling pathways regulated by androgens and estrogens at early stages of folliculogenesis may reveal factors that are involved in the mechanism responsible for its delay or acceleration. Endocrine-active chemicals (EACs) with androgenic/antiandrogenic and estrogenic/antiestrogenic activity may interfere with the natural regulation of endocrine systems affecting the normal process of folliculogenesis. Our research hypothesis was that the balance between androgens and estrogens level is indispensable during neonatal follicles formation and transition to the primary stage. Thus, the objective of the study was to elucidate the impact of EACs on the follicle formation as well as proliferation and apoptosis within neonatal porcine ovaries.
Design: A total of 24 neonatal female pigs were randomly divided into six groups.
Materials and Methods: Animals were injected with testosterone propionate (TP), flutamide (Flu), 4-tert-octylphenol (OP), ICI 182,780 (ICI) or methoxychlor (MXC) between days 1 to 10 postpartum (n = 4 per each group). TP, Flu, OP, ICI and MXC were suspended in corn oil with DMSO and the following doses were used: 20 mg/kg body weight (bw), 50 mg/kg bw, 100 mg/kg bw, 400 µg/kg (bw) and 100 mg/kg bw, respectively. Control animals were treated with corn oil with DMSO. The ovaries were collected from 11-day-old pigs and histological examination were conducted by hematoxylin & eosin staining and the number of follicles at each developmental stage were evaluated. Cell proliferation within the ovaries was performed by analysis of proliferating cell nuclear antigen (PCNA)-positive cells (immunohistochemistry). Cell apoptosis within the ovaries was done by identification of apoptotic cells by ApopTag® Peroxidase In Situ Apoptosis Detection Kit. To examine the differences between control and investigated compounds-treated groups Mann-Whitney U test was used.
Results: Histological analysis revealed that in OP and TP groups the process of folliculogenesis was accelerated while in Flu, ICI and MXC groups was delayed. Analysis of proliferation index showed the increased number of follicles with PCNA-positive oocytes in OP group, and the decreased number in Flu and MXC groups. Results from apoptosis revealed no apoptotic cells in control and MXC groups, while in TP, Flu, OP and ICI groups the staining was present only in the individual cells.
Conclusions: A strong androgen and estrogen effect was noted, resulting in increased follicle recruitment. On the other hand, all antagonists used in the experiment had an ability to delay the process of follicle activation. It seems that compounds with hormonal activity revealed specific effects on folliculogenesis in neonatal porcine ovaries, characterized by changes in proliferation and apoptosis during follicular recruitment. These results suggest that any change in steroid hormones concentration during neonatal period may alter ovarian function in adulthood.
Support: National Science Centre, Poland (Grant No. 2015/17/B/NZ9/01457)