Journal Scan

Review: Fetal Programming of Polycystic Ovary Syndrome by Androgen Excess—Evidence from Experimental, Clinical and Genetic Association Studies

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ABSTRACT

Objective

Polycystic ovary syndrome (PCOS) is a common endocrine disorder of premenopausal women, characterized by hyperandrogenism, polycystic ovaries, and chronic anovulation along with insulin resistance and abdominal obesity as frequent metabolic traits. Although, PCOS manifests clinically during adolescence, emerging data suggest that the natural history of PCOS may originate in intrauterine life.

Evidence Acquisition

Evidence from experimental, clinical, and genetic research supporting the hypothesis for the fetal origins of PCOS has been analyzed.

Evidence Synthesis

Female primates, exposed *in utero* to androgen excess, exhibit the phenotypic features of PCOS during adult life. Clinical observations also support a potential fetal origin of PCOS. Women with fetal androgen excess disorders, including congenital 21-hydroxylase deficiency and congenital adrenal virilizing tumors, develop features characteristic of PCOS during adulthood despite the normalization of androgen excess after birth. The potential mechanisms of fetal androgen excess leading to a PCOS phenotype in humans are not clearly understood. However, maternal and/or fetal hyperandrogenism can provide a plausible mechanism for fetal programming of PCOS, and this, in part, may be genetically determined. Thus, genetic association studies have indicated that common polymorphic variants of genes determining androgen activity or genes that influence the availability of androgens to target tissues are associated with PCOS and increased androgen levels. These genomic variants may provide the genetic link to prenatal androgenization in human PCOS.

Conclusion

Prenatal androgenization of the female fetus induced by genetic and environmental factors, or the interaction of both, may program differentiating target tissues toward the development of PCOS phenotype in adult life.

Circulating Inflammatory Markers in Polycystic Ovary Syndrome: A Systematic Review and Meta-analysis

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ABSTRACT

Objective

To perform a review and meta-analysis of the studies evaluating the status of serum inflammatory markers in women with polycystic ovary syndrome (PCOS).

Design

Systematic review and meta-analysis of articles published in English before January 2010 and identified using the PubMed search engine.

Setting

Academic hospital.

Patient(s)

Women with PCOS and appropriate controls.

Intervention(s)

Measurement of serum concentrations of inflammatory markers by high-sensitivity techniques.

Main Outcome Measure(s)

Meta-analyses of the mean difference in serum C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) concentrations among patients with PCOS and appropriate controls, applying random-effects models to limit interstudy variability and using appropriate estimates of evidence dissemination bias.

Result(s)

Meta-analysis of the 31 articles meeting inclusion criteria showed that circulating CRP was 96% higher in women with PCOS compared to controls (95% confidence interval, 71%-122%; z = 7.32) without evidence of dissemination bias (Egger's regression intercept, 0.45; 95% confidence interval, –2.30 to 3.21). These findings persisted after excluding five studies with mismatches in body mass, frequency of obesity or both, between women with PCOS and controls. Meta-analyses involving 10 studies of IL-6, and nine studies of TNF-α revealed no statistically significant differences between PCOS and controls.

Conclusion(s)

Women with PCOS exhibit an elevation in circulating CRP that is independent of obesity. This finding corroborates existing molecular evidence of the chronic low-grade inflammation that may underpin the pathogenesis of this disorder.

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