Altered Steroid Metabolism and Insulin Signaling in PCOS Endometria: Impact in Tissue Function

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Resumen

Background: Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine/metabolic disorder characterized by hyperandrogenemia and in most cases, by hyper-insulinemia in addition to obesity. Besides ovarian dysfunction, endometrial physiology is also disrupted since this tissue is highly dependent on the action of steroids; in case of conception cycles, high percentage of abortion is observed. Because of the endocrine/metabolic alterations, PCOS-women present high probability to develop hyperplasia and endometrial cancer, where an imbalance of cell proliferation/apoptosis processes is detected. Additionally, insulin pathway and the endometrial energetic homeostasis are also compromised.

Methods: The aim of this review was to report molecular alterations related to insulin-resistance and/or obesity in PCOS-women endometria that could drive to infertility. For this, several methods were employed: immunohistocytocchemistry, qPCR, western-blot, glucose-uptake, cell cultures, among others.

Results: Diminished levels and activity of several insulin signaling pathway molecules, like IRS-1/AS160/PKC., were detected. Concomitantly, a defect in the synthesis and GLUT4 translocation to cell surface is induced. Oral administration of metformin (insulin sensitizer) to PCOS-patients increases GLUT4 endometrial levels, improving fertility of those patients. Another relevant feature is the high percentage of obesity in PCOS-women; adiponectin is an obesity marker and elicits an insulin-sensitizer action, being diminished in plasma of obese PCOS-women similar to its endometrial level, adiponectin-receptors and APPL1, an adapter molecule of adiponectin pathway. Moreover, obesity and PCOS can induce a pro-inflammatory environment, exaggerating the alterations in insulin pathway.
Conclusion: The evidences obtained in PCOS-endometria clearly indicate that these molecular defects could partially explain the reproductive failures of these patients.

Palabras clave

Palabras clave de autor: PCOS; endometria; insulin; hyperandrogenism; adiponectin; obesity; glucose-uptake

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