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P69. Insulin and the Down-regulation of Glucose Transporter 1 in Decidualizing Endometrial Stromal Cells

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Context: Glucose transporter (GLUT) 1 is the most abundant glucose transporter in the endometrium. Low glucose levels inhibit decidualization, a progesterone-dependent differentiation of endometrial stromal cells. Successful decidualization is necessary for establishment and maintenance of pregnancy. Hyperinsulinemia is the presence of higher than normal levels of blood insulin relative to blood glucose levels. The most common disorders characterized by hyperinsulinemia are obesity and polycystic ovary syndrome.

Objective: This study aims to evaluate how chronic hyperinsulinemia affects the expression of GLUT1 in decidualizing endometrial stromal cells and whether this effect results in altered glucose uptake.

Methods: We induced in vitro decidualization of endometrial stromal cells in the presence and absence of insulin. mRNA level of GLUT1 was measured by Real-Time PCR. Involvement of the transcription factor forkhead box O1 (FOXO1) and PI3K pathway were evaluated by the use of FOXO1/PI3K inhibitors. The effect of insulin on glucose uptake was also determined.

Patients: 6 regularly menstruating healthy non-obese women.

Results: Insulin down-regulates the expression of GLUT1 mRNA in a dose-dependent manner in decidualizing endometrial stromal cells. We have confirmed that down-regulation of GLUT1 is mediated via the transcriptional inactivation of FOXO1 and is conveyed partly through the PI3K pathway. Glucose uptake was decreased by insulin in 50% of the subjects.

Conclusions: Insulin might inhibit the expression of GLUT1 and reduce the glucose uptake of endometrial stromal cells. Our previous studies show that the morphological transformation of endometrial stromal cells into decidual cells does not seem to be inhibited by insulin. However, the decreased glucose utilization might influence the metabolism of the cells and thereby affect endometrial function. The nature of these effects is a subject of our ongoing studies.

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