LIFESTYLE INTERVENTION UP-REGULATES GENE AND PROTEIN LEVELS OF MOLECULES INVOLVED IN INSULIN SIGNALING IN THE ENDOMETRIUM OF OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME

D. Ujvari

There is increasing evidence that the endocrine abnormalities in polycystic ovary syndrome (PCOS) may have complex effects on the endometrium, contributing to implantation failure and miscarriage. However, little is known about the role of insulin signaling in the endometrium of women with PCOS. Our aim was to study the insulin signal transduction in proliferative endometrium of obese women with PCOS in response to lifestyle intervention and compare to controls. Groups of obese and normal-weight women fulfilling all the Rotterdam criteria of PCOS and groups of age and body mass index (BMI)-matched healthy controls participated in the study. Seventeen obese women with PCOS completed combined diet and exercise lifestyle intervention for three months. Endometrial biopsies were collected at menstrual cycle day 6-8 and gene expression levels and immunohistochemical staining of insulin signaling pathway molecules were analyzed.

Women with PCOS exhibited significantly lower levels of IRS1 and GLUT4 mRNA in their proliferative endometrium than BMI-matched controls. After 3 months of lifestyle intervention menstrual pattern was clearly improved in 65% of obese PCOS women. BMI and fasting insulin levels were reduced significantly. Levels of IRS1 and GLUT1 mRNA were significantly up-regulated in women with improved menstrual function, as well as protein expression of several insulin signaling molecules. Serum level of SHBG, gene expression level of IRS1 and decrease of BMI and serum level of estradiol correlated to improved menstrual function. Since lifestyle intervention up-regulates, both at the mRNA and protein levels, components of insulin signaling in the endometrium of obese PCOS women in relation to improved menstrual pattern, endometrial insulin signaling appears to play an important role in endometrial function in PCOS.