Reproductive Endocrinology

REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

Intermediate Hyperglycemia and Type 2 Diabetes in Women with Polycystic Ovary Syndrome: Findings from Large Caucasian Cohort.

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Background: Insulin secretory defects and insulin resistance exists in women with polycystic ovary syndrome (PCOS) and are prerequisites for the development of type 2 diabetes (T2D). Objective: To determine the prevalence of T2D, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), as well as the factors associated with these dysglycemic conditions. Participants: 1614 women with PCOS of Caucasian origin (Rotterdam criteria) with a mean age 25.14±5.56 years and BMI 27.34±7.09 kg/m^2 comprised the study group, whereas 359 normally ovulating, not hyperandrogenic women of comparable age and BMI, served as controls. Design: Observational study. Setting: Outpatient clinics of tertiary hospitals. Main Outcome and Measures: Clinical, biochemical, hormonal and ovarian ultrasound as well oral glucose tolerance test were performed in all subjects participating in the study. Diabetes and intermediate hypeglycemia was categorised according to WHO criteria and PCOS subgroups was based on the Rotterdam criteria. Results: In the PCOS group 2.2%, 9.5% and 12,4% of subjects had T2D, IGT and IFG, respectively. In control group 1,11%, 7.5% and 8.9% had T2D, IGT and IFG, respectively. When the existence of T2D was stratified according to age and BMI, no difference was found among age and BMI subgroups or PCOS subgroups. Namely in patients aged 17-22 years, T2D was detected in 3 lean and 2 obese subjects. The corresponding distribution for patients aged 22-30 years was 4 lean, one overweight and 2 obese, whereas in those older than 31 years, 2 overweight and 5 obese suffered from T2D. Free Androgen Index (FAI), waist to hip ratio (WHR) and LDL levels were significantly higher in T2D subjects in comparison to PCOS women with normal glucose metabolism. Diagnosis of T2D was significantly associated with Free Androgen Index (r: 0.469, p<0.05), while subjects with either IFG and IGT had positive association with BMI, WHR, FAI and HOMA-IR. In controls, T2D, IGT and IFG were positively associated with BMI and androgen concentrations. Conclusions: The prevalence of T2D and IGT is significantly higher in our large cohort of PCOS women in comparison to controls. The existence of T2D is irrespective of age and BMI, and seems to be inherent for PCOS women. Hence, the evaluation of glycemic status in women with PCOS using OGTT is supported.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING II

Nuclear Corepressor; SMRT Acts as an Important Regulator for Both Beta-Oxidation and the Maturation of Myogenesis in Mouse C2C12 Cell

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Background: Silencing Mediator of Retinoid and Thyroid hormone receptors (SMRT; NCoR2) is a transcriptional corepressor which has been recognized as an important player in the regulation of hepatic lipogenesis and the somatic development in mouse embryo. SMRT protein is also widely expressed in the mouse connective tissues, for example adipocyte and skeletal muscle, and we recently reported that the mouse of global deletion of SMRT causes significant obesity which is independent from thyroid hormone signaling and thermogenesis. However, the tissue specific role of SMRT in skeletal muscle is still unelucidated. **Methods:** To clarify this, we took the gene targeting strategy for SMRT using CRISPR Cas9, and made the myogenic C2C12 clone which lacks SMRT protein (C2C12-SMRTKO; SKO). For this study, wild type C2C12 cell (WT) and SKO cell were cultured in differentiation medium (DMEM+2% horse serum) for 5-6 days, and analyses for gene expression compared two cell types were performed. **Results:** We found the significant up-regulations of muscle specific beta-oxidation related genes (ex. *Ppar delta*, *Ampk2*), and higher protein level of PGC-1A in the SKO cell, suggesting that SKO cell had similar gene profile to that of rodent skeletal muscle in the exercise test. On the other hand, confocal microscopic analysis showed SKO cell had decreased cell-fusion and loss of myotube, indicating that the morphology was similar to immature mouse myoblasts. Further gene analyses compared between WT and SKO cell demonstrated that SKO cell had higher expressions of myogenic markers;