

Anti-Mullerian Hormone Receptor Type II Gene Polymorphisms Similar Among Women With The Polycystic Ovary Syndrome (PCOS) And Controls

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Background

Polycystic ovary syndrome (PCOS) is associated with menstrual dysfunction, polycystic ovaries (PCO), hirsutism, and an increased risk of infertility. Polycystic ovaries, as evidenced by an increased proportion of primary follicles and a reciprocally decreased proportion of primordial follicles, and subsequent impairments in folliculogenesis are frequent findings in patients with PCOS. Primordial follicle growth is influenced by paracrine and endocrine factors including anti-mullerian hormone (AMH) and its receptor AMH receptor type II (AMHR2). Expression of AMH, an early follicle growth inhibitor, is normally low in primordial and primary follicles, increases to maximum levels in large preantral follicles and small antral stages, and then declines during final follicular maturation. Primordial and preantral follicles of PCOS patients have reduced AMH expression and sera of PCOS women have elevated levels of AMH. A study of the *AMHR2* gene showed that carriers of the *AMHR2* -482G allele had higher follicular phase E2 levels than non-carriers, suggesting a role for *AMHR2* in the regulation of FSH sensitivity in the human ovary. In addition, in granulosa cells of small follicles of PCOS patients, levels of *AMHR2* mRNA were higher in PCOS than in controls. Our group previously evaluated polymorphisms in the *AMH* gene and did not find relationships to fertility endpoints in PCOS patients.

Objective

The purpose of this study was to determine the role of the *AMHR2* gene as a candidate for PCOS and its component traits.

Materials and Methods

In a cohort of 287 White women with PCOS and 187 controls., we genotyped three *AMHR2* single nucleotide polymorphisms (SNPs: rs11170547, rs2002555, and rs11170553) selected based on Caucasian International HapMap data to maximize coverage of the gene. Haplotypes were also determined and evaluated. Association of SNPs and haplotypes with qualitative traits was evaluated using logistic regression; association with quantitative traits was evaluated using analysis of covariance, adjusting for age and BMI. Qualitative traits included PCOS, presence of severe oligomenorrhea, infertility, and parity. Quantitative traits analyzed included free and total testosterone, DHEAS, 17HP, SHBG, and FG score.

Results

We did not observe any genotype-phenotype or haplotype associations between *AMHR2* and any of the qualitative or quantitative traits listed above.

Conclusions

We were unable to confirm *AMHR2* as a genetic determinant of PCOS or a gene that influences the phenotype. We will continue to evaluate other related genes, specifically other members of the transforming growth factor beta superfamily, to determine if they may be associated with the dysfunction in folliculogenesis observed in PCOS patients

Support

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