Introduction and objective

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in adult women. Syndrome is characterised by hiperandrogenism, oligo/amenorrhoea and polycystic ovary morphology (PCOM) in ultrasound. Clinical signs of the syndrome usually start already during adolescent years. Non-classic congenital adrenal hyperplasia (NCAH), caused by several mutations in CYP21A2 (6p21.3) gene is the most common differential diagnosis for girls presented with symptoms of PCOS. It is diagnosed in 1/1000 women in reproductive age. NCAH is characterized with the same symptoms as PCOS, no specific clinical signs can usually be observed. Level of 17 – OH progesterone and AKTH stimulation test is the main diagnostic tool. Nevertheless, genetic testing provides more accurate diagnosis.

Objective: To assess prevalence of NCAH causing alleles among adolescent patients with PCOS.

Methods

40 adolescent patients at least two years after menarche attending paediatric gynecologist with PCOS according to Rotterdam criteria were included in the study. Hyperandrogenism was defined as Ferriman – Gallway score more than seven or elevated total testosterone (Total T), androstendione or DHEAS0 levels. DNA was extracted from venous blood using酚酚– chloroform method. Genetic variations in the CYP21A2 gene were tested by using standart Multiplex Ligation-dependent Probe Amplification test (SALSA MLPA probemix P050-C1 CAH, MRC Holland), according to methodology established by producers. Following CYP21A2 mutations were tested: Single nucleotide polymorphism (SNP) at 113 bp before the start codon; I2G sequence at 13 bp before exon 3; 8 bp deletion in exon 3 (del8bp; 706_713del8); I172N mutation in exon 4; V237E mutation in exon 6; M239K mutation in exon 6; F306+T mutation in exon 7. Research was approved by Central Medical Ethics Committee of Latvia.

Results

Median age of the study group was 16 (SD 1.4) years. Average score in Ferriman-Gallway (F-G) scale was 10.8 (SD 6.3). We detected pathogenic variants in CYP21A2 for four patients, that constitutes 10% of the tested alleles. All discovered variants were in heterozygous state, that does not establish definitive diagnosis of NCAH. Two patients had c.-113 A>G, I172N (rs6475) and other two I2G (rs6467). Characteristics of patients with established mutations are presented in Table1. MLPA testing results are showed in Figure 1. – 4.

Conclusions

As NCAH is one of the reasons for hiperandrogenism masked by clinical appearance of PCOS, genetical testing is an important tool to distinguish between these two conditions.

Prevalence of NCAH causing alleles among PCOS patients in our study was lower than in literature (usually around 10%). It could be because the test we used is designed to assess rather large rearrangements of DNA, further studies in this area are required in order to test minor DNA changes and less prevalent mutations.

Bibliography

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