Xbal and Pvull estrogen receptor alpha gene polymorphism and Y chromosome deletions in infertile vs. fertile men

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The most frequently studied single nucleotide polymorphisms are the Pvull (known as IVS1-397 T/C, or rs2234693; where the T and C allele are often reported as the p and P allele) and Xbal (also known as IVS1-351 A/G or rs9340799; where the A and G allele are often reported as the x and X allele) both located in intron 1 of the ESR1. ESR1 Xbal polymorphism was suggested to have an effect on azoospermia or severe oligospermia in males.

Objective: The aim of this study was to determine the frequencies of estrogen receptor α (ESR1) Pvull and Xbal polymorphisms and Y chromosome deletion in infertile Romanian patients and to investigate their involvement in male infertility.

Subjects and methods: The study was carried out on 49 infertile men, aged between 20 and 50 years, divided into three groups, based on spermatogenic parameters: group 0 men with azoospermia (17 subjects), group 1 men with severe oligospermia (14 subjects), group 2 men with oligospermia (18 subjects), and 34 controls with the same age without pelvic radiotherapy and/or chemotherapy in the last 6 months, known genetic aberrations, urogenital infections, bilateral orchectomy, vasectomy, occupational exposure to noxious hydrocarbons organophosphates, ionizing radiation, heavy metals. They were enrolled after signing a written consent form approved by our ethic committee. The hematological, biochemical and hormonal profiles were evaluated. ESR1 (Xbal and Pvull) polymorphisms were determined by PCR-RFLP method on genomic DNA. Genomic DNA was prepared from whole blood using the Wizard DNA Blood Purification Kit (Promega Inc.). ESR alpha (Xbal and Pvull) polymorphisms were determined by RFLP method. Screening for microdeletions in the azoospermia factor (AZF) region of Y chromosome was performed by multiplex polymerase chain reaction (PCR) with Y chromosome deletion selection system, version 2.0 (Promega Corporation).

Results: ESR Xbal polymorphism study in infertile patients revealed 5 homozygote (XX), 23 heterozygote (Xx) and 19 homoygote cases (xx). The frequency of X allele in infertile patients was 0.35, and 0.65 for x allele, $\chi^2=1.299$. ESR Xbal polymorphism study in normal patients revealed 3 homozygote (XX), 17 heterozygote (Xx) and 14 homoygote (xx) cases. The frequency of X allele in population was 0.34, for x allele the frequency was 0.66, $\chi^2=0.464$. ESR Pvull polymorphism study in infertile patients pointed to homozygote (PP), 23 were heterozygote (Pp) and 15 were mutant homozygote (pp) cases. The frequency of P allele was 0.44, and 0.56 for p allele, $\chi^2=0.137$. ESR Pvull polymorphism study in normal subjects pointed to 6 homozygote cases for PP allele, 18 heterozygote (Pp) and 10 homoygote cases (pp). The frequency of p allele was 0.44, for P allele the frequency was 0.56, $\chi^2=0.184$. 5.4% of all patients presented microdeletions in AZFc region and 2.7% in AZFb region. 8.11% in AZFb and AZFc regions.

Conclusion: Even if no statistic significance can be established, a higher percentage of homozygote x and p allele was found in group with severe oligospermia. No significant differences were found for the alleles frequency between the infertile patients and the control group.

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