GENETIC VARIANTS OF TNF-α: ASSOCIATIONS WITH PECULARITIES OF THE CLINICAL COURSE OF RHEUMATOID ARTHRITIS

Authors: Diyara Kadyrbekova, Alexandra Murtazaliyeva
Scientific research supervisor: A. Tarabayeva
S. Asfendiyarov Kazakh National Medical University, The Republic of Kazakhstan

Keywords. Rheumatoid arthritis, polymorphisms, tumor necrosis factor.

Introduction. It is commonly known that pathogenesis of rheumatoid arthritis (RA) is closely associated with dysregulation of cytokine network. One of pro-inflammatory cytokines taking part in the pathogenesis of RA is tumor necrosis factor (TNF-α). This cytokine carries a wide range of inflammatory, catabolic and immune stimulating actions. Chronic inflammation with tissue destruction, and RA severity and activity, respectively, are supposed to be a result of increased TNF-α production.

Aim. To study features of the course of RA depending on the variant of TNF-α genotype.

Materials and methods. In order to detect polymorphisms of TNF-α gene (1031 T/C, 376 G/A, 308 G/A), PCR-RFLP was used. Specific oligonucleotides for PCR were synthesized at the National Center for Biotechnology (Astana). Processing of the connection of genotypes with the level of cytokine production and activity indexes were carried out with the help of Mann-Whitney U test.

Results. Polymorphisms of TNF-α gene in positions 1031, 376, 308 were studied, and 4 different types of genome were formed.

According to the results of the study it was revealed that the variant (variant №2), which indicates the combination of wild-type homozygotes in all points (1031 T/T, 376 G/G, 308 G/G), was most common among RA patients. The second most frequent variant was the option with mutation in point 1031 C/T at homozygotes in two other locations (variant №3). The third variant due to frequency of occurrence was the option with mutation in point 308 G/A at homozygotes in the rest two investigated points (variant №1). Significant increase in eSR is revealed at variant №3 (1031 C/T) during analysis of the combination of clinical and diagnostic indicators in accordance with the above variants of the genome. However, statistically significant importance was not identified in terms of DAS. At the same time, individuals with the presence of SNP were characterized by relatively low TNF-α production, whereas RA patients with heterozygote of mutant type 308 G/A showed significantly increased production of this cytokine. Simultaneously, it was not accompanied with elevated ESR.

Conclusion. Homozygote of TNF-α gene “wild” type at points 1031, 376 and 308 is most common in RA patients. Individuals with the presence of TNF-α genotype 1031 (C/T), 376 (G/G), 308 (G/G) are characterized by relatively low TNF-α production. Moreover, it is noted that they have more active course of RA. Patients with the presence of TNF-α genotype 1031 (T/T), 376 (G/G), 308 (G/A) are characterized by increased TNF-α production, however, it is not accompanied with more severe and active RA.