GENETIC MARKERS OF SECONDARY AMYLOIDOSIS IN BELARUSIAN PATIENS WITH RHEUMATOID ARTHITIS

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Background: The development of secondary (AA) amyloidosis in rheumatoid arthritis (RA) is considered to be extensively determined by genotype characteristics. Serum amyloid A protein (SAA) is synthesized by liver under inflammatory conditions. In spite of several polymorphism described in the *SAA1* gene, particular investigator's attention is attracted to three single nucleotide polymorphisms localized in the third exon of this gene: -13T/C, 2995C/T and 3010C/T. The combination of these polymorphic variants determines three *SAA1* haplotypes – α, β and γ. The influence of the γ/γ genotype as well as γ haplotype itself on the development of secondary amyloidosis in patients with RA in Asian population (including Japanese) is described in number of studies.

Objectives: In the present study we compared the influence of the *SAA1* gene allele polymorphism in AA-positive RA with those in AA-negative RA patients. All of them were Belarusian citizens.

Methods: Native DNA was extracted from leucocytes of blood samples obtained from 45 AA-positive RA patients (1st group) and 59 AA-negative RA patients (2nd group). Toamplify a segment of the *SAA1* gene in polymorphic sites -13C/T, 2995C/T and 3010C/T it was genotyped by polymerase chain reaction (PCR) with subsequent restriction enzyme digest analysis. Statistical analyses of genotype and allele frequency comparisons of the various single nucleotide polymorphismsbetween groups were performed using the chi-square test.

Results: Genetic polymorphism of the *SAA1* gene in Belarusian AA-positive RA patients (1st group) and AA-negative RA patients (2nd group) was determined. An odds-ratio (OR) calculated for the *SAA1* α/α genotype was 45.26, and the 95% confidence interval was – 95%CI (9.9 –206.8). It was shown that the *SAA1* α/α genotype dominated in both groups and consisted 95.6% (1st group) and 32.2% (2nd group), respectively. The similar tendency was observed on allele α frequency: χ^2=47.01 (p<0,001). It's remarkable, that γ/γ genotype wasn't revealed in both groups. This genotype variant is considered to be a risk factor of secondary amyloidosis in Japanese RA patients. Furthermore, in AA-positive patients γ allele was not detected at all. Thus, presence of γ allele one can consider to be "protective" for Belarusian patients with RA as it was defined only in AA-negative group. Therefore, according to obtained data *SAA1* α/α(allele variants 2995T and 3010C) are the genetic risk factors for the development of secondary amyloidosis in Belarusian patients with rheumatoid arthritis.

The -13T allele frequency of the *SAA1* gene was 10.2% in the 2nd group; among AA-positive RA patients (1st group) this allele was revealed in 11.1%. In both groups there were no -13T/T homozygotes. Consequently, the -13T allele has no influence on the manifestation of AA-amyloidosis in Belarusian patients with RA.

Conclusions: Relative risk of secondary amyloidosis in RA patients significantly increases in *SAA1* α/αgenotype. In contrast to Japanese data, our results revealed that in Belarusian citizens (Caucasians) *SAA1*α/αisotype was the most amyloidogenic. Presence of the -13T allele in *SAA1* gene had no influence on the risk of AA-amyloidosis development in investigated Belarusian patients with RA.

Disclosure of Interest: None Declared

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