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VITAMIN D RECEPTOR GENE POLYMORPHISM IN PATIENTS WITH JUVENILE RHEUMATOID ARTHRITIS

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Introduction: Juvenile rheumatoid arthritis (JRA) is the most common rheumatic disease developing in childhood; its onset occurs before 16 years of age [1]. It is supposed that the heterogeneity of this disease is due to different factors contributed to its pathogenesis. The central role in the pathogenesis of JRA has been attributed to dysregulation of the adaptive immune response, where regulatory T cells, effector T cells and antibody-producing B cells play the leading role. Further, activated B cells produce immunoglobulins, such as rheumatoid factor (RF) and antinuclear antibodies (ANAs). The information about the role of hereditary factors in the pathogenesis of juvenile rheumatoid arthritis has increased with the discovery of the growing number of genetic loci and single polymorphisms associated with RA susceptibility [2]. The most studied susceptibility locus for this disease is the major histocompatibility complex (MHC) located on chromosome 6p. Rheumatoid arthritis is the known risk factor of osteoporosis and bone fragility [3]. Vitamin D is one of the key point that interacts with both the immune system and bone tissue. The biological effects of vitamin D are mediated by the functional activity of its receptor. More than 200 single nucleotide polymorphisms were detected in vitamin D receptor (VDR) gene that regulates its activity. VDR polymorphic alleles are the risk factor of such diseases as rheumatoid arthritis, celiac disease, systemic lupus erythematosus and many others. Thus, the study of molecular-genetic markers of JRA is highly required to reveal the hereditary predisposition and early diagnosis of this pathology.

Objectives: The aim of the study was to evaluate the distribution of VDR gene polymorphic alleles BsmI in patients with JRA.

Materials and methods: One hundred and four children were enrolled in this study. The patients were divided into three groups: 37 patients had

JRA according to ILAR classification criteria, 33 children had articular syndrome and 34 hospital controls without any signs of autoimmune or inflammatory diseases. The method of patients genotyping: BsmI (c.IVS7 + 283 G>A) polymorphism of VDR was detected by allele-specific polymerase chain reaction method with the use of reagent kit and in accordance with manufacture's instruction.

Results: It has been shown that VDR genotype GG was the most frequent among all three groups (18 (48,6%), 18 (54,5%), 20 (58,8%), respectively). In patients with JRA, it was revealed the increased frequency of allele A from 32,4% to 10,2% ($p<0,05$) as compared to the controls. In patients with articular syndrome frequency of allele A was 28,8%. In our study children with AA genotype had also earlier manifestation of articular syndrome, as compared to the patients with GA VDR gene polymorphism (8,0 (2,3–13,0) years and 13,0 (5,0–13,7) years, respectively ($p<0,04$).

Conclusions: Thus, minor A allele of polymorphic locus BsmI VDR gene is associated with JRA arising and with predisposition to earlier manifestation of the joint syndrome in patients with JRA.

Prospects for further research. It remains to be further investigated how genetic variants VDR gene may be associated with the activity of the inflammatory process in JRA patients. The finding of our future research will be allowed to answer the question if it is possible to predict complications of JRA and effectiveness of its treatment based on VDR gene polymorphism.

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