AB0014  GENETIC MARKERS OF METHOTREXATE HEPATOTOXICITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

N. Martusevich1, E. Aksenova2, K. Gudkevich3, 1Belarusian State Medical University, Minsk, Belarus; 2The Institute of Genetics and Cytology, Minsk, Belarus; 3Minsk City Clinical Hospital No 6, Minsk, Belarus

Background: Methotrexate (MT) is a first-line drug in the treatment of rheumatoid arthritis (RA). The effectiveness and tolerability of the use of MT largely determines the prognosis of the course of the disease, the speed of achieving remission. The development of hepatotoxicity (HT) is the most common adverse reaction, it is predicted in 5-12.5% of cases and often requires the abolition of MT. In this regard, predicting the development of HT seems to be an important area of research.

Objectives: to study genetic predictors of HT development in patients with RA using MT.

Methods: 44 patients with a reliable diagnosis of RA were included in study. All of the patients used MT at a dose of 15.0 (12.5-17.5) mg/week in combination with folic acid 3-5 mg/day outside of MT. The average age was 46.7 ± 12.3 years; females - 81.8% (n = 36); mail 18.2% (n = 8). The duration of RA is 5.3 ± 2.2 months. All patients were divided into two groups: the first study group (n = 17) included patients with RA who developed a HT reaction to MT, which required the abolition of MT; in the second- (n = 27) - comparison group - patients with good efficacy and tolerability of MT.

Genotypes for polymorphic alleles were analyzed in all patients: C677T (rs1801133) and A1298C (rs1801131) of the methylenetetrahydrofolate reductase gene (MTHFR); 347C>G of SLC19A1 gene encoding the folate transporter membrane carrier protein.

Table 1. The frequency of occurrence of various mutations in genes that affect the metabolism of MT among patients with RA in the study and comparison groups are presented in table 1

<table>
<thead>
<tr>
<th>Genetic option</th>
<th>Study group</th>
<th>Comparison group</th>
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<tbody>
<tr>
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<td>TT, n=17</td>
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<td>MTHFR-A1298C</td>
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<td>GG</td>
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Table 1. The frequency of occurrence of various mutations in genes that affect the metabolism of MT

<ref>When analyzing inheritance models, it was found that differences in hepatotoxicity for comparing genotypes (MTHFR-A1298C, MTHFR-C677T, SLC19A1c80A>G) were not statistically significant. A statistically significant increase in the risk of hepatotoxicity was found dominant (2.18 (1.06-4.47), x2 = 4.38, p = 0.03) and codominant (0.42 (0.19-0.92), x2 = 5.23, p = 0.02) models for the 347C>G ATIC gene. Conclusion: Thus, an increase in the risk for the dominant and codominant models for the 347C>G ATIC gene allows recommending genotyping of the alleles of this gene before MT administration in order to reduce the risk of hepatotoxic reactions.

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Results: The frequency of heterozygote rs33996649GA genotype was higher in pSS patients than HS [OR=3.143 (1–10.234), p=0.046], and also, the expression mRNA correlates with disease activity in pSS.

References:

References:

Disclosure of Interests: None declared

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AB0017

CONSTANT HISTOKRINGENER MARKER IL1B T–31C IS ASSOCIATED WITH ANAMNESIS OF BIOLOGICAL DRUGS TREATMENT IN RHEUMATOID ARTHRITIS

V. Orlenechenko1, E. Letyagina1, Y. Kurochkina1, A. Akimova1, A. Shevchenko1, M. Kordiev1,2, RICEL – Branch of IC&G SB RAS, Novosibirsk, Russian Federation

Background: Rheumatoid arthritis (RA) is chronic progressive joint disease with erosions formation. Timely and effectiveness treatment is important due to quickly structural damage and progressive losing of active motion. Synthetic DMARDs didn’t have a sufficient effect. Using biological drugs seemed like a panacea, but according to investigations at least 30-40% RA-patients lost treatment efficiency. Biological drugs act through immune cascade, that’s why mutation in regulatory region of cytokine genes may partly determine treatment failure.

Methods: One hundred two Caucasian RA-patients (age – 56 yrs [45;61]; DAS28 4.7 [3.8; 5.9]) were enrolled in our study. All of them had American College of Rheumatology (ACR)-defined RA (1987 classification criteria) and gave written inform consent. Single nucleotide polymorphisms IL1B T–31C (rs1143627), IL4 C–590T (rs2243250), IL10 C–592A (rs1800872), IL2A-590T/C (rs1800896) were determined by restriction fragment length polymorphism. Descriptive statistics, Chi-squared test were used for data analysis. Results are presented as median and 25th/75th percentiles (Me [25th percentile; 75th percentile]).

Results: The most of SNPs analyzed had corresponded to the Hardy Weinberg equilibrium (HWE). The only exception was IL1B T–31C – the frequencies were differed statistically significant from HWE (p=0.03). Forty seven (46.1%) patients were treatment with biological drugs. Homozygotes IL1B -31CС were founded in 13/47 from 47 (27.7%) vs. 6 from 52 (11.5%), p=0.042. Other SNPs didn’t demonstrated any associations.

Conclusion: Single nucleotide polymorphism IL1B T–31C (rs1143627) may be used for prognosis of basic anti-inflammatory therapy inefficiency and the needing for prescribing biological therapy.

Disclosure of Interests: None declared

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AB0018

TNFA RS1800629 POLYMORPHISM: WHAT ABOUT ITS ASSOCIATION WITH CLINICAL MANIFESTATIONS AND ANTI-TNFα THERAPY? DATA FROM A SERIES OF ITALIAN PATIENTS WITH BEHÇET SYNDROME

M. C. Padula1, P. Lecceca1, N. Lascaro1, G. G. Sorrento2, R. P. Radice2, A. R. Limongi2, T. Carbone1, A. Padula1, G. Martelli, S. D’angelo, A. Rita Tavolatrili,2, R. Bruschi,2, A. Giuseppe Salerno,2, V. A. Nasonova Research Institute of Rheumatology, Pediatric, Moscow, Russian Federation; V. A. Nasonova Research Institute of Rheumatology, Pediatric, Moscow, Russian Federation; V. A. Nasonova Research Institute of Rheumatology, Immunology, Rheumatology, Moscow, Russian Federation; V. A. Nasonova Research Institute of Rheumatology, Immunology, Molecular, and Cellular Biology of Rheumatic Diseases, Moscow, Russian Federation

Background: Behçet’s disease (BD) is one of the most widely-spread immunoinflammatory diseases of an unknown etiology, the leading manifestation of which is chronic joint inflammation, occurring in children under the age of 16. The disease is a complex of chronic arthropathies with various phenotypic manifestations.

AB0019

GENETIC POLYMORPHISM OF THE INFAMMATORY MARKER SAAR1 S12218 (-13/T) IS ASSOCIATED WITH AN ATTITUDE TO CLINICAL PHENOTYPES OF JUVENILE IDIOPATHIC ARTHRITIS

E. Fedorov1, S. Salugin2, M. Krylov3, I. Guseva3, E. Samarkina3, V.A. Nasonova Research Institute of Rheumatology, Pediatric, Moscow, Russian Federation; V.A. Nasonova Research Institute of Rheumatology, Pediatric, Moscow, Russian Federation; V.A. Nasonova Research Institute of Rheumatology, Immunology, Molecular, and Cellular Biology of Rheumatic Diseases, Moscow, Russian Federation

Background: Juvenile idiopathic arthritis (JIA) is one of the most widely-spread immunoinflammatory diseases of an unknown etiology, the leading manifestation of which is chronic joint inflammation, occurring in children under the age of 16. The disease is a complex of chronic arthropathies with various phenotypic manifestations.