AB0001  ASSOCIATION OF MDR1 GENE G2677T POLYMORPHISM WITH METHOTREXATE RESISTANCE IN PATIENTS WITH UZBEK RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the most widely prescribed disease-modifying antirheumatic drug (DMARD) for treatment of rheumatoid arthritis (RA)[1]. According to different authors, in 25-40% [3] of cases “complete clinical remission” or “low disease activity” is not achieved, by reason of refractoriness to methotrexate and this may be related to the activity of the MDR1 (ABCB1) gene which is involved in its metabolism. According to many studies on the C3435T isoform MDR1 polymorphism CC genotype is associated with methotrexate refractoriness [2]. But a certain interest is also influenced by the other isoform of the MDR1 gene (G2677T) for the presence of resistance to methotrexate.

Objectives: The aim of this research was to study the effect of MDR1 gene polymorphisms G2677T (rs2032582) on resistance to treatment with methotrexate in Uzbek patients with RA.

Methods: The study involved 76 patients with RA of Uzbek nationality and 24 healthy people. The average age of patients was 48.9±15.9 years. RA was diagnosed according to the criteria of the American College of Rheumatology (ACR). 75.6% of patients had high and 24.4% moderate RA activity (DAS28). All patients took methotrexate in monotherapy, at a dose of 7.5-15 mg for 3-6 months. All patients were genotyped by the MDR1 gene G2677T polymorphisms by using the polymerase chain reaction (PSR-Real time).

Results: Genotyping of the G2677T isoform of MDR1 gene revealed the following results: in patients with CC genotype was found in 22 patients (28.9%), GT genotype was found in 31 patients (40.7%) and TT genotype was found in 23 patients (30.2%). In patients treated with methotrexate, the following disease activity was observed in patients with CC genotype, the disease activity was DAS28>2.6, with CT genotype Das28 3.2-4.5. Patients with the TT genotype had an activity of DAS28>5.1. Despite the increase in the dose of methotrexate, the remission was not achieved.

Conclusion: TT genotype G2677T isoform of MDR1 gene is associated with resistance to methotrexate. Patients with the CC genotype are recommended to replace methotrexate with other DMARD preparations. Patients are recommended to conduct genotyping to the MDR1 gene for personal selection of drugs.

REFERENCES

Disclosure of Interests: None declared

AB0003  GENETICS IN PAIN IN WOMEN WITH FIBROMYALGIA: THE PROMISING ROLE OF REDUCING SEDENTARY BEHAVIOUR

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Background: Fibromyalgia is characterised by chronic pain and a heterogeneous presentation of other symptoms (e.g. fatigue and depression) [1]. It is widely accepted that pain is promoted by both genetic susceptibility and environmental factors such as people’s behaviours [2]. In addition to genotype individual associations and gene-gene interactions, when considering complex phenotypes such as pain, gene-environmental interactions are likely present and can help to better understand the disease (i.e. by unravelling underlying mechanisms [3]).

Objectives: To test the individual association of 64 polymorphisms (34 candidate-genes) and the gene-gene, gene-physical activity, and gene-sedentary behaviour interactions with pain and pain-related cognitions in fibromyalgia.

Methods: In 274 women with fibromyalgia, saliva samples were collected for extracting DNA. We measured physical activity and sedentary behaviour by accelerometers for a week, pain with algometry and questionnaires, and pain cognitions with questionnaires. Age, body fat, and analgesics and antidepressants consumption were included as covariates. Significance was set at P-values lower than the Bonferroni’s correction or P- and false discovery rate values lower than 0.05.

Results: The rs6311 and rs8313 polymorphisms were individually related to algometer scores. The interaction of rs4818 and rs1799971 polymorphisms was related to pain catastrophizing. Five gene-behaviour interactions were significant: the interactions of sedentary behaviour with rs1383914, rs8680, rs4880, rs165599, and rs12994338 polymorphisms were associated with the bodily pain subscale of the SF-36.

Conclusion: The HTR2A gene (individually), COMT and CPRM1 gene-gene interaction, and the interactions of sedentary behaviour with ADRA1A, CPP1A, HTR1A, COMT, and SCN9A genes were associated with pain-related outcomes in fibromyalgia females. Besides indicating the relevance of genetic background for pain and pain-catastrophizing, the observed genotype-behaviour interactions suggest that the effects of sedentary behaviour on pain may depend on the genotype of women with fibromyalgia. Future clinical experimental research should examine whether reducing sedentary behaviour is particularly beneficial for reducing pain in women with specific genotypes.