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Association between G2677T/A MDR1 Polymorphism with the Clinical Response to Disease Modifying Anti-Rheumatic Drugs in Rheumatoid Arthritis

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Abstract : Introduction: In patients with rheumatoid arthritis, resistance or poor response to disease modifying antirheumatic drugs (DMARD) may be a reflection of the increase in g-P. The expression of g-P may be important in mediating the effluence of DMARD from the cell. In addition, P-glycoprotein is involved in the transport of cytokines, IL-1, IL-2 and IL-4, from normal lymphocytes activated to the surrounding extracellular matrix, thus influencing the activity of RA. The involvement of P-glycoprotein in the transmembrane transport of cytokines can serve as a modulator of the efficacy of DMARD. It was shown that a number of lymphocytes with glycoprotein P activity is increased in patients with RA; therefore, P-glycoprotein expression could be related to the activity of RA and could be a predictor of poor response to therapy. Objective: To evaluate in RA patients, if the G2677T/A MDR1 polymorphisms is associated with differences in the rate of therapeutic response to disease-modifying antirheumatic agents in patients with rheumatoid arthritis. Material and Methods: A prospective cohort study was conducted. Fifty seven patients with RA were included. They had an active disease according to DAS-28 (score >3.2). We excluded patients receiving biological agents. All the patients were followed during 6 months in order to identify the rate of therapeutic response according to the American College of Rheumatology (ACR) criteria. At the baseline peripheral blood samples were taken in order to identify the G2677T/A MDR1 polymorphisms using PCR- Specific allele. The fragment was identified by electrophoresis in polyacrylamide gels stained with ethidium bromide. For statistical analysis, the genotypic and allelic frequencies of MDR1 gene polymorphism between responders and non-responders were determined. Chi-square tests as well as, relative risks with 95% confidence intervals (95%CI) were computed to identify differences in the risk for achieving therapeutic response. Results: RA patients had a mean age of 47.33 ± 12.52 years, 87.7% were women with a mean for DAS-28 score of 6.45 ± 1.12. At the 6 months, the rate of therapeutic response was 68.7 %. The observed genotype frequencies were: for G/G 40%, T/T 32%, A/A 19%, G/T 7% and for A/A genotype 2%. Patients with G allele developed at 6 months of treatment, higher rate for therapeutic response assessed by ACR20 compared to patients with others alleles (p=0.039). Conclusions: Patients with G allele of the - G2677T/A MDR1 polymorphisms had a higher rate of therapeutic response at 6 months with DMARD. These preliminary data support the requirement for a deep evaluation of these and other genotypes as factors that may influence the therapeutic response in RA.

Keywords : pharmacogenetics, MDR1, P-glycoprotein, therapeutic response, rheumatoid arthritis
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