TNF-α GENE POLYMORPHISMS AND JUVENILE IDIOPATHIC ARTHRITIS: INFLUENCE ON DISEASE OUTCOME AND THERAPEUTIC RESPONSE

A. Scardapane[1], R. Ferrante[2] , M. Nozzi[1], A. Savino[1], I. Antonucci, V. D'Adorante[1], L. Stuppia[2], F. Chiarelli[1], L. Breda[1]

[1]Paediatric Rheumatology Unit, Department of Paediatric, ,"G, d'Annunzio" University, Chieti-Pescara, Italy.

[2]Laboratory of Molecular Genetics, Department of Psychological, Humanities and Territorial Sciences ,"G, d'Annunzio" University, Chieti-Pescara, Italy.

Introduction: The objective of this work is to investigate the genetic contribution of TNF-α, a cytokine involved in lung inflammatory process and during hypoxia, on disease course and therapeutic response in patients with juvenile idiopathic arthritis (JIA).

Methods: 74 Caucasian patients with a diagnosis of JIA were consecutively recruited along with a control group of 77 healthy children. DNA was extracted for analysis of TNF-α gene promoter polymorphisms at position -163, -244, -238, -376 and -308 .

Results: No single nucleotide polymorphisms (SNPs) at position -163 was observed, while SNPs at position -244 and -376 were only observed in the controls. No differences were observed in the prevalence of SNPs at -238 and -308 between JIA and controls. In the group of JIA patients no significant differences were observed between the -238 and -308 G/A genotypes and different disease phenotypes. We observed the higher reduction of disease activity expressed in the carriers of -308 GG genotype respect to GA and AA genotypes after 6 and 12 months of disease. After 12 months of biologic therapy, a significant higher disease activity was observed in patients with genotype -308 AA respect to both GA and GG.

Conclusions: JIA patients carrying the TNF-α -308 GA/AA and -238 GA genotypes are associated with a worse prognosis and with a lower response to anti-TNF-α drugs.