A78 MODULATION OF GENE EXPRESSION BY LEFLUNOMIDE AND PREDNISONE DURING TREATMENT OF EARLY RHEUMATOID ARTHRITIS

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Background Many genes encoding human leucocyte antigen molecules or involved in the activation and resistance of apoptosis of T cells have a role in the susceptibility to rheumatoid arthritis (RA) and are also responsible for the heterogeneous response to conventional disease-modifying antirheumatic drugs (DMARDs) such as leflunomide (LEF).[1] LEF has a cellular antiproliferative action on activated inflammatory cells and halts important steps in the pathogenesis of RA, reducing joint inflammation.[2] Combined with glucocorticoids such as prednisone (PN), LEF can be very effective in exerting a potent synergistic effect by immunosuppressive and anti-inflammatory activities.[3] Aim To study the effects of combined LEF and low-dose PN treatment in patients with early RA through selected inflammatory gene expression in peripheral blood mononuclear cells (PBMCs).

Methods Ten patients with early RA (age 49±9 years, disease duration <2 years, DAS28 ≥5) not treated in the previous 6 months with DMARDs or biological drugs were included (after patient informed consent and EC approval) and divided into two groups. At baseline, six untreated patients (group 1, age 48±13 years) and four PN-pretreated (3 months with 5 mg/day, night time, age 51±9 years) patients received both LEF and PN together for 12 weeks. PBMCs were isolated by Ficoll centrifugation (Histopaque 1077, Sigma, Italy). Total RNA extracted by RNeasy Midy Kit (Qiagen, USA) and cDNA was synthesised from RNA using SuperScript II (Invitrogen, UK). Real-time reaction for β-actin, HIF1A, STAT4, MIF, MAPK9, STAT6, NFKB1 and TNFRSF1B was obtained using Real MasterMix SYBR Green detection system (Eppendorf, Germany). All patients were tested at baseline and after 12 weeks. Comparative threshold method was used to quantify the expression levels.[3] The expression level at baseline was normalised to 1 to compare the effects of combined LEF/PN treatments in both groups.

Results The combined LEF/PN treatment induced a statistical reduction in the expression levels of all genes analysed by quantitative real-time PCR in both groups (p=0.05–0.001), except for MAPK9 in group 1 and MIF in group 2.

Conclusions Treatment of early RA with combined LEF/PN should be started as soon as possible since a significant down-regulation of crucial genes involved in the pathogenesis of RA seems to be achieved with their concomitant administration. Poorer effects are obtained by adding LEF to patients with RA already treated with PN.

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