Anti-tumour necrosis factor agents and lipid profile: a class effect?

S P Garcês, M J Parreira Santos, F M R Vinagre, R M Roque and J A C da Silva

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mechanism may be, this case suggests that B cell depletion is effective in the treatment of arthritis along with improvement of fatigue but may have distinct effects on the haematological abnormalities in Felty syndrome.

A Salama,1 U Schneider,2 T Dörner1,3
1 Department of Transfusion Medicine and Immune Hematology; 2 Department of Medicine, Rheumatology and Clinical Immunology, Charite Universitätsmedizin Berlin, Germany; 3 Deutsches Rheumaforschungszentrum, Berlin, Germany

Correspondence to: Thomas Dörner, Charite Universitätsmedizin Berlin, Chariteplatz 1, 10098 Berlin, Germany; thomas.doerner@charite.de

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Increased cardiovascular morbidity and mortality has been documented in several chronic inflammatory rheumatic diseases. In addition to the traditional cardiovascular risk factors, disease activity itself may contribute to this increase.

Tumour necrosis factor (TNF-α), a pivotal cytokine in chronic inflammation, also affects lipid metabolism, insulin resistance and endothelial function. Therapeutic use of TNF-α blockers reduces inflammation and modifies the lipoprotein spectrum of patients. A significant increase in high-density lipoprotein (HDL) cholesterol levels has been documented after short-term infliximab therapy. However, this beneficial effect seems to be transient and more prolonged use of TNF-α blockers may lead to an increase in total cholesterol and low-density lipoprotein (LDL) cholesterol, inducing a more “atherogenic” phenotype.

The majority of clinical studies have looked at the use of infliximab. Data regarding the effect of other anti-TNF-α agents on lipid levels is scarce.

We compared the changes in lipid levels after 1 year of treatment with infliximab and etanercept, in a small group of patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA).

The study included 65 consecutive patients (36 females) with a mean age of 47.4 (SD 13.3) years, 30 patients with RA, 29 with AS and six with PsA. Forty-four patients were treated with infliximab and 21 with etanercept. At baseline, 23 (35.4%) had increased total cholesterol levels, 17 (26.2%) had increased LDL levels, seven (10.8%) had increased triglycerides and nine (13.8%) had low HDL. Thirty-three patients were on low-dose steroids and six were taking statins. There were no significant differences in lipid levels between the infliximab and the etanercept group.

After 1 year of treatment, 71.4% of patients with AS had a good response (reduction of BASDAI >50%) and 73% of RA and PsA patients had a moderate/good DAS28 response. Despite reduced inflammatory activity and reduction in steroid dosage patients developed a more “atherogenic” lipid profile. There was an increase, in the whole group, in total cholesterol (p<0.0001) and LDL levels (p = 0.02), without significant changes in HDL or triglycerides, which is in agreement with previously published studies. When analysed separately, we found an elevation in total cholesterol (p<0.001) and LDL (p = 0.003) in the infliximab group, while in the etanercept group there was a significant increase in HDL (p<0.05) and no significant changes in total cholesterol or LDL (table 1). Despite the small number of patients, the differences between infliximab and etanercept could not be attributed to a distinct clinical response evaluated
Relapse of sarcoidosis upon treatment with etanercept

Tumour necrosis factor (TNF-α) is thought to play a central role in promoting and perpetuating inflammation in sarcoidosis, and treatment with TNF-α inhibitors has been reported to be successful. 1–5 We present a patient with quiescent sarcoidosis who relapsed shortly after beginning treatment with a TNF-α inhibitor for an unrelated medical condition.

A 35-year-old woman with a history of sarcoidosis, in remission while on no treatment, and ankylosing spondylitis experienced a severe flare of inflammatory back pain that was not responsive to non-steroidal anti-inflammatory drugs. Treatment with etanercept 50 mg subcutaneously weekly was begun with marked symptomatic improvement in her back pain. Three weeks after starting etanercept, she developed dry cough, exertional dyspnoea, blurred vision with photopsia of the right eye, fatigue and fevers to 38.9°C. Etanercept was discontinued. Computed tomography of the chest showed extensive pulmonary nodules, peripherally based infiltrates, and paratracheal, subcarinal, mediastinal and bilateral hilar lymphadenopathy. Bronchoscopy revealed highly friable bronchial mucosa with scattered endobronchial nodular granulomas. Cultures of bronchoalveolar lavage fluid and lung tissue were negative. Lung biopsy demonstrated non-necrotising granulomas consistent with sarcoidosis. Treatment with prednisone 0.5 mg/kg per day and prednisolone acetate 1% ophthalmic solution resulted in prompt resolution of her anterior uveitis, respiratory and constitutional symptoms. Follow-up computed tomography scan of the chest 3 months later showed improvement (fig 1). One year after relapse of sarcoidosis, she remains in clinical remission on tapering doses of prednisone.

Contrary to previously reported cases of successful treatment of active sarcoidosis with TNF-α inhibitors, our patient experienced relapse of sarcoidosis 3 weeks after initiating etanercept to treat active ankylosing spondylitis. She had prompt clinical and radiographic improvement after discontinuation of etanercept and treatment with corticosteroids. This

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Plasma concentration of lipids at baseline and 12 months after infliximab and etanercept therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n = 65)</td>
</tr>
<tr>
<td></td>
<td>Infliximab group (n = 44)</td>
</tr>
<tr>
<td></td>
<td>Etanercept group (n = 21)</td>
</tr>
<tr>
<td>----------</td>
<td>---------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>T Chol, mg/dl</td>
<td>180 (35.2)</td>
</tr>
<tr>
<td>HDL, mg/dl</td>
<td>57.3 (20.1)</td>
</tr>
<tr>
<td>LDL, mg/dl</td>
<td>104.8 (36.2)</td>
</tr>
<tr>
<td>TG, mg/dl</td>
<td>101.6 (45.2)</td>
</tr>
<tr>
<td>T Chol/HDL</td>
<td>3.4 (1.0)</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>1.9 (0.9)</td>
</tr>
</tbody>
</table>

Base line versus 12 months (Student t test): *p<0.0001; †p = 0.02; ‡p = 0.005; §p = 0.001; ¶p = 0.003; **p = 0.01; ††p = 0.05.

* T Chol, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; Infl, infliximab; Etan, etanercept.

Correspondence to: Sandra Pinheiro Garcés da Gama, Rheumatology Department, Hospital Garcia de Orta, Avenida Prof. Torrado da Silva, 2801-951 Almada, Portugal; sandragarces@gmail.com

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