Effects of infliximab treatment on insulin resistance in patients with rheumatoid arthritis and ankylosing spondylitis

D N Kiortsis, A K Mavridis, S Vasakos, S N Nikas, A A Drosos

CONCISE REPORT

Background: Tumour necrosis factor α (TNFα) may be an important mediator of insulin resistance. Infliximab is a chimeric monoclonal, high affinity antibody against the soluble and transmembrane TNFα, which can reduce markedly the biological activity of circulating and tissue TNFα and is used to treat various autoimmune disorders.

Objective: To assess the effects of infliximab infusions on insulin sensitivity in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).

Methods: Forty-five patients (28 with RA, 17 with AS) aged 19–74 years were studied. All patients were treated with infliximab. A complete biochemical profile was obtained before and after 6 months' treatment with infliximab. The Homeostasis Model Assessment (HOMA) Index was used to measure insulin resistance and the Quantitative Insulin Sensitivity Check Index (QUICKI) to measure insulin sensitivity.

Results: In the whole study group, no significant changes of the HOMA Index or QUICKI were seen. In the tertile of patients with the highest insulin resistance, a significant decrease of the HOMA Index or increase of the QUICKI was found (p<0.01 for both).

Conclusions: The results suggest that infliximab treatment may have beneficial effects on insulin sensitivity in the most insulin resistant patients with RA and AS.

It is well established that there is increased risk for cardiovascular disease (CVD) in rheumatoid arthritis (RA). Several factors have been implicated, of which systemic inflammation is considered the major one.

Increased insulin resistance is an important risk factor for CVD. Patients with autoimmune connective tissue diseases have increased insulin resistance. Several factors have been implicated in the pathogenesis of insulin resistance. Tumour necrosis factor α (TNFα) is a proinflammatory cytokine that has a major role in the pathogenesis of autoimmune diseases and inflammatory disorders. Recently, many studies suggested that TNFα might be an important mediator of insulin resistance in animal models. Moreover, there is evidence that in insulin resistant patients TNFα overexpression occurs in adipose tissue and skeletal muscle. Weight loss in obese insulin resistant subjects results in a substantial reduction of TNFα expression and secretion, in association with a decrease in serum TNFα levels and a restoration of insulin sensitivity. Interestingly, administration of TNFα to healthy volunteers induced insulin resistance. Infliximab is a chimeric monoclonal, high affinity antibody against the soluble and transmembrane TNFα. It can reduce significantly the biological activity of circulating and tissue TNFα and is used in the treatment of various autoimmune disorders.

Very little information exists about the role of infliximab treatment on insulin sensitivity. Thus, we assessed the effects of infliximab infusions on insulin sensitivity in patients with RA and ankylosing spondylitis (AS).
improvement in insulin sensitivity was infliximab treatment. However, those with AS. Moreover, no significant correlations were observed between the insulin action indexes and age, disease duration, or disease activity.

**DISCUSSION**

In this study a significant decrease in insulin resistance was seen after infliximab treatment in the most insulin resistant patients. The possibility cannot be completely excluded that other factors might have affected the insulin sensitivity in these patients. However, the lack of change in their body weight and their dietary habits, and the dose of steroids and DMARDs (both of which can considerably affect insulin resistance), indicate that the most probable cause of the improvement in insulin sensitivity was infliximab treatment. Only one small study has previously assessed the effects of infliximab on insulin resistance. The authors found no significant change in insulin sensitivity after three to five infusions of infliximab. However, owing to the very small number of patients included (10 subjects) they did not perform a separate analysis of the patients with the highest insulin resistance. In another study, the administration of another human anti-TNFα antibody (CDP571) did not considerably affect insulin sensitivity and glycemic control in patients with type 2 diabetes mellitus. However, those subjects had longstanding diabetes mellitus (known duration of the disease averaging 9 years) and severe hyperglycaemia. In such patients, various other mechanisms may contribute to the insulin resistance, including hyperglycaemia, which has been shown to affect insulin signalling in a different way from TNFα.

In conclusion, our results indicate that infliximab treatment may have beneficial effects on insulin sensitivity in the most insulin resistant patients with RA and AS. The improvement in insulin sensitivity may decrease the CVD risk in these patients. Further prospective studies are needed in larger groups, followed up for a long period of time, in order to assess the effects of infliximab treatment on cardiovascular risk.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
<th>p Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA</td>
<td>3.01 (0.48)</td>
<td>1.89 (0.35)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>QUICKI</td>
<td>0.30 (0.008)</td>
<td>0.35 (0.013)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

All values are expressed as mean (SE).

**REFERENCES**

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Ann Rheum Dis 2005 64: 765-766 originally published online September 30, 2004
doi: 10.1136/ard.2004.026534

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