Bone mineral density in patients with rheumatoid arthritis treated with infliximab

M Vis, A E Voskuyl, G J Wolbink, B A C Dijkmans, W F Lems for the OSTA study group


METHODS AND RESULTS

This open cohort study consisted of consecutive patients with RA, who were treated with infliximab at the Slotervaart Hospital and the VU University Medical Centre. All patients fulfilled the ACR 1987 criteria of RA and had active disease (defined by the modified 28 joint count Disease Activity Score (DAS28) of at least 3.2). Infliximab was given intravenously at 0, 2, 6, 14, weeks and from the fourth infusion every 8 weeks in a dose of 3 mg/kg. At each visit the DAS28 was calculated and changes in drug treatment were recorded. BMD measurements (g/cm²) of the hip (total hip) and lumbar spine (L1–4) were performed at baseline and after 1 year on a Hologic 4500.

osteoporosis is a well known feature of rheumatoid arthritis (RA). Cross sectional studies have shown that patients with RA have a lower bone mineral density (BMD) than healthy controls. Disease activity, steroid use, and immobility are associated with loss of BMD in RA. It has been suggested that active treatment of patients with RA may prevent loss of BMD. The current most effective drugs in the treatment of RA are the tumour necrosis factor α (TNFα) blocking agents. The beneficial effects of short term treatment with infliximab on markers of bone metabolism in patients with active RA have recently been shown. From this we proposed the hypothesis that bone loss might be arrested in patients with RA during treatment with infliximab.
Letters

In total, 36 patients (29 (81%) female) were included into the study. Patients had a mean (SD) age of 53 (12) years, with a median (range) disease duration of 9.5 years (0–49). Methotrexate, prednisone, and bisphosphonates were used by 100%, 50%, and 25% of the patients, respectively. The mean disease activity (DAS28) decreased from 5.6 at baseline to 3.8 at 6 weeks and stabilised around 3.6 for the rest of the studied period. In 36 patients dual x ray absorptiometry (DXA) measurements of lumbar spine (L1–4) and in 30 patients DXA measurements of the hip were available at baseline and after 1 year. In four patients no DXA hip measurements were available because of bilateral hip replacement, and in two patients only one DXA of the hip was available owing to unknown causes.

Mean (SD) BMD at the lumbar spine increased non-significantly from 0.998 (0.205) to 1.001 (0.199) at 1 year (+1.1%, p = 0.117). BMD at the total hip decreased non-significantly from 0.857 (0.144) to 0.854 (0.132) at 1 year. (−0.3%, p = 0.683). In a linear regression model, changes in BMD at the hip or the spine were not associated with mean DAS28, prednisone use, or bisphosphonate use (data not shown).

DISCUSSION

This study indicates that BMD of the spine has a tendency to increase and that BMD of the hip slightly decreases during 1 year of treatment with infliximab. This is in contrast with previous longitudinal studies of patients with RA, in which a decrease of BMD was seen during conventional disease modifying antirheumatic drug treatment without tumour necrosis factor blockings agents (table 1).

In our view, these data suggest that treatment with infliximab can arrest generalised osteoporosis in patients with RA. This view is supported by the observation that markers of bone formation increased and markers of bone resorption decreased in the first 6 weeks of treatment with infliximab.7 We do realise that our observations are made in an open cohort study and therefore no definite conclusions can be drawn from our data.

In summary, this study suggests that treatment with infliximab has a positive effect on BMD in patients with RA. Because patients with RA have an increased risk of bone loss and, subsequently, osteoporotic fractures, this might be an additional advantage of infliximab (above the well known favourable effect on disease activity and radiological damage), and warrants further study.

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Authors’ affiliations

M Vis, A E Voskuyl, G J Wolbink, B A C Dijkmans, W F Lems, Department of Rheumatology, VU University Medical Centre, Amsterdam, The Netherlands
M Vis, B A C Dijkmans, W F Lems, Slotervaart Hospital, Amsterdam, The Netherlands

Correspondence to: Dr M Vis, Department of Rheumatology, 4A 42, VU University Medical Centre, Postbus 7037, 1007 MB Amsterdam, The Netherlands; m.vis@vumc.nl

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REFERENCES


Table 1 Summary of changes in BMD of five studies in patients with RA

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Follow up (years)</th>
<th>BMD change (%)</th>
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<tbody>
<tr>
<td></td>
<td>(n)</td>
<td>RA</td>
<td>Hip</td>
</tr>
<tr>
<td>Boers†‡</td>
<td>62</td>
<td>Early</td>
<td>1</td>
</tr>
<tr>
<td>Gough‡</td>
<td>50</td>
<td>Early</td>
<td>1</td>
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<tr>
<td>Haugeberg§</td>
<td>366</td>
<td>Established</td>
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<tr>
<td>Dolan*</td>
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<td>2</td>
</tr>
<tr>
<td>Shibuya</td>
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<td>1</td>
</tr>
<tr>
<td>This study</td>
<td>36</td>
<td>Established</td>
<td>1</td>
</tr>
</tbody>
</table>

* Percentage change calculated from data given in the manuscript; †BMD of the spine was not measured; ‡data from the patients treated with sulphasalazine alone.