

## Adalimumab arrests bone loss in the spine and hip of active rheumatoid arthritis patients with osteopenia

Sirs,

Rheumatoid arthritis (RA) not only leads to erosions and local periarticular osteoporosis (OP), but also the systemic bone loss, osteopenia or even osteoporosis. Tumour necrosis factor (TNF) inhibitors are a step forward in the therapy of RA. Beyond the effective control of the disease activity, there is accumulating evidence that this medicine may produce favourable effects on the bones (1-3). However, the consequences of present studies on this field seems to be conflicting. Therefore, we aimed to evaluate this effect in active RA patients with osteopenia.

A total of 62 patients with active RA according to the 2010 ACR/EULAR Classification Criteria (4) were included. The 28-joint Disease Activity Score (DAS28) of these patients needed to be  $>3.2$  and they had to have osteopenia simultaneously. According to the International Society for Clinical Densitometry: patients with Z-score  $<2$  SD were considered as having osteopenia (5). All the study participants provided written informed consent before blood sampling. The local ethics committee approved the study.

The 62 enrolled patients were divided into 2 groups. The study group received adalimumab treatment (40 mg subcutaneously every other week) for 12 months, while the control group received methotrexate (10-15 mg every week according to the patients' weight). Both groups were taking calcium (1.0 g/day) and vitamin D (800-1000 IU/day).

The bone mineral density (BMD) of the lumbar spine (L2-L4), femoral neck, trochanter and Ward's triangle were measured at baseline and after 6 and 12 months of treatment by dual energy x-ray absorptiometry (DEXA) (MEDLINK, France). During the study, the BMD of every patient was measured by the same machine. As well as the bone turnover markers, serum C telopeptide of type-I collagen (CTX-I) and serum procollagen type-I N propeptide (PINP) were measured by ELISA.

Compared to the baseline, BMD of lumbar spine, femoral neck, Ward's triangle and Trochanter were significantly decreased in the control group after 12 months. While in the group of adalimumab, BMD of lumbar spine did not decrease but increased (before treatment  $0.669 \pm 0.078 \text{ g/cm}^2$  vs. after treatment  $0.688 \pm 0.075 \text{ g/cm}^2$ ,  $p=0.001$ ). The BMD of femoral neck and Ward's triangle region was stable after 12 months (see Fig 1).

Compared to the baseline, serum CTX-I, a marker of bone resorption was significantly decreased by 29% ( $p=0.0011$ ) and 32% ( $p=0.0000$ ) at 6 months and 12 months in the adalimumab group, while this decline was not found in the methotrexate group. By contrast, serum PINP, a marker of bone formation was stable in both groups during the study.

Our study found that the spine and hip BMD continued to decrease with treatment of methotrexate in the active RA patients with osteopenia, but the decline was inhibited by adalimumab therapy, especially in the lumbar spine. This effect of adalimumab was also supported by a decrease in serum CTX-I. These results may derive from different effects including direct control of inflamma-

tory mechanisms, reduction of corticosteroid use and increase level activity secondary to improved health status.

Sakthiswary R. (6) concluded that TNF- $\alpha$  antagonist therapy has a positive impact on bone metabolism by suppression of bone resorption in his review article, and Wijbrandts *et al.* found that TNF inhibitors may result in an arrest of general bone loss (7). These findings (6-8) are consistent with our study. But compared to these studies, the effect in our study is stronger. The possible reason is that the RA patients in our study are more severe, with the average DAS28  $>6.0$ . In other words, inflammation in our patients was more severe than in other studies. To suppress the inflammation of RA is considered as the main mechanism for inhibiting bone loss by TNF- $\alpha$  inhibitors (6). We can conclude that perhaps the effect is stronger when the inflammation of RA is more severe.

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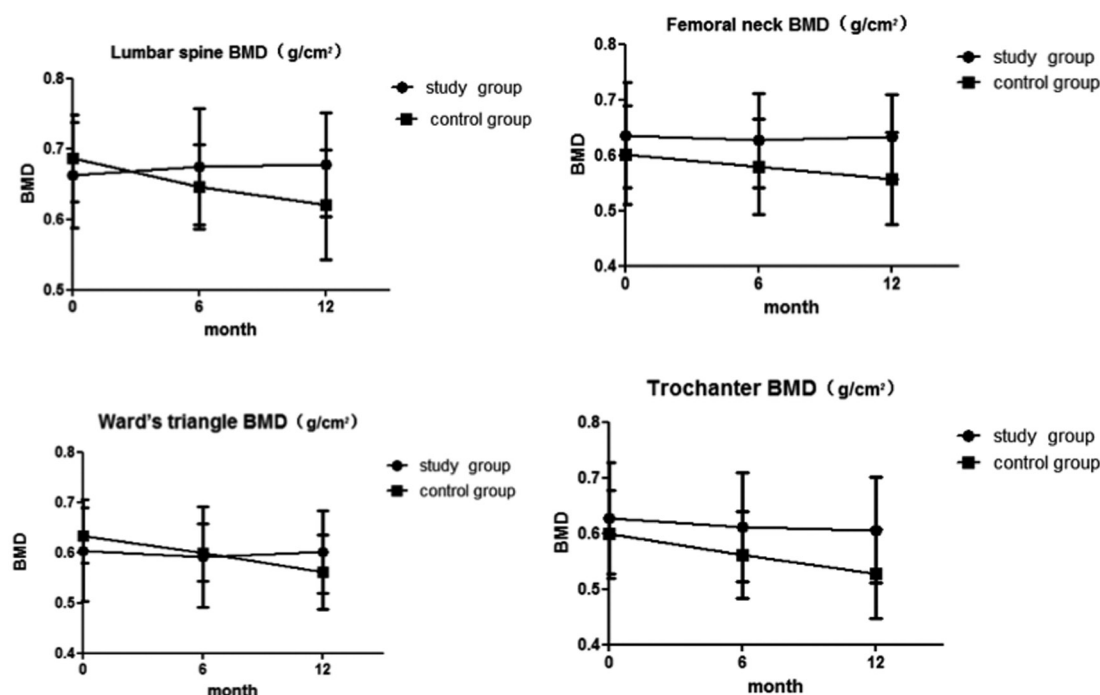
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**Fig. 1.** Changes of lumbar spine, femoral neck, Ward's triangle and Trochanter bone mineral density (BMD) at baseline, 6 months and 12 months in study group (adalimumab) and control group (methotrexate).



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