EFFECT OF BONE AND CARTILAGE METABOLISM IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ALENDRONATE

INTRODUCTION:

Rheumatoid arthritis (RA) is a systemic inflammatory disease characterized by polyarthritis. Generalized osteoporosis is a common complication of RA. In addition, disease-modifying antirheumatic drugs (DMARDs) and corticosteroids may increase extent of osteoporosis [1]. Alendronate is strong inhibitor of osteoclast-mediated bone resorption. Alfacalcidol stimulates osteoblast proliferation. Alendronate and alfacalcidol are widely used in osteoporotic patients. Recently, some biochemical markers have been developed to evaluate the bone and cartilage metabolism. Cross-linked N-terminal telopeptides of type I collagen (NTx) is used frequently to assess bone metabolism. Cleavage of type II collagen (C2C) is a newly developed cartilage metabolism marker. C2C is detected by monoclonal antibody against the specific cleavage site of type II collagen cleaved by collagenase [2]. The Disease Activity Score (DAS) is a combined index that has been developed in Nijmegen in the eighties to measure the disease activity in patients with RA. The purpose of this study was to investigate the effect of alendronate and alfacalcidol treatments on bone and cartilage metabolism in osteoporotic patients with RA. And then we examined the difference in bone and cartilage metabolism with disease activity.

METHODS:

Fifty RA patients classified according ARA criteria were included. They all were diagnosed as secondary osteoporosis. Exclusion criteria were serious hepatic and renal dysfunction, heart disease and metabolic bone disease. The patients were divided into two groups randomly. The alendronate group was given 5mg daily alendronate and 1500mg daily lactic calcium. The alfacalcidol group was given 1 microgram daily alfacalcidol and 1500mg daily lactic calcium. A complete blood count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were obtained every month. Serum bone alkaline phosphatase (BAP), serum NTx, urinary NTx, matrix metalloproteinase 3 (MMP-3), and C2C were obtained every three months. And furthermore, we classified these patients under two groups with DAS28, and then we analyzed the difference in bone and cartilage metabolism with disease activity. Lumbar spine and hand X-rays were taken. Lumbar spine and hand radiographs evaluated for compression fracture and the presence of erosions, osteopenia and joint space loss, respectively. Bone mineral density (BMD) of the lumbar spine was measured using dual-energy X-ray absorptiometry (DEXA) in all patients, and the measurement was repeated at the end of the sixth month. After initial examination, each patient was seen every month. Possible side effects were investigated by patient questioning and routine serum analysis at each visit. This study was approved by the Institutional Review Board of our hospital and informed consent was obtained from all participating patients. Wilcoxon signed-ranks test was used for two group comparisons.

RESULTS:

We studied 50 osteoporotic patients with RA; including 46 female and 4 male patients. Each twenty-five patients were allocated to the alendronate group and the alfacalcidol group. The alendronate group consisted of 24 female and 1 male, and the alfacalcidol group consisted of 22 female and 3 male. All female were postmenopausal. During follow-up, no patients were excluded from the study. The alendronate and alfacalcidol group patients’ age were 65 years (range; 48-78) and 65 years (range; 48-80), respectively. After 6 month, in the alendronate group of the BMD increased with 4.1±1.2% and in the alfacalcidol group increased with 2.3±1.3%. In the alendronate group, BAP, serum NTx and urinary NTx were significantly decreased, especially low disease activity group (Fig. 1). And low disease activity alendronate group showed a tendency to decrease C2C (Fig. 2).

DISCUSSION:

In our study, at the end of 6 month follow up, we saw statistically significant increase in BMD and improvement of bone metabolism in both groups. The increase of BMD values in alendronate group was higher than that of alfacalcidol group. And low disease activity group treated with alendronate showed a tendency to decrease C2C. The results of this study suggest that alendronate treatment improves bone metabolism and may inhibit joint destruction in osteoporotic RA patients.

REFERENCES:


Fig.1: Percent changes in BAP after 3 and 6 months of treatment. In the alendronate group, BAP was significantly decreased, especially low disease group. A: alendronate group, D: alfacalcidol group, DAS<3.2: low disease activity group

Fig.2: Percentage changes of C2C after 3 and 6 months of treatment. Low disease activity alendronate group showed a tendency to decrease C2C. A: alendronate group, D: alfacalcidol group, DAS<3.2: low disease activity group

 serious side effects were observed.