The effectiveness of a combined therapy with alendronate and alfalcacidol on BMD loss around femoral implants after total hip arthroplasty

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Introduction
Several previous studies have reported that bone mineral density (BMD) loss around femoral implants is common, particularly in the proximal femur, relatively soon after surgery. The causes of this BMD loss are thought to be aseptic loosening or stress shielding. Osteolysis due to increased osteoclast-mediated bone resorption initiated by polyethylene or metal wear particles generated from joint surface friction is said to cause not only BMD loss around implants but also implant loosening in aseptic condition. In addition, stress shielding around the implant might contribute to a decrease in BMD over the long-term.

Recently, some authors have proven effectiveness of bisphosphonate on BMD loss around femoral implants after THA. Furthermore, our study took notice of active vitamin D₃ that becomes widespread on treatment for osteoporosis. Active vitamin D₃ has been shown not simply to supply calcium as a role of native vitamin D but contribute to the prevention of bone absorption and prevent to fall down. The big trial of combined therapy with the two drugs for postmenopausal osteoporosis is starting in our country and showing the significant effect compared with bisphosphonate monotherapy.

The purpose of our current prospective study was to compare the effects of combined therapy with alendronate and alfalcacidol and alendronate monotherapy on the prevention of BMD loss around femoral implants after primary THA.

Methods
Our study enrolled 62 patients (49 females and 13 males) with hemi-ostearthritises of the hip who had undergone primary THA. The patients were randomly assigned to alendronate (bisphosphonate, n=20) monotherapy, combined therapy with alendronate and alfalcacidol (active vitamin D₃, n=20) and non-medication (n=22). Drug treatments were 5 mg/day alendronate or 1 μg/day alfalcacidol by oral administration beginning on postoperative day 1. The same type of cementless femoral component (Versys fiber metal midcoat; Zimmer Inc, Warsaw, IN) was implanted in all of these patients.

The BMD levels in the periprosthetic femur were measured at one week after surgery as a reference baseline, followed by subsequent measurements at 12, 24 and 48 weeks post-operatively. These BMD measurements were made using dual-energy X-ray absorptiometry (DEXA) (Holologic QDR 2000 system). The periprosthetic zones described previously by Gruen were adopted as the regions of interest (ROI).

The bone turnover markers were evaluated before surgery as a baseline reference and then at 12, 24 and 48 weeks after surgery. Bone specific alkaline phosphatase (BAP) and serum N-terminal telopeptides of type 1 collagen (NTx) were measured. Changes in the periprosthetic BMD and in bone turnover markers at each follow-up were converted to a mean percentage loss or gain relative to the baseline reference.

Results
The non-medication group showed a BMD loss in all ROIs at 12 weeks after surgery and an even more remarkable BMD loss in ROI 1 and 7, which are located in the proximal region of the femoral implant. The values at each measurement time in ROI 1 and 7 are significantly lower than at baseline reference (p<0.05). In comparison between each ROI, the value of ROI 7 is significantly lower than that in ROIs 2 to 6 (p<0.05) (Figure 1).

The alendronate monotherapy and combined therapy with alendronate and alfalcacidol showed slight bone loss in all ROIs except for ROI 4 at 12 weeks after surgery. Even in ROI 1 and 7, the BMD values showed slight decrease at each measurement time. There were no significant differences in the mean BMD percentages at each measurement time in each of the ROIs compared with a baseline reference.

In a comparison of the mean BMD percentages, the periprosthetic BMD (%) in the non-medication showed 83.1±16.7%, 79.7±18.6% and 73.9±16.8% consecutively, on the other hand, the periprosthetic BMD (%) in the alendronate monotherapy and combined therapy with alendronate and alfalcacidol showed 95.4±18.3% and 97.9±15.1% at 12 weeks, 92.1±14.8% and 91.6±13.3% at 24 weeks and 92.3±21.9% and 91.2±16.5% at 48 weeks after surgery respectively. Of note, the patients in the alendronate monotherapy and combination therapy with alendronate and alfalcacidol at each measurement time showed a significantly reduced periprosthetic BMD loss in ROI 7 compared with those in non-medication group (p<0.05) (Figure 2).

Discussion
1α-Hydroxyvitamin D₃ or alfalcacidol which is a active vitamin D₃ and a prodrug of 1,25(OH)₂ D₃, is also known as a major drug for postmenopausal osteoporosis in Europe and Japan. 1α-Hydroxyvitamin D₃ shows pleiotropic actions which indicate calcium absorption, reduction of PTH, mineralization, bone turnover, muscle function and risk of falls.

In fact, postmenopausal osteoporosis is frequently treated with combination therapy, however, clinical effects have not adequately investigated until today, although a few paper revealed the effectiveness of combined therapy with alendronate and 1α-Hydroxyvitamin D₃. Recently some big studies of combined treatment for postmenopausal osteoporosis are ongoing and the focus on the world’s attention.

The main point of our study is the first study to evaluate the effect of a combined treatment with alendronate and 1α-Hydroxyvitamin D₃ in prevention of periprosthetic BMD loss after THA. As a result, the effectiveness of the combined treatment was equivalent to that of alendronate alone treatment on prevention of periprosthetic BMD loss although the combined treatment was significantly effective compared with no medication.