Introduction: Aseptic loosening due to wear particle-induced osteolysis at the host-implant interface is a major factor limiting implant survival after total hip arthroplasty (THA). Factors that allow ingestion or generation of wear particles at the interface may include local bone remodeling due to stress shielding and implant micromotion. Prevention of stress-shielding and early stabilization of the host-implant interface may reduce the interface particle load and subsequent osteolytic stimulus. The bisphosphonates are a group of drugs that have powerful anti-osteoclast activity and may have a role in the prevention of both stress-shielding and wear particle-induced osteolysis. In this randomized controlled trial extension study we examined the effect of pamidronate on bone turnover and implant migration after THA.

Materials and Methods: 50 men and women undergoing primary hybrid THA for osteoarthritis were randomized to receive a single infusion of 90mg of pamidronate or placebo on the 5th post-operative day. Femoral and pelvic periprosthetic BMD was measured by dual energy x-ray absorptiometry using an Hologic QDR 4500A densitometer with metal removal software at post-operative baseline and at weeks 6, 12, 26, 52, and 104. Implant migration was measured on digitized radiographs of the hip taken at the same timepoints using dedicated migration software (EBRA). Biochemical markers of osteoclast activity (NTX-I, N-telopeptide of type-I collagen, ELISA) and osteoblast activity (Bone ALP, bone-specific alkaline phosphatase, RIA) were measured from fasting morning urine and serum samples, respectively, at pre-operative baseline and at weeks 1, 6, 12, 26, 52, and 104. Quantitative periprosthetic isotope bone scan activity was measured by single photon emission computed tomography (SPECT) 3 hours after administration of 800MBq of 99mTc-HDP at weeks 26 and 52. Clinical assessments were made using the Harris hip score and the SF-36 general health questionnaire at baseline and at weeks 12, 26, 52, and 104. Quality of femoral cementing was graded using the Barrack system. Analysis of serial data was by repeated measures ANOVA or Friedman’s 2-way ANOVA by rank. Proportional data were analysed using the χ² test with Yates correction.

Results: 44 patients completed the study and form the analysis set, of whom 22 received pamidronate. The patients in each group were of similar age, sex distribution, BMI, and baseline BMD (P>0.05). Patients in the pamidronate group had significantly less femoral, but not pelvic, bone loss than those given placebo (Figure 1, P=0.02), however, most of the femoral bone loss seen in the placebo group was transient. Pamidronate was most effective in preventing non-transient bone loss in Gruen zones 6 and 7 (P=0.004, and P=0.014, respectively). No differences in stem or cup migration were found between the study groups (Figure 2, P>0.05). At week 104 the mean total stem migration was 1.77±0.27 and 1.62±0.37 for the placebo and pamidronate groups, respectively. Total cup migration was 0.75±0.26 and 0.76±0.14. In the placebo group there was a transient early rapid rise in osteoclast activity with a peak rise of 60% that was suppressed by pamidronate therapy (Figure 3, P=0.008). By week 26 biochemical markers of bone turnover had returned to, or below, baseline, and SPECT activity in both groups was similar. Both groups underwent similar improvement in Harris hip score, and SF-36 physical component summary score (P>0.05). Age at surgery accounted for 26% (linear regression, r²=0.65, P=0.02) and 38% (r²=0.51, P=0.007) of the variability of stem and cup migration by week 104 in the placebo group, with younger subjects experiencing greater migration. Stem migration at week 104 was also inversely related to the Barrack grade of the cement mantle (r=-0.66, r²=41%, P=0.0003). Implant migration was not significantly related to periprosthetic bone loss, or other markers of bone metabolism (linear regression, P>0.05, all comparisons).

Discussion: Pamidronate therapy has a significant effect on bone turnover after THA. Single dose therapy has a duration of action of 3 to 6 months and is sufficient to prevent the transient component of femoral bone loss that is seen in the early period following surgery. Pamidronate therapy does not enhance implant stability and therefore may not have any significant implications for implant survival. Longer courses may be effective, however our results suggest that changes in bone mass are not major determinants of early implant migration whereas age at operation and cementing technique are.

Figure 1. BMD change of the proximal femur and pelvis by treatment group. PBO=placebo, APD=pamidronate.

![BMD change](image1)

Figure 2. Total migration (vector of x and y-axis) by treatment group

![Migration](image2)

Figure 3. Changes in biochemical markers by treatment group.

![Biochemical markers](image3)

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