Combined effects of zoledronate and mechanical stimulation in the mouse tibia

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INTRODUCTION

It has been shown that local bisphosphonate preserves periprosthetic bone stock, in rats and sheep [1]. In the clinical situation of load-bearing implants, where the periprosthetic bone is exposed to high mechanical demands, the modulation of the bone response by bisphosphonate remains uncertain.

Bone can adapt to mechanical loading. This relies upon the communication between osteocytes, osteoclasts and osteoblasts, through cell-cell contacts and local cytokines. Bisphosphonates inhibit osteoclasts differentiation and activity; consequently they slow down the bone turnover rate. Given the constant communication between the bone cells, the changes that affect one type of cells might have indirect consequences on the other types of cells. In the specific case of periprosthetic bone under specific mechanical conditions, this could lead to a pathological response.

The aim of the present study was to assess the effect of zoledronate, a member of the third generation bisphosphonates, on bone adaptation to mechanical loading. For this purpose, we used an in-vivo axial compression model of the mouse tibia and analyzed the effect of systemic zoledronate exposure on site-specific bone adaptation.

MATERIALS AND METHODS

Animals

Eleven C57BL6 male mice, 17±1 weeks old, were separated randomly into two groups: zoledronate (5 animals) and control (6 animals). On day 0, the zoledronate group received a single subcutaneous injection of 1 µg/kg Zoledronate (Novartis, Switzerland) while the control group received an injection of saline. The local ethics committee on animal care approved all animal procedures (Protocol#2006.1).

µCT

We assessed trabecular and cortical bone architecture of the tibias using in vivo micro-computed tomography at day 0 and day 11, with 9 µm isotropic voxel size. Trabecular thickness (Tb.Th) was evaluated at the proximal tibial metaphysis, whereas cortical thickness (Ct.Th), bone perimeter (B.Pm) and bone area (B.Ar) were evaluated at four different locations of the diaphysis (as shown in Figure 1).

RESULTS

Effects of mechanical loading and zoledronate were analyzed with two-way ANOVA and Tukey postoc-tests, p<0.05 was considered significant and, given the small number of animals per group, p<0.1 was considered as a strong trend.

DISCUSSION

Numerical analyses showed that this simple axial loading induced combined compressive and bending strains, with maximum octahedral shear strain at the postero-tibial crest (1800±40 µε) [2].

Sacrifice and mechanical tests

On day 11, while still under anesthesia for the µCT, the animals were sacrificed, the tibias extracted surgically and placed in wet conditions at 4 °C. Then, tibial biomechanical properties were assessed by 3-point bending. The ultimate force, stiffness and postyield energy to failure were calculated from the collected data. The yield point was defined by using a 0.3 N offset from the stiffness line [20].

Analysis

Effects of mechanical loading and zoledronate were analyzed with two-way ANOVA and Tukey postoc-tests, p<0.05 was considered significant and, given the small number of animals per group, p<0.1 was considered as a strong trend.

REFERENCES


ACKNOWLEDGEMENTS

Project no. 04-P2 was supported by the AO Research Fund of the AO Foundation, Davos, Switzerland.