A BIOMECHANICAL STUDY ON THE EFFECTS OF PAMIDRONATE FOR PREVENTION OF OSTEOPOROSIS IN OVARIECTOMIZED RATS

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INTRODUCTION

Animal studies show that pamidronate can be 10-100 times more potent than clodronate or etidronate in inhibiting bone resorption in vivo. The purpose of this study is to determine the effects of pamidronate on the prevention of postmenopausal osteoporosis in the femur of ovariectomized rats by conducting biomechanical analysis.

PROCEDURES

Forty-two female Sprague-Dawley rats were used for this study. At the beginning of the experiment, the animals were 17 weeks of age weighing approximately 244g. The animals were randomly divided into 3 groups: Group 1 (n=10) was sham-operated, Group 2 (n=12) bilateral ovariectomy, and Group 3 (n=20) bilateral ovariectomy plus intravenous injection of 0.1mg/kg pamidronate twice a week during the first 8 weeks. Animals were sacrificed 12 weeks postoperatively and stored at -20ºC in a freezer. Before testing, the specimens were thawed at room temperature. The femurs from each group were tested in a 3-point bending mode with an MTS 858.20 Bionix testing machine (MTS System Corp., Minneapolis, MN, USA) to obtain bending stiffness. Load was applied to the bone at the mid-point of the femur at a deformation rate of 0.01 mm/sec. Bending stiffness was measured as the initial linear slope of the load-displacement curve. In addition, the stiffness was calculated analytically. For this, the femur was assumed as an isotropic, homogeneous, and deformable material of a small size. Thus, the following relationship between the deflection, bending moment, moment of inertia, and Young’s modulus was used for analysis of bending of the femur:

\[
\frac{|v''|}{\left[1 + (v')^2\right]^{3.5}} \approx \frac{|v''|}{M_b \cdot EI} \quad \ldots(1)
\]

where \(M_b\) is the bending moment, \(v\) is the deflection, \(I\) is the moment of inertia, and \(E\) is Young’s modulus. To calculate the moment of inertia of varying cross-sections, the specimens were cut into 2 mm-thick slices with a diamond saw (ISOMET™ 1000 Precision Saw, Buehler Analyst Ltd., Lake Bluff, IL, USA). Photos of the cross-sections were taken using CCD camera (WV-BP310, Panasonic®) and the cross-sectional areas were measured using specially-developed image analysis software. Young’s modulus was calculated using the moment-area method as in Equations (2) and (3):

\[
E = \frac{PL^2}{576 \cdot \delta \cdot \frac{2L}{36} \left(\frac{8}{I_1} + \frac{19}{I_2} + \frac{37}{I_3} + \frac{49}{I_4} + \frac{91}{I_5}\right)} \quad \ldots(2)
\]

\[
E = \frac{PL^2}{576 \cdot \delta \cdot \frac{2L}{36} \left(\frac{8}{I_1} + \frac{19}{I_2} + \frac{37}{I_3} + \frac{152}{I_4}\right)} \quad \ldots(3)
\]

where \(P/\delta\) is the stiffness, \(L\) is the distance between the two supports and \(I_{i=1\ldots5}\) is the moment of inertia of each segment. Equation (2) is for specimens with 5 slices and Equation (3) is for specimens with 4 slices.
RESULTS AND DISCUSSION

Figure 1 shows the analytically calculated Young’s modulus results of each group: 12.6 ± 3.5 GPa for Group 1, 9.6 ± 2.7 GPa for Group 2, and 12.0 ± 2.4 GPa for Group 3. Young’s modulus of Groups 1 and 3 were each significantly larger (p<0.1) than that of Group 2. The difference between Group 1 and Group 3 was not significant (p=0.4). These results suggest that pamidronate treatments can raise the Young’s modulus of osteoporotic bone to levels close to that of normal bone. Differences between the load-deflection curves from the bending tests were, however, indistinguishable among the groups (Figure 2).

SUMMARY

Our biomechanical analysis showed that the Young’s modulus of the femur was increased by administration of pamidronate in a rat model of osteoporosis. This suggests that pamidronate could be effective for prevention of osteoporosis during the early period of estrogen deficiency.

REFERENCE


Figure 1: Comparison of Young’s modulus for each group.

Figure 2: 3-point bending test and typical load-displacement curves for each group.