TACSM Abstract

Impact of Anti-Resorptive Treatment on Recovery of Bone After Disuse

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ABSTRACT

Bisphosphonates (BP), drugs that inhibit bone resorption, are used to minimize bone loss in long-duration spaceflight, extended bed rest, and acute spinal cord injury; however, the long term impact of BP use on recovery of bone after disuse is not well understood. This experiment tests the hypothesis that the BP zoledronic acid (ZOL) administered 7 days before hindlimb unloading (HU) will protect against loss of bone mass during 28 days of HU by suppressing bone resorption activity while also diminishing the ability of cancellous bone formation rate (BFR) to recover following HU. Male Sprague Dawley rats (6 mo) were assigned to aging control (AC), HU, and HU+ZOL groups and subjected to 28 days of HU, then to 56 days of weight-bearing recovery (REC). One group of rats was given 2 fluorescent labels 7 days apart to measure BFR in the final week of HU and the other group was given the same labels in the final week of REC. Histomorphometric analyses of the proximal tibia and distal femur showed lower osteoclast surface, a measure of bone resorption, 35 days after injection and 119 days after injection (-50% and -75%, respectively, compared to HU). This verified that ZOL successfully suppressed bone resorption. Dynamic histomorphometry revealed that cancellous BFR was lower in ZOL+HU versus AC both immediately after HU (-96.6%) and after the recovery period (-99.9%) ($p<0.05$). However, quantitative computed tomography measures of cancellous volumetric bone mineral density (CN-vBMD) at the proximal tibia revealed that CN-vBMD was higher in ZOL+HU versus AC and HU after 28 days of HU (+120.0% and +109.5%, respectively) and higher than AC after the 56 day recovery period (+125.5%) ($p<0.05$). These data indicate ZOL is a potent suppressor of bone formation as well as resorption. While ZOL effectively inhibited disuse-induced bone loss, the prolonged suppression of BFR by ZOL after administration may be detrimental in long-term recovery of bone after disuse.