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Original Article

Hylonome

New observations on bone fragility with glucocorticoid treatment. Results from an *in vivo* animal model

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Glucocorticoid treatment frequently is associated with an increase in the risk of bone fracture, especially in the spinal vertebrae and the femoral head[1-3]. Individuals treated with glucocorticoids have alterations in bone remodeling[4-6]. These alternations in bone remodeling include an increase in bone resorption and reductions in bone formation such that reductions in trabecular bone mass and architecture occur, including reductions in trabecular thickness and trabecular number[5-8]. The mechanism behind these changes have been proposed to be alterations in bone cell viability, i.e., glucocorticoids reduce the lifespan of osteoblasts and osteocytes through apoptosis while increasing osteoclast viability[7,8]. While these proposed alterations in bone cell lifespan could explain the reduction in bone formation markers and trabecular bone architecture, neither of these observations completely explains the increased bone fragility observed in glucocorticoid-induced osteoporosis when compared to postmenopausal osteoporosis[4].

Methods

We assessed the changes in the fifth lumbar vertebral body and/or distal femur for trabecular bone structure (micro-CT and histomorphometry), elastic modulus of lumbar vertebrae trabeculae (Scanning Probe Microscopy), whole bone strength (compression testing), mineral to matrix ratio of the trabeculae (MicroRamen Spectroscopy), and bone turnover (serum and urine biochemical markers and histomorphometry) for prednisolone-treated mice and controls; and estrogen deficient mice and sham-operated controls after 21 days of treatment.

Results

We observed significant reductions in trabecular bone volume and whole bone strength in both prednisolone-treated and estrogen deficient mice compared to their controls after 21 days ($p<0.05$). In addition, significant changes within the trabecular bone surrounding the osteocyte lacunae were observed in the prednisolone-treated mice. The size of the osteocyte lacunae was increased, and elastic modulus was reduced around the lacunae. In addition, a "halo" of hypomineralized bone surrounding the lacunae was observed only in the prednisolone-treated mice and this was associated with reduced (nearly 40%) mineral to matrix ratio determined by Raman microspectroscopy.

Conclusions

Based on these results, we propose that glucocorticoids have direct effects on osteocytes, not only to induce cell death[7,8], but more importantly, to induce viable cells to modify their microenvironment. By 'leaching' mineral from their surroundings, there is both enlargement of the lacunae and a sphere of hypomineralized bone that is generated. Together, this may result in highly localized changes in bone strength. Based on these results, bone active agents that influence bone cell activity such as bisphosphonates and hPTH (1-34) might be useful agents to prevent or treat glucocorticoid-induced bone loss[9,10]. These results also suggest that glucocorticoids produce localized changes in bone strength that are in some aspects similar to estrogen deficiency (increased bone remodeling on the trabecular surface) but also different (hypomineralization around the osteocyte lacunae) that may help to explain why glucocorticoid-treated patients fracture at higher bone mineral densities than postmenopausal women with osteoporosis.

The author has no conflict of interest.

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