Glucocorticoid-induced Osteoporosis

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KEYWORDS

• Glucocorticoids • Osteoporosis • Fracture risk • Prevention

KEY POINTS

- Glucocorticoid-induced osteoporosis (GIOP) is one of the most common and serious adverse effects associated with glucocorticoid use.
- GIOP is associated with significant morbidity secondary to resultant fractures, and despite GIOP being a well-characterized problem, it remains undertreated, and prevention strategies are underused.
- This article highlights GIOP pathophysiology, epidemiologic associations, effective treatment, and lifestyle modifications that can reduce fracture risk for long-term glucocorticoid users and additionally emphasizes the importance of early intervention.

INTRODUCTION

Glucocorticoid-induced osteoporosis (GIOP) is one of the most common and serious adverse effects associated with glucocorticoid use. GIOP, the most common secondary form of osteoporosis, is associated with significant morbidity secondary to resultant fractures. Despite GIOP being a well-characterized problem that can occur rapidly, within the first few months of glucocorticoid use, it remains undertreated, and prevention strategies are underused. This article highlights GIOP pathophysiology, epidemiologic associations, effective treatment, and lifestyle modifications that can reduce fracture risk for long-term glucocorticoid users and additionally emphasizes the importance of early intervention.

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GLUCOCORTICOID EFFECTS ON BONE

Glucocorticoids lead to decreased bone formation and increased bone resorption (Fig. 1). The effects on osteoblasts, which are essential for bone formation, include decreased differentiation and maturation leading to their decreased number and function.[1,2] In addition, excess glucocorticoid results in osteoblast apoptosis, further contributing to reduced bone formation.[1–3] Osteocytes also undergo apoptosis and, because they are involved in repair of microdamage to bone, this leads to a decrease in bone quality.[1] Glucocorticoids increase the expression of cytokines, including receptor of activator of NF-kappa β ligand (RANKL), that are involved in differentiation of osteoclasts and conversely decrease those involved in inhibition of osteoclasts, with the net effect of increased bone resorption.[1] Indirect effects of glucocorticoids contribute to bone loss as well, such as decreases in calcium resorption, suppression of sex hormones and growth hormones, and alteration of parathyroid hormone pulsatility.[1] However, subclinical secondary hyperparathyroidism leading to bone resorption is considered a more minor pathway for bone loss in GIOP. Areas of exploration include determining whether there are genetic factors that may make an individual more susceptible to adverse effects from glucocorticoids. A polymorphism in the glucocorticoid receptor gene has been identified that is associated with increased sensitivity to glucocorticoids with regard to cortisol suppression and insulin response, and although lower bone mineral density (BMD) in the spine was also found compared with controls, this did not reach statistical significance.[4] To date, genetic testing has not found a role in risk stratification for GIOP.

EPIDEMIOLOGY

Up to 40% of persons receiving glucocorticoids develop bone loss over time.[5] Bone loss secondary to glucocorticoids occurs early in their course of use; most

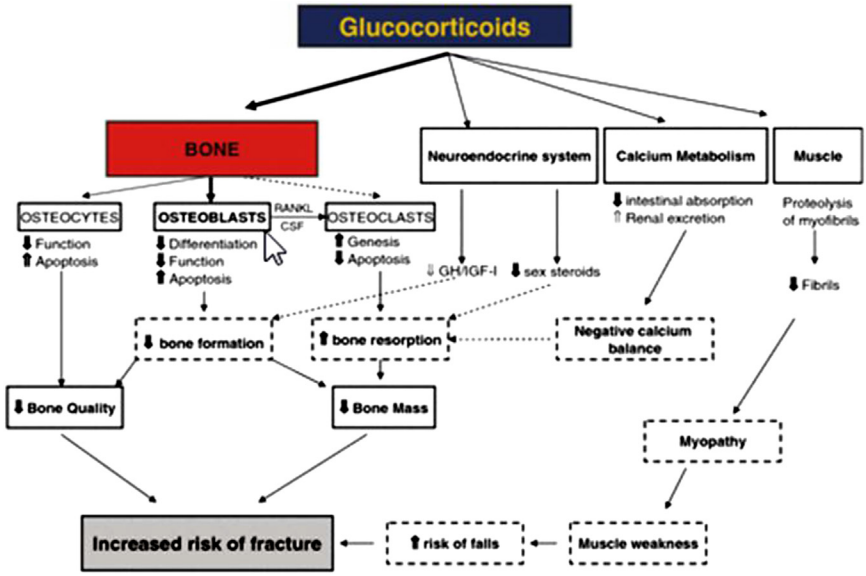

Fig. 1. Pathogenesis of GIOP. CSF, colony-stimulating factor; GH, growth hormone; IGF, insulinlike growth factor; RANKL, receptor activator of nuclear factor kappa-B ligand. (*Adapted from* Canalis E, Mazziotti G, Giustina A, et al. Glucocorticoid-induced osteoporosis: pathophysiology and therapy. Osteoporos Int 2007;18(10):1319–28; with permission.)