A Guide to Preventing Glucocorticoid-Induced Osteoporosis

Our patients with very different problems: a 30-year-old woman with rheumatoid arthritis, a 68-year-old man with poorly controlled asthma, a 52-year-old man who has received a kidney transplant, and a 46-year-old woman with inflammatory bowel disease. Yet all of these patients have at least one thing in common: an increased risk of osteoporosis as a result of long-term treatment with glucocorticoids.

Because of their anti-inflammatory and immunosuppressive effects, glucocorticoids remain a cornerstone of treatment for patients with a variety of noninfectious inflammatory diseases. However, adverse effects of long-term glucocorticoid therapy are common: osteoporosis and associated fractures are among the most serious. Prednisone therapy at doses of 7.5 mg/d or more for 6 months or longer often causes rapid loss of trabecular bone in the spine, hip, and forearm.

The American College of Radiology (ACR) updated its recommendations to help you combat glucocorticoid-induced osteoporosis.1 A key change from earlier guidelines is that recommendations are now based on the patient’s overall risk profile instead of T-scores alone. Highlights of the ACR’s report on preventive measures follow.

MECHANISMS OF GLUCOCORTICOID-INDUCED BONE LOSS

Glucocorticoids affect calcium homeostasis, sex hormones, and bone formation through a number of mechanisms. These include:

• A decrease in intestinal absorption of both calcium and phosphate and an increase in urinary calcium excretion. These actions can cause secondary hyperparathyroidism and increased serum levels of parathyroid hormone (PTH). If PTH levels remain consistently elevated, bone resorption may be increased.

• A reduction in the production of estrogen and testosterone.

• Inhibition of osteoblast proliferation and attachment to matrix, and synthesis of type I collagen and non-collagenous proteins.

The myopathy induced by glucocorticoids may also contribute to bone loss by removing natural forces on bone that occur during muscle contraction.

PREVENTING OSTEOPOROSIS IN ADULTS RECEIVING GLUCOCORTICOID THERAPY

Bone is lost most rapidly during the first 6 months of glucocorticoid treatment. Thus, the ACR recommends that you start primary preventive measures as soon as you prescribe these agents. This includes educating the patient about glucocorticoid-induced bone loss and lifestyle modifications that can help prevent such loss (Table).

Table – Measures that can help prevent bone loss in patients who take glucocorticoids

| • Use the lowest effective dose of glucocorticoid for the shortest duration possible* |
| • Encourage patients to reduce their risk of osteoporosis by: |
| — Quitting smoking |
| — Limiting alcohol consumption (2 or fewer drinks per day) |
| — Participating in a daily weight-bearing exercise program for 30 to 60 minutes |
| — Maintaining an adequate intake of calcium and vitamin D |

*Use of an alternate-day dosing schedule does not protect against glucocorticoid-induced bone loss.

During the initial history and physical examination, document any potentially modifiable risk factors for osteoporosis. Key among these are inadequate dietary calcium and vitamin D intake, smoking, and excess alcohol consumption. Inquire about menstrual history and, in men, ask about problems with infertility or erectile dysfunction. A review of the patient’s medications can also be revealing: such agents as phenytoin, cyclosporine, thyroid hormone replacement, warfarin, and antigonadotropins (including gonadotropin-releasing hormone agonists) are among the agents associated with an increased risk of osteoporosis.

Clinical factors that may indicate a greater risk of glucocorticoid-induced osteoporosis include the following1:

• Low body mass index.
• Parental history of hip fracture.
• Current smoking.
• Three or more alcoholic drinks per day.
• Higher daily glucocorticoid dose.
• Higher cumulative glucocorticoid dose.

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- Intravenous pulse glucocorticoid use.
- Declining central bone mineral density (BMD) measurement that exceeds the least significant change.

The maintenance of muscle strength is particularly important for patients who will be taking glucocorticoids for long periods. Consider referring your patient to a physical therapist who can recommend and teach specific strengthening exercises and who can offer assistive devices (canes, walkers, etc) when appropriate to help prevent falls.

During the initial visit, measure the patient’s height and weight, and assess muscle strength. Order dual energy x-ray absorptiometry to measure BMD.

However, BMD may not be the sole reliable predictor of fracture risk in patients who are receiving glucocorticoids. The FRAX tool was developed by the World Health Organization to assess the risk of fracture; it incorporates numerous clinical factors into its prediction model.2

The FRAX tool is used to calculate the 10-year probability of a major osteoporotic fracture:
- Low risk: Less than 10% probability of fracture.
- Medium risk: 10% to 20%.
- High risk: Greater than 20% (or a T score of less than or equal to –2.5).

The National Osteoporosis Foundation considers the category of high risk as the threshold for cost-effective treatment.3 Because FRAX uses an average glucocorticoid dose to calculate the 10-year risk of fracture, patients who are receiving higher doses are likely to have a greater absolute fracture risk than estimated by FRAX. In addition, a higher cumulative glucocorticoid dose and intravenous pulse glucocorticoids may increase the risk of fractures.

TREATMENT OPTIONS

Calcium and vitamin D supplementation is recommended for all patients who are starting glucocorticoid therapy. A total calcium intake (dietary and supplemental) of 1200 to 1500 mg/d is advisable. So is vitamin D supplementation to achieve “therapeutic” levels of 25-hydroxyvitamin D, or dosages of 800 to 1000 IU/d; higher dosages may be required to reach target levels.

For low-risk postmenopausal women and men older than 50 years who are receiving a glucocorticoid dosage of less than 7.5 mg/d, no pharmacological treatment is recommended. Alendronate and risendronate are options for low-risk patients taking a higher glucocorticoid dosage, all medium-risk patients, and all high-risk patients. Zoledronic acid is an option for low-risk and medium-risk patients who are receiving a glucocorticoid dosage of 7.5 mg/d or higher, as well as all high-risk patients. Teriparatide is an option for high-risk patients.

Treatment options for premenopausal women and men younger than 50 years who have a history of fragility fracture are provided in the ACR guidelines.1 There is inadequate evidence to make pharmacological treatment recommendations for patients in these groups who do not have a history of fragility fracture.

REFERENCES:
2. FRAX. WHO Fracture Risk Assessment Tool. URL: http://www.shef.ac.uk/FRAX/.