Corticosteroid-Induced Bone Loss
Prevention and Management

César Picado and Maite Luengo
Servei de Pneumologia i Allergia Respiratoria, Departament de Medicina,
Hospital Clinic i Universitari, Facultat de Medicina, Barcelona, Spain

Summary

Osteoporosis is one of the most serious adverse effects experienced by patients receiving long term corticosteroid therapy. Bone loss occurs soon after corticosteroid therapy is initiated and results from a complex mechanism involving osteoblastic suppression and increased bone resorption. There are a number of factors that may increase the risk of corticosteroid-induced osteoporosis [smoking, excessive alcohol (ethanol) consumption, amenorrhea, relative immobilisation, chronic obstructive pulmonary disease, inflammatory bowel disease, hypogonadism in men, organ transplantation].

The initial assessment of patients about to start taking corticosteroids should include measurement of spinal bone density, urinary calcium level and plasma calcifediol (25-hydroxycholecalciferol) level; serum testosterone levels should also be measured when hypogonadism is suspected.

Many different drugs have been used to prevent osteoporosis in patients receiving long-term corticosteroid therapy, including thiazide diuretics, cholecalciferol (vitamin D) metabolites, bisphosphonates, calcitonin, fluoride, estrogens, anabolic steroids and progesterone. At present, however, published studies have failed to demonstrate a reduction in the rate of fracture using different preventive pharmacological therapies in patients being treated with corticosteroids on a continuous basis.

Among the drugs studied, bisphosphonates (pamidronic acid and etidronic acid) and calcitonin appear to be effective in increasing bone density. Cholecalciferol preparations have been reported to be effective in some, but not all, studies. Limited data have shown positive results with thiazide diuretics, estrogen, progesterone and nandrolone.
When treating patients with corticosteroids, the lowest effective dose should be used, with topical corticosteroids used whenever possible. Auranofin may be considered in patients with corticosteroid-dependent asthma. Patients should take as much physical activity as possible, maintain an adequate daily intake of calcium (1000 mg/day) and cholecalciferol (400 to 800 U/day), stop smoking and avoid excessive alcohol intake. It is important to detect and treat hypogonadism in men, if present, and to replace gonadal hormones in postmenopausal women or amenorrheic premenopausal women, and to detect and correct cholecalciferol deficiency. A thiazide diuretic should be considered if hypercalciuria is present (urinary calcium excretion in excess of 4 mg/kg/day).

High-risk patients and those with established osteoporosis should be treated with bisphosphonates (cyclical etidronic acid or intravenous pamidronic acid), nasal calcitonin, or calcifediol or calcitriol. Patients receiving cholecalciferol preparations should be carefully monitored for hypercalciuria and hypercalcaemia.

A common and often clinically challenging type of osteoporosis is that caused by long term corticosteroid therapy. Such therapy is prescribed for many patients, including certain patients with bronchial asthma, systemic lupus erythematosus, vasculitis, malignancies and rheumatoid arthritis, and recipients of organ transplants. This review discusses the pathophysiology, predisposing factors, prevention and management of corticosteroid-induced bone loss.

1. Pathophysiology

In 1932, Cushing[1] described the tendency of patients with endogenous corticosteroid excess to develop bone fractures. Estimation of the prevalence of osteoporosis in these patients, given by the proportion of patients with fractures, indicates that the prevalence ranged from 20 to 70%.[2,3] Similar prevalences of fractures have been reported in patients requiring long term high-dose corticosteroid therapy.[4-6] In other studies, however, the prevalence of bone fractures in patients receiving long term high-dose corticosteroid therapy has been found to be similar to the incidence seen in healthy individuals.[7,8]

It is commonly held that corticosteroids deplete bone preferentially in the axial skeleton. The fact that bone loss in trabecular bone occurs more rapidly and markedly than loss in cortical bone results in a greater likelihood of fractures in bones with a higher proportion of trabecular bone, such as the vertebrae and ribs.[9] Recent studies, however, suggest that corticosteroid-induced osteoporosis is a generalised process causing bone loss at various sites.[10] Prospective studies have suggested that there is an initial phase of very rapid bone loss, followed by slower continued bone loss.[9-11]

Corticosteroids have been found to influence both bone formation and bone resorption.[9] The enhanced bone resorption might be explained, at least in part, by the development of secondary hyperparathyroidism, but evidence exists showing that a direct effect on bone also occurs.[9] When given initially, corticosteroids increase secretion of parathyroid hormone (PTH), probably as a result of reduced intestinal absorption, and increased renal loss, of calcium.[12-14] There is also evidence that corticosteroids potentiate the activity of PTH on osteoblasts.[9] An increase in PTH levels has been shown shortly after administration of corticosteroids, but the effect of long term corticosteroid administration is less clear.[6] The mechanism of inhibition of intestinal calcium absorption by corticosteroids is unknown. Initially, it was suggested that corticosteroids may inhibit cholecalciferol (vitamin D) metabolism, particularly the conversion of cholecalciferol to calcifediol (25-hydroxycholecalciferol). Evidence for this, however, has been contradicted by studies showing elevated, normal or depressed levels of cholecalciferol.[13-17]