



Steroid-Induced Osteoporosis; At a Glance

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Steroid-Induced Osteoporosis and the Facts

Due to its strong immunosuppressive effects, steroids are a valuable group of drugs and are widely used in the treatment of inflammatory and autoimmune diseases. With the discovery of cortisone and cortisol in the 1930s, synthetic derivatives of glucocorticoids are used successfully in many fields of medicine such as rheumatology, allergy, lung diseases, dermatology, hematology [1], Glucocorticoids (GC) in the treatment of many inflammatory conditions plays an important role. Nowadays steroids major reasons for its use; rheumatologic causes such as rheumatoid arthritis, polymyalgia rheumatica, asthma and chronic obstructive pulmonary disease. It has been reported that oral steroid use in the population is between 0.5-0.9%. The use of GC in the 70-79 age group is approximately 2.5%. [2]. During chronic use of steroids, well-known side effects such as diabetes, osteoporosis, myopathy, cataract, hypothalamic-pituitary-adrenal axis suppression, susceptibility to infections are seen. In addition, lipodystrophy and neuropsychic disorders are the most common side effects [3,4].

Steroid osteoporosis, the most common cause of secondary osteoporosis and it ranks first in iatrogenic osteoporosis and before the age of 50 years [5]. Studies have shown that oral GCs are both short and long-time use leads to bone loss and increased risk of fracture [6,7]. This loss is closely related to the cumulative dose and duration, and it has been shown that even a prednisolone dose of <5 mg per day may increase the risk of fracture [8]. In terms of the relationship between fracture risk and GC dose, epidemiological studies have shown an increase in fracture risk even in low doses of 2.5-5 mg prednisone per day. There is a dose-dependent increase in fracture incidence. The risk of fracture appears to be more related to the daily dose than the cumulative dose; this may be explained by the difficulty in accurately calculating the cumulative dose [9]. More than 10% of patients undergoing long-term GC treatment have clinical fractures, and 30-40% have signs of radiological vertebral fractures [10,11].

The highest rate of bone loss occurs within the first three to six months of GC treatment. In the first year of treatment, bone loss rate is more than 20%, but this loss tends to stabilize in 2-3%. The

use of parenteral, oral and even long-term inhaled steroids leads to significant bone loss. It is primarily the affected trabecular bone, with both high and cumulative doses of GCs leading to an increased risk of fractures in the vertebrae. Cortical bones, such as the femur, are affected later. Fragility fractures may occur in approximately 20% of patients treated with steroids in the first year of treatment [10-12]. Due to the strong connections between inflammatory cells and bone cells, the inflammatory process requiring steroid use is itself a key factor in bone fragility and is one of the determinants of rapid bone loss at the onset of steroid use [13]. Risk factors for GC-induced fracture include low bone strength at the onset of GC treatment and bone mass reduction rate in treatment; this is largely determined by the dose and duration of GC use. However, GC treatment is a potentially reversible risk factor for glucocorticoid-induced osteoporosis (GCO); If GK treatment is discontinued, bone mineral density (BMD) increases and fracture risk decreases.

In addition, the absolute risk of future fracture in an individual is significantly affected by demographic and other characteristics (age, race, sex, and associated osteoporosis risk factors). For these reasons, it is important to identify those at high risk among patients receiving GC therapy with a sufficiently high potential for damage [14]. The global prevalence of fractures in patients receiving long-term steroid treatment has been reported to be 30-50%. In a cross-sectional study, the prevalence of spine fractures was found to be 37% in 551 long-term steroid patients, and 14% of patients had two or more asymptomatic vertebral fractures; At least one vertebral fracture was reported in 48% of patients older than 70 years and in 30% of those younger than 60 years. [11] The risk of fracture in patients using steroids is almost twice as high, and this risk is even higher in vertebral fractures. In the study, a total of 244,235 people using oral steroids were compared with a control group of 244,235 patients, the risk of hip fracture was 1.6 and the risk of vertebral fracture was 2.6 times higher in the steroid group [15].

Prevalence increases with age and is the key point of preventive strategies. Some observations from epidemiological studies are important for clinical practice, as they may help identify high-risk patient groups. Some observations from epidemiological studies

are important for clinical practice, as they may help identify high-risk patient groups.

Glucocorticoid-Induced Osteoporosis-Clinical Features

The clinical manifestations of GCO are the same as for other causes of osteoporosis. Most of the time, there is no clinical finding until fracture occurs. Since trabecular bone is affected more than cortical regions, spine and rib fractures are more common. The risk of hip and nonvertebral fracture is reported to be moderate [15-18]. Vertebra fractures are the most common fractures but are usually asymptomatic. Information on GCO and related fractures in children is limited. The risk of vertebral fractures in children with systemic autoimmune disease receiving GC has been reported to be 6% after 1 year of treatment. Compared to the general pediatric population, children who receive GC (> 4 cycles of GC per year) have a relative risk of fracture increased by approximately 30% [19,20]. When evaluating the patient, besides the reason, dose and duration of GC use, fall risk factors should also be investigated. Previous fractures and fragility fractures should be questioned. Other risk factors and comorbid conditions such as malnutrition, severe weight loss or low body weight, hypogonadism, secondary hyperparathyroidism, history of thyroid disease, hip fracture, history of alcohol use (≥ 3 units / day) should be identified.

Physical examination should include osteoporosis-specific examinations such as height measurement (without shoes), weight measurement, muscle strength assessment, spinal sensitivity, deformity and reduction of the space between the lower ribs and the upper pelvis for the follow-up of asymptomatic vertebral fractures at the beginning of steroid treatment. Biochemical tests should be performed to screen for different bone diseases. Since the bone turnover is consistently low in steroid users, there are no biochemical markers to indicate bone turnover at baseline or during follow-up. However, osteocalcin can be evaluated because it is significantly suppressed in GCO. Biochemical evaluation of calcium, 25 hydroxy-vitamin D (25-OHD), liver and renal functions is recommended before starting treatment.

Treatment

Despite increasing knowledge of risk factors for fracture in GC users and the availability of effective treatments to prevent fracture, many long-term GC users do not receive treatment to prevent bone loss or are treated only after fracture occurs [21,22]. However, more than half of those treated have not been evaluated or treated for the treatment of osteoporosis [23]. Postmenopausal women and the elderly have the highest risk of bone loss and fracture among GC users [24]. Therefore, anti-osteoporotic drugs should be started immediately for postmenopausal women and men over 50 years of age, who are at high risk for GCO. However, there is little evidence that treatment prevents a new vertebral fracture for premenopausal women and young men. [8] Studies have been conducted to investigate the effect of antiosteoporosis drugs on prevention or treatment of GCO, but their duration is limited to 12-36 months [25]. Since the risk of fractures has been shown to be reduced after discontinuation of steroids, it is recommended that bone preservatives may be discontinued in this case. The most

appropriate medical treatment for patients with GCO should be monitored by the relevant physician.

General Precautions

Since the daily dose of steroids is the determinant of fracture risk, alternative applications such as continuous minimal dose reduction or intraarticular injection should be considered. Especially in elderly patients, the risk of falling due to painful lower extremity joints should also be evaluated. Physical activity or immobilization should be adjusted and planned according to the underlying condition. In order to minimize bone loss, the following general principles should be applied to each patient who has been using GK at any dose for more than ≥ 3 months [26,27]:

- 1) The dose and duration of GC treatment should be minimized, as even the doses and chronic inhaled GCs that are thought to be changed may cause bone loss. If possible, alternative treatment should be used.
- 2) Instead of enteral and parenteral GC therapy, topical treatments (inhaled GCs in asthma and GC enemas in bowel diseases) should be preferred, if possible.
- 3) Load-bearing exercises should be performed to prevent bone loss and muscle atrophy.
- 4) Smoking and excessive alcohol consumption of the patients should be prevented.
- 5) Precautions should be explained to prevent falls.

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