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Low bone mineral density can occur in children after short-term systemic glucocorticoid treatment

To the editor

Osteoporosis in children with chronic diseases has long been recognized as a major endocrine complication during the pre- and posttreatment periods, possibly triggered by the disease itself or its treatment. Despite advanced and targeted management of childhood illnesses, the use of systemic glucocorticoids (GC) remains the cornerstone of treatment for various acute and chronic conditions, including infections, cancers, autoimmune disorders, respiratory distress, and neuromuscular disorders.[1] However, bone mass, shape, and bone metabolic status continue to significantly change during childhood and adolescence; thus, children are more sensitive to the detrimental effects of GC use because it exerts both direct and indirect adverse effects on the growth plate and developing skeleton, causing chondrocyte apoptosis, premature osteocyte death, and excessive bone resorption via prolongation of osteoclast survival.[1] Although age upon starting GC and its duration of use are major osteotoxic contributors, spontaneous recovery of bone mass following treatment completion is a privilege of this specific age group.[2] Nevertheless, the extent of bone mass recovery after the cessation of therapy remains unknown. According to the International Society for Clinical Densitometry, pediatric osteoporosis is diagnosed when nontraumatic vertebral fracture (VF) is confirmed or, in the absence of VF, a clinically significant fracture history along with a bone mineral density (BMD) *z* score of less than -2.0 is measured by dual-energy x-ray absorptiometry (DXA).[3] Unfortunately, measuring BMD using DXA in younger children is challenging, and nontraumatic VF is easily overlooked due to its asymptomatic nature and normal BMD.[4] A Canadian multicenter observational cohort study determined the severity of the underlying disease, average daily and cumulative dose of GC, and duration of therapy (highest at 12 months of therapy) as predictive factors of incidental VF.[5] Although longitudinal cohorts from a large-scale population yield the most reliable results, Kuniyil et al.[6] presented a distinct study design that investigated the effect of GC on pediatric BMD for a short treatment period.

This study highlights the detrimental effects of systemic GC use on pediatric BMD. DXA-interpreted BMD data (whole-body, lumbar spine, nondominant distal radius, and total body less head) of 25 patients with heterogeneous diseases (21 with tuberculosis, 2 with juvenile idiopathic arthritis, 1 with inflammatory bowel disease, and 1 with autoimmune hemolytic anemia) younger than 18 years of age who underwent GC therapy were collected at baseline, first follow-up (at 6 weeks or end of therapy), and second follow-up (at 12 weeks of therapy) and compared them to an equal number of sex-matched healthy children. Mean cumulative GC dose and treatment duration were 1895.23±269.30 mg/m^2 and 39.48±3.42 days, respectively. A significant decline in BMD was observed at each follow-up point, and a negative correlation was found between bone densitometric parameters and cumulative GC dose and duration.

From the view of a pediatric endocrinologist, a few comments require consideration: (1) a formula for BMD *z* score calculation adopted from a study performed of children with juvenile idiopathic arthritis could not apply to disease categories of this study, while normative BMD data of Indian children was also missing; (2) posteroanterior spine and total body less head are the preferred skeletal sites of measurement recommended by the guideline, but only the baseline whole-body BMD *z* score differed significantly between patients and controls; (3) some BMD *z* scores displayed a wide range (from less than -2.0 up to 2.0), whereas the author mentioned that the presence of VF was observed in none of the subjects; and (4) patients' underlying diseases eventually required long-term GC treatment, so the clinical significance of the short-term effect may not be critical to some disease specialists.[3]

The osteotoxic effect of GC on a child's growing bones has been extensively reviewed; nonetheless, the severity of its impact appears to vary among ages and underlying conditions.[7] Although a higher dosage and prolonged duration of GC administration are the most common components of iatrogenic osteoporosis, this study clearly highlights that GC use for 2–6 weeks could still be detrimental. Most guidelines recommend the use of antiresorptive treatments, such as bisphosphonates, for the diagnosis of childhood osteoporosis.[8] More importantly, optimal GC dose reduction or withdrawal seems a fundamental principle to preventing further bone loss. Since childhood osteoporosis is frequently asymptomatic, it is not detected in the absence of routine surveillance, making VF and BMD screening prior to starting GC therapy vital[9] (Fig. 1). The growing skeleton is especially vulnerable to drug-induced osteotoxicity, but it also has the unique feature of reclaiming bone mass and density.[10] For any patients undergoing >2 weeks of GC therapy, its osteotoxic effect should be recognized; thus, bone health screening is the next step.

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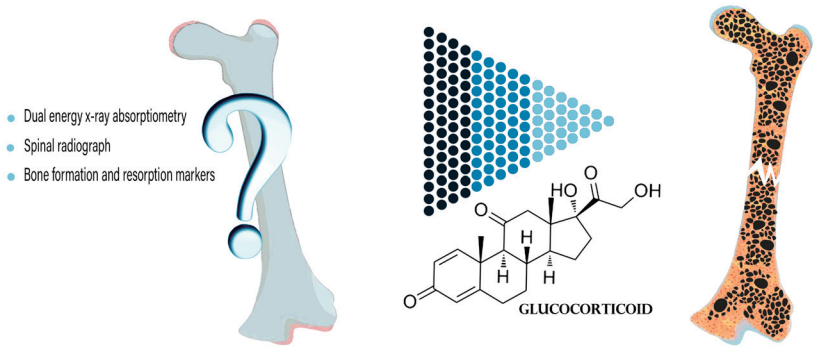

Fig. 1. Routine skeletal assessments prior to glucocorticoid therapy are critical for preventing future osteoporotic fractures.

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Key message

Osteoporosis diagnosed in children with chronic diseases is a major endocrine complication triggered by the disease itself or its treatment. Although age upon starting osteotoxic agents and the their duration of use are vital contributors, spontaneous recovery of bone mass following treatment completion is a privilege of this specific age group. For any patients short-term glucocorticoid therapy, bone health screening is the next step.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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