Low Bone Mineral Density Could Be Alarmed Within a Short-Term Use of Systemic Glucocorticoid Treatment

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Osteoporosis in children with chronic diseases have long been recognized as a major endocrine complication possibly triggered by disease itself or its treatment occurring pre- and post-treatment period. Despite advanced and targeted management of childhood illnesses, the use of systemic glucocorticoid (GC) remains the cornerstone of treatment for various acute and chronic conditions, including infection, cancers, autoimmune disorders, respiratory distress, and neuromuscular disorders. However, bone mass and shape as well as bone metabolic status continue to significantly change during childhood and adolescent period, thus children are more sensitive to detrimental effect of GC since GC exerts both directly and indirectly adverse effects on the growth plate and developing skeleton mostly causing chondrocyte apoptosis, premature death of the osteocyte, and excessive bone resorption via prolongation of osteoclast survival. Although age at start and duration of GC therapy are major osteotoxic contributors, spontaneous recovery of bone mass following the treatment completion is a privilege of this specific age group. Nevertheless, the extent of bone mass recovery after cessation of therapy is yet unknown. According to the International Society for Clinical Densitometry, pediatric osteoporosis is diagnosed either when non-traumatic vertebral fracture (VF) is confirmed or, in the absence of VF, clinically significant fracture history along with bone mineral density (BMD) Z-score measured by dual-energy x-ray absorptiometry (DXA) less than -2.0 is present. Unfortunately, measuring BMD by using DXA in younger children is challenging and non-traumatic VF may easily be overlooked due to its asymptomatic nature and occur within normal BMD. A Canadian multicenter observational cohort study determined the severity of underlying disease, GC (average daily and cumulative) dose, and duration of therapy (highest at 12 months of therapy) as predictive factors of incidental VF. Although longitudinal cohorts from large scale population are considered to yield the most reliable results, the study by
Yadav et al. presents distinct design as it has investigated GC effect on pediatric BMD for short period time.

This study highlights the importance of detrimental effect of systemic GC use on pediatric BMD. Dual energy x-ray absorptiometry-interpreted BMD data (whole body, lumbar spine, non-dominant distal radius, and total body less head) of 25 patients with heterogenous diseases (21 tuberculosis, 2 juvenile idiopathic arthritis, 1 inflammatory bowel disease, 1 autoimmune hemolytic anemia) aged under 18 years who underwent glucocorticoid therapy were collected at 3 time points: baseline, first (at 6th week or end of therapy), and second follow up (at 12 week of therapy), then compared to equal number of sex-matched healthy children. Mean cumulative dose and duration of treatment of GC were 1895.23±269.30 mg/m² and 39.48±3.42 days, respectively. As a result, 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 its duration.

From the view of a pediatric endocrinologist, a few comments need to be taken into consideration: i) a formula for BMD Z-score calculation was adopted from a study performed on children with juvenile idiopathic arthritis, thus could not apply to disease categories of this study while normative BMD data of Indian children was also missing, ii) posterior-anterior spine and total body less head are the preferred skeletal sites of measurement recommended by the guideline, however BMD Z-score for whole body at baseline only showed significant difference between patients and controls, iii) some BMD Z-scores were widely ranged (from less than -2.0 up to 2.0) whereas the author mentioned the presence of vertebral fracture was observed in none of the subjects, and lastly patients’ underlying disease are condition that eventually requires a long-term GC treatment, thereby, the clinical significance of short-term effect may not be critical to some disease specialists 3).
GC’s osteotoxic effect on child’s growing bone has been extensively reviewed, nonetheless the severity of its impact appears to vary depending on patients’ age and different types of underlying condition. Although higher dosage and prolonged duration of GC administration have been most common components of iatrogenic osteoporosis, this study clearly highlights that GC use within 2 to 6 weeks still could be detrimental. Most guidelines recommend the use of antiresorptive treatment such as bisphosphonate upon the diagnosis of childhood osteoporosis. More importantly, however, optimal dose reduction or withdrawal of GC seem fundamental principles to prevent further bone loss. Since the progression of childhood osteoporosis is frequently asymptomatic thereby go undetected in the absence of routine surveillance, above all, VF as well as BMD screening in prior to starting GC therapy is vital (Figure 1). Growing skeleton is especially more vulnerable to drug-induced osteotoxicity, but at the same time has a unique feature of reclaiming bone mass and density. For any patients undergoing longer than 2 weeks of GC therapy, GC’s osteotoxic effect should be recognized, thus bone health screening is a next step.
Footnotes

Conflicts of interest

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

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References


Figure legends

Figure 1. Routine skeletal assessment in prior to glucocorticoid therapy is critical in prevention of future osteoporotic fracture.
FIGURE 1

- Dual energy x-ray absorptiometry
- Spinal radiograph
- Bone formation and resorption markers

GLUCOCORTICOID