Steroids Cost Children Height, Not Bone Mass

BY TIMOTHY F. KIRN
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SNOWMASS, COLO. — Gathering data suggest that using glucocorticoid steroids in children may cost them height but not necessarily bone density, Dr. Lenore Buckley said at a symposium sponsored by the American College of Rheumatology.

"The issue of what glucocorticoids do to bone mass in children is an area where we are only just beginning to get some data," said Dr. Buckley of the Medical College of Virginia, Richmond.

One such cross-sectional study looked at 60 children with isolated, idiopathic nephrotic syndrome being treated with glucocorticoids, and compared them with 195 matched controls, mean age 9-10 years. Children treated with glucocorticoids were found to lose height but not necessarily bone density (N. Engl. J. Med. 2004;351: 868-75). In the group treated with glucocorticoids, 26 study participants were black, and 39 control group participants were black, according to the study data.

Previous studies have found that children lose bone mineral density when treated with glucocorticoids. But those studies looked at children with systemic illnesses, such as juvenile rheumatoid arthritis and inflammatory bowel disease, so it is not clear whether their low density was due to their treatment with glucocorticoids or to their systemic condition.

The mean height *z* score of the children in the control group was positive (0.35), whereas the mean height *z* score of the glucocorticoid treated children was negative (–0.17), the study found.

At the lumbar spine, the same bone mineral density per unit area was found in both the control and glucocorticoid treated groups, however.

"For what bone [both groups] have, the density is the same, but [the glucocorticoid group doesn't] have as much bone because they don't grow as much," Dr. Buckley said. The bone density for the treatment group could be due to the glucocorticoid, which causes weight gain, and weight stimulates bone density growth, she noted.

The mean body mass index *z* score for children with nephrotic syndrome was 1.24, while the score for controls was 0.34. There was also a higher percentage of obese children in the nephrotic syndrome group, compared with the control group (38% vs. 16%, respectively).

A more detailed look at the children's bone density found that those with nephrotic syndrome had slightly lower trabecular bone density (mean *z* score – 0.27, vs. 0), but much greater cortical bone density (mean z score 0.87, vs. 0). This situation also suggests that while there may be a process interfering with bone accumulation, there is also some compensation due to weight gain, Dr. Buckley said.

Children with nephrotic syndrome go on and off glucocorticoid treatment, which could allow for some periods of recovery, so these findings may not extrapolate to children treated chronically, Dr. Buckley noted. "What it tells us is that in the short run, these kids are not at risk for fracture—they have pretty good density," she said. "But what it doesn't tell us is the risk of fracture in the future."

Adults not taking glucocorticoids whose rate was one standard deviation below the mean as a child have a four times higher risk of fracture, studies show, noted Dr. Buckley. ■

Trabecular Bone Loss May Begin as Adults Reach Their 20s

BY KERRI WACHTER
Senior Writer

NASHVILLE, TENN. — Trabecular bone loss in both men and women may begin much earlier than previously thought, Dr. B. Lawrence Riggs reported at the annual meeting of the American Society for Bone and Mineral Research.

With his colleagues, Dr. Riggs of the Mayo Clinic College of Medicine in Rochester, Minn., used high-resolution peripheral quantitative CT (pQCT) to assess cortical and trabecular bone loss in 375 women and 325 men aged 21-97 years.

A total of 97 women were excluded from the analysis because they were receiving hormone replacement therapy, selective estrogen receptor modulators, or bisphosphonate therapy. Measurements of cortical and trabecular volumetric bone mineral density at the distal radius and the distal tibia were made at two to four consecutive annual visits.

In women, trabecular "bone loss appears to begin in young adulthood, probably in the third decade, and continues throughout life, with the suggestion of a menopausal acceleration at the distal radius," said Dr. Riggs. Cortical bone loss does not really begin until menopause.

Premenopausal women lost an average of 0.67% of trabecular bone per year at the distal radius, compared with postmenopausal women, who lost 1% of trabecular bone per year. At the distal tibia, premenopausal women lost 0.53% trabecular bone per year, compared with 0.61% trabecular bone loss for postmenopausal women.

Cortical bone loss at the proximal radius was 0.11% per year for premenopausal women, compared with 0.60% for postmenopausal women. Cortical bone loss at the proximal tibia was 0.08% per year for premenopausal women and 0.57% per year for postmenopausal women.

In men "there really is no [cortical] bone loss until the age of 70," said Dr. Riggs. Studies have shown that sex steroids begin to decline in men around this age. "Now with respect to trabecular bone loss in men, as in women, we do in fact see substantial trabecular bone loss … with more bone loss in young men than subsequently [thought]," said Dr. Riggs. This perhaps relates to changes in microstructure, he speculated.

Trabecular bone loss at the distal radius was 0.66% per year for men younger than age 50, compared with 0.53% for men aged 50 and older. Trabecular bone loss at the distal tibia was 0.68% per year for men younger than age 50 and 0.24% per year for men aged 50 and older.

Cortical bone loss at the proximal radius was 0.08% per year for men younger than 50 years, compared with 0.38% for men aged 50 and older. Cortical bone loss at the proximal tibia was 0.8% per year for men younger than 50 years and 0.22% per year for men aged 50 and older.

The early trabecular bone loss described accounts for a substantial proportion of total bone loss. "Consequently, determining the causation should be an important priority for future osteoporosis research," said Dr. Riggs.

"The onset of substantial trabecular bone loss in both sexes soon after the conclusion of puberty and at a time when sex steroid levels are, by definition, normal indicates the current paradigms for the pathogenesis of osteoporosis are incomplete," he said. ■

CLINICAL CAPSULES

Rheumatic Fever's Decline

Nonrheumatogenic types of group A streptococcus may be replacing rheumatogenic types in cases of acute streptococcal pharyngitis in children, said Dr. Stanford T. Shulman of Northwestern University and his colleagues.

This change could be contributing to the decline of acute rheumatic fever among children in the United States, based on a comparison of data on M-type isolates from children in Chicago during 1961-1968 with data from children in Chicago and nationwide during 2000-2004 (CID 2006;42:441-7).

Several rheumatic types of group A streptococcus were present in nearly 50% of 468 pharyngeal isolates from the 1961-1968 period, but comprised only 11% of 450 isolates from the Chicago area and 18% of 3,969 isolates nationwide during the 2000-2004 period.

In contrast, the proportion of several nonrheumatogenic types increased significantly between the study periods, from about 5% to nearly 28% of isolates both in Chicago and nationwide.

Rheumatic types 14, 18, 19, and 29 essentially vanished during the years between the two study periods. The other most significant decreases occurred in rheumatic types 3, 5, and 6, which comprised 35% of the Chicago isolates during the first study period, when acute rheumatic fever was still prevalent, but only 10% of Chicago isolates during the second study period, when acute rheumatic fever had become rare.

Predictive Model of Lyme Meningitis

Three conditions—a long-lasting headache, the presence of cranial neuritis, and a predominance of cerebral spinal fluid mononuclear cells—can predict Lyme meningitis in children aged 2-13 years, said Dr. Robert A. Avery of the Alfred I. duPont Hospital for Children in Wilmington, Del., and his colleagues.

Data from a study of 27 children with Lyme meningitis (LM) and 148 children with aseptic meningitis (AM) provide the first model to distinguish between the two conditions in areas where Lyme disease is endemic (Pediatrics 2006;117:1-7).

Overall, 16 of the 27 (59%) patients with LM experienced headaches longer than 3 days' duration, compared with 37 of 148 (25%) patients with AM. The average duration of headache was 7.5 days among LM patients vs. 2.8 days among AM patients.

In addition, 15 (56%) of the LM patients had cranial neuritis, compared with 5 (3%) of the AM patients. Finally, the average percentage of mononuclear cells in samples of cerebrospinal fluid was 87% among the LM patients vs. 58% among the AM patients, and 19 (70%) of the LM patients had CSF mononuclear cell levels greater than 86% compared with 42 (28%) of the AM patients.

However, high levels of CSF mononuclear cells are not specific to LM alone, and this finding must be supported by longer-lasting headaches and the presence of cranial neuritis for an LM diagnosis, the researchers noted. All three conditions made statistically significant contributions to the prediction model.

Based on a regression analysis in which all three conditions were considered, the odds ratio for LM for each variable was 2.9 for a patient with a headache lasting 14 days, 3.4 for a patient with 90% CSF mononuclear cells, and 16.9 for a patient with cranial neuritis.

Flu Shots a Must in Kids With NNMD

Flu shots are de rigueur for children with neurologic and neuromuscular diseases given their high risk of influenza-related respiratory failure.

"Children with pulmonary disease, cardiac disease, or NNMD [neurologic and neuromuscular disease] had approximately a 10% probability of respiratory failure" during a hospitalization for influenza, Dr. Ron Keren and colleagues reported. "Having two of the three chronic conditions increased the probability another three- to fourfold" (JAMA 2005;294:2188-94).

Dr. Keren, of the Children's Hospital of Philadelphia, and associates examined rates of respiratory failure in 745 children and adolescents (aged 21 years and younger) in 2000-2004. Eighty-nine (12%) had an NNMD, most commonly cerebral palsy (40%), seizure disorders (42%), and hydrocephalus/cerebrospinal fluid shunt (30%).

During the study period, 32 children developed respiratory failure; 14 of those had an NNMD, a sixfold increased risk compared with those with no chronic health problem. This risk was higher than that associated with pulmonary disease (OR 5.0) or cardiac disease (OR 4.0), both of which are accepted indications for an annual childhood influenza vaccine.

—Heidi Splete and Michele G. Sullivan

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