If we don’t monitor patients on high-vitamin D regimens for urinary calcium, they may develop kidney stones.

DR. RASTELLI

Chronic PPI Use Did Not Lower BMD in Children in Pilot Study

BY MIRIAM E. TUCKER

National Harbor, Md.—Bone mineralization was not significantly altered among 17 children receiving chronic proton pump inhibitor therapy, including 12 who were also using inhaled steroids.

Proton pump inhibitors (PPIs) are commonly prescribed for acid suppression in children with gastroesophageal reflux, sometimes for long periods. A significantly increased risk of bone fracture has been reported in adult patients receiving long-term PPI therapy (JAMA 2006;296:2947-53), and chronic acid suppression has been shown to impair calcium absorption, thereby promoting bone resorption (Am. J. Med. 2005;118:778-81).

However, this pilot study is believed to be the first to look at bone mineralization or fractures in children on PPIs. Dr. Stephanie Willot said in a poster presentation at the annual meeting of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

The 17 patients (12 boys) had a mean age of 7.8 years (range 0.8-16.7 years). All had gastroesophageal reflux disease, and the other children had intractable gastroesophageal reflux disease and were referred for bone health evaluation (Am. J. Med. 2005;118:778-81).

In addition, patients randomized to the active treatment group received vitamin D2 (ergocalciferol) at 50,000 IU/week for 8 weeks if their baseline serum vitamin D level was 20-29 ng/mL, and for 16 weeks if it was 10-19 ng/mL. Thereafter, they got 50,000 IU once monthly for the balance of the 6-month period. The control group received placebo on the same schedule.

At 2 months of follow-up, women in the high-dose vitamin D arm had significantly lower pain scores than did controls on both the Brief Pain Inventory and the Fibromyalgia Impact Questionnaire. They also scored significantly better than controls on the Health Assessment Questionnaire–Disability Index domains that specifically assessed ability to climb stairs and walk on flat ground. These benefits were no longer significant at the 4- and 6-month follow-ups, probably because by then the high-dose vitamin D had been switched to weekly or monthly therapy, Dr. Rastelli said.

In future studies, she plans to continue high-dose vitamin D for a longer period in an effort to achieve more lasting benefits. In addition, she is considering using daily cholecalciferol to maintain more stable serum vitamin D levels than is possible with weekly ergocalciferol. She is also interested in broadening the study population to include patients with vitamin D levels that are currently considered normal.

Separately, Dr. Steve N. Birrell reported on 90 postmenopausal women with breast cancer who had been on adjuvant anastrozole for a median of 16 months and were experiencing significant joint pain. They were randomized in a double-blind manner to 3 months of oral testosterone undecanoate at 40 or 80 mg/day, or placebo.

Eligibility for the trial required that patients have baseline visual analog scale scores in excess of 50 out of a possible 100 for both pain and stiffness. At follow-up assessments at 1 and 3 months, a strong placebo effect was evident, with roughly 40% of controls reporting their pain and stiffness scores had dropped below 50. However, a significant treatment benefit was seen with high-dose testosterone, with three-quarters of patients on killing/day reporting scores below 50 for both pain and stiffness at 3 months, according to Dr. Birrell, head of the breast cancer unit at Flinders Medical Centre, Adelaide, South Australia.

The safety data were reassuring, with good tolerability and no increase in serum estradiol levels in connection with testosterone therapy, which is unsurprising in light of the fact that aromatase inhibitors are widely used to block conversion of testosterone to estradiol in athletes who illicitly use anabolic steroids to enhance performance, he noted.

Dr. Birrell’s own preclinical studies suggested that testosterone treatment does not impinge upon the anticancer effects of aromatase inhibitor therapy. In fact, there was evidence of a synergistic anti-inflammatory effect that warrants further study, the surgeon continued.

The biological rationale for testosterone therapy in aromatase inhibitor–associated joint morbidity lies in the premise that affected patients have a reduced ability to convert endogenous testosterone to 5-alpha-dihydrotestosterone.

This potent testosterone metabolite appears to be important in reducing the proinflammatory interleukins present in the synovium of patients with inflammatory joint disease, Dr. Birrell explained.

“It’s really quite interesting that women on aromatase inhibitors have a significant increase in Sjögren’s syndrome, where it has been demonstrated that there is a perturbation in the ability to convert testosterone into ac- 

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score BMD of less than –1 standard deviation for age, they all had normal vol- 

ume BMD (ranging from –0.8 to 0.6 standard deviation), as did the other seven children who were older than 4 years of age, Dr. Willot and her associates reported.

In a follow-up interview, Dr. Willot said that, given the small sample size of the study and its cross-sectional nature, its implications are limited to the finding that BMD is not low in children on chronic PPI therapy. “We cannot conclude about the association between PPI and fracture risk in the future, we would like to follow our cohort to assess BMD in a longitudinal fashion to establish if a z score could decrease during the course of PPI treatment.”

Dr. Willot stated that she had no per- sonal financial disclosures.