Calcitonin Prevents Transplant-Induced Bone Loss

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Prophylactic use of calcitonin prevents the rapid initial bone loss commonly associated with high-dose steroids early after heart transplant surgery in adults, although bone mass eventually reaches normal levels after 7 years even without treatment, according to Emmanouil I. Kapetanakis, M.D., and colleagues.

Triple-drug immunosuppression treatment after cardiac transplantation usually combines cyclosporine, azathioprine, and prednisone. The long-term administration of the steroid is generally blamed for the associated bone loss and fractures seen as a complication after transplant.

In a small study of 23 patients, age-adjusted bone mineral density (BMD) values 1 year after cardiac transplant were significantly different for the 11 control group patients (BMD 61%), compared with the 12 calcitonin-treated patients (BMD 89%).

During the first 3 years of follow-up, these values reached 69% for the no-calcitonin group, compared with 90% in the treated group—also a significant difference. The calcitonin group maintained BMD within normal ranges during the entire time of follow-up.

Calcitonin is a salmon-derived polypeptide hormone approved for the treatment of osteoporosis.

However, "the BMD decline in the no-calcitonin group stabilized and was reversed during subsequent follow-up so that BMD values during the intermediate (4-6 years) and late (7+ years) follow-up periods were not statistically different," according to Dr. Kapetanakis of Washington Hospital Center and colleagues (J. Heart Lung Transplant. 2005;24:526-32).

The researchers believe their work indicates the benefits of using intranasal salmon calcitonin to prevent rapid bone loss associated with high-dose steroids early after heart transplantation. But they also said that long-term use does not seem warranted, given the natural reestablishment of BMD over lengthier periods of time.

A related small study examined the rate and etiology of osteoporosis in nine adult transplant survivors who received their new heart in adolescence. These patients were compared with an equal number of control subjects matched for age (21-32 years), sex (seven men, two women), and race (six white, one black, one Hispanic, one other), reported Adi Cohen, M.D., and colleagues (J. Heart Lung Transplant. 2005;24:696-702).

Hyperparathyroidism, mild renal insufficiency, and increased bone turnover appeared to be the key factors involved in the high rate of long-term osteoporosis seen in the transplant subjects, according to Dr. Cohen of Columbia University, New York, and associates.

BMD was measured in the lumbar spine, femoral neck, and the forearm one-third radius (DR).

Osteoporosis was present in 56% of the transplant subjects at the lumbar spine, in 33% at the femoral neck, and in 100% at the DR. Only two control subjects showed osteoporosis, and only in the lumbar spine.

Biochemically, serum parathyroid hormone (PTH) levels were threefold higher in transplant subjects than in controls.

All serum markers for bone turnover were higher in subjects than in controls, with statistically significant differences for bone-specific alkaline phosphatase and N-telopeptide. Serum calcium levels, although in the normal range, were significantly lower in the subjects than in the controls.

"Although the precise etiology of the osteoporosis remains unclear …biochemical studies suggest slightly impaired renal function and documented secondary hyperparathyroidism and increased bone turnover," Dr. Cohen and associates reported.

"This is the first study of pediatric transplant recipients to evaluate the forearm … [that is] sensitive to the catabolic effects of PTH," they added. Because the radius was also the most severely affected site, "these findings suggest a role for PTH in the pathogenesis of osteoporosis in this population."

Because survival rates after pediatric cardiac transplantation have increased dramatically, long-term consequences, such as osteoporosis, will become more evident and must be properly managed, according to the researchers. Understanding the etiology of these complications is the first step to developing treatments, Dr. Cohen and his associates said. ■