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Changes in Mineral Metabolism With Immobilization/Space Flight

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Introduction

What I would like to do is review briefly some of the studies that have been done on the effect of immobilization and weightlessness on bone. Only limited information is available on bone loss in zero g since relatively few subjects have experienced this situation.

Much of the useful information comes from the bed-rest model, which appears in many ways to be similar to the weightlessness situation. There are a number of interesting changes in mineral metabolism that occur with weightlessness. Urine calcium increases each week that the individual is immobilized (refs. 1 to 6), as does fecal calcium. Consequently, immobilized individuals develop severe negative calcium balance. This disturbance in calcium homeostasis has been shown to be associated with marked bone loss from the skeleton (refs. 5 and 6). Many years ago, it was shown that the immobilization effect on mineral metabolism was minimized by weight-bearing, but not by supine, exercises (ref. 7). Similar metabolic findings to those seen in immobilized patients were found in astronauts on the 84-day space flight (refs. 8 to 11). In some but not all individuals, bone loss was regained. In some respects, a parallel situation is seen in osteoporotic patients. These patients often have severe malabsorption of calcium, high urine calcium, and marked negative calcium balance (ref. 12). Possibly, some of the metabolic changes in these patients are due to partial immobilization caused by chronic and severe backache. Women at the time of the menopause also have rapid bone loss associated with high urine calcium levels but interestingly do not show any obvious change in absorption of calcium. The most obvious explanation for the changes that accompany immobilization is that rapid bone resorption leads to an elevated serum calcium, depression of parathyroid hormone, reduced formation of 1,25-dihydroxyvitamin D, malabsorption of calcium, and negative calcium balance. It appears that the metabolic changes associated with bone loss during weightlessness are closer to the findings in osteoporotic patients. What is interesting is why women who have rapid bone loss at the time of the menopause do not have malabsorption of calcium. Perhaps other hormones, such as cortisone, which affects absorption of calcium, may be contributors in weightlessness or immobilization. It is not clear at this moment whether the changes seen in vitamin D metabolism and malabsorption of calcium are primary or secondary phenomena subsequent to bone resorption, and more work is needed in that area.

Bone Loss in Weightlessness

There is little information on changes in bone itself during weightlessness. The results of one experiment, performed on rats in a U.S.S.R. spacecraft, showed a decrease in bone formation measured by tetracycline labeling during space flight, and this type of change in bone dynamics could contribute to bone loss (ref. 13).

The earlier space flights showed that loss of bone occurred in the radius and the os calcis (refs. 14 to 16). Further followup showed that the decrease in bone mass was reversed in some but not all astronauts (ref. 17). The last 5 years has seen the advent of new techniques for measuring bone density which are better than those used 10 years ago. These new methods include dual photon absorptiometry and computerized tomography. It has become clear from recent experimental work in osteoporosis that one cannot predict the rate of bone loss in one part of the skeleton from changes in other parts. For example, in osteoporotic patients, one sees normal radial density in about one-third of patients but very low spine density in all of them (ref. 18). Thus, I am not sure that one can assume that significant losses of bone occur in the femur or the spine during space flight even though decreases in bone density have occurred in the os calcis and the radius. Further prospective studies are needed to establish this point. Future studies should be planned to include measurement of density at multiple sites in the skeleton including the femoral neck, the spine, the os calcis, and the radius as well as measurement of total-body calcium. These measurements would give a more complete understanding of skeletal changes in immobilization. The use of total-body calcium would be especially valuable since regional changes also can be measured with the same technique.

Prevention or Treatment of Bone Loss

Other questions that need to be answered are the effects of intervention therapy on immobilization. A number of valuable experiments have examined the effect of various therapeutic agents in bed-rest studies (ref. 19). There are few data on the value of exercise in preventing bone loss. This lack partly reflects the fact that the technology for measuring different sites of the skeleton has only been available during the last 2 to 3 years. A recent study showed a correlation among spine density, femoral neck density, and fitness as measured by maximum ventilatory oxygen uptake (ref. 20) suggesting that fitness is a contributor to bone density. Presumably, most astronauts are extremely fit individuals who have probably maximized their potential for increasing bone density. Now that we have the ability to measure femoral neck density, we can look at the effect of an exercise program on the legs more carefully, since hip fracture would be one of the more severe complications of bone loss from the legs. Future experiments in space which involve prolonged space flight should provide answers to these questions. Also, since previous results were not accurate enough, one should look more closely at the recovery phase on bone since we are not sure whether bone loss due to weightlessness returns to normal. At the same time, bone density measurements can be used to detect individuals with low bone density, and I think it might be unwise to have those individuals undergo weightlessness repeatedly for several months if further studies show decreases in spine and femur density.

If significant bone loss does occur in space despite an exercise program, a strategy for preventing bone loss may be pretreatment of astronauts with agents such as the disphosphonates that significantly retard bone turnover. This idea is speculative and there are few animal data to support it, but work on immobilized animals could easily test this hypothesis.

Conclusion

We are still unsure of the accuracy of previous bone density measurements or their significance following a period of weightlessness. Rapid technological advances in the measurement of bone density will enable us now to measure bone density accurately at multiple sites in the skeleton with doses of radiation less than that given by a spine x-ray. It may not be possible to obtain this type of information before the next series of space flights take place, although the bed-rest model may provide supporting information. Extensive testing of bone density on every astronaut should be performed before and after the space flight. Prevention and treatment can only be undertaken after gathering sufficient baseline information. The use of exercise in preventing bone loss is still highly speculative, but represents a relatively easy approach to the problem in terms of study.

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