

## Fibroblast Growth Factor-23 in Bed Rest and Spaceflight

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Many nutritional factors influence bone, from the basics of calcium and vitamin D, to factors which influence bone through acid/base balance, including protein, sodium, and more. Fibroblast growth factor 23 (FGF23) is a recently identified factor, secreted from osteocytes, which is involved in classic (albeit complex) feedback loops controlling phosphorus homeostasis through both vitamin D and parathyroid hormone (PTH) (1, 2). As osteocytes are gravity sensing cells, it is important to determine if there are changes in FGF23 during spaceflight. In extreme cases, such as chronic kidney disease, FGF23 levels are highly elevated. FGF23 imbalances, secondary to dietary influences, may contribute to skeletal demineralization and kidney stone risk during spaceflight.

Presented with an imbalanced dietary phosphorus to calcium ratio, increased secretion of FGF23 will inhibit renal phosphorus reabsorption, resulting in increased excretion and reduced circulating phosphorus. Increased intake and excretion of phosphorus is associated with increased kidney stone risk in both the terrestrial and microgravity environments. Highly processed foods and carbonated beverages are associated with higher phosphorus content. Ideally, the dietary calcium to phosphorus ratio should be at minimum 1:1. Nutritional requirements for spaceflight suggest that this ratio not be less than 0.67 (3), while the International Space Station (ISS) menu provides 1020 mg Ca and 1856 mg P, for a ratio of 0.55 (3). Subjects in NASA's bed rest studies, by design, have consumed intake ratios much closer to 1.0 (4).

FGF23 also has an inhibitory influence on PTH secretion and 1 $\alpha$ -hydroxylase, both of which are required for activating vitamin D with the conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D. Decreased 1,25-dihydroxyvitamin D will result in decreased intestinal phosphorus absorption, and increased urinary phosphorus excretion (via decreased renal reabsorption). Should a decrease in 1,25-dihydroxyvitamin D be necessary to reduce intestinal phosphorus absorption, calcium absorption will also proportionally be reduced, potentially leading to skeletal demineralization. Demineralization of bone can increase kidney stone risk, a medical issue that could prove detrimental to mission success.

Given the interrelationships described above, we sought to determine circulating FGF23 concentrations in spaceflight and ground analog studies to better understand the potential effects of dietary phosphorus on bone and calcium metabolism. We analyzed serum from ISS astronauts participating in studies of bone biochemistry, including the Nutrition SMO and Pro K experiments, and we also evaluated FGF23 during extended-duration bed rest. Serum intact FGF23 levels were determined using an ELISA kit from Kainos laboratories in Japan. While initial evaluation of the data showed no changes over time during flight or bed rest, evaluation continues of FGF23 data in light of dietary factors, PTH, vitamin D status, and other biochemical and endocrine factors.

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