



Fibroblast Growth Factor 23 in Long-Duration Spaceflight

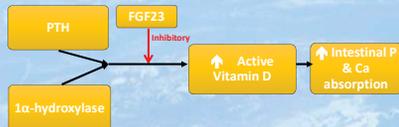
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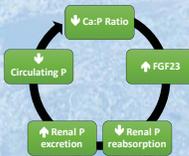


Background

Many nutritional factors influence bone, from the basics of calcium, vitamin D and phosphorus, to factors which affect acid/base balance (e.g., protein, sodium, potassium). 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 sensitive cells, it is important to determine the potential role of FGF23 during spaceflight. Elevated FGF23, secondary to dietary influences, may contribute to skeletal demineralization and kidney stone risk during spaceflight.



- FGF23 inhibits PTH secretion and 1 α -hydroxylase activity (required for activating vitamin D with the conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D).
- Decreased 1,25-dihydroxyvitamin D results in decreased intestinal phosphorus absorption, and increased urinary phosphorus excretion (via decreased renal reabsorption).
- Decreased 1,25-dihydroxyvitamin D results in decreased intestinal calcium absorption, potentially leading to skeletal demineralization.
- Demineralization of bone can increase kidney stone risk, a medical issue that could prove detrimental to mission success.
- Ideal dietary calcium to phosphorus ratio should be approximately 1:1 (3).
- The International Space Station (ISS) menu provides 1020 mg Ca and 1856 mg P, a ratio of 0.55, which falls below the nutritional requirements of greater than 0.67 (4). NASA's bed rest studies, by design, follow a 1:1 calcium to phosphorus ratio (5).
- Presented with a low dietary calcium to phosphorus ratio, increased secretion of FGF23 will inhibit renal phosphorus reabsorption, and result in increased excretion and reduced circulating phosphorus.



Increased intake and excretion of phosphorus is associated with increased kidney stone risk in both terrestrial and microgravity environments. Highly processed foods are associated with higher phosphorus content. The effects of these differences on bone research should be better understood, and in part, that was the purpose of the research reported here. Given the interrelationships described above, we sought to determine circulating FGF23 concentrations in spaceflight to better understand the potential effects of dietary phosphorus on bone and calcium metabolism.

Methods

6 astronauts (n=6, 4 female, 2 male) on International Space Station Expeditions 23 through 36 (mission duration 127-193 days, flown between 2010 and 2013). Blood samples were collected using standard phlebotomy techniques as previously described (6).

Sample Collection Timeline



- FGF23 was measured in serum samples using a commercially available ELISA kit (Kainos Laboratories, Tokyo, Japan).
- Dietary assessments were conducted for the 4 days prior to the blood collection as a part of another investigation. Crewmembers recorded all diet and fluid intake. 4-day averages were generated for intake and compared against FGF23 concentration.
- Statistical analyses were performed using Stata IC 12.1 software (StataCorp, College Station, TX). FGF23 required a square root transformation to satisfy statistical assumptions. Mixed modelling linear regression which included repeated measures among subjects was performed. Pearson correlations were determined on some selected variables.

Results

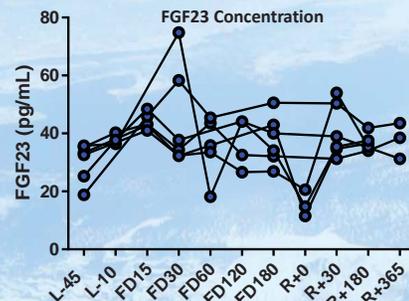


Figure 1. Serum FGF23 approximately 45 and 10 d before flight, during flight (FD15 – 180), landing (R+0), and 30-365 d after landing. There was no significant change over time. Each line represents a different subject.

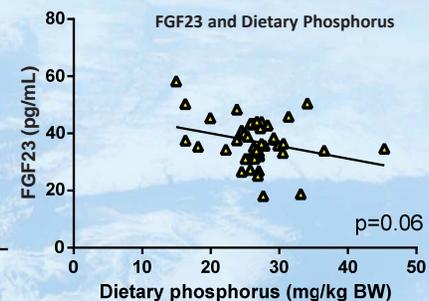


Figure 3. Serum FGF23 tended to be negatively correlated with dietary phosphorus (expressed as mg/kg BW).

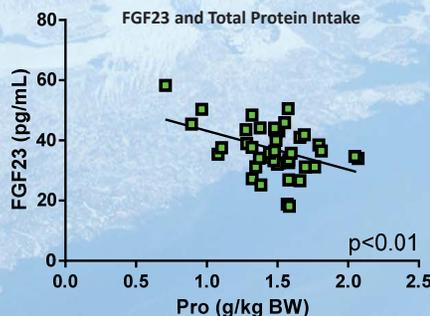


Figure 2. Serum FGF23 was negatively correlated with total protein intake (expressed as g/kg BW).

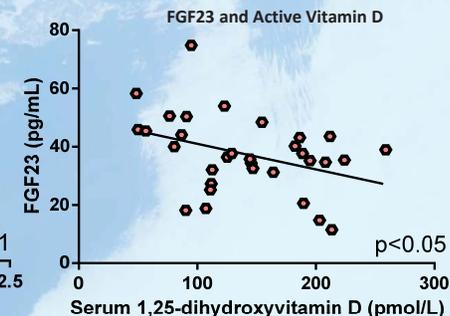


Figure 4. Serum FGF23 was negatively correlated with serum 1,25-dihydroxyvitamin D.

Summary

- FGF23 levels vary throughout the duration of flight there were no significant changes noted here.
- The negative correlation between serum FGF23 and serum 1,25-dihydroxyvitamin D is consistent with previous studies of FGF23's action to regulate active Vitamin D.
- Most astronauts take vitamin D supplements because deficiency is a chronic problem. Given FGF23's regulatory association with 1,25-dihydroxyvitamin D, it should be further studied.
- The negative correlation between protein and FGF23 could be a result of higher total protein intake, known to have a higher phosphorus content. This is further supported by the trend towards a negative correlation between FGF23 and dietary phosphorus. The strength of the correlation between serum FGF23 and total protein intake even given low subject numbers suggests that further study is required.

References

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Acknowledgments

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