Risk of Oxidative Damage to Bone from Increased Iron Stores during Space Flight

SR Zwart[1] and SM Smith[2]

[1]Universities Space Research Association, Houston, TX, [2]NASA JSC, Houston, TX

Iron stores are increased secondary to neocytolysis of red blood cells and a high dietary intake of iron during space flight. This raises concerns about the risk of excess iron causing oxidative damage in many tissues, including bone. Biomarkers of iron status, oxidative damage, and bone resorption during space flight were analyzed for 23 (16 M/7 F) International Space Station crewmembers as part of the Nutrition SMO project. Up to 5 in-flight blood samples and 24-h urine pools were collected over the course of the 4-6 month missions. Serum iron increased slightly during space flight and was decreased at landing ($P < 0.0004$). An increase in serum ferritin early in flight (217% in women and 68% in men, $P < 0.0004$), returning to preflight concentrations at landing, and a decrease in transferrin and transferrin receptors during flight indicated that a transient increase in iron stores occurred. No inflammatory response was observed during flight. The oxidative damage markers 8-hydroxy-2'-deoxyguanosine and prostaglandin $F_{2\alpha}$ were positively correlated (both $P < 0.001$) with serum ferritin. A greater area under the curve for ferritin during flight was correlated with greater changes in bone mineral density of several bone regions after flight (1).

In a separate study (2), a ground-based investigation was conducted that examined the combined effects of radiation exposure and iron overload on sensitivity to radiation injury in several physiological systems in 12-wk male Sprague-Dawley rats. The rats were acclimated to an adequate iron diet (45 mg iron (ferric citrate)/kg diet) for 3 wk and then assigned to one of four groups: adequate iron (Fe) diet/no radiation, adequate Fe diet/ radiation, moderately high Fe diet (650 mg Fe (ferric citrate)/kg diet)/no radiation, and moderately high Fe diet/radiation. Animals remained on the assigned diet for 4 wk. Starting on day 14 of experimental diet treatment, animals were exposed to a fractionated dose (0.375 Gy) of ^{137}Cs every other day (3 Gy total dose). On day 29 (24 h after last radiation exposure), animals were euthanized. Oxidative stress markers in the liver, bone, eyes, and serum were assessed. There was evidence that the iron diet contributed to DNA damage as well as radiation exposure in the liver, eyes, and bone.

Together, the results suggest that increased iron stores do constitute a risk factor for oxidative damage and bone resorption, during space flight and on Earth. Funded by the Human Health and Countermeasures Element of the NASA Human Research Program.

1. Zwart SR, et al. Iron status and its relations with oxidative damage and bone loss during long-duration space flight on the international space station. Am J Clin Nutr. 2013;98:217-23.
2. Morgan JL, et al. Increased dietary iron and radiation in rats promote oxidative stress, induce localized and systemic immune system responses, and alter colon mucosal environment. FASEB J. 2014;28:1486-98.