Bone Metabolism During Strict Head-Down Tilt Bed Rest and **CO2 Exposure**

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Objectives: Carbon dioxide (CO₂) levels on board the International Space Station reach 10× those of outdoor terrestrial levels. We report here studies assessing whether increased levels of ambient CO₂ contribute to elevated bone resorption characteristically observed with bed rest as an analog for skeletal unloading during spaceflight.

Methods: Data are reported from two ground-based studies which included 12 male and 7 female subjects placed in a strict -6° head-down tilt (HDT) position for 30 days at 0.5% ambient CO2 or 60 days with nominal environment (0.04% CO₂). Subjects were neither afforded a pillow nor allowed to use an elbow while eating to increase headward fluid pressure. Bone mineral density (BMD) and bone mineral content (BMC) were measured with dual-energy X-ray absorptiometry. Blood and urine were collected before and during HDT for analysis.

Results: There was no change in BMD or BMC. Excretion of collagen crosslinks increased during HDT (p < 0.001) with no additive effect of CO₂. Serum and urine mineral concentrations were not affected by CO₂. Serum PTH and 1,25-deoxyhydroxyvitamin D were both reduced during bed rest (p < 0.0001), likely secondary to calcium efflux from bone, but with no additive effect of CO₂ exposure. These changes reinforce the impact of decreased mechanical loading on bone and mineral homeostasis and the efficacy of the strict HDT model.

Conclusions: Exposure to 0.5% CO₂ for 30 days did not exacerbate bone resorption during strict HDT bed rest. Future research on bone metabolism at varied CO2 levels is needed to clarify a risk ceiling for bone resorption, especially as missions progress beyond low-Earth orbit.

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