

Irisin Treatment during Chronic Inflammatory Bowel Disease in a Rodent Model Improves Bone Formation Rate

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ABSTRACT

Bone is a dynamic tissue that responds to many stressors including physical stress and certain disease states. Chronic systemic inflammatory conditions, like inflammatory bowel disease (IBD), result in increased bone resorption and decreased bone formation leading to low bone mass and high fracture incidence. There currently are no effective, safe treatments for IBD. Irisin is a hormone that is released during exercise and has previously been shown to increase bone mass. **PURPOSE:** Determine if exogenous treatment with irisin can mitigate the inflammatory insult of chronic IBD on bone. We hypothesized that young male rats with induced IBD and treatment with exogenous irisin would have increased bone formation rate (BFR) and mitigated loss of bone mineral density compared to rats with only IBD.

METHOD: Male Sprague Dawley rats (2 months) were divided into four groups: controls (CON), those given dextran sodium sulfate in drinking water to induce IBD (DSS), CON rats given exogenous irisin (CON+IR), and DSS rats given exogenous irisin (DSS+IR). n per group=8. Irisin injections began one week after initiation of IBD for the remainder of the four week protocol. **RESULTS:** Peripheral quantitative computed tomography (pQCT) of the proximal tibia metaphysis showed a significant decrease in total bone mineral content and volumetric bone mineral density (cortical shell+cancellous core) in both DSS groups compared to both control groups. Dynamic histomorphometry revealed higher cancellous BFR due to irisin treatment in both CON and DSS rats resulting in DSS+IR having higher BFR than DSS. This was due largely to increases in mineralized surface indicating increased numbers of osteoblast teams. At the midshaft tibia, BFR was higher in DSS+IR, but not significantly different than DSS alone. This change was due more to increases in mineral apposition rate indicating higher activity of osteoblast teams.

CONCLUSION: In this study, we demonstrated that rats with DSS have low bone mass similar to patients with IBD. Although irisin did not mitigate this bone loss, our data indicates over time it would likely lead to improved bone mass due to increases in bone formation. Additionally, our data indicate greater improvements in BFR in the cancellous bone, a more active bone compartment, than the midshaft tibia, but slight increases in mineral apposition rate at this site demonstrate improved osteoblast activity due to irisin. Since IBD is a chronic, life-long disease, our data highlights the potential benefit of exogenous irisin treatment as well as exercise therapy for patients with IBD.