Δ Enhancing Bone Healing With Boron Salt

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Purpose: Fracture nonunion can be as high as 20% in certain clinical scenarios and has a high associated socioeconomic burden. It has been shown that bioceramics can positively affect bone healing through localized changes in the ionic environment. Boron has been shown to regulate the Wnt/β-catenin pathway, critical for bone healing, via GSK3β. Here we aim to demonstrate that the local delivery of boric acid can accelerate bone healing, as well as to elucidate how boric acid, via the regulation of the Wnt/β-catenin pathway, impacts the osteogenic response of bone-derived osteoclasts and osteoblasts during each phase of bone repair.

Methods: Bone repair was quantified using bilateral 1 mm x 2 mm femoral cortical window defects created using a burr in 20 healthy and skeletally mature C57 mice. This allowed for control and experimental groups to be in the same animal. On the experimental side, boric acid (dose 8 mg/kg) was injected every 48 hours to the defect site whereas on the control side, saline was used. Mice were divided into 2 groups and were then euthanized and their femora harvested at either the early inflammatory phase at 7 days (n = 10) or the regeneration phase at 28 days(n = 10) postsurgery. MicroCT was then used to quantify the amount of bone regeneration and neovascularization at the site of the defect. Histological analysis with staining for alkaline phosphatase (ALP) and tartrate-resistant acid phosphatase (TRAP) was used to quantify osteoblast and osteoclast activity respectively.

Results: Preliminary microCT interpretation revealed that the experimental group exhibited more bone formation, more trabeculae, less total porosity (%), as well as a more robust periosteal reaction. Histological staining showed that ALP activity was higher in boron-treated femurs when compared to controls at day 7. At day 28, the ALP-positive osteoblast activity was more important in the control group whereas TRAP-positive osteoclast activity was higher in the boron group. This early onset in osteoblast activity during the inflammatory phase and the later transition to osteoclast dominance in the regeneration phase in the boron-treated femurs suggests that boron, through the upregulation of activated β-catenin, positively upregulates osteoblast expression.

Conclusion: Localized injections of boric acid in mice bone defects accelerated and improved physiological bone healing at different stages. It is suspected that boron enhances bone healing through inactivation of GSK3β and the subsequent increase in activated β-catenin. Currently, further data quantification as well as immunohistochemistry staining for GSK3β and nonphosphorylated (active) β-catenin is being performed to confirm this proposed mechanism. The addition of this inexpensive and widely available ion could potentially become a noninvasive, cost-effective treatment modality to augment fracture healing and decrease nonunion rates in high-risk patients.

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