Δ Aminocaproic Acid Inhibits Periosteal Chondrogenesis and Promotes Periosteal Osteogenesis During Fracture Healing

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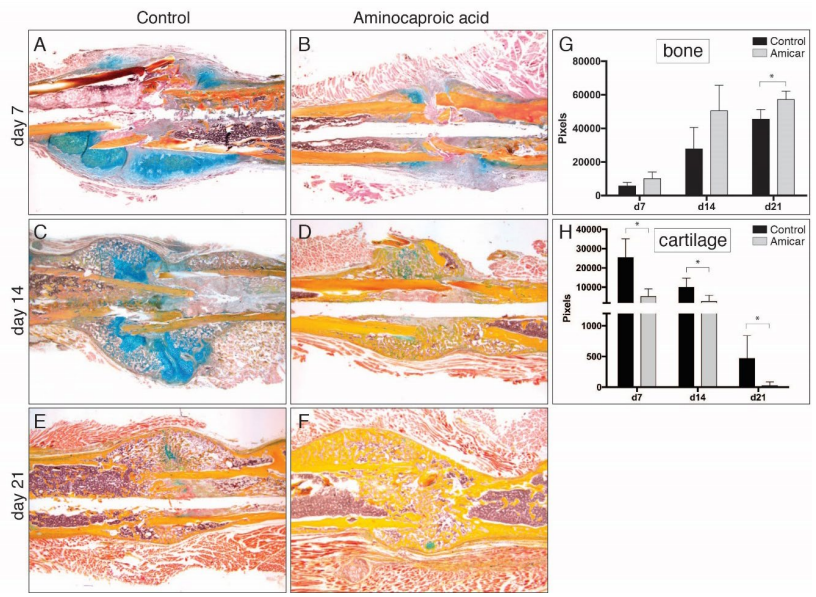
Purpose: We tested if Aminocaproic acid (AA) enhances appendicular bone healing and the mechanism of action of AA on osteoprogenitor cells (OPCs) during bone regeneration.

Methods: Bone marrow-derived OPCs were treated with varying concentrations of aminocaproic acid or control media. Cell proliferation and differentiation were assessed with standard tests. For the in vivo experiments, adult C57/BL6 mice received AA 30 minutes prior to fracture surgery and 30 minutes after surgery. A femur fracture model was utilized to assess bone formation rate, callus volume, proliferation, differentiation, and remodeling in vivo. Mice were euthanized at several days postinjury. A monocortical tibial defect model was used to study intramembranous ossification.

Results: At all examined time points, AA treatment resulted in a smaller cartilaginous soft callus, but larger bony hard callus, pointing toward an effect of AA on cell fate decisions of OPCs during fracture repair (Fig. 1). Next, we examined whether AA induces a switch from chondrogenesis to osteogenesis. We utilized a model of intramembranous bone formation to test this hypothesis. AA demonstrated a smaller bony callus than control animals. Transplantation experiments of blood clots from AA treated and control animals onto periosteal injury confirmed that AA modulated the cell fate decision from chondrogenesis to osteogenesis during fracture repair.

Conclusion: These experiments demonstrate that AA treatment during fracture healing leads to a change in cell fate of periosteal osteoprogenitor cells, with a predominance of osteogenic differentiation, resulting in a larger overall callus.



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