Δ Delayed Endothelial Progenitor Cell Therapy Promotes Bone Defect Repair in a Clinically Relevant Rat Model

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Purpose: The repair of nonunion and the restoration of bone loss secondary to trauma remains a challenge for orthopaedic surgeons. Recent experimentation in animal models has suggested that endothelial progenitor cells (EPCs) are capable of enhancing bone defect repair when applied acutely to surgically created defects. However, in the clinical context of open fractures complicated by bone loss, or in the nonunion setting, bone grafting is commonly delayed to minimize graft resorption, reduce infection risk, and allow soft-tissue healing. To date, animal models investigating EPC therapy have failed to replicate this environment. The current study sought to address this by investigating EPC therapy in a clinically relevant model of delayed treatment.

Methods: 5-mm segmental defects were surgically created in the right femur of male Fischer 344 inbred rats. Defects were stabilized with mini-plate and screws, and left empty for 3 weeks. After 3-week delay (delayed group), rats were randomized to a second surgery and treatment with either 1 million EPCs on a gel foam scaffold (n = 8) or gel foam scaffold alone (n = 8). A second group of rats (acute group) underwent the same femur fracture surgery, and were treated acutely with either 1 million EPCs on a gel foam scaffold (n = 6) or gel foam scaffold alone (n = 6). EPCs were isolated from the bone marrow of Fischer 344 rats, and subsequently expanded in culture for 7-8 days prior to transplantation. Animals were sacrificed at 10 weeks post-treatment, and defect healing was analyzed by plain radiographic assessment, microCT analysis, and biomechanical testing.

Results: Animals treated with EPCs in acute or delayed fashion achieved 100% union rate, whereas defects treated with cell-free scaffolds were united in 0% of acute controls and 37.5% of delayed controls. Furthermore, acute and delayed treatment with EPCs improved trabecular number and trabecular spacing compared to the respective control groups. Lastly, defects treated with EPCs in either acute or delayed fashion sustained higher ultimate torque compared to the respective controls.

Conclusion: Results from this study indicate that EPCs are capable of enhancing bone repair when applied to bone defects in acute or delayed fashion. Importantly, no differences in outcomes were observed between acute and delayed treatment with EPCs. These data suggest that EPC-based therapy could represent a substantial advance for the treatment of nonunions and traumatic bone defects in humans, and further research aimed at bringing this therapy to the clinical realm is warranted.

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