Δ Platelet-Rich Plasma as a Vehicle for Endothelial Progenitor Cell Delivery in Critical-Sized Bone Defects

David Ramnaraign; *Charles Godbout, PhD; Brent Bates; Emil H. Schemitsch, MD; Aaron Nauth, MD*
University of Toronto, Toronto, Ontario, CANADA

Purpose: Endothelial progenitor cells (EPCs) have successfully been used to promote bone repair in many different preclinical fracture models. However, to date, investigation in this area has relied on the use of cell culture media or saline for the therapeutic delivery of these cells. Recently, platelet-rich plasma (PRP) has been found to stimulate profound recruitment, proliferation, and differentiation of various stem and progenitor cells. Therefore the purpose of this study was to investigate the use of PRP and its effect on the ability and efficacy of EPCs to regenerate bone in a rodent critical-size defect model. We hypothesized that the use of PRP as a carrier for EPCs would improve bone healing when compared to the conventional EPC carriers including culture media, saline, or platelet-poor plasma (PPP).

Methods: A collagen scaffold seeded with ex vivo expanded EPCs (suspended in saline, PPP, PRP, or cell culture media) was placed in a surgically created 5-mm bone defect in the right femur of male rats. Controls of PPP and PRP with no cells were also used. The cells used for implantation were isolated from a sacrificed rat whose bone marrow was cultured for 7 days, while the PRP and PPP was isolated from rat peripheral blood via a 2-stage centrifugation process. Bone healing was assessed with biweekly radiographs, microCT analysis, and biomechanical testing. All animal protocols were approved by the Hospital Animal Care Committee.

Results: Radiographs demonstrated that bony union was achieved (irrespective of the carrier) in all but one of the EPC-treated animals. Notably, animals receiving PPP or PRP alone did not demonstrate any osseous bridging of their defects. MicroCT analysis further revealed a significant increase in the volume of bone regenerated among EPC-treated animals when compared to non-EPC-treated. Biomechanical testing confirmed unstable nonunion in both the PRP and PPP control groups, and crucially showed no significant differences in strength among any treatment groups receiving EPCs.

Conclusion: The use of PRP for regenerative applications in orthopaedics is appealing due to its ease of isolation and its biocompatibility. However, this study showed no significant benefit of PRP over conventional carriers for EPC therapy. Taken altogether, the results of this investigation identify saline as an appropriate and clinically relevant carrier for EPC therapy due to its efficacy, low cost, and noninvasiveness.

Δ OTA Grant