Tibial Fracture – Platelet-Rich Plasma and Bone Marrow Aspirate Concentrate (T-PAC): A Randomized Controlled Feasibility Study

James Vun, MBCHB, MRCSED*; Michalis Panteli, MD; Paul Harwood, FRCS (Ortho), MSc Anthony Howard, PhD; Nikolaos K. Kanakaris, MD, PhD; Jehan El-Jawhari, PhD; Elena Jones, PhD; Peter Giannoudis, MD, BS*
Leeds Teaching Hospitals NHS Trust, Leeds, UNITED KINGDOM

Purpose: We sought to assess the feasibility of conducting a randomized clinical trial (RCT) evaluating the effect of augmenting acute fracture healing with autologous bone marrow aspirate concentrate (BMAC) and platelet-rich plasma (PRP) in addition to standard care in patients with acute, unilateral tibial diaphyseal fractures.

Methods: This was a prospective single, patient-blinded randomized controlled trial based in a single major trauma center that has gained ethical approval. Patients were randomized at a 2:1 ratio (treatment: control arm) using an online randomization platform. Patients were eligible if they were aged 18 to 65 years, sustained an acute unilateral closed tibial diaphyseal fracture, able to provide consent, and definitive fixation with statically locked, reamed intramedullary nail or fine wire ring fixator within 14 days of injury. Autologous BMAC and PRP prepared following centrifugation of bone marrow aspirate harvested from iliac crest and peripheral blood, respectively, were injected percutaneously into fracture site under fluoroscopic guidance on the day of surgery. We assessed the safety profile of BMAC-PRP injection. Primary outcomes were time to painless weight bearing; radiological union assessed using the Radiological Union Score in Tibial Fractures (RUST) at weeks 2, 8, 12, 16, 20, 26, and 39; and patient-reported outcome measure (PROM) using the Lower Extremity Functional Scale (LEFS) at weeks 0, 12, 26, and 39.

Results: Of 54 patients who met the inclusion criteria, 45 patients were recruited and randomized. Two patients were withdrawn before surgery (1 compartment syndrome, 1 delay to operation beyond 14 days). Majority of the tibial fractures were distal third diaphyseal fractures (84%). Commonest fracture patterns were AO42A1 (47%) and AO42A3 (21%). There were no nonunionselayed unions, or deaths reported. No adverse effects, serious adverse effects, or complications were observed with BMAC-PRP injection. In the treatment group the RUST score was significantly higher when compared to control arm at weeks 8, 12, 16, and 20 ($P<0.05$). To account for the confounding effect of different fracture patterns, we analyzed and compared the largest subgroup AO42A1 (control n = 6, treatment n = 14). RUST scores were significantly higher in the treatment arm at weeks 8, 12, and 16 ($P<0.05$), reflecting quicker radiological union. Mean LEFS was higher in the treatment arm at weeks 12, 26, and 39, demonstrating clinical significance (difference by 9 points) at week 26 (treatment 62.7, control 49.7), and approaching clinical significance at week 39 (treatment 66.8; control 58.7).

Conclusion: This study demonstrated running a full scale RCT to be feasible, with a high recruitment rate. Furthermore, BMAC-PRP injection has a good safety profile, and was found to improve radiological and PROM outcomes.