Δ Treatment of Infected Bone Defects with Endothelial Progenitor Cells (EPCs) ± Local Antibiotics

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Purpose: Infection continues to present a major challenge in bone defect and nonunion management. It has previously been shown that EPCs can reliably heal critical-sized bone defects in a sterile animal model. However, the treatment effect of EPCs or EPCs plus local antibiotics on infection outcomes is unknown. Given their positive effects on bone healing and blood vessel formation, we hypothesized that EPCs would aid in the eradication of infection and that adding local antibiotics would further facilitate this outcome.

Methods: 24 animals underwent surgery to establish a critical-sized defect in the right femur and receive a low-dose inoculation of Staphylococcus epidermidis (103 CFU [colony-forming units]) at the defect site. Two weeks later, a second surgery was performed and animals were randomized to the following treatments: control/no treatment (n = 6), EPCs (n = 6), local vancomycin and rifampin (V+R) (n = 6), or EPCs plus local V+R (n = 6). Animals were sacrificed 2 weeks later. Our primary outcome was infection status based on intraoperative culture at the time of sacrifice (2 weeks post-treatment). Secondary outcomes included radiographic scoring for infection and serum inflammatory biomarker (α-2 macroglobulin) measurement. We did not assess bone healing in this study due to the short follow-up interval.

Results: Results for our primary outcome were as follows: rates of positive culture were 5 of 6 animals (83%) for controls, 4 of 6 (67%) for EPC treatment, 3 of 6 (50%) for local V+R treatment, and 2 of 6 (33%) for EPCs plus local V+R treatment. Differences between culture outcomes were not significant ($P = 0.52$). There were also no significant differences between groups on radiographic scores for infection. Serum α-2 macroglobulin analysis demonstrated that EPCs ($P<0.01$), local V+R ($P<0.01$), and EPCs plus local V+R ($P<0.01$) all significantly decreased inflammatory levels relative to controls at 2 weeks post-treatment.

Conclusion: We were unable to demonstrate a statistically significant effect of either EPCs, local antibiotics, or EPCs plus local antibiotics on infection outcomes in an infected bone defect model. However, we did observe trends towards increasing levels of infection eradication with both local antibiotics and the combination of local antibiotics and EPCs (50% and 67% rates of infection eradication, respectively). Inflammatory biomarker analysis also demonstrated that all 3 treatments reduced inflammation 2 weeks after treatment; however, it is unclear if the inflammation is solely due to infection and thereby a reliable indicator of infection status. These results support further investigation of the impact of EPCs ± local antibiotics on both infection and bone healing outcomes in the treatment of infected bone defects, with both larger group numbers and longer follow-up times.

Δ OTA Grant