Δ The Effect of Smoking Cessation on Serum Biomarkers of Fracture Healing

*Justin Kleiner, BS; **Joseph Johnson, MD**; Jeremy Truntzer; Scott McAllister; Matthew Edward Deren; Mursal Gardezi; Olivia Cummings; Melanie Ambler; Dioscaris Garcia; Christopher T. Born, MD*
Brown University, Providence, Rhode Island, USA

Purpose: Substantial information exists demonstrating the impact of smoking on wound healing, infection, and other outcomes following orthopaedic surgery. Little data exist demonstrating the effect of smoking and smoking cessation on inflammatory cytokines following fracture fixation. Our study uses a murine model to investigate the impact of smoking, and timing of cessation, on the regulation of vascular endothelial growth factor (VEGF) and transforming growth factor-beta (TGF-ß).

Methods: Our study incubated 70 mice for 4 weeks in a smoking chamber with 10 negative controls. These mice were divided into groups, with smoking cessation at 8, 6, 4, 2, and 1 week prior to fracture creation as well as at the time of fracture. A femur fracture was created and stabilized using a novel intramedullary fixation system. Blood was drawn from the mice during smoking, 2 weeks after fracture creation and 4 weeks after fracture creation. These blood samples were analyzed via ELISAs (enzyme-linked immunosorbent assays) for concentrations of VEGF and TGF-ß, and compared to continuous smoking, and smoke naïve controls. T tests were used to analyze the effect of smoking on VEGF and TGF-ß and linear regression was used to evaluate the effect timing of cessation on VEGF and TGF-ß.

Results: At 4 weeks postoperatively, the average VEGF level was significantly different between treatment groups ($P < 0.0001$). For all smoke-exposed mice, mean VEGF level was 93.733 pg/mL while the mean of non-smoke-exposed mice was 43.113 pg/mL ($P < 0.001$). Additionally, when compared to the treatment group at 4 weeks, the mean VGEF of mice that smoked continuously (48.276 pg/mL) and mice that never smoked (43.211 pg/mL) were both lower than groups that stopped smoking prior to fracture (101.90 pg/mL) ($P < .001$). At 2 weeks postoperatively, there was a significant difference between treatment groups ($P = 0.0309$), with TGF-ß higher in the groups with fewer weeks cessation; by 4 weeks postoperatively, TGF-ß was no different between groups.

Conclusion: Our study demonstrates that at 4 weeks postoperatively, mice that have started smoking, but stop prior to fracture creation, have a higher VEGF level than mice that smoke continuously or mice that never smoke. VEGF is a key cytokine involved in angiogenesis that contributes to fracture healing, and it appears that smoking cessation upregulates its production, while continuous smoking does not. Additionally, our data show that TGF-ß, an inflammatory cytokine, is upregulated by shorter durations of smoking cessation 2 weeks postfracture.

Δ OTA Grant

See pages 401 - 442 for financial disclosure information.