Paper - Basic Science

Paper Session: Fracture Healing:
Cells and Bone

Effects of TXA on Human Osteoblasts as Proxy for Fracture Healing

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Purpose: Tranexamic acid (TXA) is a popular antifibrinolytic drug used to decrease blood loss in many surgical fields and is increasingly used in orthopaedic trauma, but there is currently little published information regarding its effects on bone healing. Herein, we investigated TXA's effect on fracture healing via the basic surrogates of human osteoblast (HOB) viability, metabolism, and mineralization. In seeking to mimic topical TXA exposure in open fracture repair settings, and to determine the threshold of HOB viability with TXA, we included drug concentrations reported for fracture repairs and arthroplasties using local, topical, or intra-articular administration. The wide concentration range tested provides a more complete picture of fracture healing as TXA concentrations decrease toward those typically seen in IV administration. We hypothesized that as TXA concentration and exposure time increased, HOB metabolism would be negatively affected, but that no effect would be seen at lower typical surgical concentrations.

Methods: Primary HOBs were cultured via the explant method using arthroplasty patient donors and were seeded in 96-well plates to be cultured to 80% confluence. The cells were then exposed to TXA solutions of 100, 50, 25, 12.5, 6.25, 3.125, 1.563, 0.7813, 0.3906, and 0.1953 mg/mL for 3, 6, 12, or 24 hours. Cells were assessed for viability/metabolism using resazurin, alkaline phosphatase, and total protein assays. For mineralization testing, HOBs were grown with antibiotic-free media in collagen-coated 24-well plates to 80% confluence, were exposed to TXA at 50, 12.5, 3.125, 0.7813, and 0.1953 mg/mL for 3 or 6 hours, and were cultured with mineralizing media for 1 month before alizarin red assays were performed.

Results: HOB viability and metabolism decreased as TXA concentration and exposure time increased up to a concentration of 100 mg/mL and an exposure time of 24 hours, at which point negligible viability, suggesting significant cell death, was seen. Concentrations below 56.44 mg/mL did not affect HOB viability compared to the positive control, regardless of exposure time. Interestingly, at low concentrations at all exposure times, there was an increase in cell viability and metabolism, with 6 hours or less exhibiting a greater increase. Preliminary mineralization data seems to corroborate this, as a negative correlation between TXA concentration and mineralization was seen with all concentrations at 3 hours greatly improving and all concentrations at 6 hours slightly improving above the control.

Conclusion: We both partially rejected and partially accepted our hypothesis, for a degradation of HOB viability and metabolism occurred with increased TXA concentrations and exposure times, but at low TXA concentrations and exposure times we observed an improvement. Our data suggest that limiting TXA concentrations to a conservative 50 mg/mL when applied topically will minimize the impact on fracture healing.