Glycosaminoglycan Release from Cartilage Exposed to Tranexamic Acid

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Disclosures:

Introduction: Tranexamic acid (TXA) is a potent inhibitor of fibrinolysis via competitive inhibition of the conversion of plasminogen to plasmin. Mounting evidence suggests that administration of TXA reduces intraoperative blood loss, transfusion requirement, and decreases postoperative swelling and pain in joint replacement surgery. TXA is administered either intravenously or intra-articularly after closure of the joint capsule. Intra-articular doses from 1 to 3.5 grams have been reported. Interestingly all these studies used TXA in total joint replacements where all articular cartilage has been removed. Unknown is what effect topically applied TXA has on articular cartilage. If deemed safe, intra-articular TXA use could be expanded into a wide range of periarticular/intrarticul ar procedures to reduce post-operative hematoma and bleeding. Decreased post-operative narcotic requirement, better post-operative range of motion and accelerated rehab are all potential goals.

Glycosaminoglycans (GAG), keratin sulfate and chondroitin sulfate, provide the structural properties of cartilage and trap water within the extracellular matrix. Using a bovine cartilage explant model, we hypothesized that exposure to TXA would result in GAG release and that this release would be dependent on the time of exposure.

Methods: Cartilage samples were taken from the intercondylar groove of fresh bovine knees from a local slaughterhouse. A 4mm dermatome punch was use to take equally thick pieces of cartilage which were placed in Dulbecco’s Modified Eagles Medium supplemented with 10% FBS (v/v), penicillin-streptomycin (100 µg/ml), and 1% Fungizone. After harvest, the explants were given 24 hours to equilibrate. Explants were then exposed to either TXA at a concentration of 100mg/mL in media or normal growth medium for 2, 4, 8 or 24 hours, after which the supernatant was collected and frozen at -20° C. Utilizing a dimethylmethylene blue assay, the amount of GAG released in to the media was measured. In brief, 20 µl of sample diluted 1:2 and 180 µl of DMMB reagent were added to a 96-well plate, and absorbance was measured at 530 nm immediately. A standard curve was produced with serial dilutions of a chondroitin sulfate solution of known concentration.

Results: At each time point, on average, more GAG was released in the TXA group than the control as measured by microgram (µG) of GAG per uG of wet cartilage weight. GAG release at 8 hours for the control and TXA groups was 0.0008 and 0.0136 respectively. At 24 hours GAG release was 0.0068 in the control group and 0.0448 in TXA group. These differences were significant in both the 8 hour (p=0.003) and 24 hour (p=0.0074) groups.

Discussion: GAG release was evident at 8 and 24 hr for the control group as well as the treatment group. As hypothesized, a greater concentration of GAG was present in the media of TXA-treated explants at 8 and 24 hr, indicating an increase in cartilage matrix degradation. While the significance and exact mechanism of this GAG release is unknown it may indicate that surgeons should proceed with caution when using TXA in partial knee arthroplasty, hemiarthroplasty or any other procedure where native cartilage is retained. Currently, we are investigating the effects of TXA treatment on chondrocyte viability and links to necrotic and apoptotic cell death.

Significance: Treatment with Tranexamic acid does result in glycosaminoglycan release from articular cartilage. Until further investigation, surgeons should exercise caution when using TXA in procedures where articular cartilage is retained.

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Panteli, Michalis, Costas Papakostidis, Ziad Dahabreh, and Peter V Giannoudis. “Topical tranexamic acid in total knee
GAG Release in Response to TXA Exposure

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