Triamcinolone Acetonide Does Not Accelerate Human Cartilage Degeneration: Evidence from a Click-Chemistry Assay

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INTRODUCTION: Intra-articular corticosteroid injections are a standard therapy for controlling synovial inflammation, yet many clinicians worry that steroids hasten cartilage loss and precipitate premature osteoarthritis (OA). Prior data are conflicting, partly because tools to track matrix turnover have lacked sensitivity. We applied a novel high-resolution click-chemistry assay to test whether triamcinolone acetonide (TA) harms chondrocytes or extracellular matrix (ECM) in healthy and OA human cartilage.

METHODS: Intact femoral-condyle cartilage from cadaveric donors (mean 38 yr; n = 4; Male) and tibio-femoral cartilage from total knee arthroplasty (mean 64 yr; n = 14; 8F/6M) were harvested and cultured *in vitro*. Samples were treated with TA at either vehicle-saturated (200 µM) or clinically relevant (1 nM) concentrations. Outcomes included (1) Live/Dead™ staining, (2) qRT-PCR of catabolic (MMP13, ADAMTS5) and anabolic (ACAN, COL2A1) genes, and (3) click-chemistry labeling of newly synthesized glycosaminoglycan (GAG) and collagen to quantify synthesis and degradation.

RESULTS: *Chondrocyte Viability*: A 14-day treatment with saturated 200 µM TA did not affect cell viability in healthy ($p = 0.5$) or OA cartilage ($p = 0.82$). *Gene Expression*: In OA cartilage, 48 h of 200 µM TA down-regulated MMP13 (-75%, $p = 0.04$) and ADAMTS5 (-55%, $p = 0.02$) without suppressing ACAN or COL2A1. Healthy cartilage showed a similar MMP13 decline (-60%, $p = 0.06$), although it was not significant, and a 45% decrease in COL2A1 expression ($p = 0.002$). *Matrix Turnover:* Across 14 days, neither TA dose triggered GAG loss in healthy or OA cartilage. Continuous 200 µM TA modestly reduced GAG (-19%) and collagen (-25%) synthesis in healthy tissue ($p < 0.01$) and collagen synthesis (-27%) in OA tissue ($p = 0.008$), whereas 1 nM TA affected only collagen (-21%, $p = 0.004$) in healthy cartilage. However, two-day continuous TA exposure followed by a 14-day recovery culture produced no detrimental effect on GAG or collagen synthesis in the healthy human cartilage.

DISCUSSION AND CONCLUSION: Even at a supra-physiologic dose, TA did not induce chondrocyte death or accelerate matrix degradation. Click-chemistry assay revealed only a modest, reversible suppression of matrix synthesis, and high-dose TA lowered catabolic gene expression in OA cartilage. Given TA's insolubility in synovial fluid and tendency to remain on the cartilage surface clinically, intra-articular injections of TA are unlikely to reach chondrotoxic concentrations *in vivo*. These findings support continued use of TA for synovitis while alleviating concerns about direct cartilage harm.