In Vivo Effect of Single Intra-articular Injection of Tranexamic Acid on Articular Cartilage and Meniscus in a Rat Osteoarthritis Model

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INTRODUCTION: Tranexamic acid (TXA) has been increasingly used in arthroscopic surgeries to prevent the hemarthrosis. Despite its effectiveness, safety concerns have been raised regarding the potential cytotoxicity on articular cartilage and meniscus following intra-articular injection.

METHODS: To evaluate the impact of TXA on cartilage and meniscus, a rat model of knee instability was utilized, wherein an anterior cruciate ligament transection (ACL) surgery was followed by a single intra-articular injection of TXA at varying concentrations (0, 20, 50, 100, and 150 mg/mL) in saline. After 24 hours, cell viability assessment of the cartilage and meniscus was conducted (n=6), and gross observation and histological analysis of the medial tibial plateau and medial meniscus were conducted at the 2, 4, and 8 weeks (n=6).

RESULTS: The chondrocyte viability was significantly decreased in 50, 100, and 150 mg/mL groups compared with saline group ($P = 0.001$, $P < 0.001$, $P < 0.001$, respectively), as did meniscus cell viability ($P = 0.042$, $P < 0.001$, $P < 0.001$, respectively). At week 8, while the Saline, 20, and 50 mg/mL groups showed relatively normal appearances, the 100 and 150 mg/mL groups exhibited increased and varying severity of cartilage and meniscus degeneration. In the 150 mg/mL group, the Osteoarthritis Research Society International scores were significantly higher than those in the Saline and 20mg/mL groups ($P = 0.010$ and $P = 0.007$). Additionally, the meniscus score in the 150 mg/mL group was significantly higher than that in the Saline, 20 mg/mL, and 50 mg/mL groups 26 ($P = 0.020$, $P = 0.021$, $P = 0.031$, respectively).

DISCUSSION: Our findings indicate that concentrations of TXA at or above 100 mg/mL can lead to decreased cell viability in both cartilage and meniscus, resulting in significant cartilage degeneration in rats with anterior cruciate ligament transection. Furthermore, the use of 150 mg/mL TXA led to significant meniscal degeneration.

SIGNIFICANCE/CLINICAL RELEVANCE: It is prudent to avoid using concentrations of TXA exceeding 100 mg/mL for intra articular injection, as such concentrations may potentially result in adverse effects on the cartilage and meniscus.

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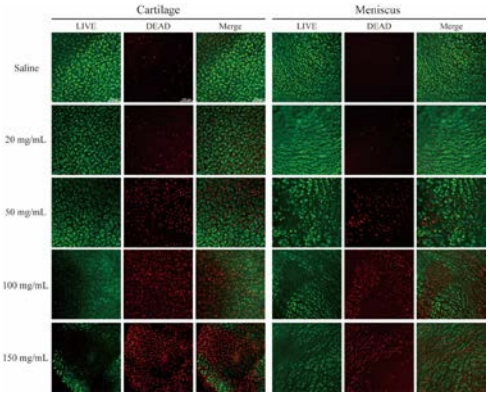

Figure 1. Representative images of Live/Dead staining for surface chondrocytes and meniscus cells at 24 hours after TXA injection (n = 6). Live cells were labeled in green fluorescence and dead cells in red fluorescence. White scale bar = 100 μm.

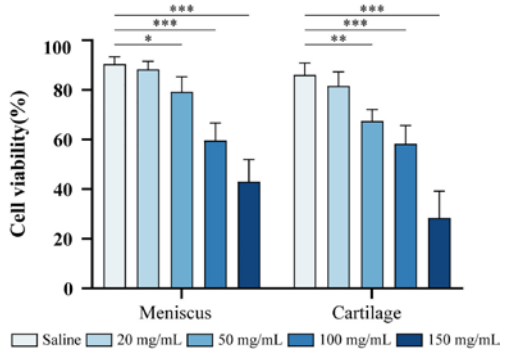

Figure 2. Average cell viability of meniscus and cartilage at 24 hours after TXA intra425 articular injection. Data are expressed as mean ± 95% CI. Quantification of the 426 percentage of Live and Dead cells using ImageJ (n = 6). One-way analysis of variance 23 / 24 427 and post hoc Bonferroni multiple comparisons test were used to compare all groups. * 428 $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.