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Intra-articular hyaluronic acid increases cartilage breakdown biomarker in patients with knee osteoarthritis

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Intra-articular hyaluronic acid has been used in treatment of patients with knee osteoarthritis. Though its effect on pain has been well studied, it is not clear how it affects the articular cartilage. This is a preliminary study to evaluate the kinetics of urinary collagen type-II C-telopeptide (CTX-II) as a biomarker of collagen breakdown in response to intra-articular hyaluronic acid injection in patients with symptomatic knee osteoarthritis. Intra-articular injections of hyaluronan were administered to ten patients with symptomatic knee osteoarthritis. Urine collection for urinary CTX-II was obtained at baseline, before each injection and once every other week for a total of 6 months. Urine CTX-II was measured using a CartiLaps© ELISA kit. There was a statistically significant increase ($p = 0.0136$) in CTX-II a week after the third intra-articular injection of hyaluronic acid (6,216 ng/mmol +/- 4,428) compared with baseline (2,233 ng/mmol +/- 1,220). This increase in CTX-II was sustained throughout the entire 6 months follow-up period (repeated measures ANOVA, $p < 0.015$). This is the first study of changes in an osteoarthritis biomarker after intra-articular hyaluronic acid injections in patients with symptomatic knee osteoarthritis. Contrary to our initial hypothesis that CTX-II levels should decrease after intra-articular hyaluronic acid injections, we found a significant increase in urinary CTX-II levels that was sustained throughout the study. These observations suggest that intra-articular hyaluronic acid injections may accelerate cartilage breakdown in patients with symptomatic knee osteoarthritis. The responsible mechanisms are unknown and warrant further study.

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