Osteochondral injury increases type II collagen degradation products (C2C) in synovial fluid of Thoroughbred racehorses

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Introduction: Type II collagen is a primary component of articular cartilage. Degradation of collagen is primarily initiated by matrix metalloproteinases (MMP-1, -8, and -13)[1]. These proteolytic enzymes have been shown to cleave the collagen triple helix into 1/4 and 3/4 length fragments. This cleavage exposes a neoepitope at the carboxy terminus of the 3/4 fragment (C2C or COL 2-3/4Clong). Type II collagen cleavage is increased in injured cartilage of humans, dogs, and horses[1–3]. The specific purposes of this study were (1) to investigate the effects of exercise and osteochondral (OC) injury on synovial fluid (SF) C2C concentrations in metacarpophalangeal/metatarsophalangeal (MCP/MTP) and carpal joints and (2) correlate these concentrations with severity of joint injury, as determined by radiographic and arthroscopic scores.

Materials and Methods: SF samples were obtained from 3 groups of Thoroughbred (TB) racehorses: (1) Rested: 20 TB horses (age range 14 to 20 months), confirmed normal by clinical and radiographic examination. SF samples were collected from metacarpophalangeal (MCP) joints (n=20) and middle (n=14) or radiocarpal joints (n=6) of these horses before the start of race training. (2) Exercised: horses from the rested group (group 1) had the same joints sampled at the end of 5 to 6 months of training. (3) OC injury: 28 Thoroughbred horses (age range 2 to 7 years) undergoing MCP (n=13), metatarsophalangeal (MTP; n=1), middle carpal (n=9), or radiocarpal (n=5) arthroscopic surgery for removal of (OC) fragments, which were injuries resulting from racing. For group 3, radiographic and arthroscopic scores were determined. Radiographic scores were assigned, using a scale of 0 to 3, for each of the following 10 criteria: joint space narrowing, osteophyte number, osteophyte size, enthesophyte number, enthesophyte size, fragment number, fragment size, soft tissue swelling/effusion, subchondral bone sclerosis, and subchondral bone lucency. Possible radiographic scores were 0 to 30. Arthroscopic scores were assigned by modification of previously described methods[4–6], with possible scores of 0 to 37. SF samples were assayed using a commercially available ELISA (C2C, IBEX Technologies, Inc). Differences between groups were determined by one-way ANOVA and a post hoc Tukey’s multiple-comparison test. Positive and negative predictive value of SF C2C for identifying OC injury was determined by Fisher’s exact test. Correlations were determined using the Spearman correlation coefficient. P<0.05 was considered significant.

Results: SF C2C concentrations in OC injured MCP/MTP and carpal joints were significantly different than rested and exercised joints (P<0.01; Figure 1). However, MCP/MTP and carpal SF C2C concentrations were not significantly different between rested and exercised groups. Arthroscopic scores were significantly higher for OC injured carpal than OC injured MCP/MTP joints (P=0.004). OC injured SF C2C concentrations were positively correlated with radiographic scores (R=0.43; P=0.03) and arthroscopic scores (R=0.52; P=0.03). Arthroscopic scores were positively correlated with radiographic scores (R=0.51; P=0.04). SF C2C concentrations ≥ 64 pmol/mL for MCP/MTP joints and ≥ 75 pmol/mL for carpal joints were arbitrarily chosen to determine predictive value for discriminating OC injured horses from rested or exercised horses. This yielded a positive predictive value of 73% and a negative predictive value of 94% for the MCP/MTP joints, and positive predictive value of 79% and negative predictive value of 95% for the carpal joints.

Discussion: Concentrations of C2C in MCP/MTP and carpal SF did not increase significantly after exercise. However, OC injury caused a significant increase in SF C2C concentrations compared to rested and exercised horses. SF C2C concentrations were correlated to severity of joint injury. Although carpal radiographic scores were not significantly higher than those for the MCP/MTP joints (P=0.06), the difference may have clinical significance when considered in conjunction with the arthroscopic scores, since carpal joints had higher SF C2C concentrations and higher arthroscopic scores when compared to the MCP/MTP joints. Therefore, it appears that OC injuries in the carpus tend to result in greater overall joint damage than in the MCP/MTP joint. This provides rationale for using different SF C2C concentrations to establish criteria for using this biomarker as a diagnostic tool for different joints. Based on these findings, SF C2C analysis may be useful for evaluation of joint injury.


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