PROGRESSIVE CHANGES IN PRO-INFLAMMATORY AND STRUCTURAL BIOMARKERS IN SYNOVIAL FLUID AND SERUM IN STANDARBRED RACEHORSES WITH TRAUMATIC OSTEOARTHRITIS

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Purpose of the work. *The object of the present study was to assess changes of pro-inflammatory and structural biomarkers in synovial fluid (SF) and serum (S) in Standardbred racehorses (STBR), diagnosed with traumatic osteoarthritis (OA) of the fetlock, over a long-term period of training. Biomarkers in SF and S could assist clinicians to predict OA progression to degenerative joint disease (DJD) in the fetlock joint during STBR racing careers.*
Materials and used methods. *Twenty-five STBR starting training between 18-24 months of age, diagnosed with fetlock joint OA as a cause of lameness, were included in a prospective cohort study. Horses were observed over a period of 5 years of continuous athletic activity. Six sound, age-matched STBR were used as controls (C). Blood and SF samples from the affected joints were collected at the first episode of lameness and repeated once a year for the consecutive training seasons (named T1 to T5). Samples were processed for interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-a (TNF-α), cartilage oligomeric matrix protein (COMP) and cross linked C-telopeptide of type II collagen (CTX-II) using ELISA kits validated for equine use. Statistical analysis were performed using a two-way ANOVA with a statistical software package (GraphPad Prism version 6.00 for Windows, GraphPad Software, La Jolla California USA) and p-value of <0,05 was considered significant.*
Outcomes. *IL-1β values in SF were significantly higher in OA group than C at T1, T4 and T5. A significant decrease at T2vsT1, and a significant increase at T4vsT3 and at T5vsT4 were noted in OA group. Serum IL-1β was significantly greater in OA horses than C only at T5. A significant increase in S IL-1β values in OA group was recorded at T5vsT1, T5vsT2, T5vsT3 and T5vsT4. Synovial fluid from OA horses had significant greater levels of IL-6 than C during the entire study period. OA group was characterized by a significant decrease of SF IL-6 at T1vsT2, and a significant increase at T4vsT3, as well at T5vsT4. There were no significant differences in IL-6 values in S between C and OA horses, and no significant differences between consecutive measurements in OA group. TNF-α values in SF were significantly higher in OA horses than C at T4 and T5. Significant increase in TNF-a levels in OA group was found at T4vsT3. Significantly higher S TNF-a values in OA group than C was recorded at T4. Values of S TNF-a were significantly increased at T4vsT3 and at T5vsT4 in OA horses. COMP in SF was significantly increased in OA than C group at T4 and T5, with a significant increase at T4vsT3. Serum COMP is significantly greater in OA horses than C at T3, T4 and T5, with a significant increase at T4vsT3 in OA horses. Significantly higher SF CTX-II in OA horses than C was found at T3, T4 and T5. Comparing SF CTX-II values in OA groups, a significant increase was found at T3vsT2, as well at T4vsT3. Serum CTX-II showed a significantly higher value in OA group than C at T4 and T5. In OA horses, a significant increase of S CTX-II value was noted at T3vsT2, and at T4vsT3. Correlation of biomarkers values from SF and S were not detected.*

Conclusions. *This is the first study reporting the assessment of OA biomarkers over a long period, which spans across the entire athletic career of STBR. Our results show that traumatic OA of the fetlock at the beginning of training is able to progress to DJD over the racing career, as it is highlighted by pronounced rise of structural cytokines (COMP and CTX-II) in SF and S. At T1 pro-inflammatory biomarkers (IL-1β, IL-6) were characterised by higher values due to early synovitis and capsulitis preceding cartilage degradation. High levels of both IL-1β and IL-6 during T4 and T5 indicated that inflammation is not only related to acute OA, but it occurs also in later stage of DJD. Because rise in both structural cytokines preceded inflammation, we conclude that pro-inflammatory cytokines rise occurred secondary to release of cartilage breakdown products in the synovial compartment. Since the value of TNF-a did not show significant increase during the initial OA stages, its trend could be related to the exercise effect in both groups. Correlations between S and SF values for the main part of studied biomarkers were unpredictable. However, S COMP seems to predict OA progression more efficiently than SF. The results of this study indicate the progressive transition from fetlock OA to DJD in racehorses and the benefit of different biomarkers in detecting cartilage damage, emphasizing diagnostic value of cytokine dosage and their values in monitoring OA treatments.*

Bibliography

1. Duclos ME, Roualdes O, Cararo R, Rousseau JC, Roger T, Hartmann DJ (2010): Significance of the serum CTX-II level in an osteoarthritis animal model: a 5-month longitudinal study. Osteoarthritis Cartilage. 18:1467-76.
2. Goldring SR, Goldring MB (2004): The role of cytokines in cartilage matrix degeneration in osteoarthritis. Clin Orthop Relat Res. 427:S27-36.
3. McIlwraith CW (2005): Use of synovial fluid and serum biomarkers in equine bone and joint disease: a review. Equine Vet J. 37:473-82.
4. Sutton S, Clutterbuck A, Harris P, Gent T, Freeman S, Foster N, Barrett-Jolley R, Mobasheri A (2009): The contribution of the synovium, synovial derived inflammatory cytokines and neuropeptides to the pathogenesis of osteoarthritis. Vet J. 179:10-24.

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