Conclusions: The present data suggest that LitoVet has anti-inflammatory properties in horses. This can possibly explain why the horses were able to improve their speed running 1000 meter and why they were more lithe after strenuous exercise.

[70] INFLUENCE OF RISEDRONATE TO BONE AND CARTILAGE METABOLISM MARKERS IN AN OVARIECTOMIZED RAT

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Purpose: It has been reported that cartilage metabolism markers are influenced by clinical administration of risedronate. We used the ovariectomized (OVX) model rat which is a postmenopausal osteoporosis model in this study and evaluated the influence of risedronate administration on bone and cartilage metabolism markers.

Methods: Ovariectomy was performed to SD rats (total 34 rats, about 6 months after birth). 0.1, 1.0 and 2.5mg/kg/day of risedronate was orally administered every day immediately after the operation for 8th weeks. Urinary D-Pyr, CTX-II and Serum CTX-I levels were determined at pre-operation, middle and end of administration. Serum COMP levels were determined at the end of risedronate administration.

Results: Serum COMP levels slightly increased in OVX group and decreased dose-dependently in risedronate administrated group. CTX-II levels showed the same changes as COMP, however the effect of risedronate decreased in 8th week. Levels of D-Pyr, CTX-II and CTX-I increased in OVX group compared in Sham group and decreased dose-dependently in risedronate administrated group. Significant positive relations were observed between D-Pyr/CTX-I and CTX-II/COMP at 4th and 8th weeks.

Conclusions: Cartilage metabolic turnover was enhanced by OVX and this enhancement was reversed by risedronate. Above data suggested that risedronate administration to OVX rat resulted in significant changes of both type I and II collagen metabolism.

[71] MECHANICAL LOADING OF MURINE KNEE JOINTS: NON-INVASIVE INDUCTION OF LESIONS?

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Purpose: Articular cartilage is essential for friction-free joint movement. Loss of articular cartilage integrity in osteoarthritis (OA) is a major cause of disability. Despite this, the factors influencing initiation and progression of OA remain poorly defined, partly due to a lack of appropriate animal models. Clinical experience and epidemiological studies indicate that joint loading promotes cartilage degeneration. Our development of a non-surgical model of mouse tibial loading through natural articulation points, offers unique opportunities to address whether well-defined and controlled joint loading induces development of OA-like lesions. Our studies will address the hypothesis that in vivo loading induces the formation of localised lesions in the articular cartilage of mouse knee joints.

Methods: In vivo loading: right knees of 22 week-old male ‘OA-prone’ Str/ort mice, ‘OA-protected’ CBA mice and mice with intermediate OA susceptibility C57BL/6, were cyclically loaded as described by De Souza et al (2005), 3 times/week for 2 (C57BL/6 and CBA) or 4 weeks (Str/ort), at a magnitude of 9N. 0.1Hz frequency with 40 cycles each day. The animals were killed 2 days after the final loading episode.

Histology: Serial 9 μm sections of the entire wax embedded knee were cut and one third of the slides stained with Toulidine blue and graded as described below.

Grading and statistics: Grading of lesion severity was achieved by the methods of Chambers et al (2002). Lesions were scored from 0 (normal cartilage) to 6 (loss of more than 80% of the articular cartilage). Each joint compartment (medial/lateral and tibia/femur) was graded separately and a grade for the whole joint also recorded. Loaded knees were compared to the contra-lateral non-loaded knees using a paired t test. Data were shown as mean±SEM.

Results: Our results show that knee joints of all three strains of mice exhibit increases in the severity of overt lesions in response to applied loads; with loaded knees showing statistically significant increases in both mean and maximum OA-grades in C57BL/6 and CBA mice, and significant increases only in the mean OA-grade in Str/ort mice. Load-induced increases in lesion severity were most marked in the lateral femur, but failed to reach levels of significance in other compartments of C57BL/6 and CBA mice. In Str/ort mice, load-induced lesions were significant in the medial and lateral femoral compartments, but tibial compartments, in which OA lesions develop spontaneously, were not significantly affected by loading.

Conclusions: In vivo murine knee joint loading can induce articular cartilage lesions in three mouse strains. The load-induced lesions were similar in mice which exhibit divergent susceptibility to spontaneous OA, namely the OA-prone Str/ort mice, the OA-resistant CBA mice, and C57BL/6 mice which exhibit a ‘normal’, intermediate incidence of OA. In addition, the location of load-induced lesions was consistently in the femoral compartment. As this differs from the predominant location of naturally-occurring lesions on the tibia of Str/ort mice, it establishes scope for comparing the progression of natural OA lesions and load-induced lesions within the same joint. Our data also provide the basis for future studies aimed at refining applied loads to develop a novel model for OA induction. Indeed, this model provides many advantages, including: non-surgical controlled induction of OA, availability of contra-lateral control joints, scope for longitudinal studies in an appropriate species that will allow us to define the most osteoarthritogenic loads, as well as the role of specific genes in OA using genetic mutant mice.