Introduction

Several experimental animal models have been developed for human osteoarthritis (OA) and used to study the preclinical efficacy of disease and symptom modifying OA drug candidates in various species.1,2 These animal models have been characterized and the preclinical efficacy of OA drug candidates has been studied using numerous microarrays scoring systems and joint pain assessments. The histopathology initiative of Osteoarthritis Research Society International (OARSI) has presented recommendations for histological OA assessment in different species to standardize the histopathological assessment of OA. Recommendations for rat samples focus on articular cartilage, synovium, joint capsule, and growth plate.3

When studying treatment effects on osteoarthritic rat bone, the histological OA assessment should be completed with the analysis of epiphyseal bone, subchondral bone plate and epiphyseal trabecular bone.

Aim of the Study

This study characterized changes in epiphyseal bone, subchondral bone plate and epiphyseal trabecular bone and assessed knee joint discomfort, pain and degenerative changes in four rat OA models, induced by intra-articular monosodium urate (MIA, 1 mg), medial meniscal tear with combined medial collateral ligament transection (MMTx), cruciate ligament transection combined with partial medial meniscectomy (ACLMT, pMMx), and ACLT alone.

Materials and Methods

Animal administration: This study was conducted using male Lewis rats with 10 weeks of age at the beginning of the study and weighing 250 ± 20 g. A total of 48 rats were randomly assigned to the following four OA models: 1. MIA+ACLT (12 rats), 2. MIA+MMT (12 rats), 3. MIA+ACLT+MMT (12 rats), 4. sham operated control group (12 rats). All animals were penned in a covered cage, for a period of 16 weeks, with a food and water ad libitum. The study was performed in accordance with the ethical guidelines of the Helsinki Declaration. The study was approved by the local animal care committee of Turku, Finland.

Histological bone analysis

Histological bone analysis was performed using standard techniques. Bone thickness above growth plate (B.Th, µm), trabecular number (Tb.N, mm⁻¹), trabecular thickness (Tb.Th, µm), epiphyseal bone area fraction (B.Ar/T.Ar, %), subchondral bone area (B.Ar, mm²), epiphyseal bone area fraction (B.Ar/T.Ar, %), subchondral bone area (B.Ar, mm²), osteophyte width (µm), cartilage degeneration width (mm), tibial score (score 0-24), and paw withdrawal threshold (g).

Summary

The amount of epiphyseal bone, subchondral bone plate and/or epiphyseal trabecular bone decreased in the rat MIA and ACLT models exhibiting mild to moderate OA changes, and increased in the rat MMT+MCLT and ACLT+pMMx models exhibiting moderate to severe OA changes.

Conclusions

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References


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