The objective of this study was to characterize tissue and structural changes in rat knee after intra-articular MIA injection, including both patellofemoral and tibiofemoral joints.

Intra-articular injection of monosodium iodoacetate (MIA) disrupts chondrocyte glycosylation through the inhibition of glycosyltransferase-3-phosphate dehydrogenase. This results in chondrocyte death and leads to osteoarthritis (OA) symptoms and joint damage. Accordingly, the injection of MIA into rat knee joint can be used widely as a chemically induced model of OA in preclinical efficacy studies for OA drugs and symptom-modifying OA drugs candidates.

Hitherto, most data of MIA-induced damage in rat knee has been obtained from tibiofemoral joint and not much information is available from patellofemoral joint. In order to improve the injection of MIA into rat knee as an animal model of OA in preclinical efficacy studies, we investigated the effects of intra-articular MIA injection on the whole knee joint including both patellofemoral and tibiofemoral joints.

The study was conducted using three months old male Lewis rats. One ring of 24 cages (designed, St.Luke’s, MD, US) of 15 g of weight was injected into the left knee joint of 12 rats and the right knee joint of 12 rats. During the study, knee joint weight distribution was measured using In Vivo Image Tester (Jitter Instrumentation, North, UK) and paw withdrawal threshold was measured using von Frey Stroem (0.5-15 g). North Coast Medical, Morgan Hill, CA, USA. Saline PBS 0.02% was used throughout the study. A 2% solution of toluidine blue was prepared using phosphate buffer for the demonstration of endochondral ossification. The cartilage degeneration is observed as denaturation of collagen fibers and degradation of proteoglycan matrices by toluidine blue staining. The cartilage degeneration was evaluated using a Faxitron machine (Faxitron X-ray Systems, IL, USA) in which the jointtissues were dissected and fixed either in formalin or ethanolic (70%). Digital radiograph were analyzed using Digirad software (Turbo Xpert, Turku University Hospital, Turku, Finland). Knee joints fixed in formaline were decalcified, embedded in paraffin and stained with hematoxylin-eosin. The sagittal sections were stained in Toluidine Blue or Safranin-O and degenerative changes in tibiofemoral joint were evaluated following the recommendations of the OARSI.

The effects of MIA injection on the joint were evaluated in terms of mechanical and histological parameters. The Paw Withdrawal Threshold was measured using the von Frey Stroem (0.5-15 g). The mechanical parameters were the paw weight distribution and the withdrawal threshold of injected and non-injected knees. The histological parameters were the histological sections of the injected and non-injected knees. The histological sections were stained with toluidine blue and toluidine blue stained sections demonstrated the presence of patellofemoral and tibiofemoral joints in the sagittal sections. Images were acquired from control knees (top panel) and toluidine blue stained (bottom panel) at 2-weeks after the injection. The images were acquired from the joint line of the left knee and the right knee.

Histology analysis demonstrated the presence of patellofemoral and tibiofemoral joints in the sagittal sections. Images were acquired from control knees (top panel) and toluidine blue stained (bottom panel) at 2-weeks after the injection. The images were acquired from the joint line of the left knee and the right knee.

Conclusions

Intra-articular injection of 1 mg MIA into rat knee induced a significant damage in the whole knee joint, including both patellofemoral and tibiofemoral joints. MIA injection induced pain-like symptoms in rat knee, including a mechanical hypersensitivity and starting at 3 days after the MIA injection.

Digital radiographs demonstrated an apparent damage including articular surface degradation in patellofemoral joint at 2 and 4 weeks after the MIA injection. Histological evaluation revealed articular cartilage worn out, patellar tendon degeneration in proteoglycan content, and synovial inflammation in MIA injected knee joints.

Fluorescence labeling demonstrated active endochondral ossification and bone formation in control knees. The endochondral ossification was impaired or ceased in MIA injected knees, especially in patellofemoral joint. Subchondral bone formation was enhanced without affecting bone volume.

When Comparing the effects in both the same site of the acidic environment, MIA induced damage was stronger in patellofemoral joint than in tibiofemoral joint.

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References