Low Dosage Of Monoiodoacetic Acid Induces Arthritis Without Bone Defect In A Rat Model.

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Introduction: Monoiodoacetic acid (MIA) is used to make a rodent arthritis model. An arthritis model by MIA is often used in order to evaluate pains in animals (1). The dose of MIA commonly used for the model is too high and results in not only cartilage degeneraiton but also bone destruction within a short period, unsuitable for morphological observation as an osteoarthritis model. The joint change induced by high dosage of MIA appears similar to that of rheumatoid arthritis, different from osteoarthritis. The purpose of this study was to examine the dose effect of MIA on cartilage and bone damage sequentially for the establishment of a rat arthritis model similar to osteoarthritis.

Methods: Male Wistar rats at 8 weeks old received a single intra-articular injection of MIA in the right knee and PBS in the left knee. The dose of MIA was 0.1, 0.2, 0.5, and 1 mg/50μl (n = 4). Articular cartilage was evaluated macroscopically and histologically at 2, 4, 6, 8, and 12 weeks. The macroscopic observation was evaluated using the modified Hayashi's score on a scale of 0-6 points. The tissue specimens were stained with safranin-o and hematoxylin-eosin (HE). Cartilage distraction was evaluated using the OARSI score on a scale of 0-24 points and the Mankin score on a scale of 0-14 points.

Results: Macroscopically, in the 0.1mg group, there was no lesion of cartilage for the first 4 weeks (Fig.1). Cartilage erosion containing several holes was observed at 6 weeks. The erosion advanced at 8 weeks and the smoothness disappeared at 12 weeks. In the 0.2mg group, the cartilage erosion containing several holes were already observed at 2 weeks. The erosion advanced gradually and the smoothness disappeared at 8 weeks. The cartilage destruction appeared in whole but the bone destruction was not observed at 12 weeks yet. In the 0.5mg and 1mg groups, the erosion appeared in whole at 2 weeks, the cartilage disappeared at 4 weeks and the bone destruction already emerged at 4 weeks. The bone was destroyed severely at 8 weeks.

Histologically, in the 0.1 mg and 0.2 mg groups, stainability for cartilage matrix already decreased at 2 weeks, further decreased gradually, and the cartilage disappeared at 12 weeks (Fig.2). Subchondral bone was focally exposed at 12 weeks in the 0.1 mg group and at 6 weeks in the 0.2 mg group. Bone destruction was not observed until 12 weeks in the 0.1 mg and 0.2mg group. In the 0.5 mg group, cartilage destruction appeared at 2 weeks, and bone destruction appeared at 4 weeks. In the 1 mg group, cartilage disappeared and bone was severely destroyed at 4 weeks. We quantified macroscopic findings by modified Hayashi’s score (Fig.3A). In the 0.1 mg group, the score was 1.0 at 2 and 4 weeks, then gradually increased at 6 and 8 weeks, and unchanged at 12 weeks. In the 0.2mg group, the score was 1.3 point at 2 weeks, unchanged at 4 weeks, then increased gradually at 6 and 8 weeks, and unchanged at 12 weeks. In the 0.5mg group, the score was 3.2 at 2 weeks, then
continued to increase rapidly at 4 weeks, then gradually increased at 6, 8, and 12 weeks. In the 1mg group, the score was 4.75 point at 2 weeks, then reached to maximum points at 4 weeks.
We quantified histological findings by Mankin score (Fig.3B). In the 0.1mg group, the score was 3.5 at 2 weeks, then gradually increased at 4, 6, 8, and 12 weeks. In the 0.2mg group, the score was 5.0 at 2 weeks, then increased rapidly at 4 weeks, and unchanged at 6, 8, and 12 weeks. In the 0.5 and 1.0 mg groups, the scores were 18 and 20 at 2 weeks, then reached to the maximum at 4 weeks.
Fig.1 Representative macroscopic features for femoral and tibial cartilage.
Fig.2 Representative histological features for medial tibial condyle.
Fig.3 Quantification for macroscopic features (A) and histological features (B) for tibial cartilage (n=4).

Discussion: There are many reports of a rat arthritis model in which higher than 1 mg MIA was used. This will be too high to evaluate cartilage because it results in rapid bone destruction. Indeed there are some reports in which low dose of MIA was used, their purpose was mainly to evaluate the pain and histopathological investigation was not performed (2). Here we demonstrated that 0.1 and 0.2 mg MIA induced early arthritis showing mild cartilage damage without severe bone damage. The dose of MIA and duration after the injection were important factors affecting severity of arthritis. Our data obtained here provide useful information for establishment of a rat arthritis model to accomplish a particular objective.

Significance: Low dosage MIA induced arthritis with cartilage damage without bone distraction. This model demonstrated the early stage of osteoarthritis, which will be useful for figuring out the mechanism of the cartilage distraction in the process of osteoarthritis.
Figure 2.
Figure 3.

A

B

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