Monoiodoacetic acid induces arthritis and synovitis dose- and time- dependent in rats

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Introduction: In a rat monoiodoacetic acid (MIA)-induced arthritis model, the amount of MIA commonly used can be too high, resulting in rapid bone destruction. There are many reports of MIA-induced arthritis models in which higher than 1 mg MIA was used in Lewis rats (1, 2), but the high dose model is not suitable for the evaluation of cartilage degeneration due to its rapid progression. Synovitis is one of the typical features of OA (3) and in clinical pathology, and synovitis can adversely affect joint function (4). However, the infrapatellar fat pad (IFP) inflammation was not reflected by the previous synovitis scoring system (5). Here, we examined the effect of MIA concentrations on articular cartilage and IFP and we also established an original scoring system for macroscopic cartilage and histologic IFP features specific to the rat MIA-induced arthritis model.

Methods: Male Wistar rats received a single intra-articular injection of MIA in the knee. The amount of MIA was 0.1, 0.2, 0.5, and 1 mg (Fig. 1A). Articular cartilage was evaluated at 2-10 weeks by MIA macroscopic cartilage score we newly established and OARSI score. IFP was also observed at 3-14 days and evaluated by the IFP inflammation score we newly established.

Results: Macroscopically, low MIA doses induced punctate depressions on the cartilage surface, and cartilage erosion proceeded slowly over 12 weeks, while higher MIA doses already induced cartilage erosion at 2 weeks, followed by bone destruction thereafter. MIA macroscopic cartilage score (Fig. 1B), OARSI histological score increased in a dose- and time- dependent manner (Fig. 1C, 2). The IFP inflammation score (Fig. 3A) peaked at 5 days in the low dose group, then decreased, while at high dose, the IFP score continued to increase over 14 days due to IFP fibrosis. There were no obvious differences in synovitis of the IFP between the 0.2 mg MIA group and in the 1 mg MIA group at 3 and 5 days. After 5 days, synovitis was reduced in the 0.2 mg group but progressed in the 1 mg group at 7 and 14 days (Fig. 3B).

Discussion: MIA-induced arthritis progression was dose- and time- dependent. These results provide valuable information to the standardization of an OA model by MIA, suitable to evaluate effects of research therapeutics.

To quantify the extent of the characterized macroscopic findings of MIA models, we established an original macroscopic cartilage scoring system for rat arthritis induced by MIA. This enabled us to provide scores to accurately reflect macroscopic findings, such as punctate depressions and erosion.

The injection of 1 mg MIA induced fibrosis of the body of the IFP. To quantitate the fibrosis in the body of the IFP, we established the IFP inflammation score, which grades “cell infiltration at the surface of the IFP” and “fibrosis in the body of the IFP’. This scoring system could make it possible to classify reversible and irreversible inflammation of the IFP. The results suggests that low amounts of MIA induce reversible synovitis, while high amounts of MIA induce irreversible synovitis.

Conclusion: Punctate depressions, cartilage erosion, and bone destruction were observed in the MIA-induced arthritis model. The pathological cartilage scoring, established here, enabled the quantification of cartilage degeneration and demonstrated that MIA-induced arthritis progressed in a dose- and time-dependent manner. IFP inflammation scores revealed that 0.2 mg MIA induced reversible synovitis, while 1 mg MIA induced fibrosis of the IFP body.

Significance: The amount of MIA administered and time after MIA injection were important factors affecting the severity of arthritis and a low amount of MIA is sufficient to produce cartilage degeneration without bone destruction, which is similar to the pathology of osteoarthritis. To quantify the findings of MIA-induced arthritis model, we established the IFP inflammation score and MIA macroscopic cartilage score.


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