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RESEARCH

Treatment of acute full-thickness chondral defects with high molecular weight hyaluronic acid: An experimental model☆

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KEYWORDS
High molecular weight hyaluronic acid;
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Abstract
Purpose: To evaluate the effect of 2 different protocols of intra-articular hyaluronic acid (HA, hylan G-F20) to articular cartilage regeneration in acute full-thickness chondral defects.
Materials and methods: Full-thickness chondral defects of 3 mm × 6 mm were performed into the lateral femoral condyles of New Zealand rabbits, treated with a single or three doses of HA. The animals were sacrificed at 12 weeks and the regenerated tissue was evaluated by direct observation and histology with the ICRS scale.
Results: Macroscopically, in both groups treated with HA the defects were filled with irregular tissue with areas similar to hyaline cartilage and others in which depressed areas with exposed subchondral bone were observed. Histological analysis showed in both groups treated with HA a hyaline-like cartilage compared to control group. However, the score of the International Cartilage Repair Society (ICRS) scale did not show differences between the groups treated with HA.
Conclusion: The use of single dose or 3 doses of AH in acute chondral lesions has a limited and similar benefit in articular cartilage regeneration.

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PALABRAS CLAVE
Ácido hialurónico de alto peso molecular;
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Artrosis

Tratamiento de lesiones condrales agudas de espesor completo con ácido hialurónico de alto peso molecular; un modelo experimental

Resumen
Objetivo: Evaluar el efecto de 2 protocolos diferentes de ácido hialurónico (AH) intraarticular (hylan G-F20) sobre la regeneración del cartílago articular en lesiones condrales agudas de espesor completo.
Material y método: Se realizaron lesiones condrales de espesor completo de 3 × 6 mm en los cóndilos femorales de conejos New Zealand, tratados con una dosis única o tres dosis de AH. Los animales fueron sacrificaron a las 12 semanas y el tejido regenerado fue evaluado mediante observación directa e histología con la escala ICRS.
Resultados: Macroscópicamente, en ambos grupos tratados con AH los defectos se rellenaron con tejido irregular, con zonas similares al cartílago hialino y otras en las que se observaron áreas deprimidas con exposición de hueso subcondral. El análisis histológico demostró en ambos grupos tratados con AH un tejido similar al cartílago hialino comparado con el grupo control. Sin embargo, la puntuación de la escala Internacional Cartilage Repair Society (ICRS) no mostró diferencias entre los grupos tratados con AH.
Conclusión: El uso de dosis única o 3 dosis de AH en lesiones condrales agudas tiene un beneficio limitado y similar en la regeneración del cartílago articular.

Introduction

Chondral knee injuries are common among athletes, especially those who practice contact sports.[1] We know that these lesions have a very limited potential for repair, including small lesions which, if untreated, may predispose toward joint degeneration with functional disability and high treatment costs.[2] Multiple treatment options have been proposed for the management of joint cartilage lesions, including subchondral drilling, microfractures, osteochondral autografts and autologous chondrocyte implantation, with poor results in some cases.[3,4] New therapeutic options to prevent the development of osteoarthritis after suffering focal chondral lesions have also been recommended, including symptomatic slow-acting drugs for osteoarthritis (SYSADOAS), such as glucosamine and chondroitin sulfate, and intraarticular injections, like hyaluronic acid (HA), with a joint protection effect.[5–8] HA is a high molecular weight mucopolysaccharide ($5–7 \times 10^6$ Da) with the viscoelastic properties of synovial fluid, which is essential to normal joint function. Thus, HA has a mechanical and healing effect on the cells of the cartilage and synovial membrane. In patients with osteoarthritis, the concentration of HA in the synovial fluid of the knee is reduced by 2–3 times and its molecular weight also decreases to minimum levels, 2×10^5 Da.[8,9]

Intraarticular injections of HA have been shown to relieve pain and improve joint function in patients with knee osteoarthritis in the short and medium term.[10,11] Experimental studies have shown that HA decreases the expression of metalloproteinases (MMP) and IL-1 in the synovium and prevents changes in the proteoglycans (PG) of the cellular matrix, reducing synovial inflammation and increasing PG content.[12–14] Kaplan et al.[15] conducted a study of acute cartilage lesions in sheep and showed that 3 doses of HA improved histological parameters and PG content of the joint cartilage.

Our hypothesis was that the use of HA increases hyaline cartilage regeneration in focal chondral lesions and that 3 injections of HA increase tissue regeneration. Therefore, the aim of our study was to evaluate joint cartilage regeneration in acute, full-thickness, chondral lesions in an animal model through 2 different treatment protocols with high molecular weight HA.

Materials and methods

We created full thickness chondral lesions in the femoral condyles ($n = 30$) of 15 New Zealand rabbits following the protocol depicted in Fig. 1. All the animals were 3-month-old males weighing between 2.5 and 3.5 kg.

The animals were kept in separate 40 cm × 40 cm × 60 cm cages under constant temperature and humidity conditions, with a light-dark cycle of 12/12 h, *ad libitum* feed and ability to roam freely, without restraints.

The research protocol was approved by the Ethics Committee of the German Clinical Medicine School-Development University. All procedures were performed under aseptic conditions, using intramuscular anesthesia with ketamine (35 mg/kg), xylazine (5 mg/kg) and acepromazine (1 mg/kg). We also used enrofloxacin (10 mg/kg) and tramadol (4 mg/kg) preoperatively and for 2 days after surgery.

Surgical technique

The cartilage defects were full thickness, 3 mm × 6 mm, created in load areas of the lateral femoral condyles of each knee, *via* a longitudinal parapatellar arthrotomy.[16] The chondral defects were created with a 3 mm osteotome up to the calcified layer, which was removed with a curette and taking care not to damage the subchondral bone. The condyles were divided into 4 groups. In group 1, no defect