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RESEARCH ARTICLE

Acupotomy versus sodium hyaluronate for treatment of knee osteoarthritis in rabbits

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Abstract

OBJECTIVE: To investigate the possible advantages of acupotomy over sodium hyaluronate injection for the treatment of knee osteoarthritis (KOA).

METHODS: Twenty rabbits were divided randomly into four groups (n = 5 in each): a control group, model group, acupotomy group, and sodium hyaluronate injection group. The model, acupotomy, and sodium hyaluronate groups underwent anterior cruciate ligament transection plus partial medial meniscectomy. Sodium hyaluronate injection and acupotomy were administered to the respective groups from weeks 5 to 8, and samples of the tibial plateau and medial condyle of the femur were collected in week 9. Vascular endothelial growth factor (VEGF) expression was assessed in cartilage and subchondral bone by immunohistochemical staining.

RESULTS: Articular cartilage degeneration was less pronounced in the acupotomy compared with the model and sodium hyaluronate groups. VEGF expression levels in cartilage and subchondral bone were increased in the model group compared with the control group ($P < 0.01$), and acupotomy had a more pronounced therapeutic effect than sodium hyaluronate injection ($P < 0.01$).

CONCLUSION: Acupotomy and sodium hyaluronate injection may both reduce degeneration in the cartilage and subchondral bone in KOA based on the results from a rabbit model, but acupotomy improved the histopathology and reduced the VEGF content more effectively than sodium hyaluronate injection, probably by reducing venous stasis and intraosseous pressure. Acupotomy may improve KOA by lowering VEGF.

Keywords: Osteoarthritis, knee; Acupuncture apparatus; Hyaluronic acid; Vascular endothelial growth factors; Venous stasis; Cartilage degeneration

INTRODUCTION

Knee osteoarthritis (KOA) is a chronic arthritis with multiple causes, triggering joint degeneration, articular cartilage damage, and degeneration of the articular soft tissue around the knee. Recent etiologic research into knee-joint diseases suggests that, in addition to age, gender, genetics, and biomechanical factors, other factors including oxygen radicals,[1,2] cytokines,[3] cartilage-degrading enzymes,[4] apoptosis,[5] high intraosseous pressure,[6] and venous stasis[7] may also influence KOA generation and development. However, the leading and secondary causes of the disease, primary and subsequent symptoms, and causes of KOA remain controversial.

Various new therapies have been developed to address these etiological factors, including pharmacotherapy with nonsteroidal anti-inflammatory drugs aimed at relieving the inflammatory reaction, sodium hyaluronate to protect or lubricate the cartilage, and glucosamine sulfate, which is a component of proteoglycan in the articular cartilage and can restrain the activity of cartilage-damaging enzymes and the production of free radicals. Although all these substances can play a role in treating KOA, their curative effects in clinical applications remain unsatisfactory. KOA is currently believed to be caused by simultaneous actions of mechanical and biological factors, which disrupt the balance of synthesis and degradation in articular chondrocytes, extracellular matrix, and subchondral bone.[8] However, some researchers believe that KOA is initiated in the cartilage,[9] while others believe that joint stress is the main or primary cause.

Acupotomy dissolution has recently been widely used for the treatment of KOA in China, with curative effects in terms of relieving pain and improving joint functions. It is administered *via* a special medical device modified from an acupuncture needle.[10]

However, the mechanisms whereby acupotomy achieves its effects remains unclear. Zhu *et al* [11] suggested that acupotomy could release adhesions or contracture of the soft tissue around the knee joint, where the knee high-stress points are located, thus reducing abnormal joint stress. Increasing recent studies using acupotomy to treat KOA have indicated the possible involvement of cytokines and inflammatory mediators,[12,13] but the mechanisms whereby acupotomy can achieve these effects remains unknown.

We investigated the effects of acupotomy compared with sodium hyaluronate injection in a rabbit model of KOA.

MATERIALS AND METHODS

Experimental animals

We used 20 healthy mature male adult rabbits (New Zealand white rabbits, clean conventional animals), aged 4 months, weighing (2.5 ± 0.1) kg, all purchased from Vital River Laboratory Animal Technology Co., Ltd., Beijing, China [SCXK (Beijing) 2010-0002]. The animals were raised in the Center for Experimental Animals, Chinese Peoples Liberation Army (PLA) General Hospital, in separate cages at a fixed temperature [(23 ± 2) ℃] and humidity (50% ± 5%). The adaptive breeding lasted for 1 week. The experimental scheme was approved by the Animal Experiment Management Committee of the General Hospital of Chinese PLA.

Main reagents and equipment

Sodium hyaluronate injection (Shipeite; principal component hyaluronic acid with 2 mL, 20 mg) was obtained from Shan Dong Bausch & Lomb (Freda Pharmaceutical Corp. Ltd., Jinan, China). Mouse anti-rabbit-vascular endothelial growth factor (VEGF) monoclonal antibody was from Abcam (London, UK). The BX-51 microscope and DP70 Image Acquisition System were from Olympus (Hataya, Japan).

Groups and animal model

Based on previous experience and the calculated sample size, we divided the 20 rabbits into four groups (n = 5 each) and assigned them to a protocol using a random contrast method, random assignment cards, and random number tables using the CHISS program (Beijing Yuanyida Co., Ltd., Beijing, China). The groups were as follows: normal control, knee joint blank model group, acupotomy group, and sodium hyaluronate injection group. Rabbits in all but the control group underwent the KOA model procedure.

The rabbit KOA model was established using an improved Hulth method.[14] Briefly, rabbits received an intramuscular injection of ketamine (Jilin Huamu Animal Pharmaceutical Co., Ltd., Jilin, China) and Sumianxin Ⅱ (Fujian Gutian Pharmaceutical Industry, Gutian, China) compound (1∶1), at a dose of 0.8 mL/kg in the thick gluteus area for about 15 min. The rabbit was then laid on its back on the operating table and the left hind leg was exposed. The knee joint was shaved and disinfected, and the rabbit was draped with an aseptic holed towel. The knee was incised medially; we cut in from the medial patellar ligament, bent the knee joint and retracted the patellar ligament, exposing the meniscus medialis and the anterior and posterior cruciate ligaments. We then cut off half of the meniscus medialis articulationis genus, washed the articular cavity, sutured each layer, and closed the wound. After revival, the rabbits were kept in the animal room with free access to food and water, with 1 h of forced activity every day. Each model rabbit was administered intramuscular penicillin sodium (40 000 U) once a day for three days from the day of the operation.

No rabbits developed infections or died during the experiment. One rabbit was chosen randomly from the model and normal control groups, respectively, and