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Original Article

Comparative Study of the Use of Intra-articular and Systemic Meloxicam to Control Experimentally Induced Osteoarthritis in Rabbit Knees☆,☆☆

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ARTICLE INFO

Article history:
Received 9 April 2013
Accepted 2 May 2013

Keywords:
Osteoarthritis
Anti-inflammatory agents
Injections, intra-articular
Knee
Rabbits

ABSTRACT

Objective: This study aimed to evaluate morphologic changes, as well as chondroprotective and intra-articular effects of meloxicam on joint repair in rabbits induced by experimental trochleoplasty, minimizing possible adverse side effects.
Methods: Thirty-five rabbits were divided into four groups: the control group, which did not undergo surgery, and operated groups, which used different ways of administering the anti-inflammatory agent: systemic, 0.2 mg/kg; intra-articular, 0.5 mg/kg; positive group control, without meloxicam. Each operated group was divided according to the periods of 7 or 30 days evaluation after surgery.
Results: Regarding macroscopic and histological evaluation of cartilage, after 30 days, most animals showed almost complete joint repair, the presence of few or no inflammatory cells; whereas part of the animals treated with meloxicam presented necrosis in the trochlear ridge and absence of inflammatory cells after 7 days. In positive control group, it was observed moderate inflammation and connective tissue proliferation. None of the animals in the operated groups showed irregularities 30 days after surgery.
Conclusion: Either intra-articular or systemic, meloxicam revealed to be favorable to be used for joint repair and control of inflammatory reaction.

☆ Please cite this article as: Vidotto VT, et al. Estudo comparativo do uso de meloxicam por via intra-articular e sistêmica no controle da osteoartrite experimentalmente induzida em joelho de coelhos. Rev Bras Ortop. 2013;48:524–531.
☆☆ Pioneering work was done in the Union of Social Integration, Brasilia, DF, Brazil.

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2255-4971 http://dx.doi.org/10.1016/j.rboe.2013.12.011

Estudo comparativo do uso de meloxicam por via intra-articular e sistêmica no controle da osteoartrite experimentalmente induzida em joelho de coelhos

Palavras chave:
Osteoartrite
Anti-inflamatórios
Injeções intra-articulares
Joelho
Coelhos

RESUMO

Objetivo: Com o enfoque no processo de reparação da cartilagem, objetivou-se analisar o uso do meloxicam, via intra-articular, para minimizar efeitos adversos causados pela aplicação sistêmica. Avaliaram-se alterações morfológicas e remodelamento do tecido cartilaginoso em modelo experimental, em joelhos.

Métodos: Usaram-se 35 coelhos, divididos em quatro grupos: grupo controle (não operado), cinco animais, e grupos tratados, 10 animais cada. A técnica usada para indução de osteartrite foi trocleoplastia por abrasão. Grupos tratados foram subdivididos de acordo com a via de administração da medicação anti-inflamatória: sistêmica (0,2 mg/kg), intra-articular (0,5 mg/kg) e controle positivo (sem anti-inflamatório). Após sete ou 30 dias de pós-operatório, a cartilagem articular foi avaliada de forma macroscópica e histológica.

Resultados: Após 30 dias ocorreu reparação da cartilagem articular em 100% dos animais que receberam a medicação sistêmica e de 90% dos animais que receberam via intra-articular, com a presença de poucas ou nenhuma célula inflamatória, enquanto que no grupo com sete dias de pós-operatório observou-se ausência de tecido cicatricial no sulco troclear e de células inflamatórias. No grupo controle operado, sem medicação, observaram-se inflamação moderada e proliferação de tecido conjuntivo fibroso, após sete dias. Em todos os grupos submetidos a 30 dias de pós-operatório observou-se discreta irregularidade na cartilagem articular, ou ausência dela, macro e microscopicamente.

Conclusão: O meloxicam via intrarticular mostrou-se favorável para uso em coelhos e obteve os mesmos resultados da administração sistêmica quanto a remodelamento cartilaginoso e controle de reação inflamatória. No entanto, sujeito a menos efeitos colaterais já descritos na via sistêmica e maior praticidade em cirurgias.

Introduction

Osteoarthrosis is the commonest aging process among mammals.[1] It is also known as degenerative joint disease (DJD) and is characterized by its non-infectious and degenerative nature. It causes destruction of joint cartilage and leads to joint deformity due to disorders of normal cell differentiation.[2–4] Although it is classified as non-inflammatory, a continuous low-grade inflammatory process is associated with DJD and this leads to osteoarthritis.[4]

The etiology of the degenerative process begins with aging, but the inflammatory or infectious diseases that destroy the cartilaginous structure, or trauma involving the cartilage, may precipitate osteoarthrosis.[2] The process is characterized by progressive erosion of the joint cartilage and leads to reduction of the joint space, subchondral sclerosis, formation of marginal osteophytes, subchondral cysts and synovial inflammation, which results in pain and reduction of functional capacity.[5]

The objectives of therapy for osteoarthritis are to diminish the pain and maintain or improve joint function. Over the last few years, many studies have investigated the potential function of anti-inflammatory and chondroprotective agents for repairing joint cartilage, controlling inflammatory reactions and decelerating the degenerative process.[3]

Non-steroidal anti-inflammatory drugs (NSAIDs) are the agents most used for alleviating pain over short and long periods of time. However, care needs to be taken in view of the possible adverse effects, such as gastrointestinal problems, hepatotoxicity and nephrotoxicity.[6–10]

With the focus on cartilage repair, the aims here were to use the technique of trochleoplasty by means of abrasion, in order to study the morphological changes and cartilaginous tissue remodeling that were induced in experimental osteoarthritis induced in rabbits, and to analyze the use of the NSAID meloxicam directly on the target, intra-articularly, which would provide an optional route for minimizing the possible adverse effects caused by systemic administration.

Material and Method

Thirty-five healthy New Zealand rabbits (*Oryctolagus cuniculus*) of both sexes, weighing between 1 and 2 kg and of age 90 days, were used. The rabbits were subjected to general clinical and orthopedic examinations and laboratory tests. The project was approved by the Ethics Committee for Animal Use of União Pioneira de Integração Social (UPIS), under protocol number 02/10.

The rabbits were randomly divided into four groups. For the surgical procedure, it was decided to standardize on the right femorotibial-patellar joint.

Control group (CG): non-operated, with five animals.

Treated groups, with 10 animals each, subdivided according to the administration route for the anti-inflammatory medication and the postoperative period (7 or 30 days):