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Original article

In vivo evaluation of porous hydrogel pins to fill osteochondral defects in rabbits☆

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ABSTRACT

Objective: This experimental study aimed to evaluate the biological performance of poly (L-co-D, L-lactic acid)-co-trimetilene carbonate/poly (vinyl alcohol) (PLDLA-co TMC/PVA), hydrogel scaffolds, as an implant in the filling (and not in the repair) of osteochondral defects in New Zealand rabbits, assessing the influence of the material in tissue protection *in vivo*.
Methods: Twelve rabbits were divided into groups of nine and 16 weeks. In each animal, an osteochondral defect was created in both medial femoral condyles. In one knee, a hydrogel scaffold was implanted (pin group) and in the other, the defect was maintained (control group). A histological analysis of the material was performed after euthanasia.
Results: The condyles of the pin group showed no inflammatory reaction and were surrounded by a fibrous capsule. The control group presented higher bone growth in the areas of the defect, but with disorganized articular cartilage, evident fibrosis, bone exposure, atrophy, and proliferation of synovial membrane.
Conclusion: The hydrogel pins are promising in *filling* osteochondral defects, generally do not cause inflammatory reactions, and are not effective in the *repair* of osteochondral defects.

☆ Study conducted at the Biomaterials Laboratory, Faculty of Medical and Health Sciences in Sorocaba, Pontifícia Universidade Católica de São Paulo, Sorocaba, SP, Brazil.

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Avaliação do desempenho *in vivo* de pinos porosos de hidrogel para preenchimento de defeito osteocondral em coelhos

Palavras-chave:
Cartilagem articular
Hidrogéis/química
Coelhos

RESUMO

Objetivo: Trabalho experimental para avaliar o desempenho biológico de arcabouços de hidrogel poli (L-co-D, L ácido lático)-co-trimetileno carbonato/poli (álcool vinílico) (PLDLA-co-TMC/PVA) como implante no preenchimento, e não no reparo, de defeito osteocondral em coelhos Nova Zelândia e verificar a influência do material na proteção tecidual *in vivo*.
Métodos: Foram usados 12 coelhos divididos em grupos de nove e 16 semanas. Em cada animal foi criado um defeito osteocondral em ambos os côndilos femorais mediais, em um foi implantado um arcabouço de hidrogel (grupo pino) e no outro foi mantido o defeito (grupo controle). Após o sacrifício dos animais, foi feita análise histológica do material.
Resultados: Os côndilos do grupo pino não evidenciaram reação inflamatória e estavam rodeados por cápsula fibrosa. Já no grupo controle, uma maior proliferação óssea foi observada nas áreas do defeito, porém com cartilagem articular desorganizada, fibrose evidente, atrofia com exposição óssea e proliferação de membrana sinovial.
Conclusão: Os pinos de hidrogel são promissores na função de *preenchimento* de defeitos osteocondrais, não ocasionam, de modo geral, reação inflamatória e não são eficazes no *reparo* de defeitos osteocondrais.

Introduction

Osteoarthritis is one of the diseases that most commonly affect humans.[1] Its prevalence increases with age, being common after 60 years.[2] The articular cartilage and the subchondral bone form a lubrication, stabilization, and uniform load distribution system, absorbing shocks and allowing movement with low friction for several decades.[2–4] Thus, cartilage protects subchondral bone from high stress and reduces normal contact pressure.[2,5] Degraded cartilage evolves to joint pain, stiffness, and decreased movement. Due to low chondral regeneration capacity, osteoarthritis is one of the most important problems in orthopedics. With increasing human longevity and the practice of sports in recent decades, osteochondral injuries have been increasingly observed.[2]

Normal joint cartilage features a solid phase consisting mostly of collagen and proteoglycans (15–32%) and a fluid phase composed predominantly of water (68–85%).[2] Hyaline cartilage consists of 10% cells (chondrocytes) and a dense extracellular matrix, composed of 60–80% water, 10–20% type II collagen fibers, and 10–15% proteoglycans. The mechanical properties of the articular cartilage allow it to transmit loads of approximately eight times the body weight, due to exudation and movement of the fluid through the pores of cartilage, conferring a friction coefficient of 0.008 μ (mi).[4,6]

The subchondral bone is a thin layer of dense, hard bone in contact with the articular cartilage, while trabecular bone is composed of an abundant matrix (collagen fibers and minerals) that serves to transmit loads.[6]

Being avascular, the cartilage depends on the vascularization of the bone marrow for the migration of mesenchymal cells responsible for the healing process.[7,8] Furthermore, superficial lesions of the articular cartilage without subchondral bone involvement have little intrinsic repair capacity.[9]

Both in primary and secondary osteoarthritis, cartilage is the tissue that undergoes the greatest damage. Morphological changes to the cartilage include loss of its homogeneous nature, fragmentation, fibrillation, fissures, and ulcerations. With disease progression, occasionally no cartilage remains and areas of the subchondral bone become exposed.[10]

Three stages can be considered in the process of tissue regeneration: necrosis, inflammation, and repair.[11,12] Nonetheless, healing of lesions restricted to the hyaline cartilage may not occur this way.[13] Superficial lesions of the articular cartilage that do not reach the subchondral bone tend not to heal.[9] In these lesions, there is a degeneration of the cartilage from the surface area; thin portions of collagen fibers with scaly appearance are observed. With lesion progression, vertical cracks with an uneven and dull appearance can be observed in the articular cartilage.[4,14]

Chondral lesions trigger an inflammatory process and the hematoma quickly organizes itself into fibrin clots, white blood cells, and bone marrow elements.

Undifferentiated bone marrow and vascular endothelium cells are converted into primitive fibroblasts, which, with input of capillaries and fibrin clots, turn into vascular fibroblastic repair tissue.[11] Depending on the mechanical and biological stimuli, this fibrocartilage tissue will form a cartilaginous tissue.[13] Newly formed bone migrates from the base of the defect to the articular surface in the area in contact with subchondral bone. Fibrocartilaginous tissue fills the transition zone and interrupts the formation of bone tissue.[4,11,14]

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