Characterization of Cartilage Degeneration in Different Models of Osteoarthritis in the New Zealand White Rabbit

INTRODUCTION:

Animal models have been used frequently in osteoarthritis (OA) research. They allow for controlled induction of OA, close monitoring of disease onset and progression, and the potential translation of findings to the human disease. Animal models are selected based on the research question, the availability of background information, size and structure of joints, and probably also financial and ethical considerations.

For a given animal model of OA, such as the rabbit knee, different interventions have been performed to explore specific aspects of disease onset and progression. For example, meniscectomy and anterior cruciate ligament transection (ACLT) have been used to mimic different injury scenarios, while exercise and immobilization have been used to assess the effects of life style choices or rehabilitation protocols on joint health. While it is implicitly assumed that a given intervention will produce similar effects on the joint, it may also be thought that different interventions cause OA of different severity and may affect different parts of the joint. However, such information is presently sparse, but might provide valuable information on the mechanisms underlying OA onset and progression.

Therefore, the purpose of this study was to describe and compare OA severity and location in the knee of New Zealand White (NZW) rabbits following different interventions. It was hypothesized that different interventions produce degenerative changes of different severity and location.

METHODS:

Thirty-two skeletally mature, 1-year-old, female NZW rabbits were obtained and studied with the approval of the Animal Care Committee of the University of Calgary. Animals were divided randomly into six groups: (1) Normal control (n = 4): rabbits received no intervention, (2) Exercise (n = 3): rabbits were made to hop 200 times per day, five days a week, (3) BTX-A injected (n = 11): rabbits received unilateral injections of 3.5 units/kg Botulinum type-A toxins (BTX-A) into the quadriceps muscles that produced approximately 80% muscle weakness, (4) BTX-A plus exercise (n = 5): rabbits received a unilateral intramuscular quadriceps BTX-A injection then they were made to hop 200 times per day, 5 days a week, (5) ACLT (n = 4): rabbits underwent unilateral anterior cruciate ligament transection (ACLT), and (6) ACLT plus exercise (n = 5): rabbits underwent unilateral ACLT, then this was followed by a percutaneous electrical stimulation of the quadriceps muscles, three times per week.

Four weeks following onset of intervention, animals were euthanatized. The knee joints were harvested, fixed, decalcified, processed, embedded in wax and then sectioned for histological analysis using standard protocols. Groups of rabbits were compared with regard to the severity and distribution of cartilage degeneration as indicated by the Mankin scores. The Mankin scoring system assesses the cartilage structure, cellularity, matrix staining, and tidemark integrity and ranges from 0 (normal) to 14 (severe OA). Mankin scores were determined and compared across five regions of the knee (retro-patellar surface, lateral and medial femoral condyles and lateral and medial tibial plateaus). Non-parametric statistical analysis was done using PASW 17 (SPSS Inc., Chicago, Illinois, USA) with α-level set at 0.05 throughout.

RESULTS:

Rabbits of the control and experimental groups showed degenerative changes of the knee articular cartilage (Fig 1). The ACLT plus exercise animal group showed greater degeneration across the different regions of the knee cartilage compared to the control, exercise, BTX-A and BTX-A plus exercise rabbit groups (p<0.05). The ACLT rabbit group also showed greater degeneration compared to the control group (p<0.05) but not to the other study groups. Also, the BTX-A plus exercise group had greater degeneration compared to that seen in the rabbits of the control group (p<0.05). Degeneration in the remaining experimental groups was statistically not different (p>0.05).

DISCUSSION:

This study shows that NZW rabbits have spontaneous knee OA by the age of 12-months. To our knowledge, spontaneous degenerative changes in knee cartilage have not been previously reported in NZW rabbits. The fact that spontaneous knee OA has not been described before might partly be explained by the selective analysis done in previous studies which often focused on specific areas of the joint rather than the entire knee (for example, Groeneboer et al, 2008).

Exercise in combination with joint instability or muscle weakness results in an acceleration of degenerative changes in cartilage. Specifically, exercise combined with ACLT seems to be the most deteriorating intervention to knee cartilage health. Exercise in combination with joint instability or muscle weakness has been suggested as a risk factor for OA initiation and progression.

The medial tibiofemoral and retro-patellar cartilages of the knee are more vulnerable than cartilages in the lateral tibiofemoral compartment. This is in agreement with arthroscopic and radiographic findings of degenerative changes in the human knee. These differences in local degeneration likely reflect differences in local loading or local tissue properties within the knee.

The limitations of this study include the small sample sizes and the relatively short follow-up period (4 weeks). Also, degeneration was only assessed histologically.

REFERENCES:


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