New in vivo animal model to create intervertebral disc degeneration and to investigate the effects of therapeutic strategies to stimulate disc regeneration

Markus Kroeber, Frank Unglaub, Haili Wang, Carsten Schmid, Marc Thomsen, Andreas Nerlich & Wiltrud Richter

STUDY DESIGN: A new rabbit model was developed that produces disc degeneration through the application of controlled and quantified axial mechanical load. OBJECTIVES: To characterize the changes associated with disc degeneration, and to evaluate the feasibility of local transfer of agents to the compressed discs to stimulate disc regeneration. SUMMARY OF BACKGROUND DATA: Studies have shown that accelerated degeneration of the intervertebral disc results from altered mechanical loading conditions. The development of methods for the prevention of disc degeneration and the restoration of disc tissue that has already degenerated is needed. METHODS: New Zealand white rabbits (n = 33) were used for this study. The discs in five animals remained unloaded and served as controls, whereas in 28 animals the discs were axially compressed using a custom-made external loading device. After 1 (n = 7), 14 (n = 7), and 28 (n = 7) days of dynamic loading, or 28 (n = 7) days of loading followed by 28 days of unloaded recovery time, the animals were killed and the lumbar spine was harvested for tissue preparation. Disc height, disc morphology, cell viability, disc stiffness, and load to failure were measured. Recombinant adenovirus encoding for two different marker genes (Ad-Luciferase and Ad-LacZ) was injected into the discs in loaded specimens and the gene expression was measured. RESULTS: The unloaded intervertebral discs of the rabbits consisted of a layered anulus fibrosus, a cartilaginous endplate, and a nucleus pulposus comparable with those of humans. After 14 and 28 days of loading, the discs demonstrated a significant decrease in disc space. Histologically, disorganization of the architecture of the anulus occurred. The number of dead cells increased significantly in the anulus and cartilage endplate. These changes were not reversible after 28 days of unloading. The stiffness and the load to failure did not change significantly in the discs after 28 days of loading, as compared with the unloaded control discs. Adenovirus-mediated gene transfer to discs was tolerated by all the animals. LacZ gene expression was found 2 weeks after injection of AdLacZ in loaded disc cells. CONCLUSIONS: The results of this study suggest that disc degeneration can be induced by axial dynamic loading in the rabbit intervertebral disc. The compressed rabbit intervertebral discs were large enough for the application of local transmitters through a percutaneous approach. We anticipate that this
animal model could be used as a basic model to study intervertebral disc degeneration and to investigate new local therapeutic strategies for maintaining disc health or initiating tissue repair.

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