INTRODUCTION: Chemonucleolysis is a minimally invasive treatment for bulging or protruding herniated discs that enzymatically removes the intervertebral matrix (ECM) of the nucleus pulposus (NP), leading to a reduction of intradiscal pressure and irritation and/or compression of the traversing nerve roots. The end result is decreased sciatica pain. The enzyme initially used for chemonucleolysis was chymopapain (CP) [2]; however, the use of CP is associated with occasional but serious side effects, such as anaphylactic shock and neurological damage. An alternative enzyme for the chemonucleolysis is Chondroitinase ABC, which specifically cleaves glycosaminoglycans, but is of bacterial origin [3]. A safer alternative for clinical use would be an enzyme of human origin that cleaves the ECM of discs. Human recombinant hyaluronidase (rhHAase) has been used as an adjuvant to increase the absorption and dispersion of other injected drugs [4]. Because this enzyme cleaves hyaluronan and chondroitin sulfate, it may be effective for chemonucleolysis. The purpose of this study was to assess the short-term effects of a single in vivo injection of rhHAase injection compared to those of CP in rabbits. Specific output measures of this study are disc height measurements, T2 quantification of magnetic resonance imaging (MRI) and static biomechanical tests.

METHODS: Surgery and Enzyme Injection: Under local IACUC approval, nine adolescent New Zealand white rabbits were equally distributed into three groups: Group 1: CP at 100 µg/disc; Group 2: low-dose rhHAase at 100 U/disc; Group 3: high-dose rhHAase at 1000 U/disc. Using a left retroperitoneal approach, the NP in two non-contiguous discs (L2/3 and L4/5) in each animal was injected with 10 µL of one of the reagents of Groups 1, 2, or 3, while the L3/4 disc was used as an internal untreated control. The disc heights were monitored weekly by x-ray for 4 weeks. At 4 weeks, the rabbits were sacrificed and intervertebral disc (IVD) segments were subjected to MRI and biomechanical assessments.

X-ray Assessments: Disc height was radiographically monitored weekly. The percent disc height index (%DHI = (postoperative DHI/preoperative DHI) x 100) was calculated as previously described [3]. The normalized %DHI = (%DHI of L2/3 or L4/5) / (% DHI of L3/4) was calculated to account for changes in disc height associated with anesthesia during x-ray.

MRI Assessment: Using a 3.0-Tesla GE MR scanner with a 3” birdcage extremity coil, T2-weighted images in the sagittal plane were obtained using a standard clinical multi-echo spin echo T2 mapping sequence. T2 quantification provides an index of proteoglycan (PG) and water content using a standard clinical multi-echo spin echo T2 mapping sequence. T2 images showed a decrease of signal in the extremity coil, T2-weighted images in the sagittal plane were obtained using a parallel saw blade into 8 mm bone-disc-bone complexes. T2 quantification data indicated rhHAase can reduce water content in aggregate, and some chondroitin sulfate chains in the aggrecan monomer.

Biomechanics: Both CP and the high-dose rhHAase groups had a significantly lower equilibrium modulus than the control group (p<0.01) (Fig. 3). In addition, each of the treatment groups was less stiff than the control group (p<0.01 for the CP vs. Control groups).


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