INTRODUCTION: Disc herniation is one of the major causes of low back pain and sciatica, particularly in the younger population. Current conventional treatment includes medication, steroid injection, physical therapy and surgery, sometimes major. Progress in minimally invasive operations, such as endoscopic discectomy, percutaneous discectomy and chemonucleolysis, has greatly benefited patients.

Chymopapain was used for many years as the enzyme of choice for chemonucleolysis. However, the use of this enzyme is sometimes associated with complications such as anaphylaxis, paraplegia or injury to the blood system. Chondroitinase-ABC (C-ABC) is commonly used to degrade the chondroitin sulfate and dermatan sulfate chains of proteoglycans (PGs). In some countries, C-ABC, injected intradiscally, has shown promise as an alternative agent for chemonucleolysis and has been suggested to have fewer side effects than chymopapain. A previous study showed that Nucleus pulposus (NP) and Annulus fibrosus (AF) cells are more effective in reestablishing a functional matrix after treatment with C-ABC than after exposure to chymopapain [1]. However, the removal of glycosaminoglycans may lead, over the long-term, to significant degradation of the injected intervertebral disc (IVD). Although matrix regeneration in IVDs treated with C-ABC occurs earlier and to a greater extent than in IVDs treated with chymopapain, disc height and PG content do not fully return to normal. Full biomechanical recovery thus probably does not occur [2].

Osteogenic protein-1 (OP-1), also known as bone morphogenetic protein-7, is a member of the TGF-β superfamily that exerts potent effects on chondrocyte differentiation and metabolism. OP-1 has been shown to stimulate IVD matrix synthesis in vitro [3] and, thus, may be useful in inhibiting and/or slowing down IVD matrix degradation in vivo. The purpose of this study was to monitor the effect of recombinant human OP-1 (rhOP-1) on the in vivo repair of IVDs co-injected with C-ABC.

MATERIALS AND METHODS: Protocol: Twenty-four New Zealand White rabbits (3 kg) were used with IACUC approval (00445). These rabbits were equally divided into 4 groups: (Control-vehicle [5% Lactose]; C-ABC [10 mU] alone; rhOP-1 [100 µg] alone; or C-ABC + rhOP-1 [10 mU + 100 µg, respectively]) co-injected). Under general anesthesia, the assigned agents (10 µl/disc) were injected into 3 levels of IVDs (L2/3 to L4/5) using the left posterolateral retroperitoneal approach for each rabbit in each group. Radiographs of the lumbar spine were taken every 2 weeks after the injections. At 4 and 12 weeks after the injections, 3 rabbits in each group were euthanatized and the IVDs were dissected and the NP and AF separated. All specimens were digested hydroxyproline as a measure of collagen by reverse-phase HPLC [4].

Biochemical Analysis: At the 4 and 12 week time points, the discs were dissected and the NP and AF separated. All specimens were digested with papain at 60°C for 24 hours. DNA content was measured by the Hoechst 33258 dye method, PG content by the DMB assay and hydroxyproline as a measure of collagen by reverse-phase HPLC [4].

Statistical Analysis: The significance of differences in the means between the four groups was assessed using ANOVA and Fisher’s PLSD as a post hoc test.

RESULTS: DHI: Significant disc space narrowing was observed 2 weeks after the injection of either C-ABC or C-ABC + OP-1, but not after injection of the control vehicle. None of the parameters studied varied significantly between the C-ABC group and the C-ABC + OP-1 group at this time point. In the C-ABC group, this narrowing was sustained for up to 12 weeks (4W: 77 ± 11%, 12W: 75 ± 8%). In the C-ABC + OP-1 group, the DHI began to return towards normal after 4 weeks and, at that time, was significantly higher than that of the C-ABC group (C-ABC vs C-ABC + OP-1, p < 0.001). At 12 weeks it was no longer significantly different from the control group (Control: 86 ± 6%; C-ABC + OP-1: 92 ± 12%) (Fig. 1).

PG Content: There were no significant differences in the normalized DNA contents of either the NP or AF among the groups at any time.

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