Effects of BMP-2 Treatment on Human Nucleus Pulposus Cells following Mechanical Stimulation

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INTRODUCTION:

Intervertebral disc disease (IDD) is predominantly caused by age-related mechanical changes on the intervertebral discs, leading to loss of disc integrity and disc pace which can lead to pain and instability in the spine. Additional risk factors for IDD include trauma, smoking, and obesity. In the literature, bone morphogenic proteins (BMPs) such as BMP-2 and BMP-7 have been shown to be upregulated with aging in degenerated discs, representing a compensatory anabolic response at the cellular level. Direct administration of BMP-2 to intervertebral discs cells has resulted in increased production of anabolic components in the extracellular matrix (ECM).

Our objective was to 1) utilize an in-vitro experiment to model IDD conditions acutely with mechanic compression of human Nucleus pulposus (hNP) cells 2) evaluate the effects of direct administration of BMP-2 on hNP cells post-mechanical compression.

METHODS:

The effects were analyzed by evaluating the gene expression of certain markers such as *ACAN* (considered an anabolic ECM marker), and *MMP-9* (considered a catabolic ECM marker). In the first part of the in-vitro experiment, confluent hNP cells were centrifuged to mimic mechanical stress (compression). The cells were divided into two experimental groups based on the magnitude of mechanical stress applied and were labeled “weak” (centrifugal force of 20g/cm^2) and “strong” (centrifugal force of 40g/cm^2). In part two, varying concentrations of BMP-2 were administered to healthy, uncompressed hNP cells to evaluate a dose response and find the optimal concentration for treatment. In the final part of the experiment, healthy cells were again centrifuged at “weak” or “strong” forces and then treated with 50 ng of BMP-2. RNA was collected for all experimental groups at 0 min, 24-hr, and 48-hour post treatments. Gene expression of the above markers was evaluated via real-time RT-PCR.

RESULTS:

After the cells were spun and treated with BMP-2, the results show that the fold change for *ACAN* gene expression was 0.28 at weak and 0.24 at strong centrifugal force after 24 hrs and 0.12 at weak and 0.04 at strong centrifugal force after 48 hrs. The fold change for *MMP9* gene expression was 0.06 at weak and 0.02 at strong centrifugal force after 24 hrs and 0.06 at weak and 0.03 at strong centrifugal force after 48 hrs. Gene expression for both anabolic and catabolic ECM markers showed a decrease from 24 to 48 hours. All values (both anabolic and catabolic ECM markers) were decreased when compared to the control group (1.0).

DISCUSSION AND CONCLUSION:

In our experiment, when looking at the gene expression of ECM markers, anabolic gene expression (*ACAN*) was decreased when compared to control. Based on these results we can conclude that, acute BMP-2 administration was not sufficient to rescue cells post mechanical compression. However, catabolic gene expression (*MMP-9*) was also decreased when compared to control, BMP-2 administration caused further downregulation of the catabolic signaling post mechanical compression. The summation of these results shows that BMP-2 shifted the balance towards anabolic signaling with acute BMP-2 administration to mechanically damaged cells, which is congruent to the findings in the current literature. Therefore, BMP/SMAD signaling pathway represents a promising therapeutic target to restore intervertebral disc composition and function in the setting of IDD, warranting future research.