The Use Of Mesenchymal Stromal Cells Embedded In Hyaluronan Hydrogel Scaffold In Treating Damaged Nucleus Pulposus In The Rabbit Annular Puncture Model: A Preliminary Report

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Disclosures:

Introduction: Damaged intervertebral discs (IVD) are treated mainly to provide symptomatic relief. It has also been demonstrated that current treatment modality results in subsequent damage to the adjacent IVDs and results in worsening morbidity. In recent years the trend of treating IVD has shifted from treating symptomatically such as those using pharmaceutical agents, instrumentations or fusion, to a more curative alternative such as disc replacements. Unfortunately, many studies have demonstrated that the use of such devices had results in many complications in addition to having a limited life span of the implanted devices. It is hypothesized that biological therapies using stem cells to augment nucleus pulposus (NP) may, in addition to providing pain relief, result in disc repair. This however, has not been previously demonstrated. A study was thus conducted to determine if the use of mesenchymal stromal cells (MSCs) in hyaluronan based HyStemTM hydrogel may in fact result in the repair of damaged IVD.

Methods: IVD damage was achieved in twelve New Zealand white rabbits through an annular puncture in the non-contiguous discs at L4-L5 level. After eight weeks, rabbits were randomly divided into three groups. Group I, was treated with MSCs in HyStemTM hydrogel, Group II treated with HyStemTM alone and, Group III received no intervention. Augmentation of NP was assessed through histological, image analyses and MRI T2-mapping of the NP after eight weeks of transplantation.

Results: There is an increase in MRI NP intensity and MRI index in group-I as compared to groups II and III (p<0.05; fig 1). Proteoglycan content was significantly higher (p<0.05) in group I as compared to groups II and III while Boo’s score of the degenerative index was significantly (p<0.05) lower in group I (8.6±1.8), than that for group II (11.6±2.3) and III (18.0±5.7; fig 2). Intensity measurement for collagen type II and aggrecan staining was significantly (p<0.05) higher in group I as compared to groups II and III (fig 3).

Discussion: The use of mesenchymal stromal cells (MSCs) embedded in hyaluronan hydrogel (HyStemTM) reduced the rate of nucleus pulposus degeneration and to a certain extent results in the reversal of the IVD degenerative process. This observation is in line with the aspirations of many current published studies. It is noteworthy that the present study has shown that adding MSCs to hyaluronan hydrogel significantly increased the quality of the repaired tissue, which was not provided by scaffold alone. This implies that the use of cells in biological therapy in IVD, in particularly multi-potent cells such as MSCs, is vital. The use of MSCs in the present study was appropriate since these cells have the ability to undergo multi-lineage differentiation and are also highly viable in vitro. Furthermore, its use in treating several conditions such as articular cartilage damage has also been shown to yield positive results and therefore the results obtained in the present study were not unexpected. Despite these robust findings, the exact mechanisms involved in the repair process observed are still not clear. It has been suggested that transplanted cell may be stimulated to produce matrix materials or even the growth factors required for increasing matrix secretion from surrounding cells. It may also be the case that the presence of MSCs retard the tissue degenerative effects of inflammatory cytokines, since these cells possesses immune-modulatory properties. While these hypotheses have yet to be answered, the present study does indicate the usefulness of using these cells in treating IVD, thus justifying the need for further investigation and exploration to be conducted in this area of research.

Significance: The results demonstrate that the use of MSCs embedded in HyStemTM may potentially result in the repair of NP in damaged IVD. Although the study is still preliminary and that the results warrants further investigation, this study does indicate the usefulness of such strategies and is therefore worth investigating further. The results of this study may have profound impact to future repair strategies involving damaged IVD.

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Figure 1 A: NP intensity measurement from MRI show regeneration at 16 weeks in MSC group. B: Nucleus pulposus MRI index.

Figure 2 A: (A1-A4) MSC and hydrogel, (B1-B4) Hydrogel, (C1-C4) Untreated defect, (D1-D4) Normal. B: Quantitative histologic evaluation of disc degeneration index using Boo’s Scoring. Significance is represented by * (P<0.05).

Figure 3 A: (A1-A3) MSC and hydrogel group with Collagen Type I, Collagen II and Aggrecan staining, (B1-B3) Hydrogel group with Collagen I, Collagen II and Aggrecan staining, (C1-C3) Untreated defect group with Collagen type I, Collagen II and Aggrecan staining. B: Quantitative evaluation of Immunohistochemistry. Significance is represented with * (P<0.05).