Global Spine Journal

Disc Regeneration Using MSC Transplanted via the Endplate Route

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Introduction

Stem cell based intervertebral disc (IVD) regeneration is quickly moving toward clinical applications.[1] However, many aspects need to be investigated to routinely translate this therapy to clinical applications, in particular, the most efficient way to deliver cell to the IVD. Cells are commonly delivered to the IVD through the annulus fibrosus (AF) injection. However, recent studies have shown serious drawbacks of this approach[2–4] suggesting that intradiscal injection through the AF route itself is not completely innocuous and may disable the treatments to therapeutic agents delivered. As an alternative we have described and tested a new surgical approach to the IVD via the endplate-pedicles (transpedicular approach). The Purpose of the study was to test MSCs/hydrogel transplantation for IVD regeneration in a grade IV preclinical model of IDD on large size animals via the transpeducular approach[5] with cell dose escalation.

Material and Methods

Adult sheep ($n = 18$) underwent bone marrow aspiration for autologous MSC isolation and expansion. MSC were suspended in autologous PRP and conjugated with Hyaluronic Acid and Batroxobin at the time of transplant (MSCs/hydrogel). Nucleotomy was performed via the transpedicular approach under fluoroscopy[6] in four lumbar IVDs and that were injected with 1) hydrogel, 2) Low doses of MSC/hydrogel [$5x10^6$ cell/ml] 3) High doses of MSC/hydrogel [$1x10^7$ cell/ml], 4) no injection (CTRL). The endplate tunnel was sealed using a polyurethane scaffold.[7] X-ray and MRI were performed at baseline and 1,3,6,12 months. Disc height and MRI indexes were calculated at each time point. Disc macro- and micro-morphology were analyzed at each time point.

Results

The MRI index showed a significant decrease in the untreated group, the disc injected with hydrogel and those injected with low MSC dose compared with healthy discs in all time points. The discs treated with high dose of MSC showed maintenance of the MRI index compared with the healthy disc. Morphologically, the grade of degeneration evaluated using the Thompson grade system[8] was in agreement with the grades observed at the MRI. The High MSC dose treated discs demonstrated abundant cartilage formation at 3 months, and to a lesser extent at 6 and 12 months. For the carrier and low MSC dose treated groups, however, there was less proteoglycan matrix.

Conclusion

An effective dose of autologous MSC [$1x10^7$ cell/ml] delivered via the alternative transpedicular approach regenerates the NP in a preclinical model of grade IV IDD. These data highlight as the disc regeneration can be achieved maintaining the AF intact via the end-plate route. This preclinical study has high translational value as large animal model with the long fallow up were used, MSCs were expanded in GMP facility simulating the clinical scenario, and the hydrogel were composed of clinically available drags and materials.

This study bring a significant contribution toward the translation of regenerative therapies for the biological restoration of degenerative changes in the IVD, which is crucial to improve present clinical treatment and life quality of several patients.

DOI: 10.1055/s-0036-1582614 ISSN: 2192-5682

Acknowledgment

The support of the Italian Ministry of Instruction, University and Research Grant (PRIN-200938NT8Z), the Young Investigator Research Grant of the Italian Ministry of Health (GR-2010–2318448) and the BIOSPINA Award of the Italian Society of Spine Surgery (SICV&GIS) are gratefully acknowledged.

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