Intervertebral Disc Repair Following Microdiscectomy Mediated by Pentosan Polysulfate Primed Mesenchymal Progenitor Cells in an Ovine Model

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Introduction

Lumbar microdiscectomy treats neural compression but fails to halt disc degeneration. Consequently, 10 – 20% of patients develop debilitating back pain and approximately 15% undergo further surgical intervention(1). In-vitro pre-incubation of mesenchymal precursor cells (MPCs) with pentosan polysulfate (PPS), enhances viability and chondrogenic differentiation, but inhibits osteogenesis(2). This study investigated the potential of PPS primed mesenchymal precursor cells (pMPCs) in a gelatin scaffold to facilitate disc repair in an ovine model.

Methods

Eighteen adult ewes underwent pre-operative 3T MRI followed by lumbar microdiscectomy at two levels. Sheep were randomized into three groups. The injured control (IC) group received no further treatment; the MPC group were implanted with non-primed MPC + scaffold; the pMPC group received the pMPC + scaffold. Necropsies were performed at six months. Analysis consisted of 3T and 9.4T MRI, gross morphological, histological and biochemical analysis for proteoglycans, collagen and DNA content.

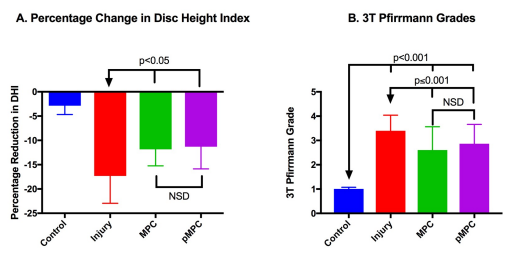

Fig. 1A. Percentage change in disc height index demonstrating significantly less loss of DHI in MPC and pMPC groups compared to injury discs. 1B. 3T Pfirrmann grades reveal significantly lower Pfirrmann grades in MPC and pMPC groups relative to injured discs.

Results

MPC and pMPC discs demonstrated significantly reduced disc height loss ($p<0.05$)(Fig. 1) and reduced Pfirrmann grades ($p<0.001$) (Fig. 2) relative to IC discs. pMPC disc segments were significantly less degenerate ($p<0.05$) than IC discs on gross morphology. Sulfated-glycosaminoglycan (S-GAG) content of pMPC discs was significantly greater than IC discs ($p<0.05$) and not significantly different to controls for the injured annulus fibrosus (AF) region and nucleus pulposus (NP) region contralateral to the injury. DNA content for pMPC discs was significantly less than IC discs for the NP & AF injury and adjacent regions. Histological analysis demonstrated increased organization and decreased degeneration in pMPC discs while MPC discs displayed increased vascular infiltration.

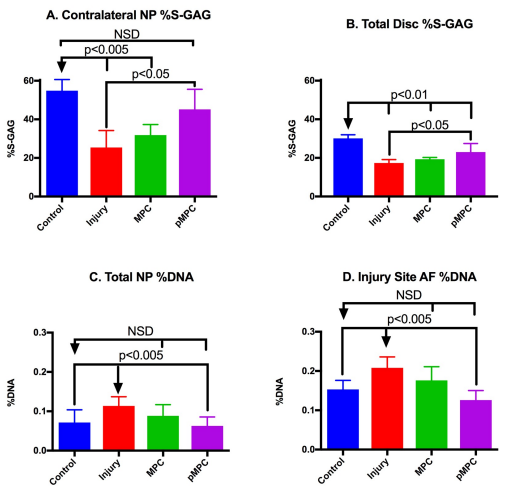

Fig 2A. Contralateral NP demonstrates increased pMPC group S-GAG compared to injury group and NSD to Control. 2B. pMPC S-GAG is significantly higher than the injury group. 2C. pMPC Total NP DNA is significantly lower than injury group and not significantly different to control. 2D. Injury site AF S-GAG demonstrates the same pattern.

Conclusions

pMPCs post microdiscectomy reduced disc degeneration, improved disc height and matrix organization, NP proteoglycan content and histological degeneration relative to microdiscectomy alone. This suggests a potential therapeutic application of pMPCs in promoting disc repair and reducing the incidence of low back pain and further surgery following microdiscectomy.

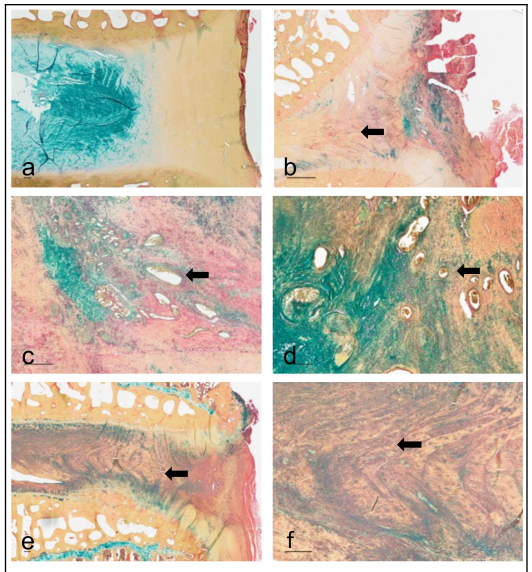

Fig 3. Alcian blue/Picrosirius red stained sections a. Control disc. b. Injured disc (Arrow demonstrating lamella disruption). c. injured discs higher power (Arrow demonstrating vascular infiltration). d. MPC disc demonstrating extensive vascular infiltration(arrow). e. pMPC discs demonstrating lamellar structure (Arrow) with reduced vascular infiltration. f. pMPC disc higher power image demonstrating lamellar structure (arrow). Scale bar=200µm.

References

1. Heindel P, Tuchman A, Hsieh PC, Pham MH, D'Oro A, Patel NN, et al. Reoperation Rates After Single-level Lumbar Discectomy. Spine 2017;42:E496–E501. doi:10.1097/BRS.0000000000001855.
2. Wu J, Shimmon S, Paton S, Daly CD, Goldschlager T, Zannettino ACW, et al. Pentosan Polysulfate binds to Stro-1+ Mesenchymal progenitor stem cells, is internalized and modifies gene expression- a novel approach of pre-programming stem cells for therapeutic application. Manuscript Submitted for Publication.