The Effect of Purified Human Bone-Marrow Derived Mesenchymal Stem Cells on Rotator Cuff Healing in an Athymic Rat

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INTRODUCTION

- Re-tear rates following arthroscopic rotator cuff repair remain high (13-64%) likely due to healing by fibrovascular scar formation, rather than regeneration of the normal insertion
- Some investigators have used “stem cells” derived from bone marrow or adipose tissue to augment repairs and improve healing
- However, variable results have been reported, likely due to the variable and small number of true stem cells in marrow and adipose tissue

OBJECTIVES

- The purpose of this study was to evaluate the ability of purified human bone-marrow derived MSCs to augment healing of a rotator cuff repair in a small-animal model, evaluating the structure and composition of the healing tendon-bone interface with histologic and biomechanical analysis
- We hypothesize that healing will be improved using a population of selected cells based on expression of specific stem cell markers

METHODS

- 52 Athymic, nude rats obtained: 26 Control, 26 Experimental
- hMSC acquired commercially (ATCC, Manassas, VA)
- Flow cytometry verified the phenotype of the cells after 5th passage as CD73+, CD90+, CD105+, and CD45-
- Procedure: Unilateral detachment and repair of supraspinatus tendon
  - Control – fibrin glue at tendon-bone interface
  - Experimental – fibrin glue with 10^6 MSC at tendon-bone interface
- Rats euthanized at 2 weeks and 4 weeks for analysis

RESULTS

Biomechanical Testing

- At 2 weeks, load-to-failure was significantly greater in the MSC group compared with the control group (11.5±2.4 N/mm vs. 8.5±2.4 N/mm, p=0.002)
- Similarily, stiffness was also greater in the MSC group compared with the control group at 2 weeks (7.1±1.2 N/mm vs. 5.7±2.1 N/mm, p<0.001)
- By 4 weeks, there were no statistically significant differences between groups

Histologic Analysis

- At 2 weeks, there was a significantly greater amount of fibrocartilage at the enthesis in the cell-treated group compared to the control group (16.6±2.9 % vs. 9.1±1.6 %, p=0.026), although the difference was not appreciable by 4 weeks

CONCLUSIONS

- Rotator cuff repair augmentation with purified human MSCs improved early histologic appearance and biomechanical strength of the repair at 2 weeks
- By 4 weeks, the effects dissipated with no significant differences between groups
- Consequently, MSCs may improve early rotator cuff healing during a period where the repair construct is vulnerable to re-injury
- Further clinical studies are necessary to determine the efficacy of MSC utilization in rotator cuff repair augmentation

REFERENCES