In Situ Forming Fibrin Gel Encapsulation of Mesenchymal Stem Cell-Exosomes Prevents Tear Progression and Promotes Healing of Partial-Thickness Rotator Cuff Tears

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INTRODUCTION:

Partial-thickness rotator cuff tears (PTRCTs) have been estimated to affect 13 to 32% of the general population, more common than full-thickness tears. Not all PTRCTs result in symptoms, but symptomatic patients often experience pain, limited range of motion, and symptoms of subacromial impingement. Based on location, Ellman classified PTRCTs into A-articular-sided, B-bursal-sided, and C-intratendinous subtypes.

Treatment for PTRCTs include conservative approaches and surgeries. Although there is no prevailing superior treatment, the current treatment of most PTRCTs usually starts conservatively (e.g., physiotherapy, non-steroid anti-inflammatory medication, and steroid injection). However, structural evolution of cuff tendons following nonsurgical care revealed considerable proportions of tear progression to larger size or conversion to full-thickness tear, and cuff tendon healing is rarely seen. Therefore, it is imperative to propose new nonsurgical techniques for PTRCTs capable of reducing tear progression and facilitating cuff tendon healing.

Recently, mesenchymal stem cell-derived exosomes (MSC-Exos), a cell-free therapeutic approach, have drawn great attention in preventing muscle degeneration and enhancing tendon-bone healing within full-thickness rotator cuff tears. Yet, it has not been investigated whether they are effective in treating PTRCTs.

Herein, we describe a rabbit model of 50% thickness PTRCTs (equivalent to clinical patient classification Ellman grade II) on the bursal side of the supraspinatus tendon, and we test the hypothesis that local administration of fibrin gel-containing adipose stem cell derived exosomes (ASC-Exos/fibrin) could promote cuff tendon healing in PTRCTs.

METHODS:

Fifty-six rabbits (112 limbs) were included in this study and assigned to 4 groups: control group (32 limbs, PTRCTs without treatment), fibrin group (32 limbs, PTRCTs treated with fibrin gel), ASC-Exo/fibrin group (32 limbs, PTRCTs treated with ASC-Exos/fibrin), and sham group (16 limbs, sham surgery). Bilateral 50% thickness bursal-side PTRCTs with 1mm (depth) × 3mm (width) × 5mm (length) on the supraspinatus tendon were established by No.11 scalpel blade and digital vernier caliper. At 6 and 12 weeks postoperatively, gross observation, thickness measurement of residual supraspinatus tendons, and histological and biomechanical analyses were performed to analyze tendon repair.

RESULTS:

At 12 weeks postoperatively, the tendon thickness (mean and standard deviation, 1.63 ± 0.19 mm) and histological score (6.25 ± 0.53) in ASC-Exos/fibrin group were significantly better than the control group (tendon thickness, 0.85 ± 0.09, $P < 0.001$; histological score, 11.38 ± 0.72, $P < 0.001$) and fibrin group (tendon thickness, 1.16 ± 0.17, $P < 0.001$; histological score, 9.00 ± 0.54, $P < 0.001$). Immunohistochemical staining of type I and III collagen and biomechanical testing of the ASC-Exo/fibrin group also showed them to be more effective in repairing PTRCTs than fibrin alone and no treatment.

DISCUSSION AND CONCLUSION: Local administration of in situ forming ASC-Exos/fibrin gel effectively facilitated the healing of bursal-side PTRCTs in rabbits. This approach may be a novel candidate for the nonsurgical management of PTRCTs.