

Mesenchymal Stem Cell Secretome: A Potential Tool for the Prevention of Muscle Degenerative Changes Associated with Chronic Rotator Cuff Tears

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Summary:

Mesenchymal stem cell secretome decreases the characteristic muscle degeneration associated with chronic rotator cuff tears.

Abstract:

Background:

Massive rotator cuff tears (MRCT) are usually chronic lesions with pronounced degenerative changes, where advanced fatty degeneration and atrophy can make the tear irreparable.

Human mesenchymal stem cells (hMSCs) secrete a range of growth factors and vesicular systems known as secretome, which mediates regenerative processes in tissues undergoing degeneration.

Hypothesis/Purpose:

We aimed to study the effect of hMSCs secretome on muscular degenerative changes on a rat MRCT model.

Methods:

A bilateral two-tendon (supraspinatus and infraspinatus) section was performed to create a MRCT in a rat model.

Forty-four Wistar-han rats were randomly assigned to six groups: control group (sham surgery), lesion control group (MRCT), and four treated lesion groups according to the site and periodicity of hMSCs secretome injection (single local injection group, multiple local injection group, single systemic injection group, and multiple systemic injection group).

Forelimb function was analysed with the staircase test. Atrophy and fatty degeneration of the muscle were evaluated at 8 and 16 weeks after injury. A proteomic analysis was conducted in order to identify the molecules present in the secretome of hMSCs that can be associated to muscular degeneration prevention.

Results:

When untreated for 8 weeks the MRCT rats exhibited a significant higher content of fat ($0.73 \% \pm 0.19 \%$) compared to rats treated with a single local ($0.21 \% \pm 0.04 \%$; $p < 0.01$) or multiple systemic ($0.25 \% \pm 0.10 \%$; $p < 0.05$) injections of hMSCs secretome. At 16 weeks after injury, a protective effect of the secretome in the multiple systemic ($0.62 \% \pm 0.14 \%$; $p < 0.001$), single local ($0.76 \% \pm 0.17 \%$; $p < 0.001$) and the multiple local ($1.35 \% \pm 0.21 \%$; $p < 0.05$) injections was observed when compared to the untreated MRCT group ($2.51 \% \pm 0.42 \%$). Regarding muscle atrophy, 8 weeks after injury only the single local injection group ($0.0993 \% \pm 0.0036 \%$) presented a significantly higher muscle mass

ISAKOS

**International Society of Arthroscopy, Knee Surgery and
Orthopaedic Sports Medicine**

11th Biennial ISAKOS Congress • June 4-8, 2017 • Shanghai, China

Paper #44

than the untreated MRCT group ($0.0794 \% \pm 0.0047 \%$; $p < 0.05$). Finally, the proteomic analysis revealed the presence of important proteins on muscle regeneration, namely PEDF and Follistatin.

Conclusion:

Our data suggests that hMSCs secretome effectively decreases the fatty degeneration and atrophy of the rotator cuff muscles.

Clinical Relevance:

We describe a new approach to decrease the characteristic muscle degeneration associated with chronic rotator cuff tears. This strategy is particularly important for patients whose tendon healing after later surgical repair could be compromised by the progressing degenerative changes.

In addition, both precise intramuscular local and multiple systemic secretome injection have showed to be promising delivery forms for preventing muscle degeneration.