The Effect of Adipose-derived Mesenchymal Stromal Cell and Running Exercise on The Biomechanical Properties of Partially Injured Achilles Tendon of Rat

[1]Choo PT; [1]Nam HY; [1]Kong P; [1]Krishnan S; [1]Zulkifli MM; [1]Kamarul T
[1]Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia.

INTRODUCTION:

Cell therapy involving mesenchymal stromal cell (MSC) was proven to be effective on tendon regeneration by improving the clinical outcome scoring and higher production of collagen and alignment. Adipose-derived mesenchymal stromal cell (ADMSC) was popularised as choice of MSC cell therapy for its ease in harvesting and high cell proliferation rate. Running exercise can speed up the tendon recovery process by increased in remodelling of extracellular matrix and biomechanical properties of injured tendon. We proposed incorporating running exercise programme on ADMSC cell therapy in tendon injury will significantly improve the biomechanical properties of tendon in animal model.

METHODS:

Adult Sprague-Dawley (SD) rat allograft adipose tissues were harvested for ADMSC isolation and culture. Twenty-four adult male SD rats were randomised into four groups, namely non-treatment-non-exercise, non-treatment-exercise, ADMSC treatment-non-exercise, and ADMSC treatment-exercise groups. Partial defect localisation was made at the right Achilles tendon. Rat in treatment group was injected with 1 X 10^6 ADMSC in 100µL immediate after skin closure. A planned 1-month thread mill running exercise programme was conducted for exercise group SD rats. All rats were euthanised at 1-month after injury and the tendons were retrieved for mechanical testing. Tendon ultimate tensile loading force (UTF) and stiffness were analysed using One-way ANOVA test.

RESULTS:

Both the mean of UTF and stiffness for the ADMSC treatment-exercise group were significantly higher than non-treatment-non-exercise group and non-treatment-exercise group (p<0.05).

Table 1: Comparing mean UTF of injured Achilles tendon among 4 experimental groups of SD rats

Variable	*n*	Tensile force (N) Mean (±SD)	*F* statistic (*df*)	*p*-value[a]
Group			8.79 (3,20)	<0.05
Non-treatment-non-exercise	6	40.14 (7.56)		
Non-treatment-exercise	6	47.59 (8.63)		
ADMSC treatment-non-exercise	6	56.53 (22.86)		
ADMSC treatment-exercise	6	79.25 (11.44)		

Note: [a]One-way ANOVA test
n = Frequency; *df* = Degrees of Freedom.

Table 2: Comparing mean stiffness of injured Achilles tendon among 4 experimental groups of SD rats

Variable	*n*	Stiffness (N/mm) Mean (±SD)	*F* statistic (*df*)	*p*-value[a]
Group			13.99 (3,20)	<0.05
Non-treatment-non-exercise	6	16.10 (5.57)		
Non-treatment-exercise	6	30.04 (11.65)		
ADMSC treatment-non-exercise	6	41.03 (14.90)		
ADMSC treatment-exercise	6	62.87 (16.73)		

Note: [a]One-way ANOVA test
n = Frequency; *df* = Degrees of Freedom.

DISCUSSIONS:

Group 4 has significant higher UTF and stiffness. ADMSC probably had gone through *in vivo* differentiation at the tendon defect site via mechano-transduction contributed by running exercise. Similar tendon circumference among all groups but different mechanical properties infers that the difference is at cellular level, likelihood of higher ratio of tenocytes to fibrous tissues had contributed to the mechanical strength of the injured tendon.

CONCLUSION:

Cell therapy using ADMSC together with running exercise have synergistic effect on Achilles tendon biomechanical properties in SD rat evidence by significant stronger UTF and stiffness.

REFERENCES:

1. Nam, H.Y et. al. Biomech Model Mechanobiol 2015; 14, 649-663.

2. Yang, X. et. al. Bone & joint research 2018; 7(10), 561–569.

3. Yin Z et. al. Stem Cells Transl Med 2016; 5(8),1106-16.