<https://doi.org/10.47660/CBR.2020.16830>

EXERCISE TRAINING ATTENUATES UBIQUITIN-PROTEASOME PATHWAY AND INCREASES GENES RELATED TO AUTOPHAGY ON SKELETAL MUSCLE OF PATIENTS WITH DERMATOMYOSITIS AND IMMUNE-MEDIATED NECROTIZING MYOPATHIES

Isabela Bruna Pires Borges^{1*}, Diego Sales de Oliveira¹, Suely Kazue Nagahashi Marie¹, Antonio Marcondes Lenario², Sueli Mieke Oba-Shinjo¹, Samuel Katsuyuki Shinjo¹

1. Universidade de São Paulo, São Paulo (SP), Brazil. 2. University of Michigan, Ann Arbor (MI), USA.

*Corresponding author: isapires@usp.br

BACKGROUND

The objective of this work was to evaluate the effects of exercise training of genes-related to ubiquitin-proteasome system (UPS) and autophagy on skeletal muscle of patients with dermatomyositis (DM) and immune-mediated necrotizing myopathies (IMNM).

MATERIALS AND METHODS

Seven patients with DM and six with IMNM (with stable disease) undergone to a combined aerobic and resistance exercise training program, twice-a-week for 12 weeks. Aerobic capacity (evaluated by a treadmill cardiopulmonary test), muscle strength (evaluated by one-repetition maximum test) and function [evaluated by timed-up-and-go (TUG) and timed-stands tests (TST)], and skeletal muscle gene expression (evaluated by RNA-seq) related to autophagy, ubiquitin proteasome and antioxidant pathways, and mitochondrial biogenesis and oxidative phosphorylation were evaluated at the baseline and after the intervention. As control group (CTRL), 10 healthy individuals (paired only with DM) were also evaluated only at the baseline.

RESULTS

The mean age of DM and IMNM patients were 49.8 and 58.5 years, respectively. The DM group showed impaired aerobic capacity and muscle strength compared to CTRL group. Genes related to UPS were upregulated, while gene related to autophagy and antioxidative system were downregulated in DM group when compared to CTRL group. After exercise training program, several genes related to UPS were downregulated, while genes related to autophagy, antioxidative system, as well as mitochondria biogenesis and metabolism were upregulated in both DM and IMNM groups.

CONCLUSIONS

Exercise training induced an upregulation of genes related to autophagy and lysosomal biogenesis in skeletal muscle of DM and IMNM patients. These results suggest an increase in recycling of damaged proteins and organelles, which could be responsible for contributing to skeletal muscle performance and endurance in these patients. Furthermore, exercise training induced a downregulation of genes related to UPS and an upregulation of few genes related to antioxidative capacity in both DM and IMNM patient groups. This, therefore, could contribute to attenuate skeletal muscle loss and to reduce the deleterious effects of oxidative stress on skeletal muscle of these patients.

FUNDING

Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP Grant No. 2019/11367-9 to IBPB, 2016/19771-5 to DSO and 2017/13109-1 to SKS) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq Grant No. 303379/2018-9 to SKS).