

Skeletal muscle oxidative metabolism in an animal model of pulmonary emphysema

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Exercise limitation, an important feature of pulmonary emphysema, a chronic obstructive pulmonary disease (COPD), has been traditionally explained by the increased work of breathing and dynamic hyperinflation (Katsura et al., 2007). However, skeletal muscle dysfunction (SMD) is a significant contributor to exercise limitation in pulmonary emphysema (ATS/ERS, 1999). The precise cellular and molecular mechanism(s) leading to SMD in pulmonary emphysema are unclear but there are evidence on mitochondrion as one of the cellular organelles involved in the pathogenesis of SMD in pulmonary emphysema (Ribera F et al., 2003). The aim of this study was to investigate the skeletal muscle oxidative metabolism, before and following a long-acting beta agonist (LABA) aerosol exposure, such as formoterol, in pallid mouse (B6.Cg-Pldnpa/J), which has a deficiency in serum α 1-antitrypsin (α 1-PI) (Cavarra et al., 2001) and develops spontaneous pulmonary emphysema (Yoshida et al., 2009).

C57 BL/6J and its congener pallid mice of 8-12 and 16 months of age, were treated with vehicle or formoterol aerosol challenge for 120 seconds. Morphological and morphometrical studies, evaluations of mitochondrial ADP stimulated-respiration and of cytochrome oxidase activity on skeletal muscle, were performed. Moreover, mtDNA content in skeletal muscle and mediators linked to muscle mitochondrial function and biogenesis as well as TNF- α and PGC-1 α were also evaluated.

The lungs of pallid mice at 12 and 16 months of age showed patchy areas of air space enlargements with destruction of alveolar septa. No significantly differences were observed in basal values of mitochondrial skeletal muscle oxidative process between C57 BL/6J and pallid mice. LABA exposure significantly improved mitochondrial skeletal muscle oxidative processes in emphysematous mice (12 and 16-months old), where the mtDNA content was significantly higher respect to 8-months old pallid mice. This latter effect was compared to a significant increase of PGC-1 α in skeletal muscles of 16-months old pallid mice, with no significant changes in TNF- α levels.

In conclusion, in emphysematous mice, that showed an increased mtDNA content, LABA inhaled exposure can improve mitochondria skeletal muscle oxidative process. The PGC-1 α could be a possible mediator of this effect.

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