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EDITORIAL

Essential amino acids to treat sarcopenia in patients with COPD?

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A shift in body composition from fat-free mass (FFM, a reflection of skeletal muscle mass) to fat mass (FM) is called sarcopenia and seems to be a physiological process of aging [1]. As COPD is predominantly present in elderly people, one would expect a comparable shift in body composition in these patients. However the decrease of FFM can be accelerated in patients with COPD [2]. Indeed, the prevalence of FFM depletion is about 30% in patients with moderate to severe COPD [3].

An abnormal loss of FFM may have a significant impact on the functional status in patients with COPD: a poor exercise performance [4], lower-limb muscle weakness [5] and an impaired disease-specific health status [6]. Moreover, various studies have shown that the FFM index (e.g., FFM in kilograms) divided by squared height (in meters, FFMI) is an independent predictor for survival, irrespective of fat mass, sex, smoking, lung function, and body mass index (e.g., body weight in kilograms) divided by squared height (in meters, BMI) [7, 8]. Also, measurement of the mid-thigh cross-sectional area with computed tomography scan gives a better prediction of survival than BMI, irrespective of the pulmonary function impairment [9]. So, it seems essential to understand the pathogenesis of muscle wasting in patients with COPD, and in turn, possible therapeutic options.

Pathogenesis of skeletal muscle wasting in COPD

Why is the loss of skeletal muscle mass accelerated in patients with COPD? To start, COPD patients have a clear loss in daily physical activities compared to age-matched healthy peers [10]. Moreover, the excessive loss of skeletal muscle mass in patients with COPD differs somewhat from loss of FFM due to physical inactivity alone [11]. The development of skeletal muscle wasting in COPD is a consequence of a form of myopathy that involves a whole cascade of metabolic modifications directly or indirectly related to the underlying disease, like fibre type redistribution, effect of hypoxia, systemic inflammation and/or malnutrition [12, 13].

Skeletal muscle wasting is always the result of an imbalance between muscle protein synthesis and breakdown. An increased whole body protein breakdown and synthesis has been found in normal weight patients with COPD [14]. Moreover, myofibrillar protein breakdown was increased in COPD patients with a decreased BMI and a decreased FFMI compared to normal weight patients and healthy peers [15-17].

Besides protein metabolism, amino acid metabolism is more extensively investigated in COPD patients with an abnormal loss of FFM. Indeed, plasma branched-chain amino acid (BCAA) concentrations (the predominant part of the essential amino acids), particularly leucine, were lower in muscle-wasted compared to non-muscle wasted COPD patients [18-20]. In addition, plasma levels of BCAA positively correlates with FFM in patients with COPD [15]. Also, skeletal muscle glutamate concentration was decreased in normal weight patients with COPD compared to healthy peers [21] and plasma glutamate concentration was positively associated with FFM [15]. These results are in line with the review of a disturbed skeletal muscle glutamate metabolism in patients with COPD [22]. As BCAA and glutamate are the predominant anaplerotic amino acids, a decreased BCAA and glutamate concentration in cachectic COPD patients could imply alterations in the substrate metabolism [23].

Management of muscle wasting in COPD

Exercise-based rehabilitation has been shown to improve FFM in patients with and without baseline loss of FFM [24, 25]. Particularly resistance training of the muscles of ambulation has resulted in improvements in FFM, muscle strength, functional exercise performance and health status [26, 27]. Moreover, neuromuscular electrical stimulation of the lower-limb muscle seems also beneficial in malnourished COPD patients [28, 29].

Muscle protein synthesis is stimulated in the recovery period after resistance exercise [30]. However, the rate of muscle protein breakdown is also increased, thereby blunting the change in the net balance between synthesis and breakdown. Although

net muscle protein balance is generally improved after resistance exercise, it remains negative. Therefore, nutrient intake is necessary to achieve positive net muscle protein balance. Indeed, ingestion of a relatively small amount of essential amino acids can effectively stimulate net muscle protein balance after resistance exercise in healthy subjects [31].

Del Negro *et al.* [32] report in the current issue of the Monaldi Archives for Chest Disease the effects of a 12-week amino acid supplementation in patients with GOLD stage 3 or 4 and an abnormal low FFM at baseline. FFM increased with a mean of 4 kilograms in the patients receiving the essential amino acid supplementation, without any change in the placebo group. These results suggest that supplementation of specific amino acids can also be a therapeutic option to stimulate protein synthesis in patients with COPD. Interestingly, physical activity also improved in the patients of the experimental group. This may also have contributed to the observed increases in FFM. Indeed, a combination of resistance training and nutritional interventions may be a promising candidate in fighting sarcopenia in patients with COPD.

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