Effects of an Exercise Test on Inflammation and Oxidative Stress Biomarkers in Patients with Metabolic Syndrome [†]

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Abstract: Metabolic syndrome is characterized by an increase in oxidative stress and chronic low-grade inflammation. The effects of an exercise test at 60–70% of the maximum capacity was evaluated on inflammatory and antioxidant response in elderly people suffering from metabolic syndrome. Exercise induced significant increases in plasma levels of inflammatory cytokines and malondialdehyde. The expression of these cytokines and antioxidant enzymes were also increased in peripheral blood mononuclear cells. In addition, plasma levels of tumour necrosis factor alpha were unchanged. In conclusion, the exercise test induces a situation of oxidative stress that promotes the activation of a proinflammatory cytokine cascade.

Keywords: aging; antioxidants; exercise; inflammation; metabolic syndrome; oxidative stress

1. Introduction

Metabolic syndrome is a cluster of common factors: hypertension, hyperglycaemia, excess of visceral fat, altered cholesterol and/or triglyceride levels that occur together, increasing cardiovascular risk and diabetes [1]. This pathology is characterized by an increase in the degree of oxidative stress and is associated with an imbalance in adipocytokine production by adipose tissue promoting chronic inflammatory status and vascular endothelial dysfunction [2]. This situation is exacerbated by the high degree of sedentary lifestyle of the population in general.

Reactive oxygen species (ROS) are a double-edged sword because they act as redox signal molecules in physiological processes but they also can induce oxidative damage and play a role in pathological processes [3]. In this sense, low-moderate levels of ROS exert stimulating effect (signalling, receptor and enzymatic stimulation), whereas a massive level of ROS inhibits enzyme activity and induces apoptosis or necrosis. During exercise, contraction processes cause an increase in ROS production and a transient situation of oxidative stress. The aim of this study is to evaluate the effects of 60–70% exercise test on inflammatory and antioxidant response in elderly people suffering from metabolic syndrome.

2. Materials and Methods

9 men over 55 years of age with a body mass index ≥ 27 and < 40 kg/m² fulfilling at least three of the metabolic syndrome parameters were tested. Physical activity consisted of a treadmill session for

30 min at an initial speed of 4 km/h that was increased progressively from min 2 until reaching 60–70% of participant's maximum ability. Blood samples were collected in heparinized tubes before and 1 hour after the exercise test.

Antioxidant and inflammatory parameters were measured in plasma and mononuclear immune cells (PBMCs). The plasma levels of intercellular adhesion molecule 1 (ICAM-1), interleukin 6 (IL-6) and tumour necrosis factor (TNF- α) were determined by ELISA according to manufacturer's instructions. Malondialdehyde (MDA) was analysed in plasma by colorimetric assay, based on the reaction of MDA with a chromogenic reagent that produces a stable chromophore with maximal absorbance at 586 nm. Gene expressions of TNF- α , IL-6, catalase and glutathione peroxidase were measured in PBMCs by real-time polymerase chain reaction (PCR) with 18S ribosomal as the reference gene. The PCR was performed using a LightCycler instrument (Roche Diagnostics) with DNA-master SYBR Green I.

Statistical analysis of data was carried out with the SPSS statistical program (Statistical Package for Social Sciences Inc., v.25 for Windows) applying the Student's t-test for paired data.

3. Results

The results evidenced a significant increase in plasma levels of ICAM-1 (+88%), IL-6 (194%), and MDA (0.3 ± 0.10 vs. 0.8 ± 0.18 pg/mL, $p < 0.001$) after the exercise test, whereas the levels of TNF- α remained unchanged.

The gene expression of the antioxidant enzymes catalase (1 ± 0.37 vs. $1.71 \pm 0.08\%$, $p < 0.001$) and glutathione peroxidase (1 ± 0.19 vs. $2.5 \pm 0.39\%$, $p = 0.001$) and IL-6 (1 ± 0.16 vs. $3.61 \pm 0.67\%$, $p = 0.003$) were significantly induced after the exercise test in PBMCs, while no changes were found in TNF- α .

4. Discussion

Aging is an inevitable process that involves a progressive loss of homeostasis and therefore, the function of the different structures of the organism over time, especially in regulatory systems such as the immune, the endocrine and the nervous systems [4]. In aging, there is an accumulation of ROS in the mitochondria that promotes a chronic oxidative stress situation contributing to the presence of oxidative damage in DNA, lipids and proteins and promoting tissues' degeneration [4].

The patients in the present study were advanced in age and symptomatic of metabolic syndrome, both of which are characterized by an increase in oxidative stress and inflammatory status. Physical activity promotes an increase in respiratory flow that leads to an increase in ROS production [5]. Accordingly, the present study has evidenced how an exercise test at 60–70% of the maximum capacity in elderly individuals with metabolic syndrome induces a situation of oxidative stress and the instauration of a pro-inflammatory environment. Exercise increases the concentration of circulating IL-6 and ICAM-1 and an induction of the expression of IL-6 and antioxidant enzymes PBMCs in response to the stress generated [6,7]. The increase in IL-6 and ICAM-1 would be indicative of the existence of an inflammatory response aimed at repairing muscle tissue damaged by exercise as evidenced by the high levels of MDA. Unlike the activation of the pro-inflammatory cytokine cascade due to an infection, the levels of TNF- α and IL-1 are not modified [8,9]. Moreover, it has been evidenced that subjects with metabolic syndrome present a higher pro-inflammatory response to exercise than that observed in healthy people of the same age [10–13]. Regular exercise practice would allow continued stimulation to maintain high antioxidant defences and contribute to the adaptive response of the body to future situations of acute stress associated with exercise. These results show how physical activity practice for healthy aging is a key point in the management and prevention of chronic diseases and therefore it would be highly recommended to promote it.

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