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Opinion Article

Obesity and exercise immunology: implication in times of COVID-19 pandemic

Obesidade e imunologia do exercício: implicações em tempos de pandemia de COVID-19

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Obesity is a major worldwide epidemic, which places a burden on society and the public health system, affecting people of all ages and all social groups in developed and developing countries, reaching 650 million worldwide [1]. Thereby, we discuss the association between obesity inflammatory state and SARS-COV-2 infection, and the role of exercise immunology as a weapon and fundamental character to the health for million people in this pandemic time.

The current pandemic situation started with pneumonia patients with an unidentified cause emerged in Wuhan, Hubei Province, China, in December 2019 [2]. There about two months later the World Health Organization (WHO) announced a standard format of Coronavirus Disease-2019 (COVID-19) [3] on the same day was named as SARS-CoV-2 [4].

The SARS-CoV-2 was considered as a member of β-CoVs [5,6] like SARS coronavirus (SARS-CoV) and MERS coronavirus (MERS-CoV) [7]. Therefore, COVID-19 demonstrated to be a predominant respiratory disease as an initial study presented 140 patients diagnosed, where the most common symptoms were fever (91.7%), cough (75%), fatigue (75%) and chest tightness or dyspnea (36.7%). However, 39.6% of them complained about gastrointestinal symptoms. 90 (64.3%) patients had comorbidity, the most common of which were chronic diseases, such as hypertension (30%) and diabetes (12.1%) [8].

Hypertension, diabetes, COPD, cardiovascular, cerebrovascular, liver, kidney, gastrointestinal diseases, in addition 60 years old, are factors relation susceptible to the infection by SARS-CoV-2 and experience higher mortality when they develop COVID-19 [9-11].

In SARS-CoV or MERS-CoV infection, there is an increased neutrophil and monocyte-macrophages influx in the severe cases [12,13]. All knowledge accumulated about previous coronavirus infections created a base to unders-

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tand that innate immune response associated to cytokines plays a crucial role in antiviral responses and against coronavirus.

Increased cytokine levels (IL-6, IL-10, and TNF-α), lymphopenia (in CD4+ and CD8+ T cells), and decreased Interferon-gamma (IFN-γ) expression in CD4+ T cells are associated with severe COVID-19 [14]. It seems that COVID-19 may have in "cytokine storm" a major role related to the involvement of IL-1, IL-6, IL-12, and TNF-α [15], creating a lung tissue damage resulting in ARDS, what can to carry to the organ failure. The risk of respiratory failure in patients with circulating IL-6 > 80 pg/ml was 22-fold higher with a median time to mechanical ventilation of 1.5 days [16].

A retrospective cohort investigated the association between body mass index (BMI) and clinical characteristics and the need for invasive mechanical ventilation in patients with SARS-CoV-2 attended in intensive care. The study reported a high frequency of obesity among patients admitted to intensive care for SARS-CoV-2. One hundred and twenty four patients (SARS-CoV-2 positive) were admitted and included during the study. Median (IQR) BMI in SARS-CoV-2 participants was higher than in non SARS-CoV-2 controls; 29.6 (26.4 to 36.5) kg/m² vs. 24.0 (18.9 to 29.3) kg/m², respectively (p < 0.0001, t-test). 47.5% of subjects presented with obesity (BMI ≥ 30 kg/m²), including class II obesity (13.7%) and with class III obesity (14.5%). This distribution of BMI categories was markedly different subjects in intensive care for severe acute pulmonary condition (SARS-CoV-2 negative), which the prevalence of obesity was only 25.8% [17].

Overweight and obese adults have circulating levels of inflammatory cytokines, such as TNF-α and IL-6 [18-20], principally, due to the action of the fat cell that secretes other mediators as monocyte chemotactic protein 1 [21]. IL-6 and TNF-α induce insulin resistance [22,23], metabolic disorders and increased cardiovascular risk seen in obesity

All this inflammatory milieu seems to induce changes in innate immunity and acquired immunity, predisposing obese individuals to infection. NK cells are also quite influenced by leptin, either in its differentiation and proliferation, both in its activation and functionality. Leptin increases IL-2 production (promotes the proliferation and differentiation of cytotoxic T cells and stimulates NK cells) and the Th1 response(T helper 1), increasing the production of INFγ (stimulates the phagocytic response of macrophages)and TGF-β (transforming growth factor β,transforming growth factor-β), while inhibits the Th2 (T helper 2) response, that is, it will decrease the production of IL-4, IL-5, IL-6, IL-10,IL-13. Obese individuals have hyperleptinemia and studies in obese mice demonstrated that NK cells, monocytes and T cells develop resistance to leptin [24]. In addition, abdominal obesity is associated with impaired ventilation of the base of the lungs and consequently reduced oxygen saturation [20].

On the other hand, moderate-intensity exercise seems to increase immune response as also as decrease proinflammatory cytokine patterns. For instance, the EVASYON (Integral Education on Nutrition and Physical Activity for Overweight/Obese Adolescents) study, a program to promote a healthy lifestyle to weight lost, decreasing serum levels of leptin and IL-8, IL-10 and TNF-α [25]. Thus, lifestyle-aimed like exercise and adequate diet interventions can decrease the inflammatory condition.

A single bout dynamic exercise (minutes) increases the total leukocyte count two- to threefold. Exercise-induced leukocytosis mainly, neutrophils, lymphocytes, and monocytes are a transient phenomenon, with normal counts

returning to preexercise levels (6-24h) after exercise cessation. A rapid lympho-cytopenia [26-28] occurs concomitantly with a sustained neutrophilia [26,29] 30–60 min after exercise cessation.

The innate cell's response to acute moderate-intensity exercise, can be demonstrated thought as the neutrophils that present phagocytosis enhanced immediately after a single exercise bout [30], as well chemotaxis [31]. After moderate intensity exercise cessation, the neutrophil oxidative burst continues to be enhanced, what is not true after exhaustive or prolonged exercise [32,33]. Other findings are related to well-trained athletes that are sensitive to the increases of training load, what present loss-making alterations in the neutrophil-monocyte oxidative burst, lymphocyte proliferation, and antibody synthesis, and NK-cell cytotoxic activity [34-38].

Furthermore, lower levels of circulating inflammatory cytokines [39], increased neutrophil phagocytic activity [40], greater NK-cell cytotoxic activity [41], indicate that regular moderate-intensity exercise can improve, or maintaining, immunity across the life [42].

An interesting point is IL-6 subtly increase during acute bouts of moderate-intensity exercise; what appears to provide protection, due to the pleiotropic nature, to immunity via directly suppressing potent inflammatory cytokines [e.g., tumor necrosis factor alpha (TNF-α)] in the lungs, creating an anti-inflammatory milieu for several hours post-exercise [43].

Obesity is a worrisome epidemic that presents itself as one more factor to contribute to the COVID-19 severe cases. Physical Activity in secure ambient, an adequate diet, and all the suggestions of the authorities are attitudes that we need to follow. Regular exercise training of moderate intensity is believed to exert beneficial effects on immune function and in maintaining health. We sought we begin to clarify the importance of regular exercise of moderate intensity and the bad relation between obesity and COVID-19 complications.

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