

Obesity and Elevated Leptin Levels during SARS-COV-2 Infection

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Obesity is a risk factor for the development of respiratory failure in SARS-CoV-2 infected patients. Leptin generated in visceral fat can contribute in ventilation system decline [1,2]. Visceral fat, lung tissue and leptin development have an interlinking role. The path to further study and care will contribute to this knowledge [3]. Leptin is a pleiotropic protein mainly synthesized into the bloodstream from white adipose tissue and could be transferred through the blood-brain barrier. Leptin is a major regulator of energy homeostasis, metabolism, neuroendocrine and immune system activity, due to its effects on the central nervous system and peripheral tissues [4].

Obesity results from a chronic excess of energy and is characterized by recurrent hyperleptinemia and resistance to central leptin. Leptin alerts the brain of the energy status in the periphery under physiological conditions, but in obesity, signals to regulatory centers in the brain that usually suppress food intake and control body weight and energy homeostasis are disturbed. Leptin resistance mechanisms comprise leptin signaling interruption in hypothalamic and other CNS neurons, reduced transport of leptin across the blood-brain barrier, hypothalamic inflammation, endoplasmic reticulum tension, and autophagy [5,6].

Leptin release assists in the multi-level regulation of the innate and adaptive immune system. Leptin signaling usually appears by binding leptin to the leptin receptor's long isoform, accompanied by JAK/STAT pathway activation [7]. Additional development of leptin promotes chemotaxis and neutrophil survival, promotes pro-inflammatory production of cytokines, chemotaxis [8,9] and higher expression by eosinophils and basophils of adhesion molecules [10,11]. Leptin also induces the recruitment and proliferation of monocytes, as well as the development of pro-inflammatory cytokines and chemotaxis [12]. Some immune cells, particularly those containing a long leptin receptor isoform, could become resistant to leptin when exposure to elevated levels of leptin for a prolonged period of time [13]. Chronic hyperleptinemia may also have adverse effects on the immune system, as shown in obesity [14]. In context, short-term increased leptin levels show an increase and higher cytotoxicity of NK cells under physiological conditions [15]. Nevertheless, chronic hyperleptinemia could generate defective NK cells in the case of obesity [14].

The body's immune response reacts to leptin as well. Leptin produces a change towards a Th1 response that is more pro-inflammatory [14], stimulates T and B lymphocytes, and inhibits T-cell regulation [15]. In the suppression of an abnormal immune response, regulatory T cells are activated [15,16]. Leptin concentrations and BMI were shown to be inversely associated with the number of regulatory T cells in patients affected by obesity [15,17].

Leptin concentrations could be further elevated in cases of obesity associated with acute inflammation, infection or sepsis [18]. In conjunction with the pro-inflammatory condition caused by obesity, increased leptin levels further play a role in causing an inappropriate or hyper-inflammatory response induced by SARS-CoV-2 infection. In addition, SARS-CoV-2 infection increased the activity of the 205 gene encoding the cytokine signaling 3 (SOCS3) suppressor in the lung epithelium [19]. This gene is a central inflammation regulator and a leptin signaling inhibitor. As a result of SARS-CoV-2 infection, increased SOCS3 expression would thus further disrupt leptin signaling and adversely affect the immune response in patients with obesity [20].

Disclosure Statement

The author declares that there are no conflicts of interest.

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