

Review Article

Exercise training increases the chance of the body's immune system to fight against the disease of Covid-19: A mini review of exercise, immune system and myokines

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Abstract

The covid-19 disease has spread all over the world since 2019 and many people have been affected by this disease. One of the main characteristics of this disease was lung tissue damage, which subsequently affected the immune system as well. In other words, since there are no registered drugs or vaccines against COVID-19, the immune system is the best defense because it supports the body's natural ability to defend against pathogens and resist infections. As long as the immune system is working normally, infections like COVID-19 cannot cause serious damage to the body. The three types of immunity are: innate immunity (fast response), adaptive immunity (slow response), and passive immunity. Strengthening the immune system can guarantee a better fight against pathogens. Exercising can help strengthen the immune system. In other words, exercise is one of the non-pharmacological factors for controlling diseases related to the immune system. Recently, it has been identified that exercise training with muscle contraction, the secretion of myokines in an endocrine form can affect all body tissues. One of the target tissues of myokines is the immune system. Therefore, this study deals with the strengthening role of the immune system due to exercise and muscle contraction in the conditions of the Covid-19 epidemic.

Key Words: Exercise, Immune system, Myokines, Covid-19

Introduction

On January 2020, the World Health Organization announced the outbreak of the coronavirus in China as a public health emergency. Which is considered a threat not only in China but for all countries. On February 11, 2020, the World Health Organization chose the official name of Covid-19 for it (X. Yang et al., 2020). The main symptoms of Covid-19 are fever, dry cough and shortness of breath. The progression of the disease ranges from upper respiratory tract infection to typical viral pneumonia, which may lead to acute respiratory syndrome, causing a combination of multi organ involvement, or death from pneumonia (Ying, Gayle Albert, Annelies, & Joacim, 2020). While covid-19 is spreading all over the world and infecting more than a million people, the fact that there is no specific medicine or vaccine against any type of virus, including SARS, MERS and the new coronavirus, is causing fear and concern among people (Chan et al., 2020). And the available vaccines have not been able to reduce the chance of contracting Corona to zero. Therefore, currently, the only advice available to deal with this disease is prevention and then strengthening the body's immune system.

Many studies have been conducted on the role of physical stress as a factor stimulating the immune system (Ticinesi et al., 2019; Sheikh & Nikbakht, 2023). Physical activity is a well-known tool to strengthen physical strength (Soleimani, Gallehdari, & Sheikh, 2023) and immune system in the face of diseases that cause inflammatory response in body (Ahmadi & Sheikh, 2023). However, due to the existence of different data in different studied populations (healthy athletes and non-athletes or patients with diabetes) (Nieman, Lila, & Gillitt, 2019), the final results are controversial. Also, in recent studies, as a result of measuring factors related to the immune system, different results have been obtained affected by changes in the intensity, duration, and type of exercise, which shows that any exercise cannot be beneficial for the immune system and for people with physiological conditions. Different exercise has different effect. Some studies show that physiological responses to physical activity are affected by the time of day a-

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-nd night (Kanaley, Weltman, Pieper, Weltman, & Hartman, 2001; Shephard & Shek, 1997). Immune-hormonal responses are not obvious (Raastad, Bjørø, & Hallen, 2000; Trine & Morgan, 1995).

Exercise and immune system

Based on the J curve (the relationship between physical activity and respiratory infectious diseases), it was observed that a person who participates in moderate and regular activities such as general sports, is less at risk of respiratory infections, compared to sedentary people. On the other hand, the possibility of infections increases in athletes who are very active (Nieman & Nehlsen-Cannarella, 1994; Nourshahi, Hovanloo, & Arbabi, 2008; Nourshahi, Hovanloo, Fariborz, & Arbabi, 2008). One of the proposed mechanisms for the increase in infectious diseases, especially respiratory tract infections in athletes, is secretory immunoglobulin (Bettendorf, 1995; Klentrou, Cieslak, MacNeil, Vintinner, & Plyley, 2002).

Immunoglobulin A (IgA) is known as one of the most important antibodies and antipathogenic defense barrier in the immune system. With the increase of this antibody under the influence of physical activity, the function of the immune system improves and the activation of the complement system and the release of products effective on inflammation, plays an important role in improving the inflammation process and dealing with local infections (Bakhtiyar et al. 2015). IgA secreted from the binding of pathogens that enter the mucosa locally, such as viruses, bacteria, etc., to mucosal cells and penetration in the lower layers of the tissue prevent (Bettendorf, 1995; Klentrou et al., 2002). On the contrary, one of the factors that cause changes in the indicators related to the immune system is the increase of cortisol (Klentrou et al., 2002; Mackinnon, 1998). The peak of IgA secretion is just opposite to that of cortisol secretion. Small increases in plasma cortisol may enhance immune responses, while higher concentrations of this hormone have an inhibitory effect. At high concentrations, cortisol causes activation. It becomes dependent on calcium endonuclease and as a result incomplete death of thymocytes. On the contrary, low amount of cortisol increases proliferative responses and production of lymphocytes.

Cortisol and IgA levels normally follow a circadian rhythm. Plasma cortisol concentration increases shortly after midnight and reaches its maximum at around 6-8 in the morning. IgA secretion naturally fluctuates throughout the day. IgA secretion is high at night and reaches its lowest level in the early morning (Arazi, Eghbali, Suzuki, & Mahdavi, 2019; Silva et al., 2019). Reports show that one of the effects of cortisol hormone is to weaken the immune system. This effectiveness has been reported when the increase in cortisol is caused by inactivity and reduced physical activity (Klentrou et al., 2002; Mackinnon, 1998).

In addition, data on the suppression of the body's immune system (through the measurement of factors related to the immune system and the risk of infectious and viral diseases) as a result of intense exercises in the morning have sometimes been reported, and one of the reasons for this effect is the high level of cortisol. Have. During and after physical activity, the level of this hormone increases. An increase in the level of cortisol affects B lymphocytes, reducing the production of immunoglobulins. However, participating in morning exercise for 8 weeks increased serum IgA levels in subjects.

Exercise and immune system factors

In addition, exercise reduces the recruitment of pro-inflammatory M1 macrophages and CD8+ T lymphocytes by limiting adipose tissue (Kugelberg, 2014 ; Sheikh, Shakeryan, Tabatbaei, & Habibi, 2023), the release of myokines such as IL-6 in active muscle, and as a result, the production of IL-1 receptor antagonists by monocytes. And macrophages, can indicate the important anti-inflammatory function of sports activity (Shirvani & Arabzadeh, 2018). Toll-like receptors (TLRs) have a potential role in pathogen recognition and innate immune response by activating various inflammatory signaling pathways (Feng & Chao, 2011).

These leucine-rich ligand-dependent receptors interact with extracellular or intracellular membrane-enclosed PAMPs. Once activated, TLRs, using the lysosomal pathway, initiate many reactions to kill the pathogen and produce a more specific immune response by creating an inflammatory reaction (Imani Fooladi, Mousavi, Seghatoleslami, Yazdani, & Nourani, 2011; Feng & Chao, 2011) more than 11 TLRs are known in humans and mice. Humans and mice have TLR1 to TLR9, but TLR10 and TLR11 are found only in humans and mice, respectively (Imani Fooladi et al., 2011). Various types of TLRs are also remarkably expressed in B cells, T cells, and DCs, which are key cells. They are expressed at the beginning of the acquired immune response (Phillips & Perry, 2013). Since TLRs are able to recognize molecules derived from viruses, fungi, and bacteria, they can detect most infections that we may encounter (Ouchi, Parker, Lugus, & Walsh, 2011; Phillips & Perry, 2013). Physical activity can change the expression of TLRs in some conditions in human and animal models (Gleeson et al., 2011). The expression of TLRs at the cellular level after long-term acute endurance exercise is reduced and causes immunosuppression after exercise and more preparation for infection in athletes (Child, Leggate, & Gleeson, 2013).

Exercise, Covid-19 and immune system

Due to the emerging nature of the Covid-19 disease, reliable results of the effect of exercise on this disease are not available. However, due to the great similarity of this virus to influenza and the way the body's immune system copes with all kinds of viruses, we can use the data of previous studies. In a large study to determine the effect of 10 months of regular endurance exercise on improving the response to influenza vaccination in older adults (a group at risk of infectious diseases due to immunodeficiency), Woods et al found that regular, moderate-intensity aerobic exercise can have a protective effect on vaccination. have annual flu so that the level of protection of antibodies was maintained throughout the flu season. While emphasizing that receiving the annual influenza vaccine is very important for these people, they concluded that regular endurance exercise with moderate intensity may be one of the ways to enhance the protective effect of annual influenza vaccination (Woods et al., 2009). Recently, new studies have been conducted with the aim of determining the role of high intensity interval training (HIIT) on various safety parameters. But their small number makes it difficult to draw firm conclusions about their impact. Yang et al investigated the effect of 5 months of Chinese Tai Chi exercise training on the immune response to influenza vaccination in the elderly. Their results showed that the amount and duration of antibody response in people participating in these traditional exercises in H1N1 and H3N2 strains increased significantly compared to inactive people (Y. Yang et al., 2007). In a systematic review study, Felkenberg et al investigated the effect of mental yoga practice on immune function, their results showed that yoga reduced the levels of IL-1 β , IL-6 and TNF α as well as improved cellular and mucosal immunity in people who they suffered from inflammatory diseases (Y. Yang et al., 2007).

Evidence shows that intense and long-term exercise when exposed to viral infections can suppress immune parameters, while moderate-intensity exercise reduces inflammation and improves the immune response to respiratory viral infections (Nieman & Wentz, 2019). Therefore, all kinds of light sports activities such as aerobic, strength, stretching, balance and even mental exercises can be used during the outbreak of the Covid-19 disease (Shirvani & Rostamkhani, 2020). Several epidemiological studies have shown that regular physical activity is associated with reduced mortality and incidence of influenza and pneumonia (Kohut, Sim, Yu, Yoon, & Loiacono, 2009). Also, in animal studies, a positive relationship between chronic exercise and improving the host's response to influenza and pneumonia was shown (Warren et al., 2015). It has also been seen in elderly people that a lifestyle combined with physical activity and exercise caused stronger and more lasting antibody responses after seasonal influenza vaccination (de Araújo et al., 2015). In general, it has been determined that mild intensity lead

to an increase in the capacity in Th1 and towards Th2, and does not affect the function of effector or key cells and increases the appropriate adaptive immune response. In contrast, intense and prolonged exercise leads to a longer and longer increase in glucocorticoids, catecholamine's and IL-6, which leads to a shift from Th1 to Th2 (which allows the virus to find a better place in the host's body and cause more damage), decrease the function of effector cells and defects in the development of appropriate adaptive immune responses. Based on the J curve, it was observed that a person who participates in moderate and regular activities, compared to sedentary people, is less at risk of respiratory infections (Nourshahi et al., 2008; Shirvani & Rostamkhani, 2020). Regulating lipid profile is one of the beneficial effects of exercise (Sheikh & Gallehdari, 2023). In addition, by limiting adipose tissue, exercise reduces the recruitment of pro-inflammatory M1 macrophages and CD8+ T lymphocytes (Kugelberg, 2014).

Exercise, myokines and immune system

Exercise can also have a positive effect on the immune system by releasing myokines and prevent the reduction of immune cells in conditions of infection such as covid-19. Muscle contraction has beneficial effects on immune diseases, and a therapeutic regimen combining regular exercise and drug therapy is often recommended for the clinical management of certain immune diseases. However, the mechanisms by which exercise produces these beneficial effects are not fully understood. Myokines are a group of peptides derived from skeletal muscles that may play an important role in this process. Myokines are produced, expressed and released by muscle fibers under contraction and have local and pleiotropic effects. Myokines such as IL-6, IL-10, and IL-1ra, which are released during exercise, mediate its health benefits. Just as exercise appears to enhance the myokine response, physical inactivity appears to impair it and could be a mechanism to explain the link between sedentary behavior and many chronic diseases, especially diseases of the immune system. Myokines can also indirectly reduce immune damage by affecting the control of adipose tissue (AT) inflammation. However, muscle tissue can directly help strengthen the immune system by increasing the secretion of some myokines such as IL-10. However, in this field, more detailed studies are needed, especially with resistance training

Conclusions

Therefore, regular exercise with low to moderate intensity can be recommended for healthy people in order to benefit from other best effects of exercise training especially with myokine secretion

(such as increasing vitality and vitality, reducing the risk of cardiovascular and respiratory diseases, reducing depression, improving sleep disorders, metabolic syndrome and...). Regular exercise training and myokine secretion benefited from improving the performance of the immune system and increasing the body's defense chances in the face of infectious diseases such as Covid-19.

What is already known on this subject?

Many studies have been conducted on the role of physical stress as a factor stimulating the immune system.

What this study adds?

Regular exercise with low to moderate intensity can be recommended for healthy people in order to benefit from other best effects of exercise training especially with myokine secretion.

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