

Lifestyle factors with immunomodulatory effect against respiratory viral infections in adults

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Abstract

The role of lifestyles on the immune system is currently being studied. Respiratory viral infections are a cause of morbidity and mortality in adults, and can cause serious conditions. A balanced diet, consumption of micronutrients and exercise have possible benefits in the evolution of these infections. A narrative review was carried out using bibliographic reviews and original articles obtained in PubMed, SciELO, HINARI and Elsevier. Studies describe that the consumption of vitamin supplements modulates the susceptibility to pathogens due to their antioxidant activity and allows the proper functioning of innate and adaptive immunity. Along with this, lipids and carbohydrates in the diet are basic elements of the immune system cells and, accompanied with 45 minutes of moderate exercise, improve the immune response and reduce the risk of respiratory viral infections. The consumption of micronutrients, moderate intensity aerobic exercise and a balanced diet, are factors that decrease the duration of symptoms due to acute respiratory viral infections in adults. However, the exact mechanism of action of exercise on the immune system is still unknown.

Keywords

Virus, life style, vitamins, immune system, exercise.

Resumen

Actualmente se estudia la importancia de los estilos de vida sobre el sistema inmunológico. Las infecciones virales respiratorias son una causa de morbimortalidad en el adulto y pueden ocasionar cuadros graves. Una dieta balanceada, el consumo de micronutrientes y el ejercicio, presentan posibles beneficios en la evolución de estas infecciones. Se realizó una revisión narrativa utilizando revisiones bibliográficas y artículos originales obtenidos por PubMed, SciELO, HINARI y Elsevier. Los estudios describen que el consumo de suplementos vitamínicos modulan la susceptibilidad a agentes patógenos debido a su actividad antioxidante y permiten el funcionamiento adecuado de la inmunidad innata y adaptativa. Acompañado de 45 minutos de ejercicio moderado, mejoran la respuesta inmune y reducen el riesgo de infecciones virales respiratorias. El consumo de micronutrientes, el ejercicio aeróbico de moderada intensidad y la dieta balanceada son factores que disminuyen la duración de los síntomas por infecciones virales respiratorias agudas en el adulto. Sin embargo, aún se desconoce exactamente el mecanismo de acción del ejercicio en el sistema inmune.

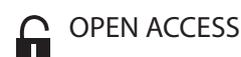
Palabras clave

Virus, estilo de vida, vitaminas, sistema inmune, ejercicio.

Introduction

The immune system is a network of elements that collaborate with one another to recognize infectious agents and coordinate their elimination¹. A sedentary lifestyle combined with a high caloric intake and high fat

content are factors that alter normal function of the system and predispose to acquire viral infectious diseases². Overweight, obesity, malnutrition and micronutrient deficiency can lead to immunosuppression, increased frequency of infections and decreased antibody response³.



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Factores del estilo de vida con efecto inmunomodulador ante infecciones virales respiratorias en el adulto

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Infections associated with respiratory-type viruses are usually self-limiting and benign; however, they can aggravate a picture, especially in immunocompromised depending on the level of vulnerability of the patient⁴. Among the agents with the highest epidemiological virulence are respiratory syncytial virus, adenovirus and coronavirus⁵.

The immune system requires multiple micronutrients to perform its functions; therefore, since the COVID-19 pandemic, several Latin American countries, are using vitamin C, vitamin D, iron and zinc⁶.

Physical activity is another factor related to the degree of immune response. Adipose tissue in obese people contains macrophages that cause low-grade inflammation, inhibiting immunity⁷. However, Simpson *et al.* establish that exercise promotes a pro-inflammatory state. Therefore, in the face of a respiratory tract infection, a healthy adult must wait for ten days to return to moderate aerobic exercise^{8,9}.

A moderate-intensity and short-duration exercise routine is recommended, as it benefits the immune system, reduces oxidative stress, increases energy generation deficiency and decreases the inflammatory response, thus limiting the development of chronic diseases¹⁰. For this reason, this research work objective is to identify the influence of lifestyle factors with potential immunomodulatory effect against viral respiratory infections in adults.

Discussion

Lifestyle factors with possible immunomodulatory effect

The World Health Organization defines healthy lifestyles as "a general way of life based on the interaction between living conditions in a broad sense and individual patterns of behavior determined by socio-cultural factors and personal characteristics"¹¹. It has been acknowledged that several lifestyle factors play an important role in positive health modification and disease prevention.

Nowadays, the role of healthy lifestyle factors as immunomodulatory agents is being studied. Some of these factors are nutrition, physical activity, sleep and the consumption of substances such as vitamin supplements, quitting smoking, avoiding alcohol and illicit substances^{12,13}.

Diet and its effect on the immune system

López *et al.* describe that the functioning of the immune system is improved by an

adequate supply of nutrients and energy¹⁴. Adequate food has been shown to have beneficial effects on the immune system, as it provides the host defenses against infections¹⁵.

The importance of maintaining a balanced diet is related to the supply of nutrients since malnutrition, either obesity or malnutrition, affects the body's immunocompetence¹⁶. These nutritional states lead to induced atrophy of the thymus and wear and tear of peripheral lymphatic tissue, increasing the risk of infections¹⁶. People with obesity have a noticeable decrease in T and B lymphocytes; however, it was not possible to conclude the mechanism responsible for the increased risk of infections or the poor antibody response in these subjects¹⁷.

An adult requires an average consumption of 2000 kcal/day to maintain immunocompetence through good nutritional status. Therefore, as the consumption of daily energy is reduced by 20 %, the risk of microbial infections and pneumonia increases¹⁵.

There must be a balance of the entry of energy into the body to strengthen the immune system; This energy source revolves around carbohydrates. However, this does not mean promoting excessive intake because it could lead to excess body mass with a negative effect on health¹⁴. Therefore, a carbohydrate-fat of 70:30 should be maintained.

As crucial as any component in diets, lipids are substances that have a strong influence on the modulation of the immune system. The composition of fatty acids present in lymphocytes is altered proportionally with those present in the diet¹⁸; therefore, De Pablo *et al.*, suggest a role of lipids provided in the diet, influencing the composition of pro-inflammatory cells of the immune system¹⁷.

Factors such as proper nutrition and sun exposure for the absorption of vitamin D (with protectors from ultraviolet rays), provide the necessary amount of nutrients and vitamins to the body in an easy and effective way. However, when neither this is not possible or proper levels, and vitamin supplements can be used¹⁸.

Consumption of vitamins and micronutrients, and risk of respiratory viral infections

Vitamins are essential nutrients that cannot be synthesized by the human body, so they are found as food supplements. Since they are antioxidants, they help in the balance of free radicals which damage the integral

structure of the cells of the immune system. Neutrophils and macrophages produce superoxide and H₂O₂ free radicals, essential for defense against invaders. In this state, vitamins are necessary to regulate the reactions released by free radicals and as a result, are related to the modulation of host susceptibility or resistance to infectious pathogens¹⁸.

Vitamin C or ascorbic acid is classified as a key antioxidant in the synthesis of collagen, carnitine and catecholamines. Also, it reduces the damage caused by free radicals, which influence ageing and tumor processes, as well as contributes to cholesterol metabolism and different chemical reactions¹⁹.

Besides reducing oxidative stress, vitamin C is accumulated in leukocytes, monocytes and neutrophils. It is believed that concentrations in these cells help prevent damage by oxidants in the environment and thus prevent these cells from being phagocytosed^{18,19}.

Vitamin D is also characterized by being an excellent modulator in the inflammatory response and in the prevention of infections. As an antioxidant, it is responsible for the protection of fatty acids present in membranes against the peroxidation of lipids, free radicals and oxygen atoms, becoming the most important antioxidant found in the lipid membrane. Serum vitamin D levels are directly involved with the formation of immune system cells, such as macrophages, monocytes, dendritic cells, and T and B lymphocytes²⁰.

Due to the immunomodulatory effect of vitamin C, a prophylactic intake is recommended to maintain adequate plasma levels of 100-200 mg/day to prevent respiratory tract infections and systemic infections¹⁹. Ran *et al.* report in a meta-analysis that vitamin C intake significantly improves symptoms such as fever (p 0,009), chest pain (p 0,03) and chills (0,01)²¹.

Vitamin C and D supplementation is recommended as these vitamins cause a significant reduction in the risk and impact of upper and lower respiratory tract infections such as the common cold and pneumonia, including the severity of the disease and the risk of death in the elderly²².

These results coincide with those of Johnston *et al.* who report that vitamin C consumption reduces the duration of the cold by 59% compared to the placebo group (-3,2 days, 95% CI -7,0-0,6, p 0,06). But the severity of the symptoms and their impact on everyday life did not differ between the two groups²⁵. Vitamin C supplementation in acute respiratory infections is not justified as

it does not reduce its incidence; however, due to its low cost and its effect on the reduction of symptoms, it can be assessed depending on the case²⁴.

Vitamin D induces antimicrobial peptides such as cathelicidin which alters the membranes of viruses, fungi and even some bacteria such as *Mycobacterium tuberculosis*²⁵. Also, this decreases the cytokine storm that occurs in severe viral infections such as Coronavirus disease; Vitamin D levels of 30 ng/mL are required for adequate vitamin D production and to reduce the incidence of respiratory infections²⁶.

The role of vitamin D in different viral infections has been described, such as the production of peptides LL 37 and β -defensin in respiratory syncytial virus infection, which prevent the entry of the virus into the body by decreasing its spread in the host²⁷. Vitamin D supplementation has also related to the improvement of results and prevention of Hepatitis C virus infection recurrence²⁶. Besides, vitamin D supplementation is recommended in patients with human immunodeficiency virus since vitamin D levels are an indicator of the prognosis of the disease and adequate levels can improve the course of the disease^{25,26}.

Daily or weekly vitamin D supplementation results in significant reduction in experiencing at least one acute respiratory infection (OR 0,88, 95% CI 0,81 – 0,96, p 0,003; NNT 33, 95% CI 20 - 101, p 0,001)²⁸. There is an important relationship between vitamin D deficiency and mortality from COVID-19, especially in older adults who have the low levels of vitamin D²⁹.

Micronutrients play an important role in the innate immune response through the development of physical barriers, regulate the activity of neutrophils and macrophages as well as inflammatory processes through the production of cytokines and their antioxidant effect; while in the adaptive response they allow an adequate lymphocyte differentiation, proliferation of cytokines, antibodies and memory cells¹⁹.

Proper nutrition is necessary for proper function of the immune system at all stages of life because inadequate consumption of micronutrients increases susceptibility to infections especially in adults in whom a wide variety of lifestyle factors produce oxidative stress³⁰.

It has been established that an adequate intake of vitamins and minerals presents benefits for the innate and adaptive immune response, mainly vitamins A, B12, C, D and trace elements such as zinc^{31,32}.

Maintaining adequate amounts of each micronutrient is crucial for the proper func-

tioning of the immune system because deficiencies of vitamins and essential elements alter the response to pathogens, since when an infection occurs, malnutrition of micronutrients is exacerbated and the demand for these increases, affecting important aspects such as alterations in the integrity of the skin and mucous membranes, chemotaxis, humoral response and cell-mediated immunity³³.

Zinc promotes the production of antibodies, influences macrophage activity and regulates lymphocyte apoptosis. It has been shown that the inclusion of this mineral in the diet, in addition to its contribution to strengthening the components of the immune system, also helps to improve intestinal absorption and promote growth³⁴; besides, zinc is a component of multiple transcription factors and enzymes and has an important role in gene expression and cell division³⁵. Zinc supplementation considerably reduces the duration of acute respiratory infections and prevents mortality in severe pneumonia³⁶. In a cohort study, zinc supplementation with 45 mg per day showed a reduction in the incidence of the common cold (p 0,067) of other infections and fever during the study³⁷.

Zinc's role as an antiviral can be separated into two categories: supplementation to improve antiviral response and zinc treatment, specifically to inhibit viral replication. They report that zinc in vitro significantly reduces influenza virus replication and inhibits elongation of the SARS-CoV-2 coronavirus³⁸⁻³⁹. Consequently, an increase in the consumption of supplements was observed as a result of the COVID-19 pandemic, which forced doctors to emphasize the adequate consumption of micronutrients and avoid an excess that can lead to symptoms such as nausea, vomiting, headache, dry skin, among others⁴⁰.

Exercise and its effect on the immune system

A sedentary lifestyle is associated with abdominal adiposity, a pro-inflammatory state, and an increased risk of infection¹⁰.

The profound impact that exercise has on the immune system has been demonstrated. Practicing physical exercise regularly promotes improvements in quality of life and can act on the immune response, reducing the risk of developing systemic inflammatory processes and stimulating cellular immunity¹⁰.

Physical exercise and training with moderate-intensity aerobic exercise, that is, up to 45 minutes, improve immune

responses to vaccination, reduce the risk of viral infections, and improve several immune markers in various disease states, including cancer and cardiovascular disease^{41,42}.

On the contrary, Walsh *et al.* demonstrate that high-intensity exercise, generally practiced by high-performance athletes, has been associated with suppressed cellular and mucosal immunity, increased symptoms of upper respiratory tract infections, latent viral reactivation, and impaired immune responses to new vaccines and antigens⁹.

Exercise practice and risk of respiratory viral infections

The proper functioning of the immune system must be boosted from before the infection occurs. Moderate-intensity aerobic exercise stimulates the exchange and redistribution of immune cells present in the circulation and peripheral tissues. Each aerobic session improves the activity of tissue macrophages and helps the movement of immunoglobulins, anti-inflammatory cytokines, neutrophils, immature B cells and lymphocytes. Intense exercise greater than one hour a day decreases the circulation of these cells. However, all this remains under debate due to the lack of studies that support this response⁴³.

Chubak *et al.* conducted a study in obese and sedentary postmenopausal women, divided into two groups, one group of moderate intensity exercise and the other group of stretching sessions, both lasting 45 minutes, for a period of 12 months, it was found that the group that performed moderate exercise had a lower incidence of respiratory symptoms than the stretching group⁴⁴.

Klentrou *et al.* found that an average of 12 weeks of moderate exercise managed to reduce the symptoms of respiratory infections and was correlated with an increase in IgA, however, there are still no studies that explain this relationship to prove this theory⁴⁵.

Another theory of immunosuppression caused by strenuous exercise is provided by Simpson *et al.*, who establish that the function of biomarkers of the immune system (NK cells, lymphocytes, neutrophils, IgA, among others) are altered for hours and even days during the recovery of the body after intense exercise, making pathogen entry more accessible the facilitating the entry of pathogens. However, although it is well known that this increases the pro-inflammatory state and can alter the immune response, the exact mechanism of action

of this phenomenon is unknown since for ethical reasons there are not many studies on the matter⁸.

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