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Immune System Response in COVID-19 Infection and the Impact of Carbohydtares on Immune System Response

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Abstract

The immune system, which has various general functions in the body, is also in close interaction with some physiological processes and body systems. The new coronavirus disease (COVID-19), which is known to have a more severe course in individuals whose immune system does not work rapidly and who has a weak immune response, has created a pandemic effect all over the world. Diet affects the composition of gut microbiota which has important effects on immunity and inflamatory responses. Fermentation of carbohydrates that reach the colon without being digested, short-chain fatty acids are play an important role in metabolism with their anti-inflammatory, anticarcinogenic, immunomodulatory and cell proliferation effects. Considering the role of the immune system in COVID-19, selection of carbohydrates from complex and high dietary fiber intake may benefit the treatment strategy in these patients by providing immunomodulatory function.

Keywords: COVID-19; pandemic; immune system; carbohydrates.

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Highlights

- Immunity is a system which is close interactions with systems, physiological processes and general functions in our body.
- Healthy nutrition is one of the cornerstones for the immune system.
- Dietary fiber intake positively affects the gut microbiota, which is important in immunity and inflammatory responses.
- The immune system plays a key role in the prognosis of COVID-19 disease.
- Providing a high fiber intake with diet benefits patients with COVID-19 by improving immune system.

What we already know

- Immunity is a system which is close interactions with systems, physiological processes and general functions in our body and healthy nutrition is one of the cornerstones for the immune system.
- Dietary fiber intake positively affects the gut microbiota, which is important in immunity and inflammatory responses.
- The immune system plays a key role in the prognosis of COVID-19 disease.

What this article adds

- High fiber intake with diet benefits by improving immune system.
- Selection of carbohydrates from complex carbohydrates intake act as an immunomodulator.
- Providing a high fiber intake may improve the prognosis and may be effective treatment strategy for patients with COVID-19.

1. Introduction

The immune system initiates a series of events in order to eliminate components that are different from the body itself. Immune system with general functions such as host defense, tissue homeostasis and system integrity; it is close interaction with physiological processes such as development, reproduction, wound healing, and body systems such as the central nervous system and cardiovascular system as well [1]. The immune response is divided into two parts, spesific and non-spesific. Spesific response includes that the initiation of recognition, activation, differentiation and proliferation, which develops between 3-7 days to 2-4 weeks after the antigen penetrates the organism, thereby activating various immune phenomena. Subsequently, a stronger line of defense, called the inducible response caused by cytokines, develops alongside non-spesific cell-mediated and humoral mechanisms in the 4 to 96 hours period. For this reason, the immune response manifests much more rapidly and effectively in people who encounter the spesific antigen again. Such that some previous infections are not undergo again or protection with vaccination can be given as an example [2]. Coronaviruses are a large family of viruses that can cause illness in humans or animals. In humans several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as MERS (Middle East Respiratory Syndrome) and SARS (Severe Acute Respiratory Syndrome) [3]. The SARS-CoV-2 virus, which causes the new Coronavirus disease (COVID-19), was first detected in Wuhan, China in December 2019, and then caused a pandemic effect all over the world [4,5]. Although COVID-19 can be asymptomatic, the most common smytoms are fever, dry cough, shortness of breath, while in severe cases pneumonia, severe respiratory failure and even death can be seen [6]. In individuals whose immune system does not work rapidly and who has a weak immune response, COVID-19 results in a more severe course of the disease because the body is a virus that is newly recognized and foreign [4,5].

SARS-CoV-2 infections develop in 3 steps;

Step 1: Patients do not show any symptoms. Reports suggested that 10-30% of patients infected with SARS-CoV-2 are asymptomic [7].

Step 2: Mild symptoms occur in patients, and therefore virus detection can be made [8].

Step 3: At this stage, where serious symptoms such as severe respiratory tract infections, pneumonia and high fever are observed and there is a life-threatening stage, hospitalization of individuals becomes indicated. In addition, the age of the patients and their underlying diseases are among the factors that affect hospitalization [9].

The SARS-CoV-2 viral load reaches its peak within the first 10 days after the onset of symptoms [10]. Symptoms can vary according to individuals [9]. A study, in China, patients were grouped as mild and severe cases by examining various parameters in terms of disease severity, including respiratory distress, resting state oxygen saturation, the ratio of partial arterial oxygen pressure to inhaled oxygen fractional concentration and the presence of serious disease complications such as mechanical ventilation, septic shock, and non-respiratory organ failure. According to this grouping, 61% of the patients are mild cases and 39% are severe cases. It has been reported that the mean viral load of severe cases is approximately 60 times higher than mild cases, and that high viral loads will result in serious clinical consequences [11]. In another study in which viral transmission was evaluated, [12] viral transmission was observed up to 30-40 days after the onset of the disease in most of the severely ill patients, while the viral load was not detected 15 days after the onset in most mild patients. On the contrary, there is a a study in the New York, USA, which included 165 cases who were presented to emergency department then discharge and 45 cases who were hospitalized. The viral load of hospitalized patients was found to be significantly lower than those discharged without hospitalization. In addition, high viral load has been associated with shorter symptom duration and shorter hospitaliastion period in all patients [13]. In order to trigger the endogenous protective immune response during the incubation period of the disease, it is important to have a good general health status and a suitable genetic structure of the host that elicits specific antiviral immunity. In other words, genetic structure causes individual differences in immune response against pathogens. In addition, successful fight and elimination of infection depends on the patient's health status and HLA (human leukocyte antigen) haplotypes [14].

2. Immune System And Carbohydtares

Healthy nutrition is one of the cornerstones for the well-established immune system and continuity of a healthy immune system. In addition, the effects and importance of various vitamin and mineral intake on immunity is an undeniable fact [15]. Although it has a major effect, one of the issues that are not emphasized is the immune system and carbohydrates. Carbohydrates are one of the macronutrients containing carbon, hydrogen and oxygen atoms and formulated as Cn(H2O)m [16]. In the 2002 report of The Institute of Medicine (IOM), [17].carbohydrate intake is 130 g / day according to the RDA for adults and children over 1 year old. This value depends on the amount of sugar and starch needed to supply the brain with adequate amounts of glucose. IOM has determined the acceptable macronutrient distribution range for carbohydrates as 45-65% of energy. For this reason, the current dietary guide recommends consuming foods containing carbohydrates, including grains, vegetables, fruits, legumes, nuts, seeds, and dairy products. From infancy, carbohydrates have a great role in the development of the immune system. Such that, breastfeeding is a very effective strategy to prevent morbidity and mortality from infancy. In addition, breast milk glycans which are containing oligosaccharides in free and conjugated forms, constitute an important innate immunological mechanism that protects babies against infections. These glycans function as soluble receptors that prevent pathogens from adhering to target receptors on the mucosal surface of the host gastrointestinal tract [18]. In the later period, fibers entering the diet with complementary nutrition contribute to the development of the immune system and the continuity of a healthy immune system [19]. Besides these beneficial effects of carbohydrates, a different approach to carbohydrates is required in COVID-19 patients. One mole of carbohydrate oxidation leads to an equal production of CO2. In respiratory distress, CO2 production should be reduced to prevent the the respiratory rate from falling. Individuals infected with SARS-COV-2 suffer from breathing difficulties. Therefore, carbohydrate intake should be reduced in critically COVID-19 patients with breathing difficulties. In these patients carbohydrate requirement is 2 g / kg / day and daily carbohydrate intake should not exceed 150 grams [20]. In the light of in patients given that partial replacement of carbohydrates with lipids in the isocaloric form reduces CO2 production by 30% per unit of calories, [21] the calorie, fat and carbohydrate intake of patients according to ESPEN [22] guidelines have planned as fat: carbohydrate ratio of 30:70 % in patients with no respiratory deficiency, 50:50 % in ventilated patients. Carbohydrates are basically substrates of energy metabolism. They affect blood glucose, insulin and lipid metabolism. In addition, intestinal transit through fermentation can provide control over colonic function, including metabolism, balance of commensal flora and intestinal epithelial cell health. They can also be immunomodulators and affect calcium absorption. All these beneficial properties have an impact on general health In particular, such as it contributes to the control of body weight, diabetes and aging, cardiovascular disease, bone mineral density, colon cancer, constipation and resistance to infection, and the strength of the immune response [19].

3. Gut Microbiota, Dietary Fiber and Immune System

Healthy nutrition modulates and supports human growth, reproduction and symbiotic microbial communities that colonizing the digestive system. The type, quality and source of our food effect and shape the structure of microorganisms in the gut. It affects host-microorganism interactions by affecting their composition and functions [23]. There is a mutual and strong interaction between gut microbiota and nutrition [24]. Dietary style affects the composition of gut microbiota, and changing dietary patterns cause changes in the gut microbiota. Gut microbiota also has important effects on immunity and inflammatory responses [25]. Dietary fiber are edible carbohydrate polymers with three or more monomeric units that are resistant to endogenous digestive enzymes and therefore are neither hydrolyzed nor absorbed in the small intestine. There are also 3 main categories. The first is edible carbohydrate polymers found naturally in foods such as fruits, vegetables, legumes and cereals. The second is edible carbohydrate polymers that obtained from food raw materials by physical, enzymatic and chemical route and with proven physiological benefits. And the third is synthetic carbohydrate polymers with proven physiological benefit [23]. Additionally in its 2002 report, IOM determined 14 g of fiber intake per 1000 kcal consumed as Adequate Intake (AI) value [17]. Dietary fiber content affects the relationship between carbohydrate quality and systemic inflammation. An inverse relationship was found between the total fiber intake in the diet and tumor necrosis factor alpha (TNF-α) and IL-6, which are important inflammatory indicators. It is known that excessive fluctuations in post-prandial blood glucose lead to the formation of nitric oxide, and as a result, it combines with superoxide to produce peroxynitrite, a powerful long-life prooxidant molecule. Consequently, consumption of high glycemic index foods has been reported to cause oxidative stress and both acute and chronic low-grade inflammation. In addition, it is known that excessive consumption of simple carbohydrates and high glycemic index foods leads to hyperglycemia, chronic inflammation, obesity, increased abdominal adipose tissue, type 2 diabetes and poor immunity [26]. Dietary fibers are classified according to several parameters, including primary food sources, chemical structure, water solubility, viscosity, and fermentability. Dietary fibers are subdivided into either polysaccharides (non-starch polysaccharides, resistant starch, and resistant oligosaccharides) or insoluble and soluble forms [23]. Bacteria in the colon use food components that reach the colon without being digested from the upper parts of the digestive tract as an energy source. The carbohydrate components that reach the colon without being digested are mainly non-starch polysaccharides, resistant starch and oligosaccharides. As a result of the fermentation of carbohydrates that reach the colon without being digested, short-chain fatty acids and various gases emerge. Acetic acid, propionic acid, and butyric acid are the most abundant short-chain fatty acids in feces [23,25]. These short-chain fatty acids are used both as an energy source in the host and play an important role in metabolism with their anti-inflammatory, anticarcinogenic, immunomodulatory and cell proliferation effects [23]. World Health Organization (WHO) defines prebiotics as nutritional components that can be selectively fermented, affecting the composition and / or activity of gastrointestinal microorganisms, and have positive effects on the well-being and health of the individual [27]. Fructooligosaccharides, inulin and galactooligosaccharides are the most common prebiotics. It is seen that most of the dietary components with prebiotic properties are carbohydrate. When the effects of carbohydrates in the regulation of intestinal microbiota are evaluated, the diet should be rich in carbohydrates that can show prebiotic properties [28]. Prebiotics have beneficial effects on immune and metabolic functions in the intestine. These effects are known to be shown by prebiotics to increase short-chain fatty acid production and to strengthen the gastrointestinal associated lymphoid tissue (GALT) obtained from fiber fermentation. GALT is the largest lymphoid tissue of the human body and contains most of the immune system cells. Peyer patches form the structure of GALT. Composed of lymph follicles, GALT has the ability to produce antigen-specific IgA. Thus, by secreting IgA on the mucosal surface, it provides an immune response with an inductive and effector function [29,30]. A healthy gut microbiota contributes to the maturation and development of the immune system. Such a mechanism is supported by short-chain fatty acids known to induce histone H3 acetylation as well as the production of colonic regulatory T cells (Tregs) in a GPR43-dependent manner [23]. In fact, a greatly altered inflammatory response was observed in mice deficient in a single G protein-coupled receptor, GPR43. In addition, the only known ligands of GPR43 are short-chain fatty acids, which are mainly a product of fiber metabolism, especially acetate and propionate [25]. Additively, maternal high-fiber feeding during pregnancy and lactation modulates the thymic microenvironment and induced autoimmune regulator (Aire) expression. Primary lymphoid tissue, a factor expressed in the thymus, is required for the maturation of T cells. With the maternal fiber intake, butyrate levels in the blood of the offspring increased and contributed to the increase of the animals' peripheral and thymic Treg amounts in a GPR41-dependent manner. This may help explain why obese people accelerate thymic aging and change primary lymphoid tissue structure. When all these findings are evaluated, the role of a dietary rich fiber and short-chain fatty acids in maintaining the normal function of the innate and adaptive immune system cannot be denied [23].

4. Conclusion

WHO recommends consuming at least 5 portions of vegetables and fruits per day before and during illnesses. Vegetables and fruits provide vitamin and mineral intake through diet. In addition, this can contribute to the daily fiber consumption, which should be taken. Selection of carbohydrates from complex carbohydrates and high dietary fiber intake act as an immunomodulator. The immune system plays a key role in COVID-19. Adequate fiber intake is important to get over the disease lightly and keep the immunity strong both before and during COVID-19 disease.

5. Recommendations

The SARS-CoV-2 virus broke out in China and created a pandemic effect all over the world. It is known that the immune system, which has many metabolic functions in the human body, significantly affects the prognosis of COVID-19. Carbohydrates are of great importance in establishing and maintaining a healthy immune system mechanism from birth to life. So much so that the selection of carbohydrates from complex carbohydrates and high fiber intake with diet act as an immunomodulator. Considering the effects of the right food preference and healthy lifestyle on the gut microbiota and immune system, it is obvious that studies on carbohydrates, dietary fiber intake, immune system and COVID-19 are insufficient. More studies are needed on this subject.

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