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ABSTRACT

Vitamin C and viral infection

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Nutrition Battling on Pandemic COVID-19: How to Survive

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Aris Wibudi[1]
[1]Omni Hospital, Pulomas, Jakarta, Indonesia

Physiology of immune response. An infection is the invasion of an organism's body tissues by disease-causing agents, their multiplication, and the reaction of host tissues to the infectious agents and the toxins produced. Hosts recognize the invading pathogens by their immune system, so without an optimal immune status, the host will not be able to eliminate the invading pathogens. The immune reaction of the host against pathogen invasion starting with innate response, the first and critical line of defense against infectious agents and often involving inflammation, then followed by adaptive response. The current medical science focused on various anti pathogens such as anti-virus, anti-bacterial and anti-fungal as disease-causing agent and pay a little attention to immune status, either innate or adaptive, whereas immune status plays a crucial role in eliminating the invading pathogens. It must be remembered that an infection is not a pathogen load only, but also the optimal responses between cellular immunity, both innate and adaptive, and humoral are essential. Innate cellular immunity is implemented by macrophage, neutrophil, natural killer cells (NK), and natural killer like T cells (NKT), whereas adaptive immunity is carried out by T and B lymphocytes. As humoral immunity, B lymphocyte produce antibodies that will collaborate with T lymphocyte, especially T cytotoxicity (Tc).

Vitamin C and Viral Infection. Micronutrients such as vitamins, minerals and trace elements influence various metabolic processes that are directly associated with immune functions, especially vitamin C and D. The adequacy of vitamin C in leukocytes plays a major role in the success of immune response, both innate and adaptive. The highest vitamin C concentrations were found in lymphocytes, monocytes, platelets and neutrophils respectively. The role of macrophage and NK cells as an innate cellular immune absolutely requires Interferon (IFN) α and β. IFN α is known to have several important roles such as: activates macrophages and NK, inhibits viral replication, and improves cellular defense against viral invasion. Several studies revealed a positive correlation between reduced IFN and higher mortality. Other study showed that vitamin C is essential in the production of IFN α and β. It can be concluded that vitamin C has very important immunomodulatory properties such as: improving chemotaxis, enhancing neutrophil phagocytosis activity, accelerating lymphocyte proliferation, and T-cell function, thereby increasing infection resistance. Theoretically, vitamin C is very useful in overcoming the infection, however numerous studies showed inconsistent results. In general, studies looked at the final results and the dose of vitamin C supplementation only, regardless of the presence of vitamin C in the circulation (desirable concentration 50 -70 μmol/L) as a reflection of tissue

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vitamin C levels. One study revealed that all critically ill patients in the ICU were found hypovitaminosis (<23 μmol/L) and vitamin C deficiency (<11 μmol/L). Patients with septic shock had significantly lower vitamin C and higher CRP compared with non-septic critically ill patients. Vitamin C concentration depends on several factors such as: intake, metabolic demand and GSTT1 gene, as well as a very important and most often overlooked is the mechanism of absorption and distribution. Thus, ideally, vitamin C supplementation is highly dependent on the initial concentration in the cells, and not on the administration dose.

Unique dual capacity of vitamin C. Vitamin C in physiologic concentration (0.2 – 2.0 mg/dL) as a very potent antioxidant, on the other hand, high concentration (>400 mg/dL) in a certain condition it becomes a pro-oxidant.

Vitamin C as antioxidant. Under physiological condition, more than 99% of vitamin C or L-ascorbic acid (AA) is in the anion form (ascorbate anion). AA is an antioxidant by donating one electron, but at the same time AA itself will be oxidized and automatically converted into ascorbate radical, but relatively unreactive compare to other free radicals, with half-life 10^{-3} seconds to several minutes. Ascorbate radical can be reduced back to ascorbate anion or become dehydro-ascorbate (DHA) by losing the second electron alternately. Hereafter DHA will be converted into oxalic acid that excreted in urine or returned as ascorbate radical.
Multiple studies alongside recent pandemic situation had provided a very valuable lesson, in particular, cytokine storm that occur as host over responses. Cytokine storm as the main cause of death can be interpreted as excessive oxidative stress. This be reflected by CRP levels, the higher CRP, the greater the oxidative stress. Increased CRP levels indicates hypo or even vitamin C deficiency. Several studies showed a significant mortality reduction in critically ill patients, those receiving vitamin C supplementation.

Vitamin C as pro-oxidant. Genuinely, vitamin C is not a pro-oxidant, but at high concentration and in the presence of oxygen and Fe^{3+}, will produce pro-oxidant by triggering peroxides (H_2O_2) formation. In the blood circulation, H_2O_2 will immediately broken down by catalase into H_2O and O_2, but in the extra cellular fluid, H_2O_2 will not change due to the absent of catalase. Researchers assumed vitamin C anti-virus properties based on the statement above.

Vitamin C absorption and distribution. Vitamin C absorption is an active transport that requires specific transporters. In the form of AA, vitamin C requires Sodium Vitamin C Transporters (SVCT1 and 2) and in the form of DHA, it requires Glucose Transporters (GLUTs). Considering that DHA transport requires GLUTs, it is important to consider the adequacy of intracellular vitamin C concentrations in those with insulin resistance, DM, hyperglycemia and insulin deficiency.

Keywords: Vitamin C, viral infection, immune system

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Corresponding author:
Dr. dr. Aris Wibudi, SpPD-KEMD
Omni Hospital, Pulomas, Jakarta, Indonesia
E-mail address: wibudiaris@gmail.com