Спортивное питание

DOI: 10.14529/hsm200416

HOW TO PREVENT COVID-19 BY MEANS OF A DAILY MICRONUTRITION PROTOCOL? AN OVERVIEW

G. Laffaye[1,2,3], *guillaume.laffaye@u-psud.fr, ORCID: 0000-0002-7414-1063,*
V.V. Epishev[3], *epishev74@mail.ru, ORCID: 0000-0002-7284-7388,*
K.A. Naumova[3], *naumova.ksenia94@mail.ru, ORCID: 0000-0002-1729-395X,*
A. Delafontaine[1,2,4], *arnaud_94150@hotmail.fr, ORCID: 0000-0002-3093-0183*

[1]*Université Paris-Saclay, Orsay Cedex, France,*
[2]*Université d'Orléans, Orléans, France,*
[3]*South Ural State University, Chelyabinsk, Russian Federation,*
[4]*Ecole d'Assas, Paris, France*

Aim. Coronavirus, also known as COVID-19, has officially been declared as a pandemic, and the world now has to manage this pandemic disease as a major public health issue at different levels, not only from a political aspect, but also from an individual aspect at the lower end of the scale. The goal of this paper is to focus on how individuals could optimize their health, and particularly their immune systems, to reduce the risk of respiratory tract infections by means of a daily micronutrition strategy. **Material and Methods.** A narrative review was conducted on 85 articles evaluating the mechanisms which allow vitamin D, vitamin C and Zinc to lower viral replication rates and reduce pro-inflammatory cytokine storm. Furthermore, we focus on high-risk populations with the prism of deficiency of these vitamins and this mineral. **Results.** According to literature, it seems that Zinc and vitamins C and D, particularly when taken as supplementation at an early stage, could be clinically useful micronutrients as adjuvant therapies in the prevention of deficiency amplification in COVID-19 unaffected and at-risk populations, and/or in the treatment of severe forms in affected patients. **Conclusion.** Further randomized control trials through the use of genomics and metabolomic techniques are needed in order to understand the role of these micronutrients in the treatment of severe forms of the COVID-19 disease in different types of at-risk populations.

Keywords: *pandemic, vitamin-C, vitamin-D, Zinc, Sars-CoV-2.*

1. Background

Coronavirus 2019 (i.e. named COVID-19 for the disease and SARS-CoV-2 for the virus itself), which was recently discovered in China, is an emerging viral zoonotic-like disease with human-to-human transmission and part of the coronavirus family which consists of seven varieties. SARS-CoV-2 is highly contagious [65]. It differs from other respiratory viruses in that it appears that transmission between humans occurs approximately 2 to 10 days before the individual becomes symptomatic [33].

It is mainly transmitted by the projection of droplets over a distance of less than 2 meters, by or from direct contact with the oropharyngeal mucosa or via a contaminated surface. This contamination can be spread to approximately 2.3 to 2.8 people by the same individual. The incubation period can extend up to 21 days. The immunization duration is unknown, and the possibility of reinfection is currently under debate. However, in order to predict the course of the epidemic and the likelihood of sustained transmission, comprehension of the transmissibility process remains crucial [53].

COVID-19 may clinically manifest itself as an influenza-like illness with fever (89%), cough (68%), fatigue (38%), sputum production (34%) and dyspnea (19%); data from the Chinese cohort observed by Guan and colleagues [33]. Other atypical clinical symptoms have also been reported, such as anosmia without nasal obstruction and ageusia [more frequent in Europe], digestive disorders [diarrhea in 30% of the cases], and dermatological problems of the vascular acrosyndrome type: Raynaud's phenomenon, frostbite

and facial erythema. A meta-analysis [85] involving 3,062 patients reported other symptoms such as muscle pain (33%), anorexia (38.8%), chest pain (35%), dyspnea (35%), shortness of breath (35%) and kidney damage (4%) [16, 19]. The phenotype of this disease can manifest itself in varying forms: mild asymptomatic or moderate (81%), severe (14%), or critical (5%). In potentially severe forms, a clinical shift is observed between the fifth and the eighth day of the disease, with a secondary onset of dyspnea, leading in most cases to transferal to intensive care.

Although the fatality ratio among patients receiving medical attention is estimated to be approximately 2% to date, the true ratio may remain unknown for a while [53]. In children, the signs are usually less severe, and are mainly manifested by a cough and fever. The number of cases of affected children is relatively low and a mild form of the disease is observed [33]. Patients at risk of developing a severe form of the disease are the elderly (> 65 years), pregnant women, and those suffering from the following health disorders: the metabolic syndrome (diabetes, hypertension, obesity with a body mass index> 30 kg / m^2); immunosuppression; associated cardiovascular and respiratory pathologies (e.g. chronic obstructive pulmonary disease, emphysema, asthma, pulmonary fibrosis and interstitial lung disease); serious chronic neurological pathologies; and patients taking certain medications (non-steroidal anti-inflammatories, converting enzyme inhibitors, angiotensin II receptor blockers, immunomodulators) [16, 24].

The median age of hospitalized patients is between 46 and 56 years old and the overall mortality is currently estimated to be between 0.5% and 0.94% but differs depending on the phenotype and the environment (Fig. 1).

To protect themselves from COVID-19, humans use their immune systems, which are "an interactive network of lymphoid organs, cells, humoral factors and cytokines" [60]: in short, immunity is acted through innate and adaptive response, determined by the speed and specificity of the organism reaction. The innate response provides quick and immediate reaction from the chemical, physical and microbiological barriers by means of elements such as neutrophils, monocytes, macrophages, complement components,

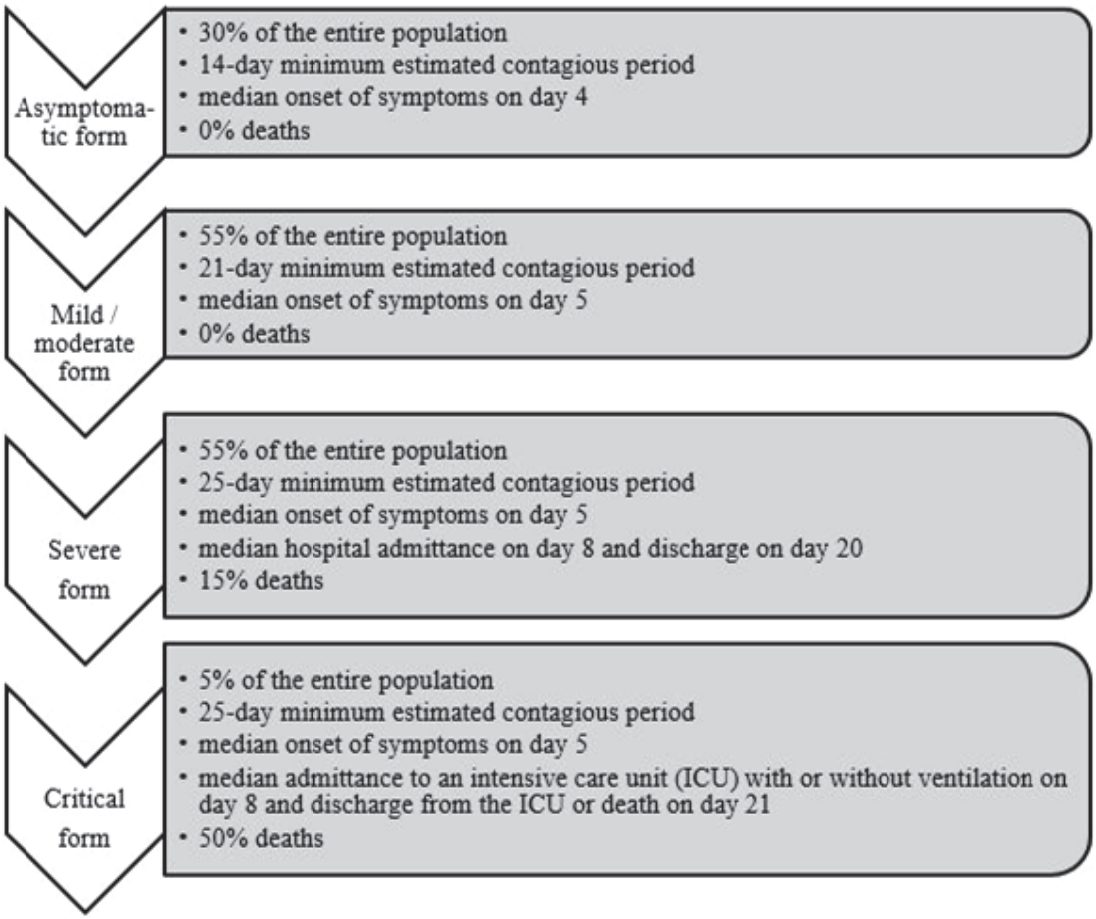

Fig. 1. Synthesis of cut-off clinical and epidemiological COVID-19 data [8–10]

cytokines and acute phase proteins. The adaptive response is more precise, but necessitates a longer period of time, from several days to weeks, to adapt its memory-based defense.

In the innate response, the central feature is the rapid recruitment and activation of neutrophils on the site of infection to eradicate pathogens, with cytokine release from activated macrophages (IL-2, IL-7, IL-10, G-CSF, IP-10, MCP-1, MIP-1A, and TNFα) [37]. COVID-19, which induces cytokine storm release [41, 71] is presumably responsible for hemophagocytic lymphohistiocytosis, a hyperinflammatory syndrome characterized by fulminant and fatal hypercytokinaemia with multiorgan failure in the severe form of the disease [56].

In the adaptive response, antigen-specific receptors on T and B cells allow a two-phase targeted response. In step 1, the antigen is recognized by the antigen specific T or B cell which leads to cell priming, activation and differentiation in the lymphoid tissue environment. In step 2, the activated T cells leave the lymphoid tissue and migrate to the site of infection or help provoke the secretion of antibodies into the blood and tissue fluids.

The adaptive immune response is considered as an indication for future vaccine development although the kinetics/titers of specific antibody correlates in severe forms of COVID-19 would need further investigation [62].

In the fight against COVID-19, approximately 150 trials [57] are in progress around the world in order to evaluate the real effect of medical treatments (e.g. antivirals, immunomodulators, antibiotics, hydroxychloroquine, …) and micronutrient therapies (e.g. vitamin C, D, zinc, thiamine…).

The use of micronutrients underlines this new interest in an old concept: adjuvant vitamin therapy in critical illness or "metabolic resuscitation". For example, Amrein et al. [2] recommend early supplementation of vitamin C and D to prevent / treat deficiency, particularly in severe acute diseases.

The aim of this article is to cross the knowledge of the roles of vitamins C and D and Zinc in the immune response and the characteristics of COVID-19, in order to focus on populations at risk and to recommend supplements to both these at-risk populations and the general public.

2. Vitamin C metabolism

Vitamin C is an essential micronutrient which protects cell membranes from damage caused by free radicals by its ability to donate electrons [11]. This contribution to immune defense is made possible through the ability of this vitamin to support both the innate and the adaptive immune systems.

Vitamin C contributes to the immune system by supporting the epithelial barrier function. Indeed, it promotes collagen synthesis in epithelial tissues [29], which protects the organism against aggressions via the skin, by building a skin and mucous barrier in contact with viruses, parasites and bacteria. Vitamin C enhances collagen synthesis and stabilization [47], protects against reactive oxygen species induced damage [51], and increases fibroblast proliferation and migration [21]. Furthermore, Vitamin C diffuses in the phagocytic cells.

Vitamin C contributes to immunity via the phagocytes [neutrophils, macrophages] by acting as an antioxidant electron donor [73]. This enhances phagocytosis and reactive oxygen species [ROS] generation [70] and also microbial killing [28], by facilitating neutrophil apoptosis and clearance at the site of infection and by decreasing necrosis [80]. Leukocytes, especially neutrophils and monocytes, accumulate vitamin C, resulting in a value 50 to a 100-fold higher than plasma concentration. This process is possible if the dietary intake of vitamin C concentration is at least 100 mg/ day.

Vitamin C enhances the differentiation and proliferation of B- and T-lymphocytes and antibody levels [74]. Moreover, it plays a major role as an inflammatory mediator by modulating cytokine production [38] and by decreasing the histamine level [40]. The modulation of cytokine activity seems to be a key factor in COVID-19, as preview research reveals the cytokine storm release to be a major contributor of the final step of the disease in symptomatic patients [71].

3. Vitamin C, COVID-19, at-risk populations and recommendations

Based on this knowledge, recent studies have tried to assess the impact of vitamin C doses on the evolution of the patient state during COVID-19 infection. In accordance with the meta-analysis of Hemilä et al. [35] which clearly shows that vitamin C in oral doses of 1–3 g/day can shorten the length of stay in an intensive care unit by 18.2%, the same team found strong evidence that vitamin C also shortens the duration of mechanical ventilation [35]. Vitamin C was most beneficial for patients with the lengthiest periods of ventilation, corresponding to the most severely

ill patients. Vitamin C has proved effective in preventing and relieving symptoms of virus-induced respiratory infections [31] with mega-doses of vitamin C [hourly doses of 1000 mg for the first 6 hours and 3 times daily thereafter]. Reported flu and cold symptoms decreased by 85% compared to the control group. A dosage of 1–6 g/day shortened ventilation time by an average of 25%. Adnan Erol [23] has proposed a mechanistic approach by using high-dose intravenous vitamin C on patients with COVID-19 pneumonia, founded on the hypothesis that vitamin C is able to reduce the hyperactivation of immune effector cells.

Erol's hypothesis [23] is that high-dose intravenous vitamin C favors the loss of immunocompetence effector cells by inhibiting glyceraldehyde 3-phosphate dehydrogenase (GAPDH) in order to prevent inflammatory hyperactivation in myeloid and lymphoid cells. In literature, a similar mechanistic approach targeting GAPDH inhibition has also been used to explore the therapeutic interest of vitamin C in human colorectal cancer with KRAS or BRAF mutations [82].

Results of meta-analyses have demonstrated that treatment with a high dose of intravenous vitamin C (50 mg/kg of body weight every 6 hours for 4 days) with glucose restriction has significant benefits over sepsis and septic shock [43]. Moreover, during infection, vitamin C levels can become depleted and a person's requirement for vitamin C increases with the infection severity [12]. A recent study [77] in the USA of 167 patients suffering from sepsis-related acute respiratory distress syndrome (ARDS) and receiving 50 mg/kg intravenous doses of vitamin C every 6 hours for 4 days, demonstrates a difference in mortality (46.3% in the placebo group vs 29.8% in the vitamin C group) with no impact on organ failure or in C-reactive protein levels. The number of ventilator-free days was also higher in the vitamin C group (13.1 vs 10.6 days in the control group). In another study, a combined vitamin C (6g per day), hydrocortisone and thiamine therapy [46] in patients with severe pneumonia reveals significant mortality benefit (17% vs 39% in the control group).

Finally, the role of vitamin C in optimizing a person's anti-oxidative capacity and natural immunity to prevent symptoms and presumably lower the mortality rate in patients with ARDS has been well documented. Megadoses of vitamin C must be controlled by medical staff. A daily intake of at least 3000 mg in divided doses [67] is recommended in order to increase the anti-oxidative system and the level of leucocytes in the prevention of COVID-19 viral infection. Vitamin C deficiency populations are smokers, people with a low intake of raw fruit, the elderly, and people suffering from antioxidant deficiencies (e.g. athletes, diabetics), or hyperglycemia-induced oxidative stress which increases the body's use of vitamin C in antioxidant fighting. Those suffering from kidney failure accompanied by a metabolic disorder of vitamin C or oxalic acid, patients with hemochromatosis and patients on a low sodium diet should avoid high doses of vitamin C in the form of sodium ascorbate (1 g providing ≈ 131 mg of sodium). Moreover, C-vitamin depletion in elderly patients with coronavirus pneumonia resulted in the aggravation of the pathological process and a fatal outcome [3, 45].

4. Vitamin D metabolism

The principal role of vitamin D is bone homeostasis. Without this vitamin, only 10% to 15% of dietary calcium and approximately 60% of phosphorus are absorbed [7]. However, over the last decades there have been an increasing number of publications on the other functions of this vitamin, and on the immune and inflammatory systems in particular. Several studies have shown the role of vitamin D in the pathogenesis of immune-mediated inflammatory diseases [64], with strong evidence of a link between a low circulating level of 25(OH)D and the prevalence and severity of these diseases. Vitamin D plays a modulating role in the tolerance and homeostasis of the immune system. B and T lymphocytes, monocytes, macrophages and dendritic cells contain significant concentrations of the vitamin D receptor (VDR), with the highest concentration to be found in the immature immune cells of the thymus and the mature CD-8 T lymphocytes [18]. Secondly, an active vitamin D metabolism by cells from the immune system is able to convert the inactive form 25(OH)D into the active $1.25(OH)_2D$ [66]. The combination of these two mechanisms allows a suppressive role in autoimmunity and an important effect against inflammation, such as the downregulation of pro-inflammatory cytokines [84]. The decrease in proinflammatory cytokines has been particularly demonstrated in the lungs by the modulation of the T-cell adaptive immunity and the subsequent decrease in the type 1 cytokines whereas an increase in the anti-inflammatory type 2 cytokines and regulatory T-cells can be observed [83].

Another study reveals that vitamin D deficiency is associated with greater inflammation and activated monocyte phenotypes (interleukines-6) in HIV-infected persons [55]. One of the fundamental roles of vitamin D is to control the cytokine levels, such as IL-6 or IL-17, allowing us to manage the cytokine storm. To benefit from this phenomenon, a high dose seems necessary, as demonstrated in a randomized controlled trial in vitamin D deficient patients. The patients administered with a high dose (4000 UI/d) of vitamin D3 compared to a low dose (400 UI/d) revealed significantly reduced nonspecific CD4 T cell activation [48]. A randomized trial consisting of 40 patients with relapsing-remitting multiple sclerosis showed a reduction in IL-17 production by the Th-cells in patients supplemented over a 6-month period with 10,400 IU/day as compared to a regime of only 800 IU/day [72].

The antiviral activity of vitamin D seems to play a key role in adequate local immune response to respiratory virus infections, acting as a local "respiratory homeostasis" through two processes: by affecting the replication of respiratory viruses or by inducing the expression of antimicrobial peptides, and therefore regulating the balance of Th1/Th2 or Tc1/Tc2 responses while inhibiting Th17 cytokine production [58, 68]. A third effect of great importance in the micronutrient approach of COVID-19 is the major role vitamin D plays in microbiota. Indeed, several papers suggest the role of vitamin D in the intestinal epithelium barrier function, and in the modulation of the bowel immune system [66]. A high level of vitamin D is associated with good gut permeability and decreased low-grade inflammation [10]. The intake of high doses of vitamin D [50 000 UI/w] affects the microbiota composition [42].

5. Vitamin D, COVID-19, at-risk populations, and recommendations

Recent publications reveal a wide range of bacterial species, such as Lautropia, Prevotella and Haemophilus, in the metagenome from the nasopharyngeal swab of a suspected case in Brazil [15] and in China [14]. Gram-negative anaerobic bacteria, Prevotella in particular, increase IL-6 in the plasma [52], causing ground glass opacity in lungs, pulmonary empyema, and cardiac injury: three classical symptoms of the severe form of COVID-19. In the SARS-Cov1 outbreak, the level of IL-6 was highly correlated with hospitalization and death [39].

Based on the vitamin D metabolism in the immune system, this vitamin seems to play a key role in reducing the risk of respiratory infection by lowering viral replication rates and pro-inflammatory cytokine concentration, while increasing anti-inflammatory cytokines. A first association between vitamin D deficiency (12 ng/mL) and acute respiratory morbidity was initially demonstrated in preterm infants: a low serum value of 25(OH)D associated with increased oxygen requirement; increased duration of intermittent positive-pressure ventilation during resuscitation at delivery; and greater need for assisted ventilation [59]. Another study of adults confirms such a link between 25(OH)D deficiency and a risk factor for acute respiratory distress syndrome (ARDS), revealing that vitamin D has trophic effects on primary human alveolar epithelial cells affecting > 600 genes [17]. Indeed, a clever hypothesis of the link between vitamin D deficiency and the COVID-19 mortality rate could be assessed by the latitude dependence. Grant and colleagues supported this hypothesis by two observational facts: firstly, the outbreak occurred in winter, a time when 25(OH)D concentration is lower, due to the minimum amount of ultra violet penetration through the atmosphere, and secondly, the number of cases in the Southern Hemisphere is lower near the end of summer [32]. Braiman and colleagues [8] tested this hypothesis, basing their studies on the data of individual country mortality and the collective COVID-19 mortality rates around the world. Despite high variability due to the multifactorial components of this disease, and considering that people living in hot countries do not necessarily expose themselves to the sun, or use sun protection if they do, the authors found that the closer people lived to the equator, the lower the mortality rate was. The latitude band with the highest mortality rate is centered around 40 degrees north (China, Iran, Italy) with a death rate of approximately 5%, which is 10–15 times higher than the mortality rate of the Southern Hemisphere. Only two counterexamples seem to contradict this relationship: the low mortality rates of Scandinavian countries and the high mortality rates due to COVID-19 in Indonesia and the Philippine. The first counterexample could easily be explained by the Nordic nations' dietary supplementation of fish liver oil and vitamin D-fortified milk [9]. A third relationship between the low concentration of vitamin D and mortality could be revealed by the increase in the mortality rate with age and obesity, both of which are asso-

ciated with a lower 25(OH)D concentration. According to several studies, 40% to 100% of elderly North Americans and Europeans are deficient in vitamin D [13] while a meta-analysis on the link obesity-vitamin D deficiency has revealed that deficiency prevalence was 35% higher in obese individuals and 24% higher in overweight individuals than in others. The well-documented higher mortality rates of these three populations (the elderly, obese individuals and people living far from the equator) seem to be linked with a low level of Vitamin D.

Based on this knowledge, populations concerned with vitamin D deficiency will be less protected from virus attacks. This deficiency is almost systematic in North European populations (except for countries with vitamin D-fortified milk), and particularly in the elderly, in obese individuals, in those with dark skin, or people who keep out of the sun (who have no direct exposure or who use solar cream with a high protection index). A daily 30–45 minutes of full body exposure at a latitude lower than Barcelona is sufficient to produce Vitamin D at a desirable 25(OH)D concentration of 30 ng/mL, defined by experts as the deficiency threshold [36]. It is recommended that these populations at risk take at least 2000 UI/d and at most 10 000 UI/d. Indeed, in order to raise 25(OH)D_2 from 20 ng/mL (deficiency) to 32 ng/mL, an additional intake of approximately 1700 UI/d of vitamin D [4] is necessary. However, the immunity impact at this serum level is low, and protects against osteoporosis only, whereas the optimal serum level to reach is between 60 and 80 ng/mL (or 180 to 200 nmol/l). Raising the level from a deficient (< 30 ng/mL) to an optimal level (60 to 80 ng/mL) decreases the risk of heart attack by 50%, multiple sclerosis by 80%, influenza by 83%, type 1 diabetes by 71%, breast cancer by 83%, and colon cancer by 80% [27, 30, 49, 78, 81].

People with diabetes, cancer, or autoimmune diseases are more likely to be affected by COVID-19 [16, 24]. In order to reduce the risk of infection in populations at risk from influenza and/or COVID-19, this optimal level must be raised by a daily intake of 10 000UI/d [32] over a few weeks in order to raise 25(OH)D concentrations rapidly, followed by 5000 IU/d. The goal should be to raise 25(OH)D concentrations above 69–80 ng/mL, with a blood control every 2 months. Vitamin D intoxication is observed when the level of 25(OH)D is greater than 150 ng/mL [79].

6. Zinc metabolism

Zinc plays a key role in the innate and adaptative immune systems. It allows the normal development and function of cells in charge of mediating nonspecific immunity (neutrophils and natural killer cells). Macrophages are adversely affected by Zinc deficiency, which, consequently, could dysregulate intracellular killing, cytokine production and phagocytosis [69]. This role against inflammation is possible by the reduction of pro-inflammatory cytokines. Indeed, the production or biological activity of multiple cytokines (IL-1, IL-2, IL-3, IL-4, IL-6, IFN-g, IFN-a, TNF-a, and migration inhibitory factors), influencing the development and function of T lymphocytes, B lymphocytes, macrophages, and natural killer cells, is dependent on zinc [20, 26, 69]. Zinc plays a part in inflammatory reduction by means of cytokine production by another mechanism: the zinc-induced upregulation of a zinc-finger protein, A20, which inhibits nuclear factor-kappa B activation via the protein TRAF pathway. Zinc contributes to mucosal and barrier immunity, and deficiency could result in skin lesions, gastrointestinal lesions with degenerative changes in the enterocytes and alterations in pulmonary function [34]. A skin barrier deficiency is instrumental in providing an open door for viruses. Zinc stimulates the thymus and the production of thymulin, which reportedly binds to high-affinity receptors, induces several T-cell markers, and promotes T-cell function including allogenic cytotoxicity, suppressor function, and IL-2 production [61]. Moreover, Zinc reveals antioxidative properties by decreasing the reactive oxygen species (ROS) by several mechanisms (i.e. the inhibition of NADPH oxidase), or its contribution to superoxide dismutase [69]. It has been proved that zinc supplementation in rats prevents pulmonary pathologies due to hyperoxia [75]. Oxidative stress induces zinc release from metallothioneins, which allows the reduction of reactive oxygen species generated by the mitochondrial dysfunction of viral infection [63]. Zinc equally plays a role in the lymphocyte cell cycle, by influencing the activity of several replication and transcription enzymes, such as the major enzyme which regulates the DNA replication: the DNA polymerase.

7. Zinc, COVID-19, at-risk populations, and recommendations

Due to the several roles of zinc in immunity and infection, this micronutrient could have a possible role in reducing the intensity of COVID-19 infections, and maybe ARDS. Indeed,

studies show a potentially adaptive lung response to stretching and a critical role of zinc in defining the tolerance of the lungs for mechanical ventilation [6]. Moreover, the SARS coronavirus RdRp template binding and elongation have shown to be reduced and inhibited, respectively, by zinc in Vero-E6 cells [76]. Zinc supplementation has revealed promising antiviral effects against rhinovirus infections, including the influenza virus [22], revealing a relationship between zinc ion availability (ZIA) values and the reduction in the number of days of the duration of a common cold. This article shows that the effect is highly dependent on the dose coupled with the zinc lozenges of different formulations. Indeed, formulations based on Zinc gluconate are able to reduce the duration of a natural cold by seven days, with a dose intake of 23 mg every 2 hours the patient is awake after an initial double dose (a total of 175 mg of Zinc gluconate) when compared to a placebo group in one study [76], while in another study the same dose, but with lower ZIA [1], reduces the duration of a cold by 4.8 days. This proves that a higher dose of ionic zinc reduces the duration of a cold by an average of 42%. Studies with low ZIA, such as Zinc orotate or Zinc aspartate showed no effect when compared to a placebo group [5].

When we summarize the scientific information available, we see the necessity of maintaining an adequate zinc balance in order to protect ourselves from viral infection. Taking Zinc supplements as a preventive and curative approach could provide an additional shield against COVID-19, by allowing an increase in host resistance to the virus and lowering the burden of disease. A minimal daily dose of 15 mg/d for adults and 20 mg/d for the elderly seems the basic advice to give as a preventive measure. However, a higher dose is necessary in curative treatment: the same dose to be administered every two hours [22] under medical supervision only, in the form of zinc gluconate or bisglycinate in order to reduce symptoms such as diarrhea and lower respiratory tract infection [44]. The toxicity is over 200 mg per day and could induce adverse effects, such as nausea, vomiting, epigastric pain, and exhaustion. Supplementation higher than 50 mg/d in curative treatment could increase the risk of immunodepression.

The elderly, obese people, and type 2 diabetics are the main targets of COVID-19 and zinc deficiency. Several conditions predispose to a high risk of zinc deficiency: inflammatory conditions, intestinal losses, hypercatabolism, renal pathologies, hypothyroidism, alcoholism, malabsorption, post-surgery, bariatric surgery, malnutrition, undernutrition, geriatrics, and digestive and hepatic pathologies (Crohn's disease, celiac disease, steatosis, pancreatitis).

8. Conclusion

According to literature, it seems that Zinc and vitamins C and D, particularly when taken as supplementation at an early stage, could be clinically useful micronutrients as adjuvant therapies in the prevention of deficiency amplification in COVID-19 unaffected and at-risk populations, and/or in the treatment of severe forms in affected patients.

Further randomized control trials through the use of genomics and metabolomic techniques are needed in order to understand the role of these micronutrients in the treatment of severe forms of the COVID-19 disease in different types of at-risk populations.

References

1. Al-Nakib W., Higgins P.G., Barrow I. et al. Prophylaxis and Treatment of Rhinovirus Colds with Zinc Gluconate Lozenges. *Journal of Antimicrobial Chemotherapy*, 1987, vol. 20 (6), pp. 893–901. DOI: 10.1093/jac/20.6.893

2. Amrein K., Oudemans-van Straaten H.M., Berger M.M. Vitamin Therapy in Critically ill Patients: Focus on Thiamine, Vitamin C, and Vitamin D. *Intensive Care Medicine*, 2018, vol. 44 (11), pp. 1940–1944. DOI: 10.1007/s00134-018-5107-y

3. Ang A., Pullar J.M., Currie M.J., Vissers M.C.M. Vitamin C and Immune Cell Function in Inflammation and Cancer. *Biochemical Society Transactions*, 2018, vol. 46 (5), pp. 1147–1159.

4. Barger-Lux M.J., Heaney R.P., Dowell S. et al. Vitamin D and its Major Metabolites: Serum Levels after Graded Oral Dosing in Healthy Men. *Osteoporosis International*, 1998, vol. 8 (3), pp. 222–230. DOI: 10.1007/s001980050058

5. Berthon G., Germonneau P. Histamine as a Ligand in Blood Plasma. Part 6. Aspartate and Glutamate as Possible Partner Ligands for Zinc and Histamine to Favour Histamine Catabolism. *Agents and Actions*, 1982, vol. 12 (5), pp. 619–629. DOI: 10.1007/BF01965070

6. Boudreault F., Pinilla-Vera M., Englert J.A. et al. Zinc Deficiency Primes the Lung for Ventilator-Induced Injury. *JCI Insight*, 2017, vol. 2 (11), e86507. DOI: 10.1172/jci.insight.86507

7. Boullion R. Vitamin D: From Photosynthesis, Metabolism, and Action to Clinical Application. *Endocrinology Philadelphia: Elsevier Saunders*, 2006, pp. 1435–1463.

8. Braiman M. Latitude Dependence of the COVID-19 Mortality Rate – A Possible Relationship to Vitamin D Deficiency? *SSRN*, 2020, 3561958. DOI: 10.2139/ssrn.3561958

9. Brustad M., Braaten T., Lund E. Predictors for Cod-Liver Oil Supplement Use – the Norwegian Women and Cancer Study. *European Journal of Clinical Nutrition*, 2004, vol. 58 (1), pp. 128–136. DOI: 10.1038/sj.ejcn.1601759

10. Caricilli A.M., Picardi P.K., de Abreu L.L. et al. Gut Microbiota is a Key Modulator of Insulin Resistance in TLR 2 Knockout Mice. *PLoS Biol*, 2011, vol. 9 (12), e1001212. DOI: 10.1371/journal.pbio.1001212

11. Carr A.C., Maggini S. Vitamin C and Immune Function. *Nutrients*, 2017, vol. 9 (11), e1211. DOI: 10.3390/nu9111211

12. Carr A.C., Rosengrave P.C., Bayer S. et al. Hypovitaminosis C and Vitamin C Deficiency in Critically ill Patients Despite Recommended Enteral and Parenteral Intakes. *Critical Care*, 2017, vol. 21 (1), e300. DOI: 10.1186/s13054-017-1891-y

13. Chapuy M.-C., Preziosi P., Maamer M. et al. Prevalence of Vitamin D Insufficiency in an Adult Normal Population. *Osteoporosis International*, 1997, vol. 7 (5), pp. 439–443. DOI: 10.1007/s001980050030

14. Chakraborty S. The Wuhan Coronavirus has Integrated in Prevotella, which Possibly Causes the Observed Extreme Virulence – as Sequencing data from 2 Different Studies in China and Hong-Kong Shows Unequivocally. *OSF*, 2020. DOI: 10.31219/osf.io/2xt3w

15. Chakraborty S. Metagenome of SARS-Cov2 from a Patient in Brazil Shows a Wide Range of Bacterial Species-Lautropia, Prevotella, Haemophilus-Overshadowing Viral Eeads, which Does not Even Add Up to a Full Genome, Explaining False Negatives. *OSF*, 2020. DOI: 10.31219/osf.io/2xt3w

16. Chen N., Zhou M., Dong X. et al. Epidemiological and Clinical Characteristics of 99 cases of 2019 Novel Coronavirus Pneumonia in Wuhan, China: a Descriptive Study. *The Lancet*, 2020, vol. 395 (10223), pp. 507–513. DOI: 10.1016/S0140-6736(20)30211-7

17. Dancer R.C.A., Parekh D., Lax S. et al. Vitamin D Deficiency Contributes Directly to the Acute Respiratory Distress Syndrome (ARDS). *Thorax*, 2015, vol. 70 (7), pp. 617–624. DOI: 10.1136/thoraxjnl-2014-206680

18. Deluca H.F., Cantorna M.T. Vitamin D: its Role and Uses in Immunology. *The FASEB Journal*, 2001, vol. 15 (14), pp. 2579–2585. DOI: 10.1096/fj.01-0433rev

19. Di X., Zhu S., Jin H. et al. Altered Resting Brain Function and Structure in Professional Badminton Players. *Brain Connectivity*, 2012, vol. 2 (4), pp. 225–233. DOI: 10.1089/brain.2011.0050

20. Dowd P.S., Kelleher J., Guillou P.J. T-Lymphocyte Subsets and Interleukin-2 Production in Zinc-Deficient Rats. *British Journal of Nutrition*, 1986, vol. 55 (1), pp. 59–69. DOI: 10.1079/bjn19860010

21. Duarte T.L., Cooke M.S., Jones G.D.D. Gene Expression Profiling Reveals New Protective Roles for Vitamin C in Human Skin Cells. *Free Radical Biology and Medicine*, 2009, vol. 46 (1), pp. 78–87. DOI: 10.1016/j.freeradbiomed.2008.09.028

22. Eby GA. Zinc Ion Availability-the Determinant of Efficacy in Zinc Lozenge Treatment of Common Colds. *The Journal of Antimicrobial Chemotherapy*, 1997, vol. 40 (4), pp. 483–493. DOI: 10.1093/oxfordjournals.jac.a020864

23. Erol A. High-Dose Intravenous Vitamin C Treatment for COVID-19. *OSF*, 2020. DOI: 10.31219/osf.io/p7ex8

24. Fang L., Karakiulakis G., Roth M. Are Patients with Hypertension and Diabetes Mellitus at Increased Risk for COVID-19 Infection? *The Lancet Respiratory Medicine*, 2020, vol. 8 (4), e21. DOI: 10.1016/S2213-2600(20)30116-8

25. Ferguson N., Laydon D., Nedjati Gilani G. et al. Report 9: Impact of Non-Pharmaceutical Interventions (NPIs) to Reduce COVID19 Mortality and Healthcare Demand. 2020, vol. 357 (9270), pp. 1777–1789. DOI: 10.25561/77482

26. Flynn A., Loftus M.A., Finke J.H. Production of Interleukin-1 and Interleukin-2 in Allogeneic Mixed Lymphocyte Cultures under Copper, Magnesium and Zinc Deficient Conditions. *Nutrition Research*, 1984, vol. 4 (4), pp. 673–679. DOI: 10.1016/S0271-5317(84)80041-X

27. Garland C.F., Garland F.C., Gorham E.D. et al. The Role of Vitamin D in Cancer Prevention. *American Journal of Public Health*, 2006, vol. 96 (2), pp. 252–261. DOI: 10.2105/AJPH.2004.045260

28. Goldschmidt M.C., Masin W.J., Brown L.R., Wyde P.R. The Effect of Ascorbic Acid Deficiency on Leukocyte Phagocytosis and

Killing of Actinomyces Viscosus. *International Journal for Vitamin and Nutrition Research*, 1988, vol. 58 (3), pp. 326–334.

29. Gombart A.F., Pierre A., Maggini S. A Review of Micronutrients and the Immune System – Working in Harmony to Reduce the Risk of Infection. *Nutrients*, 2020, vol. 12 (1), e236. DOI: 10.3390/nu12010236

30. Gorham E.D., Garland C.F., Garland F.C. et al. Optimal Vitamin D Status for Colorectal Cancer Prevention: a Quantitative Meta Analysis. *American Journal of Preventive Medicine*, 2007, vol. 32 (3), pp. 210–216. DOI: 10.1016/j.amepre.2006.11.004

31. Gorton H.C., Jarvis K. The Effectiveness of Vitamin C in Preventing and Relieving the Symptoms of Virus-Induced Respiratory Infections. *Journal of Manipulative and Physiological Therapeutics*, 1999, vol. 22 (8), pp. 530–533. DOI: 10.1016/s0161-4754(99)70005-9

32. Grant W.B., Lahore H., McDonnell S.L. et al. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths. *Nutrients*, 2020, vol. 12, e988. DOI: 10.3390/nu12040988

33. Guan W., Ni Z., Hu Y. et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *New England Journal of Medicine*, 2020, vol. 382, pp. 1708–1720. DOI: 10.1056/NEJMoa2002032

34. Hambidge K.M., Casey C.E., Crebs N.F. Trace Elements in Human Health and Animal Nutrition. New York: Academic Press, 1986. P. 1–37.

35. Hemilä H., Chalker E. Vitamin C May Reduce the Duration of Mechanical Ventilation in Critically ill Patients: a Meta-Regression Analysis. *Journal of Intensive Care*, 2020, vol. 8 (1), e15. DOI: 10.1186/s40560-020-0432-y

36. Holick M.F. Vitamin D Deficiency. *New England Journal of Medicine*, 2007, vol. 357 (3), pp. 266–281. DOI: 10.1056/NEJMra070553

37. Huang C., Wang Y., Li X. et al. Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China. *The Lancet*, 2020, vol. 395 (10223), pp. 497–506. DOI: 10.1016/S0140-6736(20)30183-5

38. Huijskens MJ.AJ., Walczak M., Koller N. et al. Technical Advance: Ascorbic Acid Induces Development of Double Positive T Cells from Human Hematopoietic Stem Cells in the Absence of Stromal Cells. *Journal of Leukocyte Biology*, 2014, vol. 96 (6), pp. 1165–1175. DOI: 10.1189/jlb.1TA0214-121RR

39. Jiang Y., Xu J., Zhou C. et al. Characterization of Cytokine/Chemokine Profiles of Severe Acute Respiratory Syndrome. *American Journal of Respiratory and Critical Care Medicine*, 2005, vol. 171 (8), pp. 850–857. DOI: 10.1164/rccm.200407-857OC

40. Johnston C.S., Martin L.J., Cai X. Antihistamine Effect of Supplemental Ascorbic Acid and Neutrophil Chemotaxis. *Journal of the American College of Nutrition*, 1992, vol. 11 (2), pp. 172–176.

41. Jose R.J., Manuel A. COVID-19 Cytokine Storm: the Interplay between Inflammation and Coagulation. *The Lancet Respiratory*, 2019, vol. 8 (6), pp. 46–47. DOI: 10.1016/S2213-2600(20)30216-2

42. Kanhere M., He J., Chassaing B. et al. Bolus Weekly Vitamin D3 Supplementation Impacts Gut and Airway Microbiota in Adults with Cystic Fibrosis: a Double-Blind, Randomized, Placebo-Controlled Clinical Trial. *The Journal of Clinical Endocrinology & Metabolism*, 2018, vol. 103 (2), pp. 564–574. DOI: 10.1210/jc.2017-01983

43. Kashiouris M.G., L'Heureux M., Cable C.A. et al. The Emerging Role of Vitamin C as a Treatment for Sepsis. *Nutrients*, 2020, vol. 12 (2), e292. DOI: 10.3390/nu12020292

44. Khaled M.B., Benajiba N. The Role of Nutrition in Strengthening Immune System Against Newly Emerging Viral Diseases: Case of SARS-CoV-2. *The North African Journal of Food and Nutrition Research*, 2020, vol. 4 (7), pp. 240–244. DOI: 10.5281/zenodo.3749406

45. Khomich O.A., Kochetkov S.N., Bartosch B., Ivanov A.V. Redox Biology of Respiratory Viral Infections. *Biochemical Society Transactions*, 2018, vol. 10 (8), e392. DOI: 10.3390/v10080392

46. Kim W.-Y., Jo E.-J., Eom J.S. et al. Combined Vitamin C, Hydrocortisone, and Thiamine Therapy for Patients with Severe Pneumonia who were Admitted to the Intensive Care Unit: Propensity Score-Based Analysis of a Before-After Cohort Study. *Journal of Critical Care*, 2018, vol. 47, pp. 211–218. DOI: 10.1016/j.jcrc.2018.07.004

47. Kishimoto Y., Saito N., Kurita K. et al. Ascorbic Acid Enhances the Expression of Type 1 and Type 4 Collagen and SVCT2 in Cultured Human Skin Fibroblasts. *Biochemical and Biophysical Research Communications*, 2013, vol. 430 (2), pp. 579–584. DOI: 10.1016/j.bbrc.2012.11.110

48. Konijeti G.G., Arora P., Boylan M.R. et

al. Vitamin D Supplementation Modulates T Cell-Mediated Immunity in Humans: Results from a Randomized Control Trial. *The Journal of Clinical Endocrinology & Metabolism*, 2016, vol. 101 (2), pp. 533–538. DOI: 10.1210/jc.2015-3599

49. Lappe J.M., Travers-Gustafson D., Davies K.M. et al. Vitamin D and Calcium Supplementation Reduces Cancer Risk: Results of a Randomized Trial. *The American Journal of Clinical Nutrition*, 2007, vol. 85 (6), pp. 1586–1591. DOI: 10.1093/ajcn/85.6.1586

50. Lauer S.A., Grantz K.H., Bi Q. et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Annals of Internal Medicine*, 2020, vol. 172 (9), pp. 577–582. DOI: 10.7326/M20-0504

51. Lauer A.-C., Groth N., Haag S.F. et al. Dose-Dependent Vitamin C Uptake and Radical Scavenging Activity in Human Skin Measured with in Vivo Electron Paramagnetic Resonance Spectroscopy. *Skin Pharmacology and Physiology*, 2013, vol. 26 (3), pp. 147–154. DOI: 10.1159/000350833

52. Leite A.Z., Rodrigues N. de C., Gonzaga M.I. et al. Matheucci Junior E. Detection of Increased Plasma Interleukin-6 Levels and Prevalence of Prevotella Copri and Bacteroides Vulgatus in the Feces of Type 2 Diabetes Patients. *Frontiers in Immunology*, 2017, vol. 8, e1107. DOI: 10.3389/fimmu.2017.01107

53. Lipsitch M., Swerdlow D.L., Finelli L. Defining the Epidemiology of Covid-19 – Studies Needed. *New England Journal of Medicine*, 2020, vol. 382, pp. 1194–1196. DOI: 10.1056/NEJMp2002125

54. Liu Y., Yan L.-M., Wan L. et al. Viral Dynamics in Mild and Severe Cases of COVID-19. *Lancet Infect Dis*, 2020, vol. 20 (6), pp. 656–657. DOI: 10.1016/S1473-3099(20)30232-2

55. Manion M., Hullsiek K.H., Wilson E.M.P. et al. Vitamin D Deficiency is Associated with IL-6 Levels and Monocyte Activation in HIV-Infected Persons. *PLoS One*, 2017, vol. 12 (5), e0175517. DOI: 10.1371/journal.pone.0175517

56. Mehta P., McAuley D.F., Brown M. et al. COVID-19: Consider Cytokine Storm Syndromes and Immunosuppression. *The Lancet*, 2020, vol. 395 (10229), pp. 1033–1034. DOI: 10.1016/S0140-6736(20)30628-0

57. Mullard A. Flooded by the Torrent: the COVID-19 Drug Pipeline. *The Lancet*, 2020, vol. 395 (10232), pp. 1245–1246. DOI: 10.1016/S0140-6736(20)30894-1

58. Nanzer A.M., Chambers E.S., Ryanna K. et al. Enhanced Production of IL-17A in Patients with Severe Asthma is Inhibited by 1α, 25-Dihydroxyvitamin D3 in a Glucocorticoid-Independent Fashion. *Journal of Allergy and Clinical Immunology*, 2013, vol. 132 (2), pp. 297–304. DOI: 10.1016/j.jaci.2013.03.037

59. Onwuneme C., Martin F., McCarthy R. et al. The Association of Vitamin D Status with Acute Respiratory Morbidity in Preterm Infants. *The Journal of Pediatrics*, 2015, vol. 166 (5), pp. 1175–1180. DOI: 10.1016/j.jpeds.2015.01.055

60. Parkin J., Cohen B. An Overview of the Immune System. *The Lancet*, 2001, vol. 357 (9270), pp. 1777–1789. DOI: 10.1016/S0140-6736(00)04904-7

61. Prasad A.S., Meftah S., Abdallah J. et al. Serum Thymulin in Human Zinc Deficiency. *The Journal of Clinical Investigation*, 1988, vol. 82 (4), pp. 1202–1210. DOI: 10.1172/JCI113717

62. Prompetchara E., Ketloy C., Palaga T. Immune Responses in COVID-19 and Potential Vaccines: Lessons Learned from SARS and MERS Epidemic. *Asian Pac J Allergy Immunol*, 2020, vol. 38 (1), pp. 1–9. DOI: 10.12932/AP-200220-0772

63. Read S.A., Obeid S., Ahlenstiel C., Ahlenstiel G. The Role of Zinc in Antiviral Immunity. *Advances in Nutrition*, 2019, vol. 10 (4), pp. 696–710. DOI: 10.1093/advances/nmz013

64. Rolf L., Muris A.-H., Mathias A. et al. Exploring the Effect of Vitamin D3 Supplementation on the Anti-EBV Antibody Response in Relapsing-Remitting Multiple Sclerosis. *Multiple Sclerosis Journal*, 2018, vol. 24 (10), pp. 1280–1287. DOI: 10.1177/1352458517722646

65. Rybniker J., Fätkenheuer G. Importance of Precise data on SARS-CoV-2 Transmission Dynamics Control. *Lancet Infect Dis*, 2020. DOI: 10.1016/S1473-3099(20)30359-5

66. Sassi F., Tamone C., D'Amelio P. Vitamin D: Nutrient, Hormone, and Immunomodulator. *Nutrients*, 2018, vol. 10 (11), e1656. DOI: 10.3390/nu10111656

67. Saul A.W. Vitamin C Protects Against Coronavirus. Orthomolecular Medicine News Service. (Preprint) (2020). Available at: http://orthomolecular.org/resources/omns/v16n04.shtml (Accessed January 26, 2020).

68. Schedel M., Jia Y., Michel S. et al. 1,25D3 Prevents CD8+ Tc2 Skewing and Asthma Development Through VDR Binding Changes to the Cyp11a1 Promoter. *Nature Communica-*

tions, 2016, vol. 7 (1), pp. 1–11. DOI: 10.1038/ncomms10213

69. Shankar A.H., Prasad A.S. Zinc and Immune Function: the Biological Basis of Altered Resistance to Infection. *The American Journal of Clinical Nutrition*, 1998, vol. 68 (2), pp. 447–463. DOI: 10.1093/ajcn/68.2.447S

70. Sharma P., Raghavan S.A., Saini R., Dikshit M. Ascorbate-Mediated Enhancement of Reactive Oxygen Species Generation from Polymorphonuclear Leukocytes: Modulatory Effect of Nitric Oxide. *Journal of Leukocyte Biology*, 2004, vol. 75 (6), pp. 1070–1078. DOI: 10.1189/jlb.0903415

71. Shi Y., Wang Y., Shao C. et al. COVID-19 Infection: the Perspectives on Immune Responses. *Cell Death Differ.*, 2020, vol. 27 (5), pp. 1451–1454. DOI: 10.1038/s41418-020-0530-3

72. Sotirchos E.S., Bhargava P., Eckstein C. et al. Safety and Immunologic Effects of High- Vs Low-Dose Cholecalciferol in Multiple Sclerosis. *Neurology*, 2016, vol. 86 (4), pp. 382–390. DOI: 10.1212/WNL.0000000000002316

73. Stankova L., Gerhardt N.B., Nagel L., Bigley R.H. Ascorbate and Phagocyte Function. *Infection and Immunity*, 1975, vol. 12 (2), pp. 252–256.

74. Tanaka M., Muto N., Gohda E., Yamamoto I. Enhancement by Ascorbic Acid 2-Glucoside or Repeated Additions of Ascorbate of Mitogen-Induced IgM and IgG Productions by Human Peripheral Blood Lymphocytes. *The Japanese Journal of Pharmacology*, 1994, vol. 66 (4), pp. 451–456. DOI: 10.1254/jjp.66.451

75. Taylor C.G., Bray T.M. Effect of Hyperoxia on Oxygen Free Radical Defense Enzymes in the Lung of Zinc-Deficient Rats. *The Journal of Nutrition*, 1991, vol. 121 (4), pp. 460–466. DOI: 10.1093/jn/121.4.460

76. Te Velthuis A.J.W., van den Worm S.H.E., Sims A.C. et al. Zn2+ Inhibits Coronavirus and Arterivirus RNA Polymerase Activity in Vitro and Zinc Ionophores Block the Replication of these Viruses in Cell Culture. *PLoS Pathogens*, 2010, vol. 6 (11), e1001176. DOI: 10.1371/journal.ppat.1001176

77. Truwit J.D., Hite R.D., Morris P.E. et al. Effect of Vitamin C Infusion on Organ Failure and Biomarkers of Inflammation and Vascular Injury in Patients with Sepsis and Severe Acute Respiratory Failure: the CITRIS-ALI Randomized Clinical Trial. *Jama*, 2019, vol. 322 (13), pp. 1261–1270. DOI: 10.1001/jama.2019.11825

78. Tworoger S.S., Lee I.-M., Buring J.E. et al. Plasma 25-Hydroxyvitamin D and 1,25-Dihydroxyvitamin D and Risk of Incident Ovarian Cancer. *Cancer Epidemiology and Prevention Biomarkers*, 2007, vol. 16 (4), pp. 783–788. DOI: 10.1158/1055-9965.EPI-06-0981

79. Vieth R., Bischoff-Ferrari H., Boucher B.J. et al. The Urgent Need to Recommend an Intake of Vitamin D that Is. *Am J Clin Nutr*, 2007, vol. 85 (3), pp. 649–650. DOI: 10.1093/ajcn/85.3.649

80. Vissers M.C.M., Wilkie R.P. Ascorbate Deficiency Results in Impaired Neutrophil Apoptosis and Clearance and is Associated with Up-Regulation of Hypoxia-Inducible Factor 1α. *Journal of Leukocyte Biology*, 2007, vol. 81 (5), pp. 1236–1244. DOI: 10.1189/jlb.0806541

81. Wei M.Y., Garland C.F., Gorham E.D. et al. Vitamin D and Prevention of Colorectal Adenoma: a Meta-Analysis. *Cancer Epidemiology and Prevention Biomarkers*, 2008, vol. 17 (11), pp. 2958–2969. DOI: 10.1158/1055-9965.EPI-08-0402

82. Yun J., Mullarky E., Lu C. et al. Vitamin C Selectively Kills KRAS and BRAF Mutant Colorectal Cancer Cells by Targeting GAPDH. *Science*, 2015, vol. 350 (6266), pp. 1391–1396. DOI: 10.1126/science.aaa5004

83. Zdrenghea M.T., Makrinioti H., Bagacean C. et al. Vitamin D Modulation of Innate Immune Responses to Respiratory Viral Infections. *Reviews in Medical Virology*, 2017, vol. 27 (1), e1909. DOI: 10.1002/rmv.1909

84. Zhang Y., Leung D.Y.M., Richers B.N. et al. Vitamin D Inhibits Monocyte/Macrophage Proinflammatory Cytokine Production by Targeting MAPK Phosphatase-1. *The Journal of Immunology*, 2012, vol. 188 (5), pp. 2127–2135. DOI: 10.4049/jimmunol.1102412

85. Zhu J., Ji P., Pang J. et al. Clinical Characteristics of 3,062 COVID-19 Patients: a Meta-Analysis. *Journal of Medical Virology*, 2020. DOI: 10.1002/jmv.25884

Received 14 September 2020

УДК 616.62 DOI: 10.14529/hsm200416

КАК ПРЕДОТВРАТИТЬ COVID-19 С ПОМОЩЬЮ ЕЖЕДНЕВНОГО ПРИЕМА МИКРОЭЛЕМЕНТОВ? ОБЗОРНОЕ ИССЛЕДОВАНИЕ

Г. Лаффайе[1,2,3], В.В. Епишев[3], К.А. Наумова[3], А. Делафонтен[1,2,4]

[1]Университет Париж-Сакле, коммуна Орсе, Франция,
[2]Университет Орлеана, г. Орлеан, Франция,
[3]Южно-Уральский государственный университет, г. Челябинск, Россия,
[4]Эколь д'Асас, г. Париж, Франция

Цель данной статьи – сосредоточить внимание на том, как люди могут оптимизировать свое состояние здоровья и работу иммунной системы с помощью пищевых добавок, чтобы снизить риск инфекций дыхательных путей. **Материалы и методы.** Был проведен обзор 85 статей, посвященных оценке механизмов, которые позволяют витамину D, витамину C и цинку снижать скорость репликации вирусов и уменьшать провоспалительный цитокиновый шторм. Кроме того, особое внимание было уделено группам высокого риска с признаками дефицита исследуемых витаминов и минералов. **Результаты.** По данным литературы можно сделать вывод, что цинк и витамины C и D, особенно при приеме в качестве добавок на ранней стадии, могут быть рекомендованы в качестве вспомогательных методов лечения для предотвращения усиления дефицита у здоровых и подверженных COVID-19 групп населения, а также при лечении тяжелых форм у пациентов. **Заключение.** Необходимы дальнейшие рандомизированные контрольные исследования с использованием геномики и метаболомных методов, чтобы выявить роль указанных добавок в лечении тяжелых форм COVID-19 в различных группах риска.

Ключевые слова: *пандемия, витамин C, витамин D, цинк, Sars-CoV-2.*

Лаффайе Гийом, доцент, Лаборатория CIAMS, Университет Париж-Сакле. 91400, Франция, коммуна Орсе, ул. Жоржа Клемансо, 15; Лаборатория CIAMS, Университет Орлеана. 45067, Франция, г. Орлеан, пр. Парк Флораль, 6749; Южно-Уральский государственный университет. 454080, г. Челябинск, проспект Ленина, 76. E-mail: guillaume.laffaye@u-psud.fr, ORCID: 0000-0002-7414-1063.

Епишев Виталий Викторович, директор научно-исследовательского центра спортивной науки, доцент кафедры теории и методики физической культуры и спорта института спорта, туризма и сервиса, Южно-Уральский государственный университет. 454080, г. Челябинск, проспект Ленина, 76. E-mail: epishev74@mail.ru, ORCID: 0000-0002-7284-7388.

Наумова Ксения Андреевна, младший научный сотрудник научно-исследовательского центра спортивной науки института спорта, туризма и сервиса, Южно-Уральский государственный университет. 454080, г. Челябинск, проспект Ленина, 76. E-mail: naumova.ksenia94@mail.ru, ORCID: 0000-0002-1729-395X.

Арно Делафонтен, научный сотрудник, Лаборатория CIAMS, Университет Париж-Сакле. 91400, Франция, коммуна Орсе, ул. Жоржа Клемансо, 15; Лаборатория CIAMS, Университет Орлеана. 45067, Франция, г. Орлеан, пр. Парк Флораль, 6749; директор по науке, Лаборатория MS2R, Эколь д'Асас. 75015, Франция, г. Париж, ул. Вилла Торетон, 4-6. E-mail: arnaud_94150@hotmail.fr, ORCID: 0000-0002-3093-0183.

Поступила в редакцию 14 сентября 2020 г.

ОБРАЗЕЦ ЦИТИРОВАНИЯ

How to Prevent COVID-19 by Means of a Daily Micronutrition Protocol? An Overview / G. Laffaye, V.V. Epishev, K.A. Naumova, A. Delafontaine // Человек. Спорт. Медицина. – 2020. – Т. 20, № 4. – С. 127–138. DOI: 10.14529/hsm200415

FOR CITATION

Laffaye G., Epishev V.V., Naumova K.A., Delafontaine A. How to Prevent COVID-19 by Means of a Daily Micronutrition Protocol? An Overview. *Human. Sport. Medicine*, 2020, vol. 20, no. 4, pp. 127–138. DOI: 10.14529/hsm200415