Sports Supplements in COVID-19 Prophylaxis

Bogdan-Alexandru HAGIU[a*], Cristina Mihaela GHICIUC[b]

[a]*Faculty of Physical Education and Sports, Alexandru Ioan Cuza University of Iasi, Toma Cozma Str. No 3, Iaşi, 700246, Romania*
[b]*Faculty of Medicine, Gr. T. Popa University of Medicine and Pharmacy, Iasi, Romania*

Abstract
Sarcopenia is an aggravating factor in the evolution of COVID-19.Avoiding its installation could be a prophylactic and curative factor.Therefore, the prophylaxis of severe forms of COVID-19 through exercise could be supported by the administration of supplements based on arginine, glutamine, n-3 PUFA or carnitine.These substances have roles in treating sarcopenia, stimulating immunity and mitochondrial biogenesis, interferon metabolism.These antioxidants could accelerate the adaptation of the vascular endothelium to exercise and thus prevent infection with SARS-CoV-2.The beneficiaries could be especially the elderly, those suffering from type 2 diabetes, liver cirrhosis, cardiovascular diseases (diseases at risk for COVID-19).Individuals with genetic defects in interferon metabolism, for the purpose discussed in this paper, should perhaps avoid n-3 PUFA supplementation.

Keywords*: sports supplements; COVID-19; sarcopenia.*

1. Introduction

During COVID-19 infection, hospitalized patients at risk for sarcopenia have an increased risk of mortality (Riesgo et al, 2021). .In a review article discussing whether COVID-19 may be a factor for cachexia in intensive care patients (Virgens et al., 2021) the following facts, taken from the literature, are set out:

* Corresponding author.
E-mail address: bogdan_hagiu@yahoo.com

- arginine and glutamine are non-essential amino acids for which the role in recovery of critically ill patients is discussed, but for striated muscles the effect is unclear (Singer et al., 2019)
- n-3 PUFAs have been shown to optimize tissue recovery (AssociaçãoBrasileira de CuidadosPaliativos, 2011)
- l-Carnitine supplementation has protective effects against several mechanisms of induction of sarcopenia, favoring protein synthesis (Esfahani et al, 2019)

These substances are used as sports supplements, namely arginine (Viribay et al., 2020), glutamine (Coqueiro et al., 2019), n-3 PUFA (Gammone et al., 2018), l-Carnitine (Sawicka et al., 2020).Given the special role of moderate-intensity exercise in preventing hospitalized forms of COVID-19 (Hagiu, 2021), the question may arise whether supplementing with certain substances in certain categories would not increase the chances of preventing COVID-19 in case of SARS-CoV-2 infection, as well as creating the premise of an easier evolution.Therefore, the paper aims to analyze the effects of these supplements on sarcopenia, immunity (its role in the fight against COVID-19 is studied – Chowdhury et al. 2020), stimulation of mitochondrial biogenesis (the main factor in preventing severe forms of COVID-19 through exercise – Hagiu, 2020). Given that exercise can improve the ability to defend against SARS-CoV-2 in individuals who are genetically deficient in interferon metabolism (Hagiu, 2021b), the paper also aims to investigate the action of these supplements on this issue.

2. Effects of arginine, glutamine, n-3 PUFA or carnitine supplementation on COVID-19 evolution

2.1. Roles for treating sarcopenia

a) Arginine and glutamine supplementation has been shown to be useful in the nutritional management of type 2 diabetes sarcopenia (Maykish&Sikalidis, 2020). It is known that diabetes itself is a risk factor for severe forms of COVID-19 (Zhou et al, 2021).

b) Although the dosage still needs to be investigated, supplementation with n-3 PUFA is a future alternative for the treatment of sarcopenia due to age (Dupont et al., 2019).

c) L-carnitine stops the decrease in muscle mass caused by liver cirrhosis (Ohara et al., 2018) the effect may be due to downregulated myostatin (Nakano et al., 2020). Data from the specialized literature suggest that pre-existing liver diseases worsen the evolution of COVID-19 (Mohammed et al., 2021)

2.2. Roles in immunity

a) l-arginine and its metabolites (e.g., ornithine and citrulline) are able to activate T-cells (Kim et al., 2018). This fact is of particular importance, as the protective role of T-cells in COVID-19 is known (Noh et al., 2021)

b) The functioning of the immune system is dependent on the intake of glutamine, this amino acid controlling the expression of specific genes (Curi et al., 2016).

c) n-3 PUFA acts on cells involved in inflammation and immunity, having anti-inflammatory and immunomodulatory effects (Calder, 2013).

d) A study in experimental animals (rats) showed that supplementation with L-carnitine may have the effect of improving immunity in elderly animals, in which there is a decline in this function (Thangasamy et al., 2008).

Stimulation of mitochondrial biogenesis

a) L-Arginine supplementation is beneficial in patients with mitochondrial etiology (Barros et al., 2021)

b) There are arguments that glutamine stimulates mitochondrial biogenesis (Sumikawa et al., 2022), (Kumar, Giri&Shaha, 2018)

c) The same activation of mitochondrial biogenesis can be obtained by supplementation with n-3 PUFA (Flachs et al., 2005).

d) Due to the ability of carnitine to act as a type 1 histone deacetylase inhibitor, supplementation can stimulate mitochondrial biogenesis in the elderly (Mccarty, DiNicolantonio& O'Keefe, 2020), category at risk for SARS-CoV-2 infection and COVID-19 complications.

2.3. *Effects on interferon metabolism*

a) Arginine has an effect on the biological action of IFNβ-1b, therefore it can be used for new formulations (Fazeli et al., 2014).

b) In vitro, an increased intake of glutamine has been shown to increase interferon-gamma production (Boelens et al., 2004).

c) In contrast, in experimental animals (mice), n-3 PUFA has been shown to reduce the expression of interferon-gamma receptors (Feng, Keisler& Fritsche, 1999).

As expected from the previous paragraph, supplementation with these substances may influence the evolution of COVID-19, including in terms of amelioration of sarcopenia:

a) The addition of oral L-arginine to standard therapy in patients with COVID-19 significantly reduces the length of hospital stay and the need for respiratory assistance to 10, but not to 20 days after starting treatment (Fiorentino et al., 2021)

b) According to some research, glutamine, as an antioxidant, can be used in the treatment of moderate-severe forms of COVID-19, resulting in a reduction in the severity of sequelae (Adebola Okunola, 2021)

c) n-3 PUFA and their metabolites have been considered to have an adjuvant role in the treatment of COVID-19 and cardiovascular complications of this disease (Darwesh et al., 2021)

d) A genetic predisposition to high plasma concentrations of carnitine may reduce the likelihood of COVID-19 disease and the severity of the disease, this supplement, a potential substitute for dexamethasone, exerting its action through its molecular functions (Li et al., 2021)

Table 1 summarizes the supplementary roles of arginine, glutamine, n-3 PUFA and carnitine on sarcopenia, immunity, stimulation of mitochondrial biogenesis, and interferon metabolism.

Table 1. Effects of supplements on sarcopenia, immunity, mitochondrial biogenesis, interferon metabolism

	Roles for treating sarcopenia	Roles in immunity	Stimulation of mitochondrial biogenesis	Effects on interferon metabolism
arginine	+ (Maykish&Sikalidis, 2020)	+ (Kim et al., 2018)	+ (Barros et al., 2021)	+ (Fazeli et al., 2014)
glutamine	+ (Maykish&Sikalidis, 2020)	+ (Curi et al., 2016)	+ (Sumikawa et al., 2022), (Kumar, Giri&Shaha, 2018)	+ (Boelens et al., 2004)
n-3 PUFA	+ (Dupont et al., 2019)	+ (Calder, 2013)	+ (Flachs et al., 2005)	- (Feng, Keisler& Fritsche, 1999)
carnitine	+ (Ohara et al., 2018)	+ (Thangasamy et al., 2008)	+ (Mccarty, DiNicolantonio& O'Keefe, 2020)	there are no data

3. Discussions

Antioxidant supplements were proposed for the elderly in combination with resistance exercises to increase muscle mass (Labonté et al., 2008). Antioxidants such as quercetin and vitamin C have been proposed for the prevention of COVID-19 (ColungaBiancatelli et al., 2020), and theoretically antioxidants can accelerate the adaptation of the vascular endothelium to effort and prevent infection with SARS-CoV-2 (Hagiu, 2021a). Supplementation with the substances discussed in the paper can be especially beneficial for the elderly, sufferers of type 2 diabetes, cirrhosis of the liver, cardiovascular diseases.Ideally, the supplement should support the prophylactic use of moderate-intensity exercise programs for severe forms of COVID-19. In those with genetic disorders of interferon metabolism, the administration of n-3 PUFA supplements would require caution.

4. Conclusions

The administration of supplements based on arginine, glutamine, n-3 PUFA or carnitine, preferably in support of moderate-intensity exercise programs, could potentiate the effects of preventing hospitalization of COVID-19 and the course of the disease. This is due to multiple metabolic pathways, to which is added the prevention or improvement of

sarcopenia.The beneficiaries are mainly the elderly, but also those suffering from type 2 diabetes, liver cirrhosis, cardiovascular diseases.In the case of a genotype characterized by poor interferon metabolism, n-3 PUFA supplements should be avoided.

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