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Mini Review

Covid-19 Response: The Importance of Amino Acids, Trace Elements and Polyphenols for Immune Competence

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Abstract

The Covid-19 pandemic is a challenge for both CAM practitioners and CAM users. An adequate immune response is required for both a Covid infection and a Covid vaccination. The adequacy of the immune response depends very much on an individual's nutritional status. The body users a range of substances to defend itself that require dietary amino acids and trace elements. Free radicals are used to attack microorganisms and antioxidants are used to quelch the free radical activity. Additionally, white blood cells derive 50% of their ATP from glutaminolysis. Glutamine is depleted at high levels of physical activity, including sport, and following burns or operations. A diet low in protein leads to impaired immunocompetence. Unfortunately, a large number of the world population fails to meet the daily requirement of 1.5 to 2.2 g/kg of high-quality protein necessary for good health. This is true even for the elderly in high income countries. Similarly with the trace elements. Large numbers of people live in areas of the world where there are low levels of iodine and selenium in the soil. This results in low levels of these elements in foods procured locally. Other trace elements such as copper, iron and zink are difficult to absorb due to the presence of phytic and oxalic acids in vegetable foods. This is less of a problem for meat eaters as these minerals are found at high levels in meat. In contrast, for vegans and vegetarians whose primary source of protein is grains and pulses, the presence of phytic acid in these foods inhibit absorption of the copper, iron and zinc from plant sources. Women are particularly at risk as their reproductive system requires higher levels of protein, iron and iodine. Ensuring adequate nutrition is the priority for long term immunocompetence.

Keywords: Immunocompetence; COVID; Glutamine; Arginine; Cysteine; Taurine; Zinc; Iron; Iodine; Copper

Abbreviations: RNS: reactive nitrogen species; ROS: reactive oxygen species; SOD: superoxide dismutase

Introduction

The Covid-19 pandemic is a challenge for both CAM practitioners and CAM users. An adequate immune response is required for both a Covid-19 infection and a Covid-19 vaccination. The adequacy of the immune response depends very much on an individual's nutritional status.

CAM therapies can be subdivided in many ways, one of which is

a) nutritional therapy, and

b) non-nutritional therapies.

The later contains herbalism, acupuncture, zone therapy, homeopathy, etc.

Nutritional therapies can be further subdivided into

a) food therapy, and

b) nutrient therapy,

for example, eating fatty fish or ingesting fish oil extracts.

This paper will focus on which nutrients are necessary for a normal functioning immune system and then examine which

groups are at risk for nutrient deficiency and subsequently reduced immune competence.

The Immune System

Both the innate and the acquired immune systems require amino acids, derived from dietary protein, to synthesise cytokines, antibodies, complements, lysosomes and other immunoproteins [1]. The immune cells produce free radicals, containing oxygen or nitrogen, to attack viruses and other microorganisms. These free radicals include both reactive oxygen species (ROS) and reactive nitrogen species (RNS): hydroxyl radical, superoxide anion radical, hydrogen peroxide, hydrogen sulphide, singlet molecular oxygen, hypochlorite, nitric oxide radical and peroxynitrite radical. A balance between the free radicals and antioxidants, including β-carotene, C vitamin, E vitamin, ubiquinol, uric acid, is necessary for proper physiological function. If free radicals overwhelm the body's ability to regulate them, a condition known as oxidative stress ensues [1]. The immune response to Covid-19 response has been outlined in detail [2].

Key Nutrients

The primary amino acids involved in these processes are arginine, cysteine, glutamine, glycine and taurine. Taurine has a key role in quelching ROS and RNS [1] as well as acting as a cell membrane stabilizer [3]. Iron is involved in the production of the superoxide anion hydroxide from hydrogen peroxide. Copper, manganese and zinc are involved in the production of hydrogen peroxide via the enzyme superoxide dismutase (SOD) Iron, selenium and the amino acid glutathione (consisting of the amino acids cysteine, glutamine and glycine) are involved in the conversion of hydrogen peroxide via the enzyme catalase.

Iodine is involved in the production of hypochlorous acid from hydrogen peroxide via the enzyme myeloperoxidase Polyphenols and the amino acid arginine are involved in the production of nitric oxide radical, and peroxynitrite radical [4]. Furthermore, polyphenols inhibit arginase and so increase the availability of arginine [1].

Glutamine also functions as the primary energy source for leucocytes. Glutaminolysis provides at least 50% of the ATP used by lymphocytes and macrophages. Furthermore, the oxidation of glutamine provides energy for the rapidly dividing cells in the bone marrow, which produce leucocytes, and for immunologically challenged lymphocytes [5]. Excessive physical activity, including sport, depletes glutamine and may lead to a weakened immune defence. Glutamine is the primary energy substrate for fibroblasts and after burns or following operations glutamine plasma levels drop for months [6].

Dietary Sources of Key Nutrients

Protein is found in large quantities in animal meats, both muscle and offal, and seafood. Protein is also found in grains and pulses in medium quantities together with large amounts of carbohydrates. Non-animal protein is not balanced for postprandial muscle storage and some essential amino acids are used for energy [7]. However, the amino acids we are interested in for the immune system are not essential ones, so we are more interested in the amount of protein ingested. Protein is generally very well digested and absorbed by the small intestine [4].

The World Health Organization Committees estimated mean daily protein requirements for adults as 0.66 g/kg with a population requirement of 0.8 g/kg, based on nitrogen balance studies. However, recent studies recommend a greater daily intake of 1.5 to 2.2 g/kg of high-quality protein with pregnant women and those over 65 years having greater protein requirement [8].

Taurine makes up 0-1% of the body's mass. It is not a true amino acid, but a β-amino sulfonic acid, and is not incorporated into proteins. It needs to be obtained from the diet as only limited amounts are produced from cysteine [3]. Taurine is found in small quantities in meat and in relatively large quantities in seafood, but not in eggs or milk. Non-animal foods contain only a trace of taurine [3,9] and consequently, vegetarians and vegans have low levels of taurine. Taurine, in daily doses of 2,000 to 3,000 mg, is useful in treating thrombocyte aggregation that can occur following COVID infections and vaccinations. On the other hand, taurine is not useful for thrombocytopenia.

Iron is found in two dietary forms heme and nonheme. About 60% of the iron in animal foods is in the heme form, which is more easily absorbed, whereas non animal sources of iron are in the nonheme form, e.g. green leafy vegetables, potatoes and legumes. Enhancers of nonheme iron absorption include sugars, acids and animal products. Inhibitors of nonheme absorption include polyphenols (including those found in tea and coffee), oxalic acid, phytic acid (found in whole grains, legumes, lentils, nuts and seeds) and the cations calcium, manganese and zinc. Due to pregnancy and the loss blood during both menstruation and childbirth, women have a greater need than men [4].

Zinc is found at higher levels in animal products and better absorbed form animal products than from whole grains and legumes. Zinc absorption is enhanced by an acid environment. Like iron, zinc absorption is inhibited by polyphenols, oxalic acid and phytic acid as well as calcium and iron. Zinc is needed at higher levels during sexual maturation and for fertility and reproduction [4].

Copper is found at high levels in offal and oysters. Other meats and seafood contain reasonable amounts as do nuts, seeds and potatoes. Copper absorption is enhanced by acids and inhibited by phytic acid and the cations calcium, iron and zink [4].

Iodine is found in seafood but not in freshwater fish. Iodine deficiency is widespread and afflicts up to 50% of the world's population, particularly those living in mountainous or lowland non-coastal regions. In high income countries the introduction of iodized salt has largely eliminated iodine deficiency. Absorption

of iodine is very high, about 90% [4]. Pregnant and breastfeeding women have a much higher need of iodine.

Selenium is found at high levels in seafood and Brazil nuts and medium levels in muscle meats, grains, milk and eggs. Wheat, broccoli, onions, asparagus, cabbage and garlic will hyperaccumulate selenium from the soil. Foods grown on soils with low levels of selenium will also be low in selenium. These areas include New Zealand, Scandinavia and parts of China and Russia. Selenium is well absorbed although absorption is inhibited by phytic acid [4].

Manganese is found in high levels in whole grain cereals, nuts, leafy green vegetables and pineapple. Compared to the other trace elements less is known about manganese. It appears that less than 5% of oral intake is absorbed and that absorption is inhibited by phytic acid and oxalic acid [4].

Treatment with Nutrients

The amino acids can be combined into a powder, with two exceptions. Citrulline replaces arginine, which is a precursor to arginine and tastes much more neutral. Cysteine, due to its sulphur taste needs to be taken in capsules. Suggestion for a 10ml scoop delivering 7000mg amino acids, dosage 1-4 scoops/day in water.

Glutamine 3500 mg, Citrulline 2000g, Glycine 1000mg, Taurine 500mg Plus Cysteine 500 -2000 mg/day Trace elements can be taken in a Multi Vitamin Mineral preparation: 1 - 2 doses daily. Single dose: Iron 5-10 mg, Zinc 10 mg, Copper 1 mg, Iodide 150 µg, Selenium 150 µg, Manganese 2 mg. Polyphenols are found whole foods such as fruits, berries, vegetables, coffee, tea and wine.

Conclusion

Amino acids and trace nutrients are essential for normal immune function and so in CAM treatments should be prioritised above immunomodulatory and immunostimulatory treatments, except in acute situations. While supplements are useful to restore nutrient levels, dietary adjustments are necessary for long term planning. In vegan and vegetarian diets, the presence of phytic and oxalic acids, as well as the low levels of protein, taurine and easily absorbable trace minerals, suggest that these diets are marginal and not optimal for immune competence. Whether these diets can be modified e.g., by fermentation, remains a challenge. Furthermore, consumers may resist changes to their traditional foods.

Acknowledgement

None.

Conflict of Interest

The author owns a company in Sweden selling nutritional and herbal products.

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