Review Article

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Tips to Boost Innate Immune System to Fight Viruses with a Focus on COVID-19: A Short Review

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ABSTRACT

This review article aims to educate the public from an immunological point of view with regards to protecting themselves from being infected with COVID-19 and to boosting their innate immune response to fight COVID-19 viral infection because as it is well known, there is neither 100% COVID-19 treatment nor a fully successful protective vaccine up to date, and the solution depends on two main factors prevention and raising the immunity. Boosting the innate immune system is summarized in this review which includes consumption of healthy immuno-fortified food, drinking enough amounts of water, avoiding alcoholic drinks, getting enough sleep, reducing the level of stress, exercising, avoiding smoking (debatable with regards to COVID-19), smiling and laughter, optimism, and listening to music. These points, if followed carefully, would work as a robust protective shield against COVID-19 and any other viruses. This review article shed the light on the most important tips to boost the innate immune system, hence fighting pathogenic microbes including viruses. It is a well-known fact that viruses are very hard to be treated. The only successful method to kill viruses is by stimulation of the immune system. COVID-19 is a viral disease that spread very quickly to threaten the entire world (pandemic). Boosting the innate immune system would help a lot to fight this viral disease and this review article lists the most beneficial tips, which could help to prevent infection and even accelerate the cure.

KEYWORDS: COVID-19; Innate immunity; No effective treatment; Prevention; Tips

ABBREVIATIONS: ARDS: Acute Respiratory Distress Syndrome; CDC: Centers for Disease Control and Prevention; COVID-19: CO= corona, VI= virus, D= disease, and 19= 2019; FDA: Food and Drug Administration; IgA, IgG, IgM: Immunoglobulin A, G or M; PBMCs: Peripheral Blood Mononuclear Cells; PCR: Polymerase Chain Reaction; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; WBCs: White Blood Cells; WHO: World Health Organization

INTRODUCTION

Google Scholar was used as the main search tool for collecting data with regards to the topic "boosting immune response". These keywords have been applied while searching for scientific references, which include "boost immunity", "maximize immunity", "raise immunity", "doubling immune response", and "COVID-19". Further to that, certain well-known websites have been visited such as WHO and FDA to look at the most recent facts published concerning the global battle against the COVID-19 pandemic. The main source for the vast majority of the accessed references used in this review was downloaded from the Online Library of The University of Nottingham, UK.

Factors to Confront COVID-19

Prevention tips: These are well known which include sterilization, good hand washing, wearing facemasks, social distancing...etc. [1,2], because known prevention methods for COVID-19 are also published on the WHO and CDC websites [3,4]. These WHO's recommendations are still controversial but not well-established scientific truths. However, WHO was initially against facemask for the general public, then changed its policies for some reasons.

Note to the public: All the medicines used to treat COVID-19 are experimental and do not have FDA approval except a few

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medicines which are not fully reliable to 100% cure COVID-19 infection such as remdesivir, dexamethasone, convalescent plasma etc. Anyway, Some-COVID-19 drugs, such as hydroxychloroquine, even tend to slow down inflammation and immune processes in addition to ivermectin (FDA approved anti-parasitic drug) where there were claims to show fair antiviral effect against COVID-19 but this is still controversial.

Boosting Immune Response

It has been mentioned earlier that the solution to fight COVID-19 disease depends on prevention and raising immunity. Asymptomatic COVID-19 patients (people without any clinical symptoms but tested positive to PCR) are apparently resistant [5]. The interpretation for showing no clinical symptoms in asymptomatic COVID-19 patients was attributed to having a strong immune defense represented by significantly elevated levels of T and B lymphocytes (important in adaptive immunity) as well as high levels of NK cells (innate immunity) compared with symptomatic patients [6]. Moreover, single-cell immune analysis confirmed a strong immune response in asymptomatic COVID-19 patients who exhibited elevated levels of expressed NK cells' genes isolated from the peripheral blood mononuclear cells (PBMCs) samples and upregulation of interferon-gamma expressed in effector CD4+ and CD8+ T lymphocytes as well as NK cells [7]. Therefore, the author hypothesizes that boosting innate immunity may help to fight COVID-19 by showing asymptomatic status or at least developing a mild disease.

The most common prevalent type of immune response against COVID-19 within asymptomatic patients is "innate immunity" which is known as a frontline defense mechanism against any invading microbe [8]. Innate immunity consists of multiple antiviral factors such as phagocytes (mainly macrophages), plays role in phagocytic activity which engulfs any invading pathogenic microbe during early infection, thus plays an important role in innate defense mechanism [9], complement system, non-specific neutralizing antibodies (IgA), Natural Killer (NK) cells, certain cytokines such as type I and II Interferons (potent antivirals) and others [10-12].

An innate immune response may show an exaggerated level of cytokines produced by monocytes [9], which play a major role in respiratory damages in COVID-19 cases, that may be fatal in some cases due to cytokine storm as reviewed in the literature [13]. Cytokines' storm is curable to some point in COVID-19 patients because it can be inhibited by immunosuppressive medications such as steroids which are already used in the therapeutic protocols [14].

However, innate immunity-driven cytokine storm is not always the reason for death in COVID-19 patients because asymptomatic patients compared to symptomatic showed increased levels of mature neutrophils, T helper 17, and growth factors that are associated with cellular repair, whereas lower rates of monocytes and systemic proinflammatory cytokines in the peripheral blood [15].

Asymptomatic cases survived worldwide and no one died including those with mild symptoms. A possible explanation is that they had a powerful innate immune response that dealt with the virus early. Asymptomatic COVID-19 patients were about 80% examined positive to SARS-CoV-2 subjected to RT-PCR [5], in addition to some recovered from mild or moderate infection showed negative titers of IgM and/or IgG measured by ELISA [16]. Plausible clarification is that they possessed protective innate immune response represented by the activity of certain cells such as macrophages, NK cells [17-19], IgA [12,20], complement system, and certain activity of any anti-viral cytokines such as type 1 interferon or gamma interferon [21,22] and other known elements of innate immunity, which dealt with the virus properly and efficiently without shifting towards adaptive immunity, thus IgG was seronegative [16,23,24].

The question here is: how do we raise an innate immune response to face COVID-19 disease? How can we build a robust frontline immune defense mechanism (powerful innate immunity)? The answer is summarized by the following points:

Consumption of healthy immuno-fortified food, vitamins, and minerals: A detailed review article written by Mahmood and Al-Ameen [25] addressed detailed information about the main types of food beneficial to boost the immune response. The list of these immuno-fortified food, vitamins and minerals includes garlic [26], onions [27], citrus fruits [28], broccoli and spinach [29], red pepper [30], ginger [31], almonds and other nuts [32,33], turmeric [34], chicken soup, green tea and black tea [35], honey [36], yogurt [37], fish [38], red meat [39], avocado [40], vitamin D [41], vitamin A [42], zinc [43], vitamin C [42] and vitamin E [44]. The role of each of above mentioned immuno-fortified food is essential in defending against microbes (mainly viruses) which is represented by the activation of lymphocytes (both B and T cells) which works as a natural antiviral and are mostly used as immunotherapy (anti-COVID-19) as mentioned in the literature [45-47]. Above mentioned food activates T cytotoxic (CD8+T cells), which is the key factor for killing viruses (for example SARS-CoV-2, the causative agent of COVID-19) in addition to the neutralizing antibodies (immunoglobulins, IgM and IgG) which are secreted by plasma cells differentiated from stimulated B cells [48-52].

Drinking enough amounts of water raise immunity: Water is included in the composition of all the cells of the body (including immune cells) and its deficiency will cause a weak performance in those cells, especially white blood cells (immune cells). Therefore, adequate quantities of water must be drunk (3 to 4 liters per day) and it is preferred to drink it at time intervals short for no more than an hour to avoid intracellular dryness including immune cells [53]. For more information, see [54].

Avoiding alcoholic drinks raises immunity: Alcoholic drinks destroy and damage immune cells and it has been shown to have a very negative effect on the immune system; thus, avoiding them as much as possible is highly recommended. It has been observed that drinking alcohol can cause pneumonia, increase the possibility of acute respiratory distress syndrome (ARDS), which is one of the main dangerous outcomes of COVID-19 clinical symptoms [55,56]. In addition, it has been found that it causes the following: liver disease (cirrhosis), various cancers, increase risk of complications after surgery delays cure of infection, delay wound healing, increase risk of sepsis, and a long list of negative and harmful effects on the body [57-62].

Getting enough sleep: It has been notified that sleeping long enough and not staying up improves the functioning of the immune system cells, specifically T lymphocytes. T cells play a major role in fighting intracellular pathogens such as viruses, bacteria, and cancers [63]. In addition, adequate sleep reduces the release of stress hormones epinephrine and norepinephrine which improves the overall functioning of the immune system [64,65]. On the other

hand, staying up late reduces the levels of melatonin, which plays a crucial role in raising the efficiency and performance of the immune system. Thus, sleep deficiency causes weakening of the immune system [66-71]. For more information, see [72].

Reducing the level of stress: It has been observed that psychological pressure leads to destruct immune system and lower body resistance to various diseases. It has been shown that stress causes low levels of inflammatory cellular cytokines (protein substances secreted by white blood cells that perform multiple functions with an important immune response); [73-77].

Exercising regularly, which helps control weight and improves the immune system: Generally, physical exercise is very important and beneficial to the body and the immune system in particular. It has been observed that doing more exercises is associated with an increase in blood circulation activity, white blood cell functions and increases the body's resistance to diseases [78,79]. On the other hand, it has been detected that excessive exercise (especially bodybuilding) can lead to immune stress, muscle tear, and many other harmful effects [80-85]. For more information, see [86].

Avoid smoking (because it inhibits immunity): Smoking can destroy the immune cells, the immune system especially the respiratory system, and causes damage to the genetic material of the DNA of any type of mammalian cells. This is due to the presence of highly toxic nicotine and tar substances in the respiratory cells [87-90]. In a study, it has been observed recently that the severity of clinical symptoms of COVID-19 disease in smokers was doubled more than those in non-smokers. The symptoms included shortness of breath, suffocation, difficulty breathing, severe pain, and lastly, the duration of the disease in smokers is longer than in non-smokers, and finally, it was thought that it is one of the causes of death for patients is attributed to smoke [91,92]. On the other hand, studies showed that smokers are less affected by COVID-19 and express asymptomatic, mild, or moderate clinical symptoms and that was attributed to the antiviral effect of nicotine and tan in tobacco [93-95]. Therefore, smoking is debatable with regards to COVID-19 patients as reviewed by recent studies [96-98].

Smile and laughter raise immunity: It has been shown that smiles and laughter improve the performance of the immune system, reduce the secretion of cortisone, and increase the chance of a person's resistance to diseases [99]. This can be achieved via improving physiological and psychological functions, modifying moods, and eliminating the risks of stress and psychological pressure. Currently, it has been recommended to get rid of depression and other psychological diseases during this COVID-19 pandemic [100-107].

Optimism and a positive attitude raise immunity: It has been noted that spreading fear, panic, and anxiety shatters the body's immunity and makes viruses more virulent and deadly in the face of this weakened immunity [108-114]. It has been proven that optimism can improve the overall conditions of health of cancer patients. It has been found that optimists provide better health due to boosting the level of immunity [115,116]. Optimism boosts immunity by initiating some biological mechanisms. Optimism stimulates high concentrations of immunoglobulin A (IgA), a secretory antibody that works non-specifically against many microbes and plays an important role in innate immunity as described in a contemporary study [117]. Another mechanism by which optimism can boost immune defense mechanism is by inhibiting cortisol (a well-known immunosuppressive steroidal hormone) as well as stimulation of mononuclear cells (mainly monocytes and lymphocytes) to produce antimicrobial cytokines such as interferons and interleukins that play an important role in cell-mediated immunity, and thus raising immunity [117,118]. Moreover, it has been shown that optimism greatly improves general health conditions and might be a reason to survive longer than other cancer patients [108,119,120]. Thus, listening to bad news scares people, worries, and terrifies them, which leads to the destruction of their immunity due to the massive secretion of cortisol from the adrenal gland which is known as an immunosuppressive hormone [108,121,122]. Therefore, it is vital to avoid these frustrating things as much as possible.

Listening to music boost immune response and induce relaxation: Listening to music is one of the most important supporting activities to boost the immune system and that was proven by empirical research. A study conducted on psychological patients who suffered from variable mental health problems found that music cured depression and relieving anxiety as well as improved social resilience in the music-treated patients compared with control patients who have not been treated with music [123]. Listening to music can improve the overall health condition through improving mood [124]. Most Muslims believe hearing the Quran can change their mood to the best plus remove stress and anxiety, so it is an immuno-stimulant to boost immunity. Not only that, but music also has a magic effect on removing stress and many medical benefits and that was deeply investigated in a systematic review done on 1076 scientific articles, 18 of them were applied on 1301 patients [125]. Listening to music perioperative decreases the levels of cortisol which is a neuroendocrine substance, and its inhibition hugely improves the immunological response to surgery [125]. Listening to music could work in many directions that affect neurochemical systems which enhance motivation, induce pleasure, remove stress and arousal, boost immunity (improves overall psychoneuroimmunological status), and potentiate social affiliation [126,127]. The mechanism of action of music and how it has an impact on the immune response was reviewed by [127] who attributed the role of music in the expansion of lymphocytes (both B and T cells) as well as the increasing number of total immunoglobulins.

CONCLUSION

COVID-19 pandemic is a vital health dilemma that has been grown over a year ago. Up to date, there is no effective authenticated drug or vaccine for COVID-19. Thus, the ways of its fighting COVID-19 via well-established preventive measures and booster immune system. Boosting immune system achieved via good food supplement, drinking an adequate amount of water, avoiding alcohol consumption, cessation of smoking (debatable with regards to COVID-19), regular health exercise, and adequate sleep intake overcome stress and to be optimistic.

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