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Zinc may have a potential role in taste malfunctions treatment for COVID-19 patients

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Abstract

The novel COVID-19 virus has ongoing signs and symptoms, one of the signs and symptoms that is discovered recently is loss of taste, some pieces of research suggested that COVID-19 patients may have zinc deficiency however the main undiscovered concern is whether the virus is a causative or those patients had deficiency pre COVID-19, approximately they found 57.4% COVID-19 patients have low zinc serum levels which may indicate an advantage to administer a therapeutic approach for zinc deficiency for those patients. Pervious research experienced with common cold symptoms and zinc administration and resulted in conflicting data. More recently, Cochran review indicates zinc may be useful for common cold patients only if administered within 24 hours onset of symptoms. It was known previously for upper respiratory tract infections to cause loss of taste; this concern might be possible for COVID-19 patients further research and clinical control trails are needed for confirmation because its safety might be a concern.

Introduction

A novel virus has been reported in Wuhan, China on 2019 [1]. It is a disease caused by an immense family of viruses that cause symptoms ranging in severity from slightly acute symptoms such common cold to extremely sever symptoms and diseases such as Middle East Respiratory Syndrome (MERS-Cov) [2]. The WHO declared the disease caused by this virus has become a global pandemic with 66,729,375 confirmed cases and 1,535,982 deaths reported on December 8th2020. Nevertheless, there are ongoing data to investigate its signs and symptoms [3]. COVID-19 patients may have a cytokine storm which could be defined as an immense release of a variety of proinflammatory cytokines such as tumor necrosis factor- alpha (TNF-alpha), interleukin (IL-1b) and (IL-6) [4].

Zinc is an essential micronutrient in the body [4,5]. It plays a crucial role in the immune system in which it works as a signaling molecule as well as a basic compound for thymulin hormone which plays an important role in differentiation and maturation process of the T-cells inside the thymus gland [4]. This trace mineral may be ranked as the secondary abundant metal in the body [6]. The optimum daily zinc intake ranges would be 3 mg and 16 mg [7]. This mineral food sources are often considered as a primary source for human in addition to the breast milk during infancy [6]. This metal is absorbed through the gastrointestinal track via intestinal zinc transporters [6]. According to Nelms, *et al.* [8] the data for the beneficial effects of zinc for common cold patients are conflicting which raised a question for weather zinc may be useful for COVID-19 patients and what are the possible roles for it, since these two diseases may share some common signs and symptoms. For common cold, some findings suggested it may be useful for those patients, however other findings suggested it may be harmful, perhaps loss of taste is a very common drawback among common cold patients, and two interesting symptoms for zinc deficiency could be losing taste and male hypogonadism [7]. The aim of this journal article is to review some of the literature for a possible correlation between zinc and COVID-19 patients. Firstly, this journal article is going to discuss new symptoms for COVID-19 patients. Secondly, it will discuss zinc deficiency among COVID-19. Thirdly, it will present some of the findings for zinc in common cold. Then, it will present some data for male hypogonadism and COVID-19. Finally, it will present the suggested theory about COVID-19 which is it may cause zinc deficiency since it was known for zinc deficiency to cause male hypogonadism and loss of taste further research and clinical control trails are needed to confirm this suggestion.

New symptoms for COVID-19

There are ongoing data for the signs and symptoms for this novel virus. Patients have some common symptoms such as fever, cough and body aches [1]. Gauiter and Ravussin [9] elucidate two new symptoms for this disease that were not reported previously these are losing taste (ageusia) and loss of smell (anosmia) [9]. Passarelli, *et al.* [10] found that 81.6 % of COVID-19 patients present with ageusia, and 74.8 % presented with anosmia. Parma, *et al.* [1] suggest that COVID-19 may cause sensory-neural disruption [1]. Equils, *et al.* [6] illustrate the pathogenesis mechanism for ageusia for COVID-19 patients may be due to direct or indirect local toxic effect for the SARS-Cov-2 on the neural cells [6]. However, it might be well knowing for upper respiratory tract infections (URI) to be associated with olfactory disorders [1].

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Key words: *coronavirus disease 2019 (COVID-19), zinc, severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), Zinc Deficiency, Angiotensin-Converting Enzyme-2 (ACE2), upper respiratory tract infections (URI), loss of taste, hypogonadism, erectile disfunction (ED), tumor necrosis factor- alpha (TNF-alpha), interleukin (IL-1b) and (IL-6)*

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Zinc deficiency among COVID-19

Zinc deficiency appears into sight by a set of features such as weight loss, loss of taste and sexual negative side effects among males in which those who are zinc deficient may suffer from delayed sexual maturation and hypogonadism. Gustin which is a zinc metalloprotein carbonic anhydrase VI (CA6) presents in acinar cells of salivary glands such as parotid and submandibular less than the optimum secretion of salivary gustin result in a taste and smell function reduced [11]. Lab results indicating low zinc statues might be useful, however it may not reflect cellular zinc deficiency due to the internal homeostatic mechanisms. Nevertheless, the clinical effects of the deficiency can be shown regardless to lab results the normality. Jothimani, *et al.* [7] have done a prospective observational study lasted from seventeenth May 2020 to twenty seventh May 2020 by measuring fasting zinc levels for (n=47) COVID-19 patients. They found that those patients have low serum zinc levels which defined as a zinc level of <80 μg/dl compared to healthy counterparts who were the hospital staff members (n=45) with no comorbidities and those who participated were signed on an informed consent [7]. They found that almost 57.4% of those patients were zinc deficient and had high complications such as prolonged hospital stay [7]. However, there are some concerns that need to be pointed out such as the sample size was small to confirm this information and the authors did not indicate pre-COVID-19 zinc status, so it is not clear if it is a causation or an epiphenomenon making its difficult conclude on this topic. In addition, the study did not show if those patients were symptomatic COVID-19 patients or asymptomatic COVID-19 patients, but it was obvious because those patients were in the hospital. Yasui, *et al.* [12] claim low serum zinc levels were seen in almost all sever causes in Yasui's hospital, the causes were either clinical zinc deficiency or subclinical deficiency [12].

Despite the lack of data, some findings suggest zinc may have a beneficial effect for COVID-19 patients. To illustrate, in vitro experiments zinc demonstrated antiviral activity by a SARS-CoV RNA polymerase inhibition [13]. There are some indirect evidences that suggest zinc might has the ability to decrease the activity of a known receptor for SARS-Cov-2 which is angiotensin-converting enzyme-2 (ACE2) [13].

Alexander, *et al.* [14] point out about a possible positive outcome for zinc in those patients. They illustrated in their review about two cause reports that investigated zinc's role. In the first cause report, four COVID-19 patients ranging in ages between 26-63 years were treated with zinc lozenges salts. Dosages between 115 to 184 mg of zin per day during 10 to 14 days duration, and those patients were recovered. Another cause report from the same source Alexander, *et al.* [14] illustrated patients aged 38-74 who had gastrointestinal manifestation zinc sulfate administration in the dosage of 220 mg every day for 5 days duration with hydroxychloroquine and azithromycin resulted in recovery for those patients [14]. However, those two were cause reports which is difficult to make a solid conclusion based on. In addition, the former report did not indicate which type of zinc has been administered for those patients. Also, their pre-COVID-19 zinc status were unknown in this review. In addition, taste loss and further taste improvement were not mentioned in this review.

Zinc in common cold

Data may be contentious. Nelms, *et al.* [8] point out that there were conflicting pieces of evidence for a beneficial effect of zinc lozenges and nasal sprays for common cold as a treatment to reduce the disease's duration [8]. Nelms, *et al.* [8] report that zinc supplementation at the recommended levels (12.8 milligram of zinc or lozenge) for every 2-3 hours, within the primary 24-hours may reduce symptoms severity and duration, however, nasal spray that contains zinc might cause damage for smell sensation [8]. NIH [15] also points out zinc nasal spray may cause anosmia (loss of smell). There are concerns related to the exact safety for the cold zinc containing nasal sprays and lozenges [15]. Saper and Rash [5] claim current data do not support zinc usage for upper respiratory tract infection, however it may be tolerated with the normal recommended dosages. In 2013, a Cochrane review elucidates that zinc in the form of lozenges or syrup may have a positive outcome for common cold healthy people, however according to them it must be taken within the 24 hours of onset symptoms [16]. They conclude that it is difficult to make a firm recommended dosage and formulations that could be used for those patients [16]. Their point is a valid point because data are still scarce for zinc usage for common cold patients, however if those patents were given zinc from its natural food sources or tested for a possible deficiency and then treated accordingly, the loss of taste may be resolved further studies and clinical control trails are needed.

Male hypogonadism and COVID-19

The presences of hypogonadism and reproductive issues among males who are affected by COVID-19 may need to be considered for researchers specially with the known facts about the crucial role of zinc for males. On April 30th 2020 almost only 35 countries reported valuable data regarding gender prevalence in COVID-19 confirmed causes [17]. However, the influence on male urogenital organs by this virus is still not evaluated and assessed yet [18]. According to Bendayan, *et al.* [19] The SARDS-CoV-2 virus uses certain receptors to invade the human cells which are the same receptors believed to be expressed in the testis specifically in the sspermatogonia, Leyding cells and Sertoli these receptors are angiotensin-converting enzyme 2 (ACE2) [19]. Sansone, *et al.* [20] suggest that erectile disfunction (ED) among COVID-19 survivors might be a consequence for this disease. They conducted a review of the literature that aimed to investigate the reproductive health issues for COVID-19 survivor, they found that subclinical hypogonadism and endothelial dysfunction is present among these patients, and they recommended andrological assessment and treatment for them [20]. Giagulli, *et al.* [21] claim that COVID-19 seems to own unfavorable clinical impacts for infected males than females [21].

Conclusion

In conclusion, zinc deficiency causes signs and symptoms one of those symptoms are losing taste and to some extend male hypogonadism, in addition loss of taste is a common drawback among common cold patients and zinc has been used in the past for them, however the results were conflicting. There are some possible theories behind this issue that worth clinical trials and further studies one suggested theory could be COVID-19 may cause zinc deficiency as a side effect from the infection and thus those patients developed taste loss and male hypogonadism in the light of some data that are suggested zinc deficiency may be present with COVID-19 patients as well as some genders discriminations caused by this novel virus such as male reproductive system. Administering zinc for treating this deficiency might be useful, however the safety of zinc for those patients may be a concern due to the unknowing facts about this virus. We do not know about zinc's role and this novel virus yet and further research and randomized control trails is further needed.

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Conflict of interest

There is no conflict of interest.

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