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Hydrothermotherapy in prevention and treatment of mild to moderate cases of COVID-19

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ABSTRACT

COVID-19 is a new contagious disease caused by a new coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 is a disease that has reached every continent in the world; it has overloaded the medical system worldwide and it has been declared a pandemic by the World Health Organization. Currently there is no definite treatment for COVID-19. We realize that host immunity is a critical factor in the outcome of coronavirus 2 infection. Here, however, we review the pathophysiology of the disease with a focus on searching for what we can do to combat this new disease. From this, we find that coronavirus is sensitive to heat. We have thus focused on this area of vulnerability of the virus. The emphasis of this hypothesis is on the action of body heat—internal (fever) and external (heat treatment)—in activating the immune system and its antiviral activities, and specifically related to the coronavirus. We hypothesize from this review that heat treatments has the potential to prevent COVID-19 and to decrease the severity of mild and moderate cases of Coronavirus. We propose heat treatments for this uncontrolled worldwide coronavirus pandemic while studies are being done to test the effectiveness of heat treatments in the prevention and treatment of COVID-19.

Introduction

The first case of this new pathology appeared late in December 2019 as pneumonia of unknown cause in Wuhan, China. The cluster of new cases seem to be linked to a seafood wholesale market [1]. Further research identified the cause of this new pathology to be a new virus [2] officially called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of virus [3]. Cases of this disease have been reported in all continents and the World Health Organization declared it a pandemic the 11 of March 2020 [4]. This new disease is called COVID-19 which means coronavirus disease 2019 [5]. The new, current corona virus causes very diverse clinical symptoms from asymptomatic disease to severe acute respiratory syndrome [6] that may lead to death.

Discussion

Pathophysiology of the severe acute respiratory syndrome coronavirus

The epidemiological history of COVID-19 is that the virus was originally transmitted in Wuhan, China from a meat market that sold

animals. The virus enters the nose and throat where the virus finds cells that are rich in a cell surface receptor called angiotensin-converting enzyme 2 (ACE2) [7]. The virus requires the ACE2 receptor to enter the cell, the same as SARS-CoV-1 [8]. Person to person transmission is the way the infection continued to spread to others [9]. It spreads mainly via respiratory droplets in a manner similar to influenza but non-respiratory virus particles have also been documented in eyes, blood and stool [10].

The most common manifestations of the infection is at the prodromal phase and it can last a week or so. This phase of the disease includes fever, myalgia, dry cough, loss of smell and taste, fatigue and diarrhea. If the immune system can't stop the virus it will continue to attack the body further and develop dyspnea and lymphopenia as it attacks the alveoli in the lungs and other organs. The alveoli are especially vulnerable since they are also rich in ACE2 receptors that allow the virus into the cell [11]. The challenging patients continue to deteriorate and develop acute respiratory distress syndrome and super infections [12]. Even asymptomatic patients after CT studies (computed tomography) show bilateral ground-glass opacities [6]. One third of those infected developed blood clot abnormalities and an increase in D-dimer [13]. This abnormality may explain why diabetic and hypertensives have poor

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prognosis after contracting COVID-19 since those patients may already have previously damaged blood vessels [14].

The innate immune response seems to be the important factor that determines the outcome of COVID-19 for each individual. An important type of protein that helps regulate the activity of the immune system is the type I interferons (IFNs). These proteins elicit an anti-viral response involving IRF3/IRF7 antiviral pathways [15]. When secreted they stimulate macrophages and natural killer (NK) cells. In the case of viral infections, interferons are secreted by infected cells preparing the body against a possible viral infection. Previous research has documented how SARS-CoV-2 suppresses or delays type I interferons (IFN), specially in the initial infection [16]. It is thought that it suppresses the immune system which may explain why some people don't present with symptoms early in the disease, as interferon is also involved in producing fever (pyrogenic) [17]. A study analyzing the evolution of a mild case of SARS-CoV-2 showed a dramatic decrease of NK cells and monocytes, which seem to be a target of the virus [18]. Patients with lower response of IFN tend to have poorer prognosis and higher risk of death from coronavirus infections [19]. People with chronic diseases (cardiovascular disease, hypertension, obesity, diabetes, etc.) seem to be more prone to the infection with the SARS-CoV-2 [20] possibly due to the fact that SARS-CoV-2 infects also the endothelium and triggers inflammation [21]. Conversely, children have a strong immune reaction against viral infections [22] and that may explain why less than 2% of all confirmed COVID-19 infections in the USA are from children even though children are 22% of the entire US population [23].

Fever and artificially induced fevers

The pathophysiology of the coronavirus appears daunting but there is much we can do about it. The way to approach this unnerving disease is to understand and select a weak point of the virus and attack its weakness. Coronaviruses are vulnerable to heat, basic pH and acid pH [24]. The virus seems to like lower temperatures as it is more stable at 39.2° F [25]. We explore the potential effect that fever or artificially induced body heat can have on the infection.

The term hydrothermotherapy come from three Greek words—"Hudor," meaning water, "Thermo," meaning heat, and "Therapeia," meaning healing—Some authors called it hydrotherapy. It is the intelligent application of water in any form, including ice and steam, either internally or externally, for the healing of disease [26]. Hydrothermotherapy is a unique mechanism that creates an artificial fever in the human body. One benefit of fever in an infection is better survival of the host and another is a shorter duration of the disease [27]. Heat by itself has an antiviral effect. When a container of human cells and rhinovirus was immersed in a 113° F hot water bath, the heat suppressed the multiplication of the virus by 90%, but did not kill the human cells [28]. Infectious agents may trigger fever, which is a defense mechanism [29]. Fever is usually triggered when monocytes meet pathogens and this results in an increase of IL-1 [30], which is what triggers the fever response since IL-1 is a pyrogen [31]. IL-1 is also involved in the activation of the cellular and humoral immune response against the pathogen [30]. Fever promotes migration of leukocytes and neutrophils to the area where the pathogen is [29] and it activates T Cell function [32]. Genes involved in the activation of the interleukins have been identified. The most important pathway is the nuclear factor kappa B (NF-kB), which is responsible to activate IL-1, IL-6 and IL-8 and it has an effect on two other pathways—the p53 protein and the heat-shock factor protein 1 (HSF1) [33].

Hydrothermotherapy has been used by multiple cultures. The Finnish people for thousands of years have used the Finnish sauna and across the world there are other analogs of the Finnish sauna such as the Sentō and mushi-buro in Japan, the hammam in Turkey, the Mesoamerican temescal and the sweat lodges among native Americans [34]. Some of the oldest records point to 3000 BCE in India where they were giving heat treatments with steam baths [35]. Sauna is probably the

most studied hydrothermotherapy treatment [36]. The person sits in a wood room with a heater (electric or wood) with rocks on top that provides the heat. The Turkish bath tends to be humid while the Finnish sauna has high temperature and dry air [34]. The temperature tends to be from 176° F to 212° F at the level of the face [37] with a relative humidity of 10 to 20% [38]. Humidity is increased as water is poured over the hot rocks. The usual duration of the sauna among adults is between 5 and 20 min follow by a quick cool-down to stop sweating, studies show that the cool down stage increases WBC count [39]. Children also take a sauna once a week with their parents, at which time the baths tend to be shorter in duration (5–10 min) and with lower temperature [40].

In Finland some cool down moderately at room temperature while some enjoy rolling on the snow or jumping in ice cold water [41]. The rapid cooling has a positive effect on the cardiac and vascular functions [42,43]. However, patients with cardiovascular problems should not cool by immersion in cold water; they should use a gradual cooling method such as a shower [44].

During the sauna the body temperature is elevated to 102° F within 15 to 20 min. This causes dilation of blood vessels in the skin; it produced a loss of about 1 lb of weight due to sweating; it increased heart rate; and it reduced peripheral resistance [45,46]. The hematological effects of sauna are increases in hemoglobin, white blood cell count, and platelets within normal limits [47]. Sauna also decrease the level of Serum C-reactive protein (CRP) [48], a marker of systemic inflammation. High levels of CRP, i.e., high levels of inflammation, could have an adverse effect on immunity [49]; while lower levels of CRP are associated with less systemic inflammation. There is evidence to show that sauna reduce the incidence of the common cold [50]. White blood cells were increased in a small study (n = 9) after a single session of Finnish sauna; the response was greater in athletes and included increases in neutrophils and monocytes [51]. A cohort study of Finnish sauna users demonstrated a decrease in systemic inflammation and oxidative stress [52].

Another advantage of heat treatments is that hyperthermia treatments result in high levels of IL-6 without activating IL-1-beta or tumor necrosis factor (TNF) [53] potentially preventing cytokine storms (dysregulated immune response) because an increase of IL-6 by itself seems to decrease inflammation [54]. The isolated increase of IL-6 is the way exercise decreases inflammation [55], which is the same way for fasting [56] and for plant-rich diets [57]. The effect of hyperthermia on the coronavirus infection by way of the interferon function seems to be optimal at higher temperatures, 104.9° F [58]. Hyperthermia induces the synthesis of gamma interferon in cell cultures [59]. In rhesus monkeys hyperthermia increased alpha interferon and non-interferon antiviral factors [60]. All this possibly counteracts the effects of the virus since interferon has the ability to slow or stop viral infections [61]. Another possible mechanism of how hyperthermia may work against viruses is the increase of membrane fluidity in both virus and target tissues [62] that affects the specific viral pathogenesis related to release, assembly, penetration and attachment of the virus with the cell that it is trying to attack [63]. The benefits of the sauna are not only the benefits related to the immune system but also benefits on other systems including the cardiovascular [64], respiratory [65], and integumentary systems [66].

Cautions with the use of saunas have been documented, but they are uncommon. A review of deaths in Finland of people using the sauna from 1990 to 2002 shows that there were less than 2 cases per 100,000 inhabitants, but the conclusion was that the most common cause of deaths in saunas was the use of alcohol and that it should be avoided [67]. The role of saunas *per se* in death is unknown. A perspective on deaths related to saunas is that the risk of sudden death [68] and myocardial infarctions [69] are lower while taking a sauna than during other daily events. In other words, sauna may protect against sudden death and myocardial infarction. A separate study reported no health risks from sauna to healthy people from childhood to old age [70]. Electron

microscopy of the lungs after sauna documented how no damage happened to the airway epithelium [71]. Thus, the benefits of taking a sauna in comparison to the potential risks are overwhelmingly in favor of sauna for health in general and particularly in cases of mild infection with coronavirus. One absolute contraindication for sauna that Finnish researchers propose is high fever [41].

Hot baths are another means of heating the body and improving immune markers. A small study (N = 12) was done in vitro and in vivo [27]. The participants were submerged in hot water at 103° F in order to simulate an artificial fever and test its effect on monocytes and TNF- α . In the in vitro part of the study it was shown that the receptors CD14 and CD11b, that are helpful in infections, were increased after the water treatment. When the in vivo part of the study took place 3 h after the hyperthermia the response of monocytes to endotoxins was improved as documented by greater TNF- α release. The conclusion of this study was that hydrothermotherapy activates monocytes and prepares them to respond to infections [27]. A separate small study (N = 7) was designed to test the effect of hydrothermotherapy followed by a cold application on the immune system. The heat followed by cold therapy significantly increased the number of white blood cells, granulocytes, lymphocytes and monocytes. The researchers concluded that the brief cold following the heat treatment was effective in increasing the white blood cell count, the NK cell activity and the IL-6. Physical exercise before therapy had a synergistic effect on the immune system [72]. Hyperthermia stimulates cytokine release in a similar way as fever [60,61].

Large scale use of hydrothermotherapy

During the Spanish flu pandemic of 1918 [73] that killed 50 to 100 million people [74] there were health centers known as sanitariums for the treatment of disease and for health education in lifestyle [75]. Hydrothermotherapy was used in sanitariums as a means of assisting the body to combat various types of diseases [76,77]. The hydrothermotherapy used in these sanitariums were hot water baths, fomentations, steam baths and wet sheet packs. Mortality from the Spanish flu in the general public hospitals ranged from 13 to 40 percent [78]. It was stated that the Army camps offered the best treatment available against the Spanish flu [79] and the death rate from the pandemic at these hospitals where hydrothermotherapy was not used was 6.7% [79]. A report from that time showed that of the 1123 documented flu cases at the sanitarium 446 treated were treated as inpatients (receiving hydrothermotherapy) and 677 as outpatients (also receiving hydrothermotherapy). Only 1.3% of Sanitarium inpatients with the flu died and 3.8% of outpatient died [79]. Even though there are numerous uncontrolled factors to consider, hydrothermotherapy appears as a significant factor associated with survival from the Spanish flu.

There is a potential case of the benefit of hydrothermotherapy against COVID-19. The European Centre for Disease Prevention and Control of The European Union reported on 11 of June 2020 that in Europe there were an average of 226.7 ± 186 (mean \pm SD) cases of COVID-19 per 100,000 population for all member countries [80]. In our calculation, Finland and Estonia were then excluded from the other countries because sauna is part of the culture in these countries and it is practiced at least once a week among the population. Excluding Finland and Estonia from the rest of the European countries increased the average of cases in Europe to $232.9 \pm 191/100,000$. The number of cases per 100,000 population in Finland were 127.6 and 148.2 in Estonia. The average reported deaths from COVID-19 per 100,000 population were 18.3 ± 23.4 in Europe without Finland and Estonia, 5.9 in Finland, and 5.2 in Estonia [80].

There are numerous factors that determine the number of cases of COVID-19 in any community or country. Also, this report above is merely a report and not a study of cause and effect. It is of interest to us, however, to note that there is a lower than average number of COVID-19 cases in the two countries that practice regular heat treatments as

compared to the average for the other European countries—54.7% in Finland and 63.6% in Estonia as compared to the rest of Europe. Far more important than the lower number of cases is the remarkably lower number of deaths from COVID-19 in Finland (32.1%) and in Estonia (28.3%) as compared to the rest of Europe considered as 100.0%. It would be hard to compare worldwide data with other countries due to limited testing and reporting in other countries [81]. Nevertheless, the community use of heat treatments is consistent with a lower prevalence and a lower death rate from COVID-19.

How to heat the body against COVID-19

This report highlights the effectiveness of inactivating the coronavirus by heat, ideally followed by cold to stimulate the immune response. The emphasis is not on the method but on the fact that heat may inactivate the virus. The reality is that any method to heat the body is better than none. And a readily accessible method for the larger portion of the population is more effective than the best method that is accessible to relatively few. Following the model of Finland and Estonia of regular heat treatments followed by cold, we propose the regular use of home hydrothermotherapy as the means of hot and cold treatment of choice during this pandemic. It is a home heat treatment method that uses tools typically available in the home—water, a means for heating water, a large kettle with lid for steam, towels, a container for foot bath, and a chair or stool. A hot shower followed by a cold shower could potentially have some of those benefits. These home tools are accessible to most people worldwide.

The hypothesis—attacking corona virus infections with heat

All the evidence cited above may be reduced to two major conclusions: 1) elevating the body heat weakens the virulence of the virus and/or improves body immunity [24,25] and 2) the use of heat treatments (such as steam baths, sauna or hot baths using water 92°f to 104°f) appears to be associated with a lower incidence of viral infections and lower death rates from viral diseases including COVID-19, when applied for 5 to 20 min followed by cold (as shown by the Finnish and Estonian populations) [80,79]. The application of these modalities does not necessarily require expensive equipment. Constructing a sauna or paying to use it could be an expensive investment but hydrothermotherapy can also be applied with simple equipment such as pails, towels and hot water, things available worldwide.

We thus hypothesize that frequent treatments of heat followed by cold are the effective first line approach in the prevention and treatment of mild to moderate coronavirus 2 infections. We further hypothesize that if this approach is followed by large numbers of individuals in each community the impact of coronavirus 2 on the world population will be significantly decreased.

Conclusion

SARS-CoV-2 is a dangerous virus that has caused a world-wide pandemic. This virus, however, is susceptible to elevated body heat and elevated body heat also enhances the immune system. We thus hypothesize that frequent treatments of heat followed by cold are the effective first line approach in the prevention and treatment of mild coronavirus 2 infections.

We recommend for all stages of COVID-19 that the most accessible method of hydrothermotherapy interventions should be used. We urge that this hypothesis be implemented for the prevention and treatment of COVID-19 while we wait for results from studies designed to test the effectiveness of heat to improve the immune system function and treat COVID-19.

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Conflict of interest statement

None of the authors declare any conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110363>.

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