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Proposed Protocol for Self-Immunization against COVID-19

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Abstract

Prophylactically taking a small, less than preventative, dose of Hydroxychloroquine can improve an individual's odds against COVID-19 upon accidental exposure. This allows the patient to lead a normal life and acquire broad natural immunity through a mild infection. The infection should be detected and terminated by appropriate anti–SARS-COV-2 medicines as soon as possible to minimize asymptomatic spread by that individual.

This is the proposed hypothesis. It is accompanied by a sample regimen suitable for a clinical trial.

Introduction

The coronavirus SARS-CoV-2 continues to evolve. The emergency-authorized vaccines give only short-term protection against new variants. Vaccine-resistant variants are frequently more infectious than the earlier variants were. Eradication of COVID-19 is unlikely [1]. It is possible that variants escaping vaccine-elicited immunity, resistant to natural immunity, and more virulent than the current Delta variant, will arise soon. Although there are well-known treatments for COVID-19 and preventative protocols, many of which are based on Ivermectin [2], acquiring broad immunity is preferable for the majority of people.

This paper proposes a self-immunization protocol intended to allow individuals to live normal lives and to acquire natural immunity in a safer way than by simply hoping.

The natural immunity to COVID-19 [3] includes mucosal immunity [4] [5] and systemic immunity. No long-term mucosal immunity is elicited by the emergency-authorized vaccines, administered intramuscularly. Natural systemic immunity comprises antibodies, B-cells, and T-cells against about a dozen coronavirus proteins. The best emergency-authorized vaccines introduce only the spike protein to the body, and most of the neutralizing antibodies elicited by them target just a few small areas in the receptor-binding

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domain of the spike. Point mutations in or next to these areas sharply decrease the neutralizing effects of the antibodies and the vaccine-elicited immune response [6].

Methods

This is a theoretical paper proposing a practical COVID-19 self-immunization regimen, which should be clinically tested.

A person with no immunity to SARS-CoV-2 or only narrow immunity from a spike vaccine can acquire broad natural immunity, including systemic and mucosal components, by exposure to coronavirus spreading in the community, while living their life as normal, when not intentionally attempting to become infected. There is a risk of contracting more than mild COVID-19 in adults, especially with novel variants. Here, it is proposed to minimize such risk by taking a small dose of hydroxychloroquine (HCQ) pre-exposure.

HCQ strongly accumulates in lungs, especially in the lung epithelial lining. The HCQ lung to plasma concentration ratio can reach hundreds to one [7]. In severe COVID-19 patients, a ratio of 40:1 was detected after receiving just 400 mg of HCQ [8]. Ivermectin can accumulate in lungs only to the ratio 3-4:1.

Normally, SARS-CoV-2 infects the upper respiratory tract (URT) first, and then travels down to the lungs, where it achieves its highest load, both in concentration and absolute numbers. In the proposed regimen, HCQ is expected to protect the lungs while the virus is allowed to replicate in the URT for a couple of days. Conveniently, the nasal epithelium has a much higher concentration of ACE2 when compared with alveoli [9], thus allowing viral replication in a relatively safe part of the URT.

HCQ Prophylaxis Studies

Multiple studies of pre-exposure prophylaxis with HCQ, conducted in healthcare workers in India in 2020, have shown that such prophylaxis is very effective (reduces the risk of COVID-19 infection by 80–90%) when the HCQ dose exceeds 2400 mg, but proportionately less effective at lower doses [10] [11] [12] [13] [14] [15]. For example, [12] suggests that 1200 mg of HCQ are much more effective than the baseline 800 mg (4.5x fewer infections), 1600 mg are more effective (9x fewer infections and all infections are asymptomatic), and 2000 mg even more effective (30x fewer infections, all asymptomatic). One randomized controlled trial [13] measured infection by seropositivity and reported a 90% decrease in seropositive individuals among those with more than 2400 mg of HCQ in pre-exposure prophylaxis.

There are studies directly confirming that COVID-19 cases, breaking through pre-exposure prophylaxis with HCQ, are less severe than the average [16] [17]. One retrospective comparison of rheumatic patients, taking HCQ for RA control [16] found 7 deaths among 78 COVID-19 cases in the non-HCQ group. There were no deaths among 31 COVID-19 cases in the HCQ group. Another study of healthcare workers in India [17] have also shown lower rate of hospitalization (2 out of 7) and no severe disease among confirmed symptomatic cases on HCQ prophylaxis, compared with higher rate of hospitalization (9 out of 13), including two cases requiring oxygen, in the arm not on HCQ prophylaxis.

Post-exposure prophylaxis with HCQ was also very successful at preventing PCR-detectable infection. Given HCQ after exposure, none of 193 elderly (median age 82 years) hospital patients with comorbidities was infected, according to the observation [18] in February 2020.

Intermediate Conclusions

These and other studies suggest that using intermediate (sub-prophylactic) doses of HCQ, such as 800–1600 mg, should allow immunity acquisition by exposure and possible natural infection, while protecting the lungs and other tissues.

It is useful to dose HCQ for COVID-19 treatment and prophylaxis per kg of mass. Assuming a typical COVID-19 patient weighs 80 kg (rather than the standard 70 kg), a 400 mg dose is expressed as 5 mg/kg.

The considered sub-preventative load is 10–20 mg/kg. Too large an amount is likely to diminish the acquired immunity or prevent seroconversion entirely [13], while too low an amount would place the person at an undesirable level of risk. The exact dosage for an individual is a function of the individual vulnerability (calculated from the age, comorbidities, and the immunity status) to the virus variants likely to be encounters. It should be determined in clinical trials.

During a respiratory virus epidemic, individuals attempt to maintain their immune system, keeping it in good shape by moderately exercising, getting a good night's sleep, assuring their intake of vitamin D (preferably by exposure to sunlight), and by taking extra vitamin C and Zinc. Here, it is assumed that the person using this protocol follows these commonsense practices.

Today, effective rapid antibody tests (RATs, also known as lateral flow assays) are available. It is a good idea for any infectable individual to have these in the home and to know how to correctly use them.

Here, dominance of the current Delta variant is assumed. It has been reported that the Delta variant is distinguished by an incubation period of only 3–4 days [19]. When considering whether to do the self-

immunization, one should first evaluate his or her immune status. A middle-aged person who has had symptomatic COVID-19 within six months might be sufficiently immune. Recent (within three months) vaccination an mRNA vaccine also provides sufficient immunity. Otherwise, if possible, the person should take a commercial N-protein antibody test. Sufficiently immune individuals need not bother with additional self-immunization.

Proposed Self-Immunization Protocol

The person takes the loading dose of HCQ of 5 mg/kg per day for 2–4 days. No maintenance is needed for at least two months. After taking the loading dose, the person carries on with their normal life. The immunization starts when there is a community spread of COVID-19 or when the person is exposed to COVID-19 at an event.

The person self-tests daily with a nasal swab RAT. The RAT is expected to show positive results on or before the day when the nasopharynx viral load becomes infective to other people. It is expected that that will happen before symptoms occur because of preloading with HCQ. When the RAT becomes positive or the person feels COVID-19 symptoms, he or she takes one dose of Ivermectin at 0.2–0.4 mg/kg [20]. At this early time, this is expected to halt viral replication.

Of course, if the individual becomes sick (with more than very mild symptoms) and suspects COVID-19, he or she should contact a physician and seek normal treatment for COVID-19, possibly including antibiotics and/or Fluvoxamine.

If possible, the individual should take a commercial test for N-protein antibodies 3–4 weeks after detecting the infection, or if no infection has been detected for a month. The test is expected to come back positive.

Options and Modifications

Additional medications and/or nasopharyngeal sanitation might be used along with Ivermectin, as recommended in early treatment protocols [20].

An option for more vulnerable persons is to take a higher amount of HCQ with the intent to develop mucosal immunity without infection and seroconversion.

If the person was exposed to COVID-19 and knows the date of exposure, s/he can take Ivermectin 2–3 days after that date, regardless of the results of RATs.

Taking Ivermectin before getting infected terminates the attempt at self-immunization. Another attempt can start 4–8 weeks later.

RATs cannot be fully trusted. Currently, the best RATs detect SARS-CoV-2 only in 50% of asymptomatic cases [21] [22]. Yet, for higher viral titers enabling substantial transmission, RATs have an up to 87% detection rate [23]. Also, when used correctly, RATs give almost no false positives.

An individual can also launch this self-immunization protocol post-exposure by starting to take HCQ on the day of exposure and starting RATs 2–3 days later. Of course, this would work only if there were no community transmission, and the exposure can be accurately detected.

Zinc

In addition to its own anti SARS-COV-2 properties, HCQ is a Zinc ionophore. None of the mentioned prophylaxis studies [10] – [15] have used Zinc, but additional Zinc supplementation is likely to increase the effectiveness of HCQ. This subject needs additional research beyond the scope of this paper.

Remarks

If the person undergoing this self-immunization protocol becomes sick with COVID-19, pre-loading with HCQ makes the treatment with HCQ-containing protocols easier. Usually, HCQ is the slowest component in such protocols.

This self-immunization protocol should not be used close to vaccination or soon after contracting the COVID-19 virus. Contraindications for HCQ and Ivermectin must be respected.

Results

It is proposed to take hydroxychloroquine in a sub-preventative dose before being exposed to SARS-CoV-2 to acquire broad natural immunity while living a normal life. For additional safety, the individual should self-test for infection daily. On detection of infection by a test or by symptoms, the individual should take Ivermectin and/or another quick and safe anti SARS-COV-2 medicine.

Discussion

It important to stress that the parameters, determining the risk of developing more than mild COVID-19, are changing quickly. New variants and subvariants appear all the time. For a vaccinated individual,

decay of the antibodies, the danger of ADE, and possible acquisition of additional immunity by exposure are additional factors.

It seems that SARS-CoV-2 has been getting more infective in parallel with large part of the population acquiring some immunity against it, both trends partially compensated each other and became underestimated.

It should be noted that with COVID-19, individual immunity is not two states (immune or vulnerable), nor is it a range from naïve to immune. Uniquely in the history of epidemics, the population has multiple combinations of vaccination (V) and infection (I): neither, V, I, IV, and VI. Immunity caused by each of these events rapidly changes in time and in relation to coronavirus variants.

Daily RATs and quick anti-viral treatment are needed because the person undergoing this self-immunization regimen is likely to have fewer symptoms at the same nasopharynx viral load, compared with an unprotected person. If left undetected or untreated, this person might become a "silent carrier," as with individuals who become infected after receiving an intramuscular vaccine [24]. Testing would be unnecessary if all individuals in the community (a dorm, a village, military quarters etc.) undergo such immunization at the same time.

May 2020 Indian MOH advisory

An early Indian government advisory [25] mistakenly recommended that healthcare workers take a small HCQ loading dose of 800 mg, followed by a 400 mg maintenance dose weekly. The initial dose was too low to prevent infection, and a sufficient protective level was achieved only after 2–4 weeks of maintenance [12]. The mixed success of that advisory has likely seeded confusion about the effectiveness of HCQ as a prophylaxis. With hindsight, it should have been recommended to take a loading dose of 2,800 mg and then a 200 mg weekly for maintenance.

No Competing Interests

The author declares no competing interest. No funding was provided for this work.

Disclaimer

This is not medical advice.

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