



Mass Chemoprophylaxis with Ivermectin against COVID-19 Pandemic: Review and Authors' Perspective

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Abstract

The current COVID-19 pandemic is a catastrophic health challenge widely spreading all over the world, caused by coronavirus "SARS-CoV-2" infections. It has been started for more than one year ago; and panic and fear are still dominated among people because of the ease with which infection spread among communities, as well as the high morbidity and mortality. Many preventive measures have been taken to prevent its spread, including physical body distancing, wearing face masks, etc. Unfortunately, the frequent mutations of the virus have made it resistant to usual measures such as use of convalescent plasma from patients cured from infections. Several vaccines have been developed and administered as an urgent measure to combat the infection. Such vaccines could be not available for all countries especially that of low- and middle income. Moreover, the time for development of an approved vaccine in the normal situations that might reach about 10 - 15 years, is not available for vaccines used in the current pandemic. On the other hand, ivermectin, a drug approved by FDA as a broad-spectrum antiparasitic drug, has been clinically tried in prophylaxis of COVID-19 patients' contacts and proved high efficacy. It is a safe and effective drug and has given tremendous results in protection against acquiring COVID-19 infection in all studies. Therefore, we suggest that ivermectin could be used for mass chemoprophylaxis without mentioned risks on populations. This measure might assist in combating the current COVID-19 outbreaks.

Keywords: COVID-19; Coronavirus Infection; Current Pandemic; Ivermectin; SARS-CoV-2

Introduction

COVID-19 is an emerging catastrophic health event widely spreading all over the globe. It results from infection by a novel virus belonging to coronavirus family of zoonotic pathogen named

Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2). It appeared for the first time in China in December, 2019 and then widely spread all over the world [1].

Most countries all over the world have reported large numbers of cases. COVID-19 virus has infected more than 110 million confirmed cases with at least 2.5 million deaths worldwide up to 3 March 2021 [2]. It has been expected that the numbers of cases could rise dramatically in the next few months if there are no measures to be taken from all countries at the same time to stop the vicious cycle of infections. Therefore, it is essential to break the circle of infection that continues from December 2019 till present. The aim of the current review was to highlight the trials made in this regard focusing on role of ivermectin in prophylaxis.

Methods

The previous literature has been reviewed on the various scientific journals and websites including PubMed, Google Scholar and others using keywords including SARS-CoV-2, current pandemic, convalescent plasma, COVID-19 vaccines, prophylaxis, ivermectin and clinical trials.

Results and Discussion

The route of virus transmission among populations occurs directly through respiratory droplets and secretions of infected cases or carriers, and indirectly through touching the contaminated inanimate surfaces and hence infection transmission through mucous membranes. Based on the epidemiological studies, the incubation period of the SARS-CoV-2 ranges from one to fourteen days; and the virus has been found to be contagious in the carriers or asymptomatic patients [1].

The clinical manifestation of patients with COVID-19 varies from mild symptoms such as fever and cough to severe picture including pneumonia, severe acute respiratory syndrome and perhaps kidney failure with a high mortality rate. Elderly patients and those suffering from other co-morbidities such as diabetes and heart and lung diseases are noticed to be at a higher risk of developing severe morbidity and high mortality rate following COVID-19 [1].

Unfortunately, the available management and vaccine prophylaxis of the SARS-CoV-2 infections have not been well-developed yet. The available medications are mostly supportive only [3].

To overcome the pandemic, most countries have tried to prevent the infection spread through adoption of some hygienic health instructions and measures including physical distancing, using face masks, avoiding the crowded areas, respiratory etiquette at sneezing and coughing and frequent hand cleaning. Moreover, such measures included patients' contacts tracing, isolations of suspected

cases, and re-arrangement of infrastructures of health care systems for treatment of severely infected patients who are in need for hospitalization, oxygen therapy and mechanical ventilation [1]. All these strategies might require a long-term health educations' programs to raise the health knowledge about COVID-19 among people for proper recognizing and practicing the protective measures.

In the absence of definite or accurate urgent COVID-19 management, the application of such protective measures could be essential to break the vicious circle of infections' transmission through potential prevention of the people from being infected and hence minimizing the disease dissemination.

Based on use of convalescent plasma (CP) as a successful therapy for previous epidemics and outbreaks for one century since 1918, it has been also recommended for the current pandemic [4]. Despite approval of FDA "US Food and Drug Administration" for use of CP in treatment of COVID-19 cases, however, the report published by University of Minnesota after reviewing ten randomized controlled studies has concluded that it has no effect regarding survival or even improvement of the clinical status of patients [5]. In addition to the insufficient investigations regarding CP use in COVID-19 outpatients, the collected data from clinical trials on hospitalized patients have not proved CP efficiency for treatment of cases [6,7]. Use of CP for prophylaxis is based on antibodies developed in body of a donor recovered from COVID-19 and transmitted to the recipient in order to neutralize SARS-CoV-2 spike protein [4]. On the same line, the Sweden authority added that such herd immunity could protect the more vulnerable groups of populations. However, such policy has been failed with more cases of deaths resulting from COVID-19 in Sweden appearing to be higher than reported in a country like Germany by about five times [8]. This leads to direction of the research efforts to development of vaccines depending on mechanisms other than antibodies that might develop in human body following previous infections.

In context of development of vaccines against COVID-19 viruses, many of them have appeared. They included Moderna "RNA-based", Inovio "DNA", Sinopharm "inactivated vaccines" and AstraZeneca "nonreplicating virus-based vectors" vaccines [9]. All these vaccines have been approved as emergency use. The normal time for the development and production of vaccines in normal situations to be approved for human use ranges from ten to fifteen years. The previously fastest developed vaccine was that of mumps; and took about five years. However, in this emergent pandemic and due to

its urgent need, the time has been reduced to few months in order to help in saving the population from the danger of increasing morbidity and mortality. All current vaccines don't pass through the full approval process; and instead approved for emergency use especially for the most vulnerable persons and those in front lines of combating infections such as health care members [10]. Thorough experimental "pre-clinical" investigations as well as vigilant clinical trials are essential to produce safe and effective vaccines in order to avoid the possible serious adverse effects. Therefore, all individuals have been requested to assign an informed consent before taking vaccinations. All current vaccines are still under study and assessment. This might not be completely clarified before passing some years.

Despite the wide spread of vaccination against COVID-19, the WHO has stressed on the importance of continuous taking precautions. Presence of virus mutations might limit the efficiency of the existing vaccines. Moreover, the extent to which vaccines protect the persons is not yet clearly identified. Therefore, it has been suggested to continue the precautions after vaccinations including wearing face masks, keeping a physical distance at least one meter from others, cover cough and sneezing and clean hands [11].

Ivermectin is essentially a broad spectrum antiparasitic drug; previously used for treatment and control of many parasitic diseases including filariasis, malaria and onchocerciasis [12]. In April 2020, the Monash University in Australia suggested the drug as a possible treatment for COVID-19 [13]. Meanwhile, many studies and clinical trials have confirmed the use of ivermectin as a potential chemotherapeutic drug against spread of coronaviruses. These trials have begun in Egypt on May 31, 2020 [14]. Thereafter, the trials and studies confirmed the trend towards use of ivermectin for prophylaxis against the current pandemic [15-20]. Use of ivermectin might save the globe from the current pandemic if used in mass prophylaxis. It is an available, cheap and safe drug; previously approved by FDA. It is suggested to be administered for prophylaxis at one dose of 200 - 300 µg/kg repeated two days later [20].

Mechanism of ivermectin is suggested to be through inhibition of the host importin α/β -1 nuclear transport proteins, that form the key for process of intracellular virus' transport [21]. Moreover, it might protect the human cell membrane from the attachment of spike protein of SARS-CoV-2 [22]. Antiviral broad-spectrum of ivermectin in vitro against viruses causing some diseases such as yellow fever, HIV, Zika and dengue has been interpreted that the

drug could be a host-directed agent [21,23-25]. Other authors stated that ivermectin has anti-inflammatory properties could be of benefit in combating COVID-19 [26-28]. Despite such in vitro activity, some authors denied any clinical benefit for ivermectin in protection against these viruses [29]. The WHO also said that the evidence is inconclusive; and added that ivermectin could be used only for treatment [30]. On the contrary of this line, a study from Colombia didn't support use of ivermectin in the treatment through investigation including 400 patients [31].

On the same line of previous authors who recommended ivermectin use for mass treatment of parasitic diseases [32]. we also suggest it but for mass chemoprophylaxis of the current COVID-19 pandemic based on the previous mentioned studies which used it for the same purpose. The WHO declared ivermectin as a safe drug and could be used a large scale [33]. We agreed the opinion of other authors that the ivermectin could be administered for prophylaxis from COVID-19 until effective and safe vaccines become available [34]. Lois., *et al.* in a multicenter study proved effectiveness of ivermectin in treatment COVID-19; and added that such effectiveness is more in early stages than in delayed ones [35]. These results support the evidence of ivermectin use in chemoprophylaxis before spread of coronavirus within human body and hence establishment of its serious complications that might be the cause for mortality. COVID-19 causes multiorgan dysfunction in severe cases. The dysfunction might involve acute failure of lungs, kidneys, liver and cardiovascular system [36].

Unlike vaccines, using ivermectin for prophylaxis does not give long immunity for the individuals but might provide temporary protection against the current pandemic. Therefore, we suggest it to be administered for populations of a locality, all of them, at the same time. It could be taken at a single dose; could be repeated after two or three days. The dose is recommended according to body weight (BW) as follows: 15 mg for person of 40 - 60 kg BW; 18 mg for 60 - 80 kg BW and 24 mg for those of more than 80 kg BW [20]. The reported side effects are minimal reported in few percentages of population; and includes diarrhea, abdominal pain, dizziness and sleepiness [17,20].

Conclusion

To date, the accumulated data demonstrating the efficacy and safety ivermectin use against COVID-19 infections support its immediate use on large scales based on the minimal risks versus

great benefits' calculation associated with the current pandemic. Therefore, it might be the time to capitalize on potential of use of ivermectin. It could be adopted as an effective low-cost alternative to other measures such as vaccines especially in low- and middle-income countries in view of their low resources and huge population size. All health efforts must be occupied in saving lives and controlling the pandemic in these countries and hence all over the world. In this case, until a proper safe and efficient vaccines become available, it might be suggested to be used in mass prophylaxis to protect lives and to end the dilemma of such pandemic crisis.

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Conflicts of Interest

There are no conflicts of interest.

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