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Combating 2019-nCoV Amidst the Pandemic Scare

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Abstract

2019-nCoV is the third consecutive coronavirus spread during the last 2 decades, but this time, unlike the previous two occasions, has achieved a pandemic proportion threatening widespread loss of human lives and a massive setback to the global economy. The situation warrants drastic measures in terms of preventing the spread of the virus and treating the virus-infected patients. The development of a new vaccine is a time-intensive option. Although efforts are underway to find possible pharmacological options, e.g., chloroquine, hydroxychloroquine, existing antiviral agents, etc., in the meanwhile we may work on the combinatorial interventional approach of combining drug therapy with passive immune therapy. It would be prudent to use a convalescent serum therapy approach with the serum from COVID-19 patients who have recovered from the infection.

Keywords

Coronavirus, COVID-19, Immunotherapy, Passive, Chloroquine

1. Introduction

At the time when I am writing this manuscript, more than 76,000 2019-nCoV infected patients have died, out of a total of more than 1,362,000 cases reported around the world in more than 190 countries, and the number is increasing relentlessly every hour of the day [1]. From amongst the remaining patients, 94% (nearly a million patients) have mild condition while 5% of patients are seriously ill. These figures are alarming and warrant drastic measures to stop the situation from sliding down further to prevent any human catastrophe. Although concerted efforts involving the researchers in both academia and pharmaceutical industries are underway to restrain the spread of infection and find its treat-

ment, there is little insight in terms of vaccination or pharmacological options for the treatment of 2019-nCoV infected patients [2]. Several anti-viral drugs with the diverse mechanism of action, attacking the virus by interfering with its attachment to the cells to its replication and exit from the infected cells, are currently being assessed for their efficacy against 2019-nCoV [3]. The latest breakthrough in the pharmacological management of 2019-nCoV infection has been reported with the use of chloroquine (CQ) and hydroxychloroquine (HCQ), which has given some hope amidst the existing COVID-19 scare [4]. CQ and HCQ are the semi-synthetic derivatives of quinine; cinchona bark-derived alkaloid with proven antimalarial activity although these anti-malarial drugs have nearly lost their clinical use due to the malarial parasite developing resistance [5]. Encouraged by the data from QC and HCQ against SARS-CoV [6] [7] and their successful use in Wuhan, China, a research group from Marseille, France has published the results of a non-randomized open-label single-arm study in confirmed cases of 2019-nCoV infected patients. The patients received 600 mg daily dose of hydroxychloroquine (in three divided doses of 200 mg each) with or without azithromycin in hospitalized patients [8]. The data showed 70% of the HCQ treated patients as virologically cured on day 6 as compared to 12.5% control patients from another center who declined to be treated with the study protocol. Additionally, treatment with azithromycin synergistically enhanced the effect of HCQ. Efforts are also underway to screen the existing armory of antivirals against 2019-nCoV. Wang *et al*., have reported that HCQ combined with nucleotide analog remdesivir was effective to inhibit 2019-nCoV *in vitro* [9]. Currently, 2 phase-III randomized open-label trials (NCT04292899; NCT04292730) sponsored by the National Institute of Health (NIH), are in the phase of enrolment to assess remdesivir in persons with COVID-19. Similarly, Europe is also starting clinical trials involving 3200 patients for the assessment of some anti-viral agents including remdesivir and CQ [10].

Incidentally, chloroquine has been included in the guidelines issued by the National Health Commission of the Peoples' Republic of China (NHCPRC) for the treatment of 2019-nCoV caused pneumonia. This short paper discusses the possible use of passive immunotherapy with chloroquine and its derivatives as a combinatorial therapeutic intervention for 2019-nCoV infected patients.

2. Coronaviruses

Coronaviruses constitute a large family of enveloped, positive single-stranded RNA viruses, which are mostly found in the animals but some of them have potential infectivity in the humans with pathogenic consequences, mostly related to the upper respiratory tract. 2019-nCoV is the third major spread of coronaviruses after Severe Acute Respiratory Syndrome (SARS)-CoV and Middle East Respiratory Syndrome (MERS)-CoV during the last 2 decades, inflicting heavy losses in terms of human life, as well as a serious global economic setback [10] [11]. Whereas both SARS-CoV and MERS-CoV were of zoonotic origin, the ori-

gin of 2019-nCoV is still debatable [12].

3. Convalescent Serum Therapy for Passive Immunization: A Viable Option for COVID-19 Patients

Passive immunization strategy is not new to the treatment of both bacterial and viral infections as it started in the 20th century with the use of animal sera to passively support the compromised immune system of patients using specific antibodies from an exogenous source. Subsequently, with the advancements in the purification and fractionation technology, the use of animal sera was replaced with the human-derived sera [13]. However, since the inception of hybridoma technology by Kohler and Milstein in the early 80's and the subsequent advent and progress made therein, the use of monoclonal antibodies (MAbs) and their derivative fractions have substituted the use of animal and human sera for many diseases. MAbs provide a renewable source of preparations with high specificity and standardized potency. Currently, more than 80 FDA approved MAb preparations are available in the market for patients with pathological conditions encompassing from cancer to cardiovascular pathologies [14]. Recent advancement in the passive immunization approach is the use of the chimeric antigen receptor T-cells (CAR T-cells) approach [15].

The passive immunization approach may be given serious consideration as a viable option to passively immunize the 2019-nCoV infected patients by convalescent serum therapy wherein serum obtained from the patients who have survived and recovered from the infection can be used [16].

Passive immunization offers the patient a short-lived protection, which may vary in duration from a few weeks to a few months. The use of human serum has been extensively studied in culturing of the donor cells for *in vitro* expansion and has been preferred over animal serum to enhance their immunological acceptance by the recipient post-engraftment. Similarly, autologous patient serum is regularly used as a medium to suspend cells for transplantation in cell-based therapy procedures. The use of convalescent patient serum is surely a superior choice in terms of curtailed immunogenicity as compared to blood plasma preparations due to their depleted protein contents. The situation warrants optimization of protocols in accordance with the existing Good Manufacturing Practices to initiate a drive to collect 250 - 300 ml blood from nearly 293,000 convalescent patients to secure nearly 4.5×10^7 ml of their precious serum that may be enough to treat the patients with an active infection under the prevailing circumstances. Moreover, combining convalescent serum therapy to enhance the compromised immune system of the patients with the pharmacological intervention using CQ, HCQ, and anti-viral agents etc., the combinatorial approach may allow the researchers to treat 2019-nCoV infected patients. While pharmacological intervention will provide anti-viral effects, serum therapy will be supportive for the depleted immune system of the patient. The use of combinatorial approach will allow ample time to researchers to develop an anti-2019-nCoV

vaccine, assess the effectiveness of the existing anti-viral drugs, and search for effective novel molecules against the novel coronavirus without the further loss of human lives.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations and Acronyms

2019-nCoV= 2019 novel Coronavirus
Chloroquine= CQ
COVID-19= Coronavirus disease-19
Hydroxychloroquine= HQ
Middle East Respiratory Syndrome (MERS)-CoV
MAbs= Monoclonal antibodies
Severe Acute Respiratory Syndrome (SARS)-CoV