An overview of possible solutions putting an end to the COVID-19 pandemic

Saina Adiban Afkham[1,2], *Amirhossein Hessami*[1,3], *Amene Saghazadeh*[1,4], *and Nima Rezaei*[4,5,6]

[1]Systematic Review and Meta-analysis Expert Group (SRMEG), Universal Scientific Education and Research Network (USERN), Tehran, Iran; [2]Department of Biotechnology, Islamic Azad University (IAU), Tehran, Iran; [3]Student Research Committee, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran; [4]Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran; [5]Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran; [6]Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Tehran, Iran

Abstract. In early 2020, a novel coronavirus, SARS-CoV-2, started to spread throughout the world. The World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) as a pandemic on March 5, 2020. This 2020's pandemic has to date caused about 200,000 deaths and is still affecting the lives of people worldwide. No solitary solution can overcome the multidimensional challenges associated with the problem of COVID-19. Here, we provide a rapid overview of possible solutions offered by the epidemiological, pharmacological, immunological, and artificial intelligence fields of science on the COVID-19 pandemic. The simultaneous application of all these solutions might bring the world close to an end to the COVID-19 pandemic.

Key words: COVID-19, solution, epidemiology, immunology, artificial intelligence, pandemic

Introduction

There have been lifechanging pandemics in the history of humankind, including but not limited to the Athenian Plague 430 (B.C.), the Antonian Plague, the Justinian Plague, and the Black death as historical examples of pandemics, and the Spanish flu, HIV pandemic, Swine flu, H1N1/o9 pandemic, and Ebola outbreak as modern ones. These outbreaks have contributed to economic, political, and social changes that determined the way the world goes (1). A pandemic refers to community-level outbreaks resulted from human-to-human transmission in two or more countries in one World Health Organization (WHO) region (2). The use of the word 'pandemic' is case sensitive as it can lead to misuse of resources and related consequences. On March 5, 2020, the WHO declared the coronavirus disease 2019 (COVID-19) as a pandemic caused by a novel coronavirus, SARS-CoV-2, while the economic cost of the COVID-19 outbreak exceeded two trillion U.S. dollars on March 6, 2020 (3). The possible sources of costs include workdays lost due to illness, a shock to population and labor force, fear of infection, which lead to a decline in consumer demand, and costs related to disease prevention (4). The COVID-19 outbreak has also imposed an excessive pressure on the healthcare workers in particular due to extended work hours, potential quarantines, and assignments outside their practice area.

Epidemiological Solutions

Programs controlling respiratory infection outbreaks include pharmaceutical and non-pharmaceutical interventions (NPI). The use of NPIs in the early stage of a pandemic, when no effective vaccines or pharmacological interventions are available yet, is necessary to reduce the spread of infection. These interventions include isolation, social distancing, personal protective measures (hand hygiene, mask-wearing), social distancing, and remote healthcare (5). Many countries involved by the COVID-19 pandemic have quarantined cities, and put certain restrictions in place. From the viewpoint of epidemiology, three different scenarios might direct us to an end of the pandemic: herd immunity, track and trace, and total lockdown (6).

Herd Immunity

Herd immunity happens when an adequate number of people get infected and, therefore, will become immune to the infectious disease, and this immunity is enough to slow down the spread of the disease (7). This scenario aims to constitute a large immune population: "you're going to let the virus run entirely and then ultimately the virus will slow down at the point that it is has infected a substantial segment of the population so that it starts to slow its spread" as John Daley explained (6). Under the current condition that there is no specific treatment for COVID-19, the strategy of the herd immunity causes the high cost – that is, the lives of the elderly and at-risk populations (7).

Track and Trace

It is another strategy that applies to small and isolated areas: "You basically look around at any infection you can find, work backward to find out who were all people they had been in contact with, test them, and if they test positive, isolate them" as described in (6). Simulation models confirm that contact tracing and case isolation would be beneficial for controlling COVID-19 (8).

Total lockdown

China successfully used the strategy of total lockdown in Wuhan for controlling COVID-19 pandemic (6). However, this method raises economic and social issues like bankrupting local businesses and a possible shortage of essentials.

Pharmacological Solutions

There are 260 clinical trials registered in Clinicaltrials.gov and 781 trials registered at the WHO International Clinical Trials Registry Platform (ICTRP) until April 3, 2020 (9). Numerous companies are working separately toward finding a drug for COVID-19 (10). The currently available pharmacological options for COVID-19 are medicines used for the treatment of previous outbreaks, including the Middle Eastern Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) (11).

Chloroquine: An 80 years old antimalarial agent

Chloroquine is an old antimalarial drug that can interfere with the pH-dependent steps and thereby result in antiviral effects against coronaviruses. It also can exert anti-inflammatory effects by reducing interleukin-6 levels. Studies confirm the efficacy of Chloroquine in reducing SARS-CoV-2 replication and controlling the infection (12) and suggest inhibition of attachment of the SARS-CoV-2 viral spike to gangliosides as a possible mechanism of action of this agent (13). Chloroquine offers a relatively safe drug at a reasonable cost for the treatment of COVID-19 (14). Clinical studies provide evidence of viral load reduction with the use of hydroxychloroquine (a derivative of chloroquine) in patients with COVID-19. However, patients receiving hydroxychloroquine did not differ from patients not receiving that in clinical improvement. Potential side effects of hydroxychloroquine include arrhythmia, QT prolongation, and cardiotoxicity, especially in critical cases. Further randomized trials are necessary for the assessment of the efficacy of chloroquine and its derivative, hydroxychloroquine, in patients with COVID-19 (15). At present, these drugs should be prescribed with caution under cardiac monitoring, daily ECG evaluation, and twice-weekly blood testing (16).

Remdesivir: A 21st-Century Development

Remdesivir has shown its antiviral effects against RNA viruses, including SARS-CoV and MERS-CoV (17). In an *in vitro* study by Wang *et al.* (12), this agent showed promising results in inhibition of SARS-CoV-2. It acts as an RNA-dependent RNA polymerase inhibitor interfering with RNA replication of coronaviruses (18-20). The compassionate use of Remdesivir could confer benefits for patients with COVID-19 (21). It is currently under investigation for its efficacy in randomized clinical trials (15).

Lopinavir/Ritonavir: An HIV medication for COVID-19

Lopinavir and Ritonavir are antiretroviral protease inhibitors which their combination has shown efficacy in treating human immunodeficiency virus (HIV) infection (22). This combination was also effective in improving the clinical outcomes of patients with SARS (23). However, a clinical trial showed no superior efficacy of Lopinavir/Ritonavir compared to the standard care in patients with COVID-19. Conversely, observational studies showed that Lopinavir/Ritonavir was effective in lowering body temperature and improving abnormal biochemical indexes (24). Overall, future research is needed to resolve controversies on the use of this combination for COVID-19 (15).

Immunological Solutions

Adaptive immunity solutions

WHO announced that there are 41 candidate vaccines (25) and nine companies working on COVID-19 vaccines (26) until March 13, 2020. A vaccine is known as useful when it can induce humoral immunity and lead to the production of neutralizing antibodies. However, the induction of cell-mediated immune responses is beneficial in viral infections as well (27). Potential targets for a vaccine against viruses include killed whole virus, live-attenuated viruses, viral subunits, virus-like particles, viral vectors, and nucleic acid vaccines (27, 28). The process of development of new vaccines comprises an exploratory stage, pre-clinical stage, clinical development, regulatory review and approval, manufacturing, and quality control (29). It is, thus, reasonable that it takes at least five years to obtain a vaccine with a satisfactory overall coverage rate (30). Then, for the implementation of an optimal vaccine at national levels, years of research are required to identify and reduce the potential harms of a vaccine. It should be noted that "A rush into potentially risky vaccines and therapies will betray that trust and discourage work to develop better assessments," as Shibo Jiang expressed (31).

Passive immunity solution

Adoptive immunity solutions are useful, but they take time to be developed. Under critical conditions, like the current COVID-19 pandemic, one possible solution is the use of passive immunization, which has been successfully used for treatment and prevention of viral infections, including Ebola, Hepatitis B, and HIV. By transfer of antibodies, passive immunization would help to treat the infection by blocking viral entry to cells, enhancing cytotoxicity by natural killer cells, neutralizing virus directly, or inducing the complement system (32).

Convalescent blood products (CBP), including convalescent plasma (CP), convalescent whole blood (CWB), and convalescent serum (CS), are a method of passive immunization and have been under attention in large epidemics (33), such as Ebola, SARS, and H1N1 (34). FDA has approved this method for treating critically ill patients (35), and the early clinical studies have shown promising results (36). It has, however, limitations, including the risk of infection transmission to healthcare personnel, lack of adequate donors, and the risk of transfusion-transmitted infection (33). This method is yet needed to be assessed in larger trials.

Artificial Intelligence Solutions

During the COVID-19 pandemic, the importance of digital healthcare like telemedicine and the power of technology for better problem solving have been revealed. Artificial intelligence (AI) offers a means of integration between different fields of science that can facilitate problem-solving and complex decision-making.

AI for Prevention

AI techniques can simultaneously process data that comes from multiple sources in various countries. Data analysis of patients with COVID-19 would allow healthcare workers to offer up-to-date prevention recommendations (37). Machine learning approaches can be used for the analysis of clinical data from COVID-19 patients, lead to the earlier and more valid diagnosis of patients with COVID-19, and therefore help track the spread of COVID-19.

AI for Diagnosis

The healthcare systems are turning to AI-based methods to control and monitor COVID-19. For example, they have installed AI systems that detect a feverish person's face with a simple facial scan (38). AI was also beneficial in the diagnosis of COVID-19 patients by processing chest computed tomography (39) and even by detecting abnormal respiratory patterns (40).

AI for Treatment

The use of AI in bioinformatics provides us with a more precise structure of the causative agent of COVID-19 pandemic, SARS-CoV-2, and its possible mechanisms of pathogenesis. It would help the process of vaccine development and drug discovery to be more successful (41). AI-based systems can also be used to identify and even prioritize therapeutic candidates for COVID-19.

Conclusion

Here, we reviewed solutions for the 2020's pandemic of COVID-19. Epidemiological solutions should be used in the early phases of a pandemic to reduce infection transmission. While pharmacological and adoptive immunity solutions to the problem COVID-19 are still in infancy and it would take time for them to become evolved and ready for application to humans. As for the previous infectious outbreaks, passive immunization has shown promising results in patients with COVID-19. Finally, AI-based technologies offer an exciting means to improve productivity and accelerate the process of vaccine development and drug discovery for COVID-19.

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Correspondence
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Prof. Nima Rezaei
Children's Medical Center Hospital,
Dr. Qarib St, Keshavarz Blvd
Tehran 14194, Iran
Tel: +9821-6692-9234
Fax: +9821-6692-9235
E-mail: rezaei_nima@tums.ac.ir, rezaei_nima@yahoo.com