

IDENTIFY THE CURRENT TRENDS RELATED TO THE TREATMENT AND PREVENTION OF COVID- 19

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Abstract

The novel coronavirus (COVID-19), SARS-CoV-2 is a severe pandemic infecting people throughout the globe. First originated from Wuhan, China it has affected almost every country of the world and is still spreading very rapidly. Most of the countries are adopting various procedures of prevention such as isolation, quarantine and proper clinical care of the infected persons. An important task for scientists and researchers is to find an efficacious treatment for the deadly disease. Currently, various agents such as corticosteroids, hydrochloroquine, convalescent plasma, and vaccines are being studied to treat COVID-19 patients.

Key Words- COVID-19, Drugs, Remdesivir, Hydrochloroquine, Vaccine

INTRODUCTION

The novel coronavirus is a new type of virus that's part of the Coronaviridae family. It was previously referred to as COVID-19 or 2019 coronavirus. The SARS-CoV-2 virus is composed of a single-stranded RNA that's surrounded by various proteins. It was first identified in China in 2019. The coronavirus has been considered a global health emergency by the World Health Organization. As of April 2019, it has caused over 200 million cases and killed almost 4.5 million people.

The infection of COVID-19 spreads very rapidly through direct contact with the droplets released into the surroundings from an infected person while sneezing and coughing. The virus also spread when an individual touches a surface contaminated with the virus as the virus survives for several hours on surfaces when it comes in contact with them. The common symptoms of the disease include fever, cough and difficulty in breathing. In severe infections pneumonia and acute breathing problems are evident leading to death in many cases. However, scientist and researchers around the globe are still making immense efforts to clearly understand the pathogenesis of the SARS-CoV-2 infection. In the absence of a definite strategy for its management, majority of the countries are following various procedures such as enormous testing, contact tracing, isolation and quarantine procedures along with implementing compulsions such as social-distancing, usage of mask and sanitizers etc. All these measures have been effective in slowing down the pace of the spread of the disease. Therefore in order to effectively manage this newly emerged pandemic there is an urgent need for newer and advance diagnostic, prevention and treatment strategies throughout the world.

The present research review highlights the major advances in therapeutics and vaccine development that have been used against the COVID-19 infections throughout the globe.

1. Convalescent Plasma Therapy

Convalescent plasma is the plasma from an individual who has successfully recovered from COVID-19 infection. It is a passive immunotherapy has been used in the treatment of various infectious diseases in the past but its effectiveness in case of SARS-CoV-2 is still being studied. In the current pandemic situation the convalescent plasma can be an easily accessible source of antiviral antibodies. This strategy has been found to be effective in reducing mortality rates and duration of hospitalization in patients suffering from SARS (Soo *et al.*, 2004). Similar results have been observed in COVID-19 patients (Chen *et al.*, 2020). Convalescent plasma containing SARS-CoV-2-specific IgG antibodies is transfused in patients which can deactivate virus and by the activation of the complement system help in the elimination of virus (Langhi *et al.*, 2020).

However, various significant aspects of CP therapy are of prime concern before its application on patients with maximum efficacy. These aspects include the dose, time and frequency of this passive immunotherapy. Standardization of appropriate amount IgG and neutralization antibodies is necessary for maximum effectiveness. Early application of the therapy, at the inception of symptoms, is an important aspect which can be helpful in increasing the effectiveness of CP therapy. In a study on SARS patients who received Convalescent Plasma therapy before 14 days post infection, showed that the therapy was more effective during this time duration. Therefore indicating that early administration can be more efficacious.

2. Recent Drug Development

The introduction of a new drug requires a prior clinical assessment for its safety and efficacy before its use in the patients. Thus, the outburst of corona pandemic forced the scientist and researchers to scrutinize the currently available drug regimen for corona treatment. They have also achieved some success in this regard and various antiviral, antiparasitic and hypertensive drugs have been found to be effective. All these drugs can be classified into two major categories:-

• Drugs against the viral pathogen

a. **Remdesivir:-** Remdesivir is an antiviral drug that has been shown to be effective against various types of viruses. It is a nucleotide-dependent polymerase inhibitor that can be used to treat patients with respiratory syncytial virus infection. Gilead Sciences has developed Remdesivir for the treatment of Ebola virus infection. It has been tested in various non-human models. Remdesivir works by activating nucleoside triphosphate metabolites which in turn obstructs the activity of RNA polymerases. Although the drug is still undergoing clinical trials for the ebola treatment, its intravenous administration in patients suffering from COVID-19 reduced the recovery time duration by 31 percent. However, the mortality rate was not reduced to a significant level. This is also suggestive of the significance of administration time and dose of the drug as well as the fact that this drug alone is not sufficient enough to control the infection and prevent mortality (Alanagreh *et al.*, 2020; Rosa *et al.*, 2020). Combination of Remdesivir with other drugs can be another alternative for the treatment of COVID-19. It has been found that during acute infection various inflammatory cytokines are produced at a much higher rate than normal i.e. the cytokine storm, which causes a positive feedback on various immune cell. Thus the incorporation of an anti-inflammatory agent can prove to be very helpful in this regard. Baricitinib is one such agent which is being investigated in combination with Remdesivir.

b. **Hydroxychloroquine:-** Hydroxychloroquine is commonly used for the treatment of systemic sclerosis, arthritis, and malaria. It has anti-inflammatory properties and is considered an effective treatment against certain infectious diseases. Studies have shown that hydroxychloroquine can prevent SARS-CoV-2 infection. It can also trigger an anti-inflammatory response by suppressing the terminal glycosylation of an ACE2 receptor. This drug can also be used with azithromycin to treat COVID-19.

c. **Lopinavir-ritonavir combination:-** This combination drug is used to treat HIV infection in adults and children. It works by combining with other antiretroviral drugs. A study showed that adding lopinavir-ritonavir to ribavirin reduced the chances of adverse clinical effects among patients with SARS. In vitro and in animal models, lopinavir-ritonavir has shown activity against respiratory diseases like Middle East respiratory syndrome (MERS).

d. **Aldehyde based Indole-2-carboxamide compounds:-** These two drugs are known as 11a and 11b, which are Aldehyde-based compounds that can target the main protease of SARS-CoV-2. In vivo and in-vitro studies have shown their potential to prevent infection.

e. Other Drugs- Host Focused

The severity of the respiratory distress experienced by patients with SARS-CoV-2 depends on the level of pro-inflammatory cytokines that they produce. Currently, various drugs are being used to improve the condition of these patients.

Some of them are:-

a. **Tocilizumab:-** A monoclonal antibody known as tocilizumab is expected to improve the lives of people with COVID-19 by preventing the onset of cytokine storms and regulating the body's temperature.

b. **Prednisolone and Tacrolimus:-** A number of drugs known as steroids such as tacrolimus and prednisolone can also be used to treat COVID-19. These agents can inhibit the growth of pro-inflammatory cytokines in the body. It has been theorized that these substances can help lower the severity of the disease. Clinical trials are currently being conducted to see if these drugs can decrease the pathological expression of COVID-19 in patients.

c. **Lisinopril and Losartan:-** A targeted approach to the renin-angiotensin-aldosterone system (RAAS) can help minimize the chances of infection during COVID-19 treatment. Studies show that anti-ACE drugs could be helpful in treating COVID-19 patients. One alternative strategy is to use human ACE2, which is a soluble protein that can convert angiotensin II to angiotensin.

d. **Camostat mesilate**:- Camostat mesilate is a drug that can be used to treat patients with chronic pancreatitis and postoperative reflux esophagitis. It has been shown to inhibit the development and spread of SARS-CoV in a mouse model. The drug acts by blocking the host protease TMPRSS2, which is a key component of the human coronavirus.

e. **2-deoxy-D-glucose (2-DG)**:- Various organizations, including the Indian Defence Research Organization and Dr. Reddy's Laboratories, have collaborated to develop 2-DG. According to reports, it has been effective against SARS-CoV-2. 2-DG is indicated for the treatment of covid-19 patients suffering from respiratory failure. It is believed that this drug can improve the patients' recovery rate and decrease their supplemental oxygen dependence. 2-DG can be used as a light-based therapy to reduce the viral replication during the early stages of the disease.

3. Stem Cell Therapy

Stem Cell therapy is one of the significant Cell-based therapies, is an important approach towards treatment of diseases for which designing a treatment regimen has been quite problematic and challenging. Studies have shown that stem cells can resist viral infection caused by the expression of certain genes. Hematopoietic stem cells protect themselves against the infection of the oncolytic Myxoma virus. Although many countries have started clinical trials related to the use of stem cell therapy for treating SARS-CoV-2 infection, the obstacles to this therapy's path are still significant. Mesenchymal stromal cells are known to have high potential due to their low invasive procurement procedure and their safety and efficacy. Different sources of MSCs are known to contain different components such as bone marrow, cord blood, adipose tissue, and peripheral blood.

4. Chimeric Antigen Receptor T-Cell Therapy

Chimeric antigen receptor or CAR-T therapy is a promising procedure that uses a patient's own cells to attack cancer. Through this process, the CAR-T cells can recognize and bind to a tumor antigen. CAR-T therapy is a type of cancer immunotherapy that targets B cell malignancies. It has been shown to be effective against various types of cancers and infectious diseases. In 2011, A study conducted on CAR-T cells revealed that they could target the corona virus. They exhibited a potential comparable to the recovery of CD8 T cells from SARS-infected patients. Although CAR-T cells can be used to treat SARS-CoV-2 infections, their use has limitations. For instance, they can't be used to kill COVID-19 cells due to their pathogen-specific T cell receptors. Instead of using viral transduction, CAR-T cells could be engineered through mRNA electroporation. The CAR-T cells should also be able to overcome the toxicity caused by cytokine storm, which can increase the severity of an infection.

5. Vaccines

The development of a vaccine involves a lengthy and expensive process. This process is usually carried out due to the high attrition rates and the number of candidates. A new pandemic model can provide a more flexible and adaptable approach to the production of vaccines. The growth of vaccines against SARS-CoV-2 has gained pace due to the significant pandemic issue that has arisen in recent years. Various innovative approaches have been utilized in the vaccine development process. In 2003, certain SARS-CoV-2 vaccines were initiated in human clinical trials to minimize the time needed for the development of the vaccine.

The first human trial of a novel RNA-based vaccine was conducted by Moderna Therapeutics in 2013. The company was working on developing a series of vaccines for various infectious diseases. Instead of animal tests, scientists conducted human trials based on the results of previous studies. This procedure saves time and allows them to conduct studies on humans. CanSino Biologics, a company based in China, launched a vaccine candidate based on the company's studies on the adenovirus. Other companies also started developing similar vaccines. A clinical trial for BTN162, which is made up of the nucleic acid RNA combined with a glycol-containing lipid nanoparticles, is expected to start within the next couple of years. Other developers of mRNA vaccines are Pfizer and Altimmune. A live-attenuated version of the adenovirus is in development by India's Serum institute and Codagenix. Meanwhile, the Geno-Immune Medical Institute in China is working on developing two other vaccines that use the same strategy.

The selection of the most effective method of vaccine development is still a debatable issue with numerous vaccines such as covaxin, covishield, sputnik etc being widely used in the vaccination program throughout the world. A successful development of a vaccine for large-scale production requires the involvement of various clinical trial phases.

CONCLUSION

COVID-19 is a dangerous emerging infectious disease caused by SARS-CoV-2 and characterized as atypical pneumonia. New drug development or exploring the already used drugs, plasma and stem cell therapies, vaccines are the pivotal intermediations which can greatly

help in curbing this global pandemic. The first step in stopping the spread of the infection is to develop a diagnostic test that can detect the infection rapidly and accurately.

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