

Emerging Therapeutic Options for COVID-19

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ABSTRACT

BACKGROUND

COVID-19, the “pandemic”, “public health crisis” etc., are the news headlines every morning which is threatening the people and developing a feeling of fear and anxiety amongst the people in almost all the countries across the globe. Scientists, doctors and all other health care professionals are making continuous and tremendous efforts in searching and developing different ways to control the outbreak of the pandemic viral disease. Also, development of new drugs, testing efficacy, and clinical trials of the old available drugs and efforts for development of vaccination for COVID-19 to prevent its occurrence in the near future is still ongoing. But unfortunately, there exists no single particular approved / recognized treatment or drug for the COVID-19 patients yet. This review article is aimed at enlightening most of the preventive measures and treatment options that are available and described in the literature.

KEY WORDS

Covid-19, SARS, Prevention, Treatment.

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BACKGROUND

Corona Virus Disease - 2019 or COVID-19 which was earlier known as 2019 novel corona virus (2019 - nCoV) or severe acute respiratory syndrome corona virus 2 (SARS - CoV-2) originated in animals such as bats and spread throughout the world. First evidence of such disease is from Wuhan city, Hubei Province, China in the month of December 2019. Emergence of this virus from China to other countries of the world is considered as life-threatening public health crisis worldwide and later was announced as pandemic by WHO (World Health organization).¹

The clinical characteristics of COVID-19 are unpredictable that ranges from no symptoms to acute respiratory distress syndrome (ARDS) and multi organ dysfunction. Fever, cough, sore throat, headache, fatigue, muscle pain and difficulty in breathing are the commonest clinical features. Conjunctivitis seen in some patients. Thus, it is difficult to distinguish it from other respiratory infections. In a division of patients, in the first week or its end, the disease can progress to pneumonia or respiratory failure and eventually death. It affects elderly population more as compared to young. This is because aging is associated with increased risk of functional dependence leading to frequent hospitalization and increased mortality. This in turn leads to poor quality of life and thus there is need for long term and higher healthcare facilities.^{2,3}

Different treatment options starting from symptomatic treatment to the definitive one and from simple pharmacological agents or supportive therapies to the invasive therapies are mentioned in the literature and also tried in the positive patients as well as suspects of COVID-19. In-vitro studies are also carried out for development of new drugs and vaccines. This article focuses on compilation of all such available treatment options and discussing their efficacy and effectiveness in the treatment of COVID-19. Also, we are not attempting to recommend any of the treatment as none is approved by the WHO yet.

Prevention

Prevention is better than cure. As rightly quoted, the first step in the treatment of COVID-19 is its prevention and control of the spread. Transmission of the virus from one human to another can be prevented by certain simple tools of prevention. It includes three important aspects; a) Isolation b) Quarantine c) Social Distancing and Community containment.⁴ Adequate isolation play crucial role in prevention of disease by restricting the transmission of the virus from one person to another.¹

Adequate Isolation

Isolation can be described as the separation of the infected persons from the non-infected ones or healthy individuals or non-infected but patients with debilitating diseases who are prone to any opportunistic infection. Isolation rooms with negative pressure in the hospital set ups are helpful in this purpose.⁴ As the incubation period of the disease is longer isolation is must to reduce the shedding of the virus during the incubation period. The mean incubation period was found as 5.2 days to 12.5 days at different confidence intervals in a study by Qun Li.⁵

Quarantine

It is an important tool in controlling of any communicable disease since olden times. Quarantine implies interruption in the social contact. People are restricted at their present place till the situation gets under control. This practice was done in Italy in way back in 14th century when ships arriving at Venice port with plaque-infected passengers the ships were anchored at ports.⁶ Also, in the year 2003, during the SARS epidemic in China quarantine was implemented and it was a successful preventive measure for control of SARS disease.⁷ As the clinical features of COVID-19 are similar to SARS, quarantine is considered as effective preventive measure here also.

Social Distancing and Community Containment

Reduction in the interactions between people is termed as social distancing. It helps in prevention of transmission of virus in people who are yet to be diagnosed or asymptomatic. Also due to failure of identification of such patients; they are not isolated but carry a potential risk of transmission. Social distancing is important tool in such cases.⁴ These measures are considered important where disease is known to have a community spread. But it is not sufficient in controlling the disease, community containment should be practiced which means ensuring only vital supplies and restricting a wide population such as a region, place or city.⁸

TREATMENT OPTIONS FOR COVID-19

Symptomatic or Supportive Therapy

As definitive treatment is yet to be developed and approved, the first line therapy for the COVID-19 positive patients is the symptomatic relief of the symptoms. Supportive therapy is important for boosting the immunity. It includes proper nutrition and hydration of the body. Screening of the patients with symptoms but negative for viral testing should be considered.

Respiratory Support

Under respiratory support comes oxygenation. According to the "Diagnosis and Treatment of Pneumonia caused by COVID-19" (updated to version 6) issued by National Health Commission of the People's Republic of China currently due to lack of antiviral therapy, supportive and respiratory treatment is focused.² Decreased ventilation causes increase in pCO₂ and decrease in pO₂ levels. During apnoea stores of oxygen falls rapidly. So, oxygenation helps in maintaining the balance.^{9,10} Almost all positive patients of COVID-19 responded well to the oxygen therapy as they mainly suffer from hypoxia and pneumonia like symptoms. For the patients with refractory hypoxemia, WHO recommended ECMO therapy that is Extracorporeal Membrane Oxygenation.¹¹

Pharmacological Agents

No particular pharmacological agents or drugs are currently approved for Corona Virus Disease-2019 (COVID-19). Although some authors have been tried, recommended and done some clinical trials using the available drugs. These drugs are described in the literature by many authors according to

their effectiveness in treatment of COVID-19 cases. Some of them are described as follows:

Anti-Viral Agents

As we know no drug is yet approved for COVID-19. Some of the anti-viral agents that were previously used and successfully cured diseases such as SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome), on the basis of experience of these drugs in SARS and MERS they are also tried in COVID-19 cases and the results were variable. Drugs which were used includes the protease inhibitors such as ribavirin and lopinavir-ritonavir. Studies by Chen N et al. have shown that ribavirin alone was less effective. Outcomes were enhanced when ribavirin was used along with lopinavir-ritonavir combination.¹²

In other studies, antiviral agents such as neuraminidase inhibitors-oseltamivir, ganciclovir, lopinavir-ritonavir were used in combination therapy and were given to children. Results of the study by Xu XW showed that all the children recovered and there was no need of intensive care in such children who were on this antiviral therapy.¹³ Such antivirals either existing or new antivirals can respond rapidly but one should consider the neurological side effects due to them. In a study by Balwani M et al. they used 2 new antivirals for treatment of HCV (Hepatitis C Virus) infection which were sofosbuvir and daclatasvir but they stopped it later because data was not available about the neurological side effects.¹⁴ Further studies and clinical trials are required to recommend a particular anti-viral drug.

Anti-Malarial Agents

Chloroquine and hydroxychloroquine are the known anti-malarial drugs and are commonly used for the treatment of malaria from many years till date.¹⁵ Studies and clinical trials showed that this drugs are effective in the treatment of SARS as well as COVID-19. Various mechanisms of action were described for the working mechanism of the chloroquine in viral diseases other than malaria. Mechanism of action includes inhibition of pH-dependent phases in the process of replication of the viral DNAs, immunomodulatory effects such as suppression of the factors like TNF-alpha and Interleukin 6.² Combination of certain drugs with chloroquine have also shown improved results than using chloroquine alone. For example, when chloroquine was used along with azithromycin (a drug used for severe respiratory diseases and upper respiratory tract infections) in an open-label non-randomized clinical trial, results showed that this is a synergistic combination and is effective against COVID-19. Also azithromycin is known to be effective against EBOLA virus as well.¹⁶ Other authors also mentioned use of systemic corticosteroid treatment such as methylprednisolone¹⁷, antifungal agents and monoclonal antibodies therapy¹⁸ for the treatment of COVID-19. Success rates were variable and no promising benefits were mentioned.

Convalescent Plasma Therapy

Kai Duan et al. in their study checked the viability of convalescent plasma (CP) to treat COVID positive patients. The results were obtained from 10 cases and showed that one dose of CP - 200 ml was well tolerated by the patients. Also, it could

significantly enhance the neutralizing antibodies which in turn leads to disappearance of viremia in 7 days. Clinical symptoms and para-clinical criteria rapidly improved within 3 days. These results indicate that CP can serve as a promising rescue option for COVID-19 but other studies and recent updates also stated that there are complications. So it is still a controversy. The optimal dose, time, clinical benefit of CP therapy needs further long-term investigation in well controlled trials.¹⁹ Further clinical trials and studies are required to come to a concrete conclusion.

CONCLUSIONS

COVID-19 outbreak has challenged social, economic, medical as well as public health sectors of almost all the countries of the world. Rather than developing fear and anxiety, it is the duty of each and every individual to prevent and control the spread at individual level. As a health care professional, responsibility is little more on us. Future impact of the condition is still questionable. Therefore, apart from complaining about the difficulties that we are facing due to social distancing and lockdown, efforts should be made to prevent the further spread and extension of the pandemic. Further interventional studies and clinical trials for the approved drugs for COVID-19 are required. Early development of the vaccination will also help in reducing anxiety amongst people.

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