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Review Article

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Review on Overview of COVID-19 Treatment Strategies

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ABSTRACT

Pneumonia like illness was caused by the novel coronavirus, designated as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 can be easily transmitted through coughs and sneezes of infected persons, or if comes in contact with a contaminated surface. In 2020, the coronavirus disease 2019 (COVID-19) was declared a global emergency. Its prevalence and fatality rate are quickly rising, but treatment options for this deadly disease remain restricted. The pandemic of COVID-19 necessitates the quick testing of new therapeutic options. According to the data, hydroxychloroquine is the first drug used to treat disease. The antiviral agent's like umifenovir, remdesivir, and fevipiravir are thought to be the most promising in terms of improving the health of infected people. Many randomised and controlled clinical trials are being conducted to better validate the safety and efficacy of these agents in the treatment of COVID-19.

Key-words: Antibiotic therapy, Acute Respiratory Syndrome, COVID-19, Novel coronavirus, Severe Acute Respiratory Syndrome

INTRODUCTION

The new unknown pneumonia-like illness started spreading in Wuhan in December 2019, the capital of Hubei Province in the People's Republic of China, which was named as 2019-nCoV by WHO on February 11, 2020. It was caused by the novel coronavirus, designated as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1-3]. Till now over 3.47 Crores confirmed COVID-19 cases and over 4.77 lakh COVID-19-related deaths have been reported in India [4]. It was believed by the Epidemiologists that the Seafood Wholesale Market in Wuhan and its trading of live wild animals was the point of origin of SARS-CoV-2 [5]. Asymptomatic People can also spread the virus as they remain contagious for up to 20 days [3].

It became very difficult to manage the rapid and global spread of SARS-CoV-2, so there was an immediate urgency to discover promising targets for the treatment of COVID-19. There were no approved drugs against SARS-CoV-2. Drug development in these urgent situations was not an appropriate option so there was reusing of already-approved drugs, which might help to treat the disease.

Drug development approach- COVID-19 treatment was urgently needed at the time of the pandemic and uncontrollable situation of the World. Initially, the nature of this virus was not known, all diagnosis was made clinically and according to radiographic findings. There was no cure by antibiotic so all other common respiratory infections were excluded as an antibiotic was not working and the situation became uncontrollable and fatal in some cases. Later on, many hospitals and health centres developed well-equipped labs to detect COVID-19 disease by both Molecular and serological methods.

Some of the studies mentioned the policy of first identifying symptoms of COVID-19 and then using the drugs that are used for those symptoms, then the diseases are correlated with the symptoms that are developed in COVID-19 patients, and the drugs related to that disease are prescribed to treat COVID-19 disease [6].

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Some studies mentioned that for effective and safe treatment, drug repurposing (repositioning) is a promising approach [7].

Drug development is a multistep process, it includes concept, laboratory preclinical testing, clinical trial development with phase I to phase III trials that typically require more than five years to market the drugs with proper safety and efficacy of the new compound. Laboratory testing requires continuous research on microorganisms and animals, filing for regulatory statutes, such as via the FDA, to initiate clinical trials of new drugs on humans, the multistep procedure for the approval and marketing of the new drug.

Drug re-purposing (Repositioning)- Till now the US Food and Drug Administration (FDA) approved no specific therapy for COVID-19 so a new policy known as drug repurposing was done in which the use of many previously approved drugs, were an efficient approach to drug discovery.

For effective and safe treatment, drug re-purposes (repositioning) is a promising approach. During the COVID-19 pandemic, drug repurposing is the clinical research process of rapidly screening the safety and efficacy of already existing and approved drugs for other diseases and is analyzed to be used for the people with COVID-19 infection. Drug repurposing has several advantages over drug development; repurposed drugs are generally safe for hospitalized COVID-19 people, long term clinical trials are not needed to obtain endpoints proving safety and post-infection efficacy with no serious side effects. It can be rapidly and easily supplied in the market, hospitals worldwide in less time and is cost-effective [8].

The different clinical trials are done and still ongoing by the WHO named Solidarity that compares single and dual treatment like namely, remdesivir, lopinavir/ritonavir, lopinavir/ ritonavir with interferon beta 1-alpha, and chloroquine or hydroxychloroquine (now not used) [9,10].

Different drugs proposed for Covid-19 Treatment- For effective and safe treatment, drug repurpose (repositioning) is a promising approach. The proposed analysis intends to provide a list of already-existing and approved drugs that could show promise in treating COVID-19.

Anti-malarials- Two antimalarials, Chloroquine and Hydroxychloroquine having anti-inflammatory and immunomodulatory activities, have shown inhibitory activity for SARS-CoV-2. It was proved in studies on SARS-CoV-1 and MERS-CoV [11]. These medicines have positive in vitro clinical trials but have limited data for use [12].

Macrolide antibiotics- Azithromycin is a macrolide antibiotic that is just given to enhance the effect of hydroxychloroquine, but still has limited data [13].

Antivirals- Lopinavir/ritonavir is used as combination therapy against COVID-19. Both in combination is CYP3A4 inhibitor. Lopinavir itself is a human immunodeficiency virus type 1 (HIV-1) protease inhibitor, Lopinavir with Ritonavir could block the main protease of SARS-CoV-1 thus inhibiting viral replication but research has not proved the results [14,15].

Remdesivir, a monophosphoramidate prodrug of an adenosine analogue, was developed during Ebolapandemics. It was very effective in previous epidemics of SARS-CoV-1 and MERS-CoV. It acts as RNA chain terminator by binding to the RNA-dependent RNA polymerase (RdRp), thus act against SARS-CoV-2 *in vitro* conditions. Clinical trials are underway but till now no clinical data has proved the successful treatment and clinical improvement [16].

Umifenovir an antiviral drug inhibits the step of viral fusion with the targeted membrane used by Influenza and SARS-CoV2 viruses [17]. Molnupiravir is an antiviral drug, inhibiting the replication of few RNA viruses, and can be used for the treatment of COVID-19 [18].

Nirmatrelvir is Novel protease inhibitors. Its X-ray crystal structure (PDB: 7SI9 and 7VH8) of the SARS-CoV-2 protease inhibitor PF-07321332 is bound to the viral 3CLpro (Mpro) protease enzyme. It is a promising drug [19].

Plasma- Convalescent plasma from recovered patients having neutralizing activity is claimed by many researchers so plasma infusion can be used as a treatment by transferring it to recipients. The results of these clinical trials were further negated by the WHO [20].

Monoclonal antibodies- Tocilizumab, a humanized monoclonal antibody, inhibits both membrane-bound and soluble forms of interleukin-6 (IL-6) receptors. Initially, it was given for rheumatoid but it is considered to be the effective and complementary treatment in cytokine-release syndrome disease. Tocilizumab can be effective in inhibiting cytokine storm, including IL-6, thus

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can be prescribed in patients with coved-19 to avoid severe outcomes [21].

Casirivimab/imdevimab, a combination of two monoclonal antibodies used for the treatment and prevention of COVID-19. The combination of two antibodies is intended to prevent mutational escape.

Bamlanivimab and etesevimab is a combination of two monoclonal antibodies, bamlanivimab and etesevimab, administered together via intravenous infusion as a treatment for COVID-19. Both types of antibodies target the surface spike protein of SARS-CoV-2 [22].

Tixagevimab/cilgavimab is a combination of two human monoclonal antibodies that bind the spike protein RBD. It can be used to prevent COVID-19 [4,23]. Regdanvimab (Regkirona) is a human monoclonal antibody used for the treatment of COVID-19. The antibody is directed against the spike protein of SARS-CoV-2 [24,25].

Human recombinant soluble ACE2 (hrsACE2)- It can block the early stages of SARS-CoV-2 infections. ACE2 is considered to be the common receptor for many coronaviruses even for SARS-CoV-2. It can prevent the interaction of SARS-CoV-2 andACE2 so it can be used to treat patients with COVID-19; however, it is not clear whether hrsACE2can block the growth of SARS-CoV-2 [26].

Dornasealfa- It is a recombinant human deoxyribonuclease. Dornase alfa acts as a mucolytic by cleaving extracellular chromosomal DNA from neutrophil extracellular traps. It is used in COVID-19 patients, who have acute respiratory distress syndrome and progressing to hypoxemic respiratory failure, such patients having thick mucus in bronchi, and bronchiectasis which can be cleared by this work and it is considered to be the major step in recovery [27,28].

CONCLUSIONS

SARS-CoV-2 pandemic has led to an impact on global health and the economy. It sets an example for the development of healthcare infrastructure including laboratory infrastructure. The Discovery of drugs targeting essential viral proteins is one of the major treatment strategies. Many clinical trials and screening are done on various drug candidates. Some of these agents were already in use for other previous applications (repurpose drugs). They are good and effective in vitro against SARS-CoV-2 study. Due to urgent need, the drug development is not safe and takes more than five years so drug repurposing is the major step for the effective treatment of the COVID-19 pandemic. It buys time for discovering newer drugs.

The newer drugs are available and are being used but their studies are still warranted by the treating physicians.

CONTRIBUTION OF AUTHORS

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