Review Article

Existing therapies of coronavirus diease-2019 treatment under consideration: A technical note

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ABSTRACT

Coronavirus diease-2019 (COVID-19) is a pandemic outbreak in the world and is the leading cause of severe acute respiratory syndrome. At present, no new drug that selectively used for COVID-19 treatment is available. Existing drugs with alternative mechanism of action found beneficial and show faster recovery rate in COVID-19 patients. Drugs with anti-malarial, anti-arthritic, anti-hypertensive, anti-cancer, and immunomodulatory activity found useful in COVID-19. However, usage of these drugs is limited due to lack of clinical trials and safety. In this review, we discussed brief overview of existing treatment of COVID-19.

Keywords: Coronavirus diease-2019, existing drugs, severe acute respiratory syndrome, new drug application, efficacy

INTRODUCTION

Coronavirus disease-2019 (COVID-19) is a viral disease initially originated in Wuhan, China, and now spreading each country in world. COVID-19 is a major health hazard and a classified as pandemic in various countries.[1] At present, more than 20 lakh people suffer from this disease and about 1 lakh deaths have been reported for this disease. Many people infected with the COVID-19 virus will develop mild-to-moderate respiratory disease and recover without any special treatment being needed.[2] Older people and those with underlying health conditions such as cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to experience serious illness. The transmission rate of this disease is rapidly high. When an infected person coughs or sneezes, the COVID-19 virus spreads mainly by droplets of saliva or discharge from the nose, so it is important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow).[3]

There are no new COVID-19 drugs or therapies available at this time. Since, new drug discovery through identification of lead molecules, preclinical and clinical testing, and post-marketing requires millions of dollars and efforts.[4] A new molecule comes in the market takes 10–15 year time which is quite huge.[4] At present, scientists working on existing drugs and observe for potential COVID-19 inhibiting efficacy. About 47 existing drugs have been tested and 4–7 drugs found clinical effective in COVID-19. However, strong scientific literature regarding safety and official approvals for these drug molecules is still pending. This commentary highlights some of the hit drugs in the marked with COVID-19 clinical applicability.

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INVESTIGATIONAL DRUGS UNDERGO EVALUATION FOR COVID-19

Hydroxychloroquine: An Antimalarial Drug

A proven antimalarial drug having selective inhibiting activity for different plasmodium species was found to inhibit the replication of various intracellular organisms including severe acute respiratory infection-coronavirus disease (SARS-CoV-2) *in vitro*.[5] During *in vivo* clinical trials, hydroxychloroquine significantly inhibits the viral load by 70%. A synergistic combination with broad-spectrum antibiotic azithromycin was found significantly found to inhibit 100% of viral load, as compared with hydroxychloroquine alone.[6] The mechanism behind that hydroxychloroquine induces endosomal pH and selectively inhibits glycosylation of the cellular receptors of SARS-CoV-2. In addition, the selective inhibition of quinone reductase enzyme by hydroxychloroquine cleaves SARS-CoV-2 spike protein which makes them a broad antiviral agent.[6,7] Hydroxychloroquine is still in Phase-III trails and COVID-19 inhibiting activity is still yet to be established.

Ivermectin: An antiprotozoal drug

Ivermectin is active against the majority of parasites with nematode. These can also be used in treating infestations of arthropod ectoparasite, such as scabies. Its primary indications are for onchocerciasis diagnosis and for strongyloidiasis.[8] Researchers have identified its antiviral activity for COVID-19 and found that ivermectin kill this virus within 48 h in cell culture experiments *in vitro*. However, this drug has proven antiviral activity on other viruses including human immunodeficiency virus, dengue virus, and influenza virus.[9]The mechanism of antiviral activity against COVID-19 activity is still yet to be established. However, it is thought that nuclear transport inhibiting activity of ivermectin blocks the nucleocytoplasmic shutting of SARS-CoV-2. This drug is now evaluated in preclinical trials for potential effects in humans for safety and efficacy.

Losartan: An antihypertensive drug

Losartan is a selective antihypertensive drug and angiotensin receptor blocker II used to treat high blood pressure. Researchers have found that angiotensin-converting enzyme (ACE) involves in binding of COVID-19 and enters the cells for viral replication.[10]The selective inhibition of ACE by losartan blocks the entry of virus to infect cells in the body. However, it was also concluded that losartan could be effective in COVID-19 patients with previous hypertension-related complications.[11] Moreover, acute lung inflammation involves over activation of renin-angiotensin system (RAS). Hence, selective blockade of RAS could be a potential pathway for COVID-19 treatment. However, no scientific data are yet to be available for proven efficacy with COVID-19.

Mycobacterium W (MW) vaccine

MW is a saprophytic cultivable mycobacterium contains enriched antigens of *M. tuberculosis* and *Mycobacterium leprae* and is widely used as an immunomodulator.[12] This vaccine was previously developed for prevention of leprosy and tuberculosis. Scientists have found that body of patients with COVID-19-induced cytokines storm due to overactivation of T-cells in innate immunity.[12,13] MW inhibits the cytokines storm and thus benefits the patients and help to decrease mortality. Different trials were conducted in postgraduate institute Chandigarh, AIIMS, Bhopal, Delhi, reported safety of MW vaccine in COVID-19 patients. However, scientific data pertaining to the treatment of this vaccine in COVID-19 patients are in the way.

Tocilizumab: An immunosuppressive agent for arthritis

Tocilizumab is the first marketed antibody blocking interleukin-6 (IL-6) by targeting IL-6 receptors and has shown its safety and efficacy in rheumatoid arthritis therapy.[14] In a study published by Fu *et al.*, the findings of the treatment with tocilizumab are encouraging as symptoms of COVID-19 in critically ill patients improved dramatically. Of those 21 patients, within 2 weeks of tocilizumab treatment, 20 patients were recovered and discharged.[15] The mechanism behind the blockade of IL-6 by tocilizumab inhibits the excessive inflammatory response of the immune system, particularly inflammatory cytokines and monocytes. The inhibition of inflammatory storm could be a targeted therapy for tocilizumab in COVID-19 treatment.

Thalidomide: An anticancer drug and immunomodulator

Thalidomide exhibited various adverse effects on babies when pregnant women exposed to this drug to treat morning sickness. The drug has been repurposed in recent years, despite its dark history, and is an approved treatment for multiple myeloma (a form of cancer of the blood cells) and leprosy complications.[16] However, thalidomide has several different effects within the body – which is why researchers look at it as a possible therapy for COVID-19. This can, for example, suppress the inflammatory response of the immune system, making it effective against inflammatory conditions. Recent study conducted by Chen *et al*. studied the possible combination of thalidomide with low-dose glucocorticoid. Results found that this synergistic combination helps to inhibit cytokine storm and lung exudation and improves orally immunity. However, no preclinical and clinical trials yet to be started for thalidomide.[17]

CONCLUSION

COVID-19 is a captivating its place as a major health hazard in the world. At present, new drug application approval takes about millions of dollars and 15–20 years time from discovery to marketing. Hence, scientists find out the COVID-19 inhibiting activity on existing drugs which could be provide immediately to the public for decreasing mortality. In future, we hope that standard treatment will be available and the entire world will win this fight.

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