Review Article

Indian Journal of Communicable Diseases
Volume 7 Number 1, January – June 2021
DOI: http://dx.doi.org/10.21088/ijcd.2395.6631.7121.4

Pharmacological Management of Coronavirus Disease 2019

Divya Krupa Muniyandi

How to cite this article:
Divya Krupa Muniyandi, Pharmacological Management of Coronavirus Disease 2019. Indian J Comm Dis.2021;7(1):27–30.

Author's Affiliations: Scientific and Medical Writer, Springer Nature Technologyand Publishing Solutions, Pune, Maharashtra 411013, India.

Corresponding Author: Divya Krupa Muniyandi, Scientific and Medical Writer, Springer Nature Technology and Publishing Solutions, Pune, Maharashtra 411013, India.

E-mail: pmdivya@yahoo.co.in

Abstract

The incidence and vast spread of the coronavirus disease 2019 has been quite rapid across the globe. There is no medicine approved solely by the FDA for the management of COVID-19 infection. Only symptomatic management is carried out in patients with the available medicines in the market. This review provides an overview of the drugs which are being used primarily for the management of the infection across the globe. The number of drugs being used is comparatively less, hence to provide a view on the mechanism and pharmacology, this review has been carried out. Data on drugs like remdesivir, dexamethasone and tocilizumab have been included in this review, along with supportive care from Siddha to help the medical fraternity to decide on the treatment regimen for COVID-19. Data on the current use of drugs in hospitals were provided by a medical practitioner and are included in this review.

Keywords: COVID-19; Management; Remdesivir; Dexamethasone; Tocilizumab.

Introduction

Coronavirus disease 2019, also known as COVID-19, is an infectious disease, recognized as a global pandemic by the WHO. The etiology of the infection is identified to be a novel coronavirus.[1]COVID-19, is turning out to be a "digital infodemic", meaning all data sources being flooded with far-reaching information, both accurate and inaccurate data across the globe.

Historical details reveal that the virus was first named as coronavirus in 1968, and the naming was due to the crown-like morphology of these viruses when observed under an electron microscope. Coronaviruses can be classified into three genera or groups (I to III) based on their serological cross-reactivity, which has been confirmed by more recent genome sequence analysis. Animal pathogens like TGEV of pig, feline infectious peritonitis virus(FIPV), porcine epidemic diarrhea virus (PEDV), and the human coronaviruses (HCoV-229E and HKU1, causing respiratory infections are included under group I coronaviruses. Group II encompasses veterinary pathogens like BCoV, equine coronavirus, porcine hemagglutinating encephalomyelitis virus, and human coronaviruses OC43, NL63 causing respiratory infection.[2]

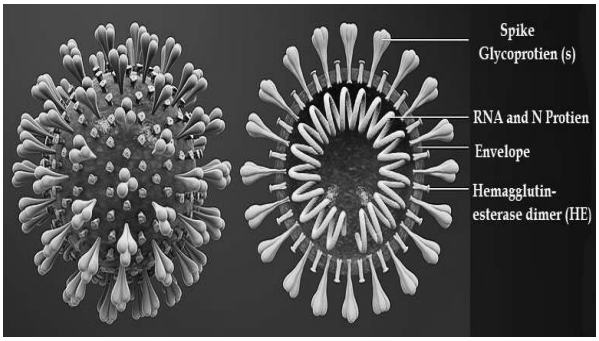


Fig. 1: Structure of coronavirus.[15]

The novel coronavirus, also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously called 2019-nCoV), was first identified in an outbreak of respiratory illness patients in Wuhan City,

Hubei Province, China. It was reported to the WHO on December 31, 2019, which was declared as a global health emergency in January 2020. In March 2020, it was declared by the WHO that COVID-19 is a global pandemic.[3]

Currently used drugs in treatment of COVID-19 have the ability to result in more harm than good. Hence, going by Hippocratic injunction of Medicine 'primum non nocere', let us try to first, do no harm to patients. In every 100 patients on ventilator for 28 days, 60 are likely to recover and 12 patients survive using the new drug.

The FDA has not approved any drugs or biologics for the purpose of preventing or treating COVID-19. On May 1, 2020, REMDESIVIR was identified as the first drug, to receive emergency use authorization (EUA) from the FDA. Since preliminary data revealed a faster time to recovery of patients who were hospitalized with severe form of the disease, this drug was utilized. Hydroxychloroquine was one of the drugs which was initially thought to have some benefit in COVID-19, but it exposed patients to risks without any proof of clinical benefit. Currently, drugs essentially required for ventilated and critically ill patients and the widespread use of inhalers used for COPD or asthma are in demand. Few of the existing drugs in the market have shown in vitro antiviral activity and may achieve adequate absorption, distribution, metabolism and excretion in the plasma with the currently approved doses being used.[3]

Remdesivir

Remdesivir, is a broad-spectrum nucleotide analog antiviral prodrug, developed by Gilead Sciences. It received emergency use authorization (EUA) from the US FDA in the treatment of severe COVID-19, confirmed or suspected cases seen in adults and children who were hospitalized. Trials of an inhaled nebulized formulation have aimed to identify if the drug can be used on an outpatient basis and in earlier stages of the disease. [3]

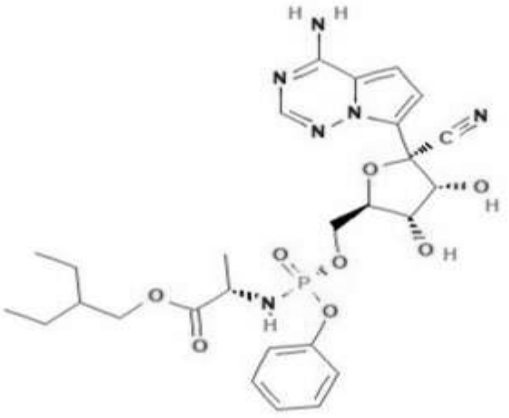


Fig. 2: Chemical structure of Remdesivir.[12]

Molecular formula: $C_{27}H_{35}N_6O_8P$

Synonyms: 1809249-37-3, 3QKI37EEHE,GS5734, GS 5734 [WHO-DD], GS-5734, GS5734

Molecular weight: 602.6 g/mol[16] Remdesivir acts by the mechanism of inhibiting the replication of other human coronaviruses associated with high morbidity in tissue cultures of SARS-CoV in 2003 and MERS-CoV in 2012. On April 29, 2020, EUA for the drug was given based on preliminary analysis of data from the Adaptive COVID-19 Treatment Trial (ACTT). The analysis included 1,063 patients who were hospitalized with the diagnosis of advanced COVID-19 and lung involvement, where remdesivir showed faster recovery rate (31% faster time) than placebo with a significance of $P<0.001$.[3]

In April 2020, Grein J *et al,* carried out a compassionate use study of remdesivir in 61 patients who were hospitalized with COVID-19, and had SARS-CoV-2 confirmed with an oxygen saturation of 94% or less when on oxygen support or when breathing ambient air. The data from 53 patients were analysed. Baseline characteristics showed that 57% were on mechanical ventilation and 8% were having extracorporeal membrane oxygenation. After 18 days, during the median follow-up, 68% showed an improvement in oxygen support class, including 57% on mechanical ventilation who were extubated. The mortality rate observed in the study was 13% and 47% were discharged. Invasive ventilation showed a difference in mortality rate in the patients: those who received it had 18% mortality rate while it was found to be 5% in those who were not on invasive ventilation.[11]

Dexamethasone

Dexamethasone is a corticosteroid medication used for the treatment of a plethora of indications which includes respiratory conditions as well. In June 2020, in the Randomized Evaluation of COVID-19 Therapy (Recovery) trial, dexamethasone was recommended for COVID-19 patients having severe respiratory symptoms. The molecule was able to reduce deaths by one-third in those requiring ventilation and by one-fifth in those needing oxygen. The mechanism of action of the drug is it acts by dampening down the immune system. In some cases, the immune system goes into overdrive and its reaction can attack the body's own cells and prove fatal. The drug is only suitable for patients in hospital receiving oxygen or mechanical ventilation. Recovery trial conducted by the University of Oxford reported that dexamethasone could be used in the list of drugs which could reduce deaths due to COVID-19.[4]

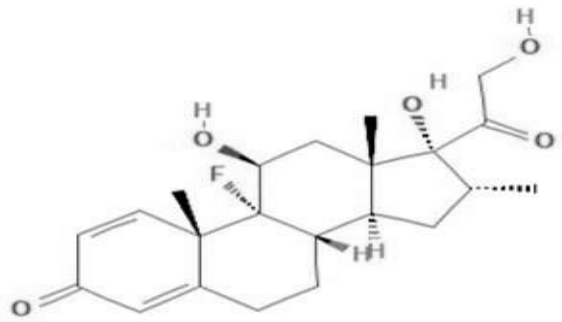


Fig.3: Chemical structure of Dexamethasone.[13]

Molecular formula: $C_{22}H_{29}FO_5$

Synonyms: Dexamethasone, 50-02-2, Decadron, Dexamethazone, Maxidex

Molecular weight: 392.5 g/mol[17]

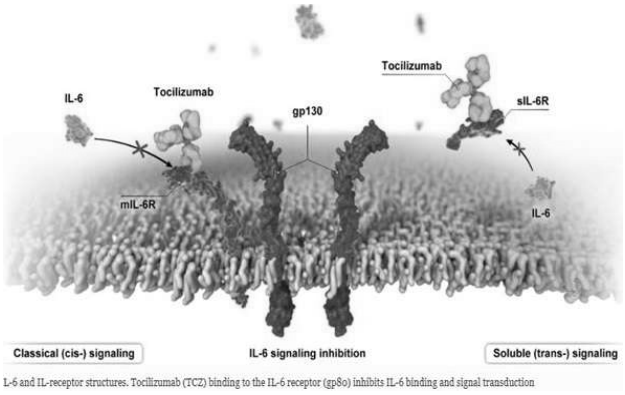
The human body's first immune response to infections is to start with the production of cytokines, which can be defined as a class of special proteins having inflammatory properties.

Cytokine production causes inflammation and fever. Severe COVID-19 occurs due to an over-reaction by the immune system, which leads to cytokine storm or an excessive inflammatory response. The cytokine storm is capable of causing life-threatening lung inflammation and damage, which are seen in severely and critically ill COVID-19 patients. Since dexamethasone has anti-inflammatory effect, it is capable of bringing down the excessive inflammatory response.[4]

The World Health Organization and an article in Lancet published during the early stages of the COVID-19 pandemic stated that corticosteroid drugs may possibly even be harmful and are not recommended for treatment of COVID-19 patients. This statement was based on the use of steroids in the previous coronavirus epidemics caused by SARS-CoV-1 and MERS-CoV.[4]

Tocilizumab

Tocilizumab is a recombinant humanized monoclonal antibody IL-6 receptor antagonist used in the treatment of inflammatory and autoimmune conditions. Currently, it is being used in studies to treat severely ill patients with COVID-19.[5]



IL-6 and IL-receptor structures. Tocilizumab (TCZ) binding to the IL-6 receptor (gp80) inhibits IL-6 binding and signal transduction

Fig.4: Mechanism of action of tocilizumab.[14]

Protein chemical formula: $C_{6428}H_{9976}N_{1720}O_{2018}S_{42}$

Synonyms: Altizumab

Protein average weight: 148000.0 Da[18]

Interleukin-6 (IL-6) is one of the key cytokines in cytokine storm induced by infection. Cytokine storm is seen in patients with rapid progression of COVID-19. The progression of COVID-19 from severe to critical causes severe cytokine storm, secondary acute respiratory distress syndrome. This is followed by shock, tissue perfusion disorders, and multiple organ failure. Hence, addressing the issue of cytokine storm becomes a vital part of rescue of severe patients. The US FDA has approved tocilizumab for cytokine release syndrome (CRS). Cytokines are small proteins secreted by cells primarily used for signaling and communication between cells, regulating immune responses, hematopoiesis, cell growth and differentiation, and repair of damaged tissues by receptor binding. When bacteria and viruses invade the human body, the immune system responds by the release of a large number of cytokines. The uncontrolled cytokine release will cause systemic inflammation, due to the over-immune phenomenon of cytokine storm.[6]

Management of Covid-19 in Tamil Nadu–Herbal Prospects in Supportive Care:

The use of siddha medicines to support in the recovery of patients with corona infection has been observed in Tamil Nadu. Since clinical studies with siddha medicines have not been carried out, the therapeutic effect can only be considered as a supportive measure.

The National Institute of Siddha in Chennai has given its view on use of siddha medicines for coronavirus infection and its efficacy. Since ancient times, plants have been a source of medicine for mankind for various diseases. They can be considered as the best treatment options for the disease because of their ability to cause the lowest possible side effects when compared with other therapeutic options.[7]

Extracts formulated from herbs have shown efficacy in curing viral fevers like dengue, multi-organ failure seen in corona fever and acute liver fever. The drug is capable of treating the viral infection within 24 hours to 40 hours[8].

The Siddha concoction, KabaSuraKudineer, is widely used across the state as an immunity booster.[9]

The guidelines released by the Ministry of Ayush, Government of India for Siddha practitioners treating Covid-19 gives an overview of the therapeutic options for prevention of the infection. It gives a common advisory and the list of antiviral medications from Siddha for the treatment of the infection. The common advisory includes points on having herbal water infusion made of dried ginger (chukku), injithenooral/ginger tea/liquorice tea as hot beverages, avoiding milk at bedtime, if needed for children, it can be given after adding quarter spoon of turmeric and pepper, steam inhalation with tulasi/nochi (Vitexnegundo) leaves/turmeric, gargling water boiled with salt and turmeric, avoiding allergic foodstuff, and environmental sanitation through neem leaves fumigation is advised.[10]

The anti-viral siddha formulations include kabasurakudineer (60 ml twice daily after food), Nila Vembukudineer (60 ml twice daily after food), Visha Surakudineer (60 ml twice daily after food), Pavala Parpam (100 mg twice daily with honey), and Velliparpam (100 mg twice daily with honey).[10]

The anti-viral siddha herbs include:

Siddha Herb	Botanical Name	Formulation	Dose
Inji	Zingiberofficinale	Injisurasam	10 Ml Od
Thulasi	Ocimum Sanctum	Thulasikudineer	60 Ml Bd
Milaku	Piper Nigrum	With Thulasi As Kudineer	
Karunjeerakam	Nigella Sativa	Karunjeerakachooranam	1 Gm Bd
Keezhanelli	Phyllanthusniruri	Keezhanellisamoolam	2 Gm Bd
Athimadhuram	Glycyrrhizaglabra	Athimadhurachooranam	1 Gm Bd
Vellaipoondu	Allium Sativum	Poonduthaen	
Cittramutti	Sidacordifolia	Cittramuttikudineer	30 Ml Bd
Seenthil	Tinosporacordifolia	Seenthilchooranam	1 Gm Bd
Manjal	Curcuma Longa		
Elumitchai	Citrus Limonia	Volatile Oil	
Vembu	Azadirachtaindica		

Note: Antiviral activity of the above mentioned drugs and formulations against COVID-19 is not established and is not being claimed.[10]

Conclusion

Addressing a novel infection is always a herculean task. Hence, in today's scenario, the healthcare professionals are striving hard to cure the global pandemic of COVID-19 by symptomatic management. Through this review, the details of the medications being used are elaborated to help them achieve their goal with a better understanding of the drugs as well as the infection.

Conflict of Interest:I declare that there is no conflict ofinterest.

References

1. https://www.who.int/health-topics/coronavirus#tab=tab_1
2. https://mmbr.asm.org/content/mmbr/69/4/635.full.pdf
3. https://emedicine.medscape.com/article/2500116-overview
4. https://health.economictimes.indiatimes.com/news/pharma/dexamethasone-game-changer-in-the-covid-19-battle/76817741
5. https://www.drugbank.ca/drugs/DB06273
6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7183818/
7. https://nischennai.org/nis-covid19.html
8. https://health.economictimes.indiatimes.com/news/diagnostics/siddha-doctor-from-tn-claims-to-have-invented-cure-for-coronavirus/73691161
9. https://scroll.in/bulletins/275/exploring-normals-old-and-new
10. https://www.ayush.gov.in/docs/siddha-guidelines.pdf
11. Grein J, Ohmagari N, Shin D, Diaz G, et al. (2020). Compassionate use of remdesivir for patients with severe Covid-19. The New England Journal Of Medicine, 10.1056/NEJMoa2007016
12. https://pubchem.ncbi.nlm.nih.gov/compound/121304016
13. https://pubchem.ncbi.nlm.nih.gov/compound/5743#section=2D-Structure
14. https://link.springer.com/article/10.1007/s00228-020-02864-6/figures/1
15. https://asm.org/Articles/2020/January/2019-Novel-Coronavirus-2019-nCoV-Update-Uncoating
16. https://pubchem.ncbi.nlm.nih.gov/compound/Remdesivir
17. https://pubchem.ncbi.nlm.nih.gov/compound/Dexamethasone
18. https://www.drugbank.ca/drugs/DB06273