

A Review on Remdesivir: A Probable Cure for Covid-19

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Abstract

The current scenario of the world is very critical as there is a global Pandemic of COVID-19 looming around in the world. It has claimed lives of millions of people and has adversely affected the health of millions. COVID-19 is an infectious disease caused by the novel corona virus. This disease is highly contagious in nature and hence it was regarded as the global pandemic by World Health Organization. There are many researches going on to either find a vaccine or find a cure for this deadly disease. Remdesivir is one such medicine which is proposed to be a probable cure for COVID-19. This medicine proved effective in the past for treatment of the ebola virus infection and the Middle East respiratory syndrome (MERS) infection; due to this researches on this medicine to be a potential cure were done. In a number of researches done in this area it was found that when remdesivir was administered to the infected individuals the recovery rate of the infected people was faster when they were given this medicine as compared to those who were not. This paper discusses about the medicine remdesivir in detail; from its discovery, functioning in human body to its chemical composition. The researches done and the clinical results of the medicines are also discussed which all point in the direction that this medicine could pose to be an aid in curing the corona virus disease.

Key words: Corona virus, Remdesivir, Contagious, Medicine, Pandemic, Research.

INTRODUCTION

COVID-19 disease comes from a large family of Coronavirus. It is an infectious disease that causes respiratory diseases to animals and humans. Corona virus encompasses some similar types of diseases like Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). COVID-19 was discovered in the year 2019 and the first case recorded was in a Chinese city, Wuhan.^[1] With the passage of time this disease spread into other cities and then gradually to other countries as well. Due to this reason World Health Organization declared COVID-19 as a global pandemic. This disease gets transferred from one person to another easily because as an infected person sneezes or coughs the saliva droplets get dispersed in the surrounding and thereby infect the things nearby. Hence as soon as any other person comes in contact with those infected things they also carry the virus with them and eventually get infected either by touching their nose, mouth or eyes. Some of the early signs of COVID-19 are:

- Fever
- Dry Cough
- Fatigue
- Body pain
- Nasal Congestion
- Conjunctivitis
- Sore Throat

- Loss of taste and smell
- Head Ache

The symptoms can vary from person to person. As this disease has more severe effect on people with low immunity hence people above the age of 60 years are more susceptible to the adverse effect of this disease. Researchers are constantly trying to find a cure and vaccine for this disease. Extensive research is done on various drugs that have proven useful earlier in treating similar type of diseases. Some of those drugs are remdesivir, rabivirin and favipiravir to name a few.^[1]

Remdesivir: Background

After the collaboration of pharma company Gilead Sciences, the U.S. Centers for Disease and Prevention and the U.S. Army Medical Research

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Institute of Infectious Diseases, the remdesivir drug was developed by Gilead Sciences. Remdesivir belongs to the broad spectrum antiviral group and was initially developed and researched for the treatment of Ebola Virus in the year 2014.^[2] It is a nucleotide analogue prodrug which helps in controlling the viral replication. Following further researches some researchers proved that it was also a potential cure for coronavirus disease like SARS-CoV-2. This strategy of interfering with the replication of the virus is quite common among various broad spectrum antiviral drugs. Remdesivir works in the human body by getting converted into an imposter which is called as a nucleoside analog. The nucleoside analog is a genetic copy that falsely resembles adenoside. Due to this when the actual virus starts replicating it also includes this analog into a new genetic material strand.^[3] As soon as this happens the replicating process stops in the human body by giving sufficient time to the immune system to fight off the viral infection. Remdesivir depicts anti-viral activity both *in vivo* and *in vitro* in the body against various viral pathogens like Ebola, SARS, MERS and SARS-CoV-2. This drug is also classified as prodrug because any prodrug does not have anti-viral activity inherently. They get activated by the enzymes when they enter into a cell. As soon as this drug is activated in the body to show anti-viral activity it remains activated for a period of one day within the cell of the host body that is been infected by this virus. Remdesivir shows anti-viral activity against many RNA viruses and hence it has been researched extensively so as to study its effect on human body to cure COVID-19.^[4,5]

Working of the drug

Remdesivir is a C-adenosine nucleoside analogue that is a mono phosphoramidate prodrug. Remdesivir drug enters inside the cells into an alanine metabolite, which further processes into the monophosphate derivative and finally it gets converted into the active nucleoside triphosphate derivative. Since remdesivir is a nucleotide analogue drug hence it is not highly cell permeable. Therefore after they reach inside the cell they need diphosphorylation and triphosphorylation in order to create nucleoside triphosphate (NTP).^[6] This nucleoside triphosphate is then used by the RNA-dependent polymerases for genome replication. In this case, nucleoside triphosphates are disintegrated into viral RNA with the help of viral RNA-dependent RNA polymerase. While giving this drug as a medicine to any patient one thing must be kept in mind. It is that Remdesivir should always be given by intravenous infusion. This is done because if this drug is taken orally by the patient then it is easily broken down by the liver.^[7,8]

Effect of Remdesivir on other diseases

Some of the other diseases with which remdesivir is associated are

1. **Ebola Virus Disease (EVD)** - Ebola virus (EBOV) was discovered in the year 1976. It comes under the umbrella of the family called Filoviridae. EBOV causes hemorrhagic fever after entering into the host body which eventually leads to the death of the infected person. The body fluids such as saliva, urine, blood and seminal fluid are responsible for the spread of EBOV. The contaminated surface also spreads the virus if any person comes in contact with it. Like any other viral agent when ebola virus enters the host body, the immune system of the host becomes activated to fight off any foreign agent in the body. However, if the immune system fails to fight against the virus then this virus destroys the immune response and starts to replicate in the body with increased speed. Therefore the infected person is first isolated and then other medical treatments are given to that person. Till date no particular cure has been discovered for the treatment of ebolavirus disease still few drugs proved useful during the time of ebolavirus outbreak in from 2013 to 2016. One such drug is Remdesivir. Remdesivir was discovered at the time of ebolavirus outbreak as the most promising drug against ebolavirus disease. Further *in vitro* results

indicated a more extensive evaluation in EBOV-infected macaques. In this evaluation it was found that remdesivir reduced viral replication and enhanced the chance of survival, some clinical signs of this viral disease and pathophysiological blood markers. Post this discovery of the drug it was administered under compassionate use to patients with ebolavirus disease (EVD).^[9] However this administration of drug was halted after the result of an interim analysis of the first clinical trial depicted that this drug shows inferiority to treatments with monoclonal antibodies. This clinical trial aimed to evaluate different therapeutic agents against the ebolavirus disease to check their efficacies.

2. **Severe Acute Respiratory Syndrome (SARS)** - First identified in the year 2003, the SARS coronavirus causes a chronic pneumonia in the infected person. The first case identified was in Guangdong, China in the year 2002. This epidemic spread and affected as many as 26 countries worldwide. It is an infectious disease and can be transferred from one person to another. The transmission is most during the second week of illness when the virus excretion is at maximum through respiratory secretion and stool. Symptoms of SARS include - very high fever, dry cough, sore throat, problems breathing including shortness of breath, headache, body aches, loss of appetite, malaise, night sweats and chills, confusion, rash and diarrhea. The remdesivir drug was again used as a prospective cure for SARS. Various researches and studies took place in relation to the effect of this drug on the treatment of SARS. However with passing time the cases of this disease reduced and there could not have been any substantial proof whether this drug could have been the cure for this coronavirus or not.^[10]

3. **Middle East Respiratory Syndrome (MERS)** – It is a type of coronavirus disease that is caused by MERS coronavirus and leads to respiratory problems to the infected person. It was first identified in Saudi Arabia in 2012. Later the disease spread into many other countries like United Arab Emirates and Republic of Korea. Out of the total number of infected people, 35% die due to MERS coronavirus. Symptoms of this disease are – fever, cough, shortness of breath, diarrhea, pneumonia and other gastrointestinal symptoms. It is different from other type of coronaviruses as it is not easily transferred from one person to another. The infection gets transferred only when there is very close contact with the infected person. Therefore healthcare centers are most susceptible to this disease. Although there is no cure or vaccine developed till date for this disease. Yet several studies found that the use of remdesivir drug could enable the development of a cure for MERS. Trials done on monkeys showed that this drug did prevent the infection if it was given before. It also improved the condition of monkeys who already got infected. It is evident that remdesivir has been constantly studied upon to find the vaccine and cure for the coronaviruses. The recent outbreak of COVID-19 has also made it even more essential to conduct extensive research in this area.

4. **A cure for COVID:** Coronavirus Disease which is caused by the virus called SARS-CoV-2 infects a cell in the human body and overtakes the cells' operation. By taking over the operation of the cell the virus starts making the cell as the virus making factory by forcing them to replicas of the virus. These replicas are arranged in a series in the body. Therefore when remdesivir drug enters the body the virus infected cell considers it as one of its factories to make replicas. Since it is not actually the part of the virus chain therefore it creates a blockage inside the cell and prevents it to create further replicas of the virus. Therefore the replicating process of the virus inside the body gets reduced after the intake of remdesivir drug. The initial remdesivir molecule was retrieved from a small-molecule group of 1,000 varied nucleoside and nucleoside phosphonate analogs. These molecules were arranged and created in this manner from many

years through anti-viral research that depicted the potential of these molecules to target any emerging RNA viruses like SARS coronavirus, MERS coronavirus and even some of the viruses of flaviviridae family like dengue and zika virus.^[11-14]

Clinical Studies: Various clinical studies have been carried out on the remdesivir drug to prove its efficiency and potential in treating diseases like COVID-19. Also such studies depict any side-effects from such drugs. Some of these studies are mentioned below. It has been seen that the *in vitro* and *in vivo* animal models have been proved useful in proving the effectiveness of remdesivir against SARS-CoV-2 and other similar coronaviruses. A recent *in vitro* study was conducted on remdesivir drug to measure the antiviral activity against SARS-CoV2. This study aimed to depict an IC₅₀ of 770 nM and an IC₉₀ equal to 1,760 nM along with the cytotoxic concentration of more than 100 mM.^[15] Along with this another study conducted by Sheahan *et al.* and De Wit *et al.* illustrated that Remdesivir had the enough potential in halting the replication and reducing viral pathology against such Coronaviruses. This study showcased *in vivo* efficacy of Remdesivir. Such studies along with the safety profile of Remdesivir in the clinical trials against Ebolavirus aid in the assessment of remdesivir as a potential therapeutic drug for reducing effects of SARS-CoV-2 I this current pandemic outbreak.^[16]

In the study it was found that remdesivir drug showed huge *in vitro* anti-viral activity against zoonotic and human pathogens coming from families of various viruses. However the anti-viral activity of this drug has showed consistent results when studied against Filoviridae, Coronaviridae, Paramyxoviridae, Pneumoviridae and virus family. Remdesivir contains three HCoV endemic strains linked with respiratory illness also other less common types like MERS coronavirus, SARS coronavirus and the novel SARS-CoV-2 that causes COVID-19. Even though a large numbers of preclinical researches have been *in vitro* in nature. Yet remdesivir has shown positive effect on non-human primate (NHP) models of viruses like Nipah virus and MERS. Studies also found that this drug is not much effective against the Flaviviridae virus family. Also it shows moderate performance against viruses causing Dengue, Hepatitis C and Yellow Fever. Remdesivir shows least or negligible effect against tick-borne flaviviruses like Kyasanur forest disease, Omsk hemorrhagic fever, Alkhurma hemorrhagic fever, tick-borne encephalitis.^[17]

A study was conducted by Beigel *et al.* on the patients who exhibited lower respiratory tract infection and were hospitalized due to COVID-19. The aim of the study was to analyze the recovery time taken by a patient by getting discharged from the hospital when they were given certain amount of remdesivir dosage. This trial was a double-blind, randomized, placebo-controlled. The drug was intravenous remdesivir given to adults who were hospitalized due to Covid-19. In a random manner patients were assigned to get remdesivir. The dosage included 200 mg on day 1 and 100 mg thereafter for the period of 9 more days. The analysis of this study demonstrated that the average recovery time of patients receiving remdesivir was 10 days as compared to 15 days for those patients who did not receive any remdesivir dosage during hospitalization. In the result of the study it was found that total of 1062 patients underwent the random selection and then were given the dose of the medicine remdesivir and the other group received the placebo medicine.^[18]

RESULTS

In the research of Beigel *et al.* it was found that those who received remdesivir had a median recovery time of 10 days (95% confidence interval [CI], 9 to 11), as compared with 15 days (95% CI, 13 to 18) among those who received placebo medicine. These clearly point out to the fact that

remdesivir can prove to be a potent drug to cure the novel Coronavirus infections. The data of this research clearly suggested that remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection.

CONCLUSION

In these trying times of the Pandemic of COVID-19, a possibility of a cure in form of the remdesivir medicine has come as relief. This paper discusses about the medicine remdesivir in light of its discovery, chemical composition and its working in the human body. The paper also studies how this medicine proved to be useful in the past in cases of the ebola virus outbreak and MERS virus outbreak. In light of these studies only the clinical trials of remdesivir began on patients of COVID-19 as well and it was found that the results were in favor and the medicine did assist in early recovery of the infected patients as compared to those who were administered some other form of medication. Through various studies quoted in the study it is clear that remdesivir does speed up the recovery process and can be used as a cure for the corona virus infection. But still more extensive research is needed in this area and any substantive conclusions can only be drawn through more in-depth research and clinical study on remdesivir medicine.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

WHO: World Health Organization; **SARS:** Severe Acute Respiratory Syndrome; **MERS:** Middle East Respiratory Syndrome; **COVID:** Corona Virus Disease.

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