

Case Report

A case report: remdesivir effective in the treatment of severe category COVID-19

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Received: 04 August 2020

Accepted: 02 September 2020

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ABSTRACT

Since the first cases were reported in December 2019, infection with the severe acute respiratory corona virus 2 (SARS-CoV-2) has become a worldwide pandemic. COVID-19 the illness caused by SARS-CoV-2 is overwhelming health care systems globally. In the absence of a proven effective therapy, current management consists of supportive care, including invasive and noninvasive oxygen support and off-label or compassionate-use therapies, including anti-retrovirals, anti-parasitic agents, anti-inflammatory compounds, and convalescent plasma. Amongst these experimental therapies, remdesivir a broad-spectrum antiviral drug has shown some promising results. We present a successfully treated patient of severe acute respiratory illness by SARS-CoV-2 with remdesivir along with standard management protocol. Reporting a case with aim to add favoring evidence for remdesivir in the treatment of SARS-CoV-2.

Keywords: Remdesivir, COVID-19, SARS-CoV-2

INTRODUCTION

In December 2019, a set of people in the Wuhan city of China were diagnosed with pneumonia with an unidentified cause, which was later discovered to be the 2019 novel corona virus (COVID-19) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has created a global health scare with international apprehension due to its massive spread. A highly potent and pathogenic COVID-19 viral infection with incubation period ranging from two to fourteen days, transmitted by inspiration or contact with infected droplets. The transitional resource of origin and transfer to humans is not known, however, the rapidly developing pandemic has confirmed rapid human to human transfer which has caused it to be labeled as a pandemic.¹

The symptoms of SARS-CoV-2 infection vary widely, from asymptomatic disease to pneumonia and life-

threatening complications, including acute respiratory distress syndrome, multisystem organ failure, and ultimately, death. Older patients and those with pre-existing respiratory or cardiovascular conditions appear to be at the greatest risk for severe complications.²

World health organization (WHO) classifies the disease into mild, moderate and severe categories.

Mild disease symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia. Moderate disease pneumonia adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea and fast breathing) but no signs of severe pneumonia, including SpO₂ ≥ 90% on room air. Severe disease severe pneumonia adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO₂ < 90%

on room air.² Severe disease is associated with increased mortality which is out of proportion to the clinical condition of the patients, even the mortality rate is a point of concern in moderate disease. Unfortunately, due to lack of specific treatment the situation was worse. More than 80 clinical trials have been on going to test coronavirus treatments, including some drug repurposing or repositioning for COVID-19.³ Based on the trials some categories as an experimental therapies like tocilizumab, remdesivir, convalescent Plasma Therapy. Based on the limited evidences remdesivir has shown most promising results. With this case report we wish to add some favourable evidences on remdesivir.

CASE REPORT

A 59-year-old male patient presented to Dhiraj hospital casualty with low grade fever, dry cough and acute progressive shortness of breath since two days, He is a known case of hypertension since past two years and was on tablet amlodipine 10mg daily. The patient had a positive contact history with COVID-19 patient in the neighbour-hood. On initial physical examination, patient is febrile with temperature 100.4 F, tachypneic with respiratory rate of 34 breath/min, with SPO₂ of 86% room air, patient also had tachycardia with heart rate of 112 bpm, and blood pressure of 130/84 mm Hg with arterial blood gas showing PaO₂/FiO₂ 68, patient was admitted in the COVID-19 suspect ICU with probable diagnosis of severe Acute respiratory distress syndrome with COVID-19, and initiated management along with oxygen therapy with non-re-breather mask (NRBM) and then had to be kept on non-invasive ventilation as not maintaining O₂ saturation [Chest x-ray was suggestive of bilateral peripheral and basal infiltration with consolidation. (Figure 1) Other treatment as per according to the existing protocol the patient was started on hydroxychloroquine (HCQ), azithromycin, and broad-spectrum antibiotics. Nasopharyngeal and oropharyngeal swab for real-time reverse transcription polymerase chain reaction (RT-PCR) for COVID-19 was sent which came positive the same day.

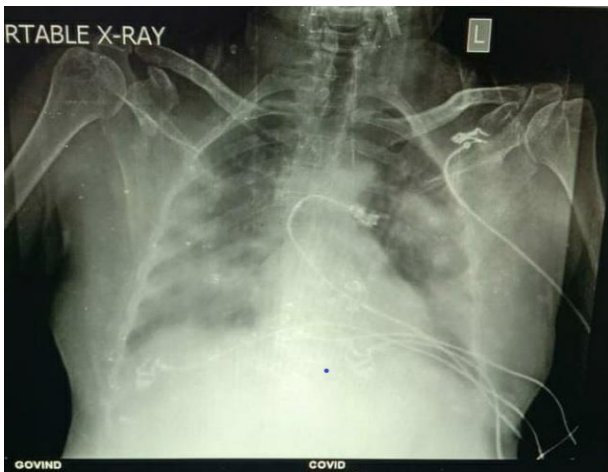


Figure 1: Chest X-ray on day 1.

Other investigating findings are, complete blood count was suggestive lymphocytopenia with normal total count, acute phase reactants were raised with ESR-97, CRP-114, and serum ferritin- 471, LDH- 475 and with raised D-Dimer levels of 1200. Patient was diagnosed as a case of severe acute respiratory distress syndrome (ARDS) with SARS-CoV2 steroid in the form of methylprednisolone and anticoagulant in the form of Low-molecular-weight heparin (LMWH) were added.



Figure 2: Chest X-ray on day 3.

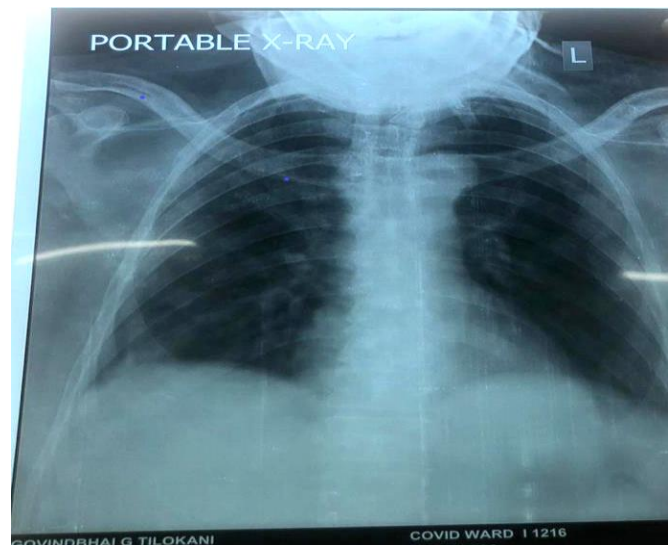


Figure 3: Chest X-ray on day 5.

This treatment along with continuous non-invasive ventilation were continued for 2 days, However, his oxygen requirement on the basis of FiO₂ increased from 60% to 90% over the due course, with increased respiratory distress and tachypnea. Patient being in the severe category with poor response to the initial therapy and with deteriorating clinical condition, investigational therapy with Inj. remdesivir was planned to reduce viral infectivity, viral replication, and the aberrant host inflammatory response remdesivir with a 200 mg IV loading dose followed by remdesivir 100 mg IV

maintenance dose every 24 hours for the next 5 days. Supportive measures as per standard protocol along with steroids and low molecular weight heparin were continued. In next 24 hours after the loading dose of remdesivir the patient's clinical condition improved in form of his PaO₂/FiO₂ from initial 68 was improved to 190 and thus the FiO₂ of the NIV was reduced to 60%. Repeat X-ray was performed on day 3 and day 5 (Figure 2 and 3) of remdesivir which should significant radiological improvement. There was clinical improvement on day 5 present and lab investigations on day 5 after the administration of remdesivir revealed no lymphocytopenia with improved acute phase reactants (CRP-1.45, ESR-22, LDH 225, and Serum ferritin-124). Later patient oxygen demand in terms of FiO₂ gradually decreased and he was shifted from non-invasive ventilation to oxygen therapy, initially with NRBM and later to nasal prongs. At present the patient is clinically stable without oxygen support and with significant radiological and clinical improvement. Patient was discharge on 14th day of admission. After the repeat RT-PCR test was negative.

DISCUSSION

The pandemic emergence of SARS-CoV-2 infection, which is characterized by progressively severe pneumonia and ARDS that leads to a high mortality rate among hospitalized patients, challenges the medical community to evaluate rapidly any possibly effective antiviral drug. On the basis of in vitro studies of different coronaviruses (including SARS-CoV-2), it seems that a number of drugs may be candidate treatment options, including lopinavir, chloroquine, HCQ and Remdesivir.

Remdesivir exhibits broad-spectrum antiviral activity against RNA viruses, and former studies with RNA-dependent RNA polymerase (RdRp) from Ebola virus (EBOV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have shown that delayed chain-termination is remdesivir's conceivable mechanism of action. Remdesivir, formerly known as GS-5734, is a mono phosphoramidate prodrug of an adenosine analog that was developed in response to the Ebola outbreak in West Africa from 2014.

Remdesivir binds to RdRp and acts as RNA chain terminator. It exhibits effective in vitro activity against SARS-CoV-2 with an EC₅₀ at 48 h of 0.77 μM in Vero E6 cells. Few studies conducted have shown comparable activity against other zoonotic coronaviruses with EC₅₀ values of 0.07 μM demonstrated for both SARS-CoV-1 and MERS-CoV.⁴ Remdesivir is very discerning for viral polymerases, hence a low propensity to cause human toxicity. In addition, it has shown to have a wide therapeutic index in a human airway epithelial cell model. The drug also exhibits a high genetic hurdle to resistance in coronaviruses and has an extended intracellular half-life that permits for once-daily dosing.⁵⁻⁷ We had reviewed the literature with great interest for the

successful application of remdesivir to cure a COVID-19 patient, and clinical trials indicate that this drug may have significant potential as an antiviral, and thus we report our case as an experience with remdesivir.

Grein et al conducted a study with 53 Covid-19 patients in January 2020 and they observed 68% showed an improvement in the category of oxygen support after a median period of 18 days. In our case the patients supplemental oxygen requirement decreased over a period of 14 days which is very much comparable.⁸ Also in our case on serial chest X-rays we found a significant radiological improvement as shown in (Figures 1-3). There are some limitations to this report that must be considered. Our context comes from a single patient treated with Remdesivir in the course of the disease. This patient also received HCQ, broad spectrum antibiotic, methylprednisolone (MPS). It is possible that these medications may have impacted his clinical course.

CONCLUSION

Remdesivir might be crucial for ensuring an efficient treatment, decrease mortality and allow early discharge in relation to COVID-19. Ongoing randomized, placebo-controlled trials are critical in delineating its efficacy and the importance in the treatment and prognosis.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Jain A, Pandya H, Reddy P, Shah A. A case report: remdesivir effective in the treatment of severe category COVID-19. *Int J Res Med Sci* 2020;8:3742-5.