Indian Journal of Clinical Anaesthesia 2021;8(Special Issue):5–9

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical Anaesthesia

Journal homepage: www.ijca.in

Original Research Article

Evaluation of role of remdesivir in covid-19 patients outcome: A retrospective analysis

Vengamamba Tummala[1,*], **Chilamakuri Kalyani**[1], **Saikrupa Vadlapudi**[1], **Nagalaxmi Jangiti**[1], **Beri Abhilash Sai**[1], **Kotha Balasubramanyam**[1]

[1] *Dept. of Anaesthesia, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India*

ARTICLE INFO

Article history:
Received 29-01-2021
Accepted 24-03-2021
Available online 21-10-2021

Keywords:
Remdesivir
COVID 19
Elderly patients
Hypoxia
Oxygen supplementation

ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Remdesivir, a broad spectrum antiviral agent, is currently the only drug that is approved by the Food and Drug Administration for the treatment of COVID-19. It is recommended for use in hospitalized patients who require supplemental oxygen. There are insufficient data either for or against to recommend for routine use of Remdesivir in high risk patients who doesn't require supplemental oxygen.
Aim: To evaluate the efficacy of Remdesivir in covid positive patients.
Materials and Methods: A retrospective analysis of 300 patients was done, out of which 150 patients belong to Group 1 and 150 patients belong to Group 2. Group 1-Elderly patients with comorbidities who doesn't require supplemental oxygen Group 2- Patients requiring oxygen supplementation (SpO2 88% to 94% on room air).
Results: Group 1 patients were discharged earlier than Group 2 patients.
Conclusion: Elective use of Remdesivir has a definitive role in prevention of progression of disease especially in high risk susceptible individuals.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first case was identified in Wuhan, China, in December 2019. It has since spread worldwide, leading to an ongoing pandemic. The WHO declared corona outbreak as a public health emergency of international concern. In India, first case of covid 19 was reported on 27^{th} January 2020 in Kerala.[1] Despite great efforts, there is no definitive treatment for this disease. However, prevention and management are the best options. Considering the impact of the disease on the public health, we conducted a retrospective cohort study on evaluation of efficacy of Remdesivir in COVID 19 positive patients. Remdesivir, a nucleotide analogue prodrug that inhibits viral RNA polymerases, has shown in vitro activity against SARS-CoV-2. Remdesivir, a broad spectrum antiviral agent, is currently the only drug that is approved by the Food and Drug Administration for the treatment of COVID-19. It is recommended for use in hospitalized patients who require supplemental oxygen.

2. Remdesivir

Remdesivir is a phosphoramidate prodrug of an adenosine C-nucleoside.[2]

* *Corresponding author*.
E-mail address: bvengamamba@gmail.com (V. Tummala).

https://doi.org/10.18231/j.ijca.2021.097

By entrance into respiratory epithelial cells in the human body, the prodrug may be efficiently metabolized to a nucleoside triphosphate as an active form.[3]

The active form can prevent the replication of several coronaviruses in the lung epithelial cells. The nucleoside analogue drug inhibits the RNA-dependent RNA polymerase (RdRp) by competing with the usual counterpart adenosine triphosphate (ATP). The nucleoside analogue is incorporated into the generating RNA strand and causes a delayed stop in the viral replication process.[4]

The exoribonuclease of the virus that usually proofreads and corrects the replication errors cannot work against the active form of Remdesivir.[5,6]

3. Aim

To evaluate the efficacy of Remdesivir in covid patients in two groups. Group 1-Elderly patients with comorbidities who doesn't require supplemental oxygen Group 2- Patients requiring oxygen supplementation (SpO2 88% to 94% on room air).

4. Objective

To evaluate the time taken for full recovery.

There are insufficient data either for or against to recommend for routine use of Remdesivir in patients who doesn't require supplemental oxygen. For patients at high risk of disease progression, the use of Remdesivir may be appropriate.

So, we collected retrospective data of patients who were administered Remdesivir. Group 1-Electively, i.e., elderly with comorbidities without oxygen requirement (high risk) with or without resting tachycardia and SpO2 more than or equal to 94% and Group 2-patients requiring oxygen supplementation.

5. Materials and Methods

We collected all the data from Katuri medical college and Hospital and two other private hospitals in Guntur, Andhra Pradesh. Our hospital was first private teaching hospital in the state which was declared as Covid treatment centre. After confirmed positive RT-PCR or COVID 19 Rapid antigen test, patient was admitted and baseline investigations, ECG, CXR and covid profile were sent for all patients.Once after baseline investigations were within normal limits like LFT, RFT, We administered Remdesivir 5 doses (200 mg on Day1 followed by 100mg for four days) to all patients.

Elderly patients with comorbidities who doesn't require supplemental oxygen were taken into Group 1. Most of these patients received loading dose of Remdesivir within first week of onset of symptoms.

Even after giving three doses of Remdesivir, a patient in Group 1 complained of momentary shortness of breath on minimal work and SpO2 was 88% on room air which improved to 96% on room air within few minutes without oxygen requirement. X- ray of this patient showed minimal viral pneumonitis. Remaining two doses of Remdesivir was given to this patient and was discharged on 10^{th} day. This is to emphasise the role of Remdesivir in high risk patients.

Patients with SpO2 of less than 94% on room air at the time of admission and the patients who developed hypoxia after admission who were on supportive treatment were taken into Group 2 and were given 5 doses of Remdesivir. Oxygen supplementation was given to all these patients with targeting SpO2 of atleast 94%. We observed definitive symptomatic improvement in these patients within 24hrs after giving loading dose of Remdesivir.

Few patients had elevated Sr. Creatinine on Day 1, so, bolus dose of 100mg of Remdesivir was given on Day 1. Repeat Sr.Creatinine on Day 2 was normal for few patients and these were given 100 mg for next 5 days (Full dose of Remdesivir was given in 6 days).

We admitted symptomatic covid positive post renal transplant patient with complaints of fever, cold, cough who had renal transplantation done at our institute with SpO2 of 95% on room air and was given half the doses of Remdesivir for 5 days. Patient recovered well and was discharged after 2 days. This patient was not taken into our observation as full doses of Remdesivir was not given.

But patients with elevated Sr.Creatinine and GFR less than 30ml/min were given half of the dose (100mg on Day1 followed by 50 mg on four days) of the Remdesivir with serial monitoring of Sr.Creatinine. As these patients were not given full dose of Remdesivir, these patients were not taken into our observation.

All the patients were given anticoagulants in both the groups. Initially started on Inj. Enoxaparin 0.4ml s/c BD and dose was adjusted based on D-Dimer assay. Remdesivir and corticosteroid therapy was not overlapped unless they developed hypoxia in Group 1. Corticosteroid therapy (Inj.Dexamethasone 4 mg i.v. BD) was started in Group 2 along with Remdesivir. Supportive treatment like Vitamin C 500mg TID, Zinc supplements 5mg OD, cough syrup, levocetirizine and montelukast, antacids inj. Pantop 40mg i.v. OD were given. Antibiotics were added according to clinical situation like Tab. Azithromycin 500mg OD, Tab.Doxycycline 100mg BD, Inj. Monocef 1 gm i.v. BD and Inj. Piptaz 4.5gm i.v TID to prevent secondary bacterial infections. Regular medications which they were using previously were continued.

After starting corticosteroids, hyperglycemia was noted in all patients irrespective of their previous glycemic status and glycemic control was achieved using Insulin.

All the non diabetics and diabetics with borderline hyperglycemia were controlled with inj. Mixtard s/c BD doses. All diabetics with high blood sugar levels were controlled by Inj.Lantus 30U H/S which maintains basal

glucose levels and inj. H.Actrapid was given TID according to GRBS sliding scale.

Serial chest X-rays were done on alternate days.

Oxygen supplementation was given to Group 2 patients targeting SpO2 atleast 94%. If target SpO2 of 94% was not achieved with facemask, they were connected to Non Invasive Ventilation. FiO2 was adjusted to attain SpO2 of 92 to 94%.

All the patients were advised prone position depending on their tolerance.

By 10th day, we stopped steroids in Group 1 patients. In Group 2 patients, steroids were continued till SpO2 of 94% on room air was attained and tapered gradually.

Low molecular weight heparin was continued in both the groups till the time of discharge.

Most of the patients were discharged on 10^{th} day of admission in Group 1. Group 2 patients took mean of 20 days for discharge.

Advised Tab. Apixaban 5mg OD for 10 days followed by Tab. Ecosprin 150mg for 20 days and incentive spirometry in both the groups at the time of discharge.

6. Results

A retrospective analysis of 300 patients was done, out of which 150 patients belong to Group 1 and 150 patients belong to Group 2.

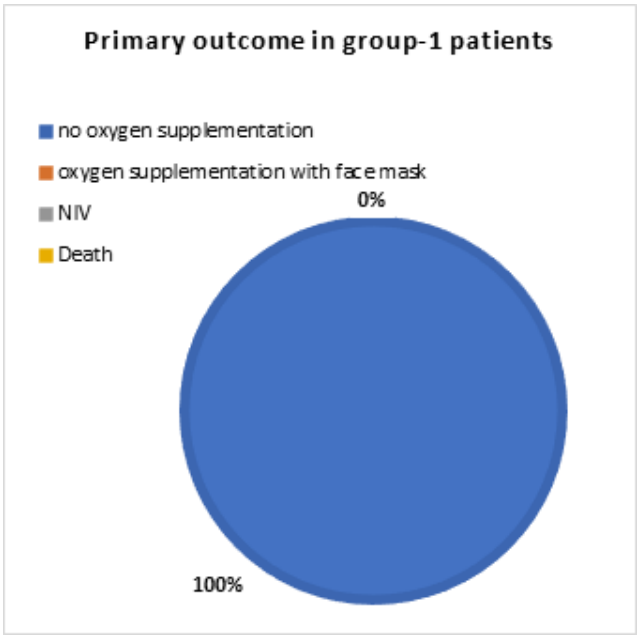

Fig. 1:

Group 1 patients discharged without oxygen requirement during their course of disease. All the patients in Group 2 were given oxygen supplementation with face mask, out of which 14% (21 patients) were connected to NIV to maintain SpO2 of 92 to 94%. Of which, 5% (8 patients) expired.

Table 1: Baseline patient characteristic

	Group 1 (n=150)	Group 2 (n=150)
Sex		
Males	80	84
Females	70	66
Comorbidities		
DM	47	24
Hypertension	58	45
CAD	30	25
Other	15	36
No	0	20
WBC count		
4000 to 10000	79	55
<4000	26	36
>10000	45	59
Sr.Creatinine		
0.6 to 1.2	126	132
>1.2	24	18
AST, ALT		
0 – 40 IU/lt	150	150
>40 IU/lt	0	0
LDH		
<245 U/lt	10	6
>245 U/lt	140	144
D DIMER		
<250 ng/ml	73	42
>250 ng/ml	77	108
CRP		
10 to 20 mg/lt	68	36
>20 mg/lt	82	114

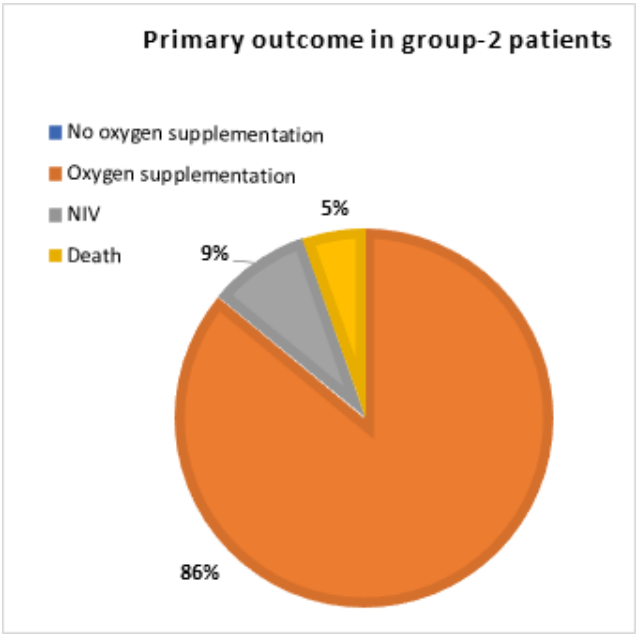

Fig. 2:

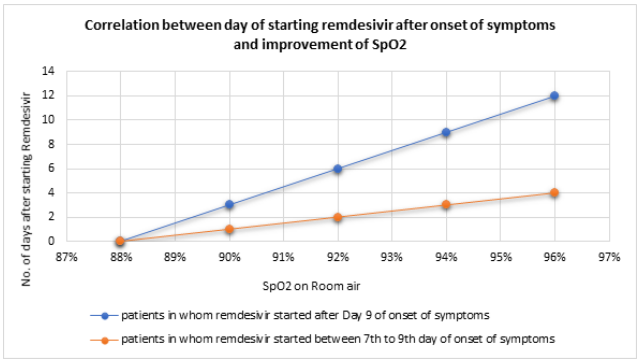

Fig. 3:

The earlier the administration of Remdesivir from the day of onset of symptoms, lesser the time taken to attain SpO2 of 94% to 96% on room air.

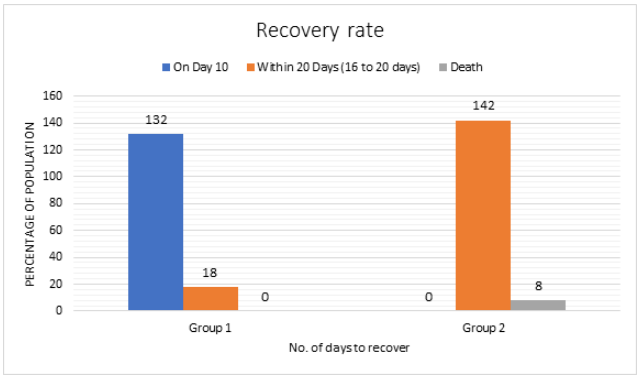

Fig. 4:

As we administered Remdesivir during viral replication phase, outcome was good in Group 1 patients when compared to Group 2 patients.

Group 1 patients did not have any post Covid symptoms like fatigue, headache, cough, myalgias, loss of appetite and weight loss.

Group 2 patients had post Covid symptoms like fatigue, cough, headache, myalgias, loss of apetite and weight loss.

7. Discussion

Remdesivir is a broad spectrum anti-viral agent that has shown a significant inhibitory effect in vitro and in vivo studies against SARS-CoV-2.

Animal studies clearly hinted that early administration of Remdesivir was more effective like in other acute viral diseases.[7] From this point of view, treating patients those already have respiratory failure, may not represent the optimal use of Remdesivir.

Early Administration of Remdesivir showed a significant reduction in viral load in Broncho Alveolar Lavage and also decreased the pulmonary infiltrates in SARS CoV2 infection of rhesus macaque model. Thus, it demonstrated both antiviral as well as clinical effects.[7]

Moreover, Remdesivir was found to be a potent inhibitor of SARS CoV2 replication in human nasal and bronchial airway epithelial cells.[8] These outcomes encouraged its use in patients with SARS-CoV-2 infection (COVID-19).

A preliminary report (April 29, 2020) from an interim analysis of an ongoing double-blind RCT recently suggested that Remdesivir had a 31% faster time to recovery, compared to the placebo ($p < 0.001$), in patients with COVID-19.[9]

The "compassionate use" of Remdesivir and purported benefit in patients with COVID-19 have been reported in some of the case series, over the last couple of months. The first high-profile single case report from Washington, USA that was published in New England Journal of Medicine (NEJM) got attention about remdesivir.[10] This study showed improvement of saturation from 94 to 96% with no requirement of supplemental oxygen after receiving single dose of Remdesivir with significant changes in X-ray.

Improvement was seen in 100% of patients with mild (receiving no supplemental or low flow oxygen) and 71% of patients with moderate (receiving high flow supplemental oxygen) COVID 19 at baseline.[11] Our analysis also showed the same results.

An exploratory analysis of Gulliead study suggested a larger benefit, if Remdesivir was initiated early within 10 days of onset of symptoms.[12]

A study of Wang et al showed that adverse effects were similar in both Remdesivir and placebo group.[13]

Although there were noted minimal complications like rash, diarrhoea, hypotension, renal and hepatic dysfunction,[14] we didn't notice any side effects in our study.

8. Conclusion

Remdesivir appears to have optimal safety profile and have a definitive role if started before manifestation of hypoxia especially in high risk elderly patients.

Elective administration of Remdesivir in high risk patients decreases the incidence of post Covid symptoms and most of them are leading near normal life after discharge.

However to date, except Remdesivir, there are no clinically approved specific or effective medicines to prevent or treat COVID 19. So, elective use of Remdesivir has a definitive role in prevention of progression of disease in high risk susceptible individuals.

Further studies are required for evaluation of role of Remdesivir in elective use in high risk patients.

9. Source of Funding

None.

10. Conflict of Interest

None.

References

1. Andrews MA, Areekal B. First confirmed case of COVID-19 infection in India: A case report. *Indian J Med Res*. 2020;151(5):490–2.
2. Siegel D, Hui HC, Doerffler E. Discovery and synthesis of a phosphoramidate prodrug of a Pyrrolo[2,1-f][triazin-4-amino] adenine C-nucleoside (GS-5734) for the treatment of Ebola and emerging viruses. *J Med Chem*. 2017;60(5):1648–61.
3. Warren TK, Jordan R, Lo MK. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. *Nature*. 2016;531(7594):381–5.
4. Tchesnokov EP, Feng JY, Porter DP, Götte M. Mechanism of inhibition of Ebola virus RNA-dependent RNA polymerase by remdesivir. *Viruses*. 2019;11(4):326.
5. Liu W, Morse JS, Lalonde T, Xu S. Learning from the past: possible urgent prevention and treatment options for severe acute respiratory infections caused by 2019-nCoV. *Chembiochem*. 2020;21(5):730–8.
6. Agostini ML, Andres EL, Sims AC. Coronavirus susceptibility to the antiviral remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. *MBio*. 2018;9(2):e00221–18. doi:10.1128/mBio.00221-18.
7. Williamson BN, Feldmann F, Schwarz B, Meade-White K, Porter DP, Schulz J, et al. Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2. *bioRxiv*. 2020;doi:10.1101/2020.04.15.043166.
8. Pizzorno A, Padey B, Julien T, Trouillet-Assant S, Traversier A, Traversier A, et al. Characterization and treatment of SARS-CoV-2 in nasal and bronchial human airway epithelia. *bioRxiv*. 2020;doi:10.1101/2020.03.31.017889.
9. NIH clinical trial shows Remdesivir accelerates recovery from advanced COVID-19. Available from: https://www.nih.gov/news-events/news-releases/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19.
10. Holshue ML, Debolt C, Lindquist S. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020;382:929–36.
11. Singh AK, Singh A, Singh R, Misra A. Remedesvir in Covid 19: A critical review of pharmacology, preclinical and clinical studies. *Diabetes Metab Syndr*. 2020;14(4):641–8.
12. Gilead announces results from phase 3 trial of investigational antiviral remdesivir in patients with severe COVID-19. Available from: https://www.gilead.com/news-and-press/press-room/press-releases/2020/4/gilead-announces-results-from-phase-3-trial-of-investigational-antiviral-remdesivir-in-patients-with-severe-covid-19.
13. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet*. 2020;395(10236):1569–78.
14. Summary on compassionate use remdesivir Gilead. Available from: https://www.ema.europa.eu/en/documents/other/summary-compassionate-use-remdesivir-gilead_en.pdf.

Author biography

Vengamamba Tummala, Professor https://orcid.org/0000-0001-6918-642X

Chilamakuri Kalyani, Assistant Professor

Saikrupa Vadlapudi, 2nd Year Postgraduate

Nagalaxmi Jangiti, 2nd Year Postgraduate

Beri Abhilash Sai, 1st Year Postgraduate

Kotha Balasubramanyam, 1st Year Postgraduate

Cite this article: Tummala V, Kalyani C, Vadlapudi S, Jangiti N, Sai BA, Balasubramanyam K. Evaluation of role of remdesivir in covid-19 patients outcome: A retrospective analysis. *Indian J Clin Anaesth* 2021;8(Special Issue):5-9.