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Original article

To Compare the Outcome of Patients Who Are Receiving Remdesivir within 10 Days of Symptom Onset to those Receiving Remdesivir after 10 Days of Symptom Onset

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Abstract

Background: A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in December 2019 as the cause of a respiratory illness designated Covid-19.Several therapeutic agents have been evaluated for the treatment of Covid-19, but no antiviral agents have yet been shown to be efficacious.

Remdesivir (RDV) is the only antiviral drug registered currently for the treatment of COVID-19 after a few clinical trials with controversial results. The purpose of this study was to compare the outcome of patients who are receiving Remdesivir within 10 days of symptom onset to those receiving Remdesivir after 10 days of symptom onset. ***Objectives:*** To compare the outcome of patients who are receiving Remdesivir within 10 days of symptom onset to those receiving Remdesivir after 10 days of symptom onset. ***Materials and Methods:*** A retrospective study was conducted on 100 patients admitted to ESIC MC & PGIMSR MODEL HOSPITAL BENGALURU during the study period from July 2020 to December 2020. Data were collected from case files of patients presenting to the Department of General Medicine Triage and COVID Ward/ICU at ESIC Bangalore fulfilling the inclusion criteria. ***Results:*** In the study, the percentage of patients who were discharged were 93.2% in the patients who received Remdesivir within 10 days of onset of the symptoms and 75% in patients who received Remdesivir more than 10 days of onset of the symptoms. The death was significantly lower among those were received Remdesivir early (<10 days) i.e. 6.8%, while 25% among those who received the same treatment late (>10days). This observation is significant with a p-value of 0.039. ***Conclusion:*** The study concludes that there is a significant improvement in the outcome of the patients who have received Remdesivir within 10 days of onset of symptoms in comparison to those who have received Remdesivir after 10 days of onset of symptoms.

Keywords: ***COVID-19; Remdesivir; Outcome***

Introduction

Coronavirus disease 2019 (COVID-19) is a major global public health and socioeconomic crisis, with over 71 million cases identified worldwide and more than 1.6 million deaths (as of Dec 2020) [1]. As a result, considerable international efforts are underway to find effective treatments involving multiple possible mechanisms. No therapy was fully approved for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at the time of writing. Remdesivir, a prodrug of an adenosine analog that inhibits viral RNA dependent RNA polymerase was recently granted Emergency Use Authorization by the US Food and Drug Administration [2]. Remdesivir has in vitro activity against SARS-CoV-2 [3,4], and early clinical data suggest promise as a treatment for COVID-19 [5-7]. Preliminary reported findings from the randomized National Institute of Allergy and Infectious Diseases (NIAID) Adaptive COVID-19 Treatment Trial indicated benefits of a 10-day course of remdesivir versus placebo, including significantly faster (32%) recovery time and numerically lower mortality [7]. Additionally, an open-label, randomized clinical trial (GS-US-540–5773) comparing 2 remdesivir courses demonstrated that outcomes of 5-day and 10-day regimens of remdesivir were not significantly different and had acceptable safety [6]. Although a randomized study in China failed to demonstrate the statistically significant clinical benefit of

remdesivir [8], the study was underpowered because of lack of enrollment and early study closure due to local disease control [9]. Although additional comparative trials are ongoing, data comparing remdesivir to a standard of care remain limited. Thus, in this study we compare the mortality and hospital stay in patients of COVID-19 receiving Remdesivir within 10 days of symptom onset to those receiving Remdesivir after 10 days of symptom onset.

Aims and objectives

To compare the outcome of patients who are receiving Remdesivir within 10 days of symptom onset to those receiving Remdesivir after 10 days of symptom onset.

Materials and Methods

Data were collected from a total of 100 patients presenting to the Department of General Medicine Triage and COVID Ward/ICU at ESIMC and PGIMSR from July 2020 to December 2020, Bangalore fulfilling the inclusion criteria and exclusion criteria.

Inclusion criteria

1. Adult patients (18 years and above) with either RT-PCR or Rapid Antigen Test positive for COVID-19 (moderate to severe).

Exclusion criteria

1. COVID-19 mild cases
2. Intubated patients.

Data were collected from case files of patients admitted to the COVID ward and ICU. History, Laboratory investigations (TLC, N:L, D-dimer, Ferritin, CRP and LDH) and radiological investigations were collected.

Method of Statistical analysis

Data were entered into a Microsoft Excel datasheet and were analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as a test of significance for qualitative data. Continuous data were represented as mean and standard deviation. Pearson correlation was done to find the correlation between two quantitative variables and qualitative variables respectively.

Results and Analysis

Age and Sex distribution

In these patients, age ranges from 17 to 90 years, with a mean age of 55 (+/- 14.36).

Table 1: Age distribution

AGE GROUP	<30	5
	31-40	8
	41-50	22
	51-60	32
	61-70	22
	71-80	6
	ABOVE 81	3
Total		100

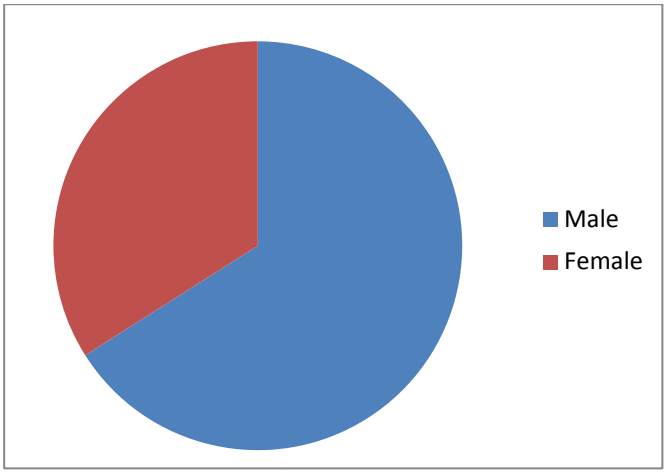

Figure 1: Sex Distribution

Males constituted 49.6% and females constituted 50.4% in our study.

Comorbidities

48.5% of the patients had comorbidities which include Diabetes Mellitus, Hypertension, Asthma, COPD and Ischaemic Heart Disease.

Patient condition

While comparing the onset of symptoms to the initiation of Remdesivir, the patients who received treatment within 10 days of onset of their symptoms, it was evident that there was a significant association of the early initiation of Remdesivir with the patient's condition and outcome.

Table 2: Patient's condition

			Patient's Condition		Total
			Deteriorated	Improved	
Day of onset of Remdesivir from the onset of symptoms	<10 days	Count	7	81	88
	>11 days	Count	3	9	12
Total		Count	10	90	100

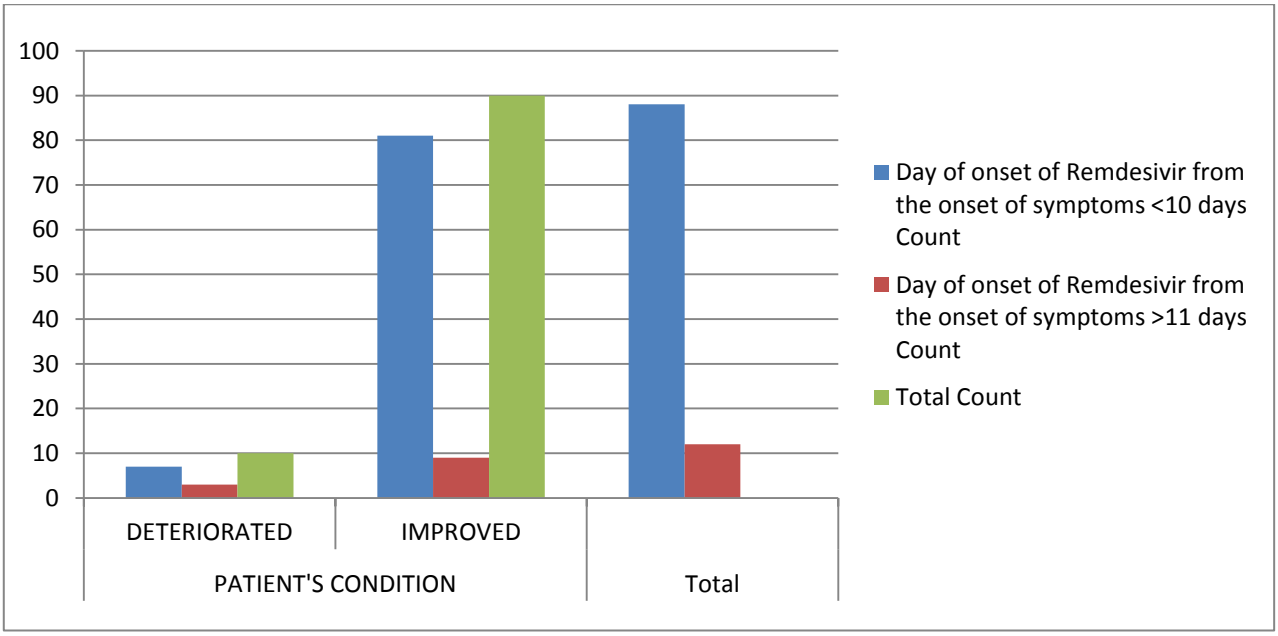

Figure 2: Patient's condition

In our study, out of 100 patients, 88 of them received Remdesivir within 10 days of onset of symptoms whereas 12 patients received Remdesivir after 10 days of onset of their symptoms. The population of patients who presented late to the hospital and the onset of Remdesivir was more than 10 days was compared with the population of patients who presented early and received Remdesivir within 10 days of onset of the symptoms, it was observed the patients who were given Remdesivir within 10 days of the manifestation of the symptoms showed improvement in their condition (92%), while only 75% of the patients who were treated with Remdesivir beyond 10 days of being symptomatic showed improvement. This was statistically insignificant with a p-value of 0.065

Patient outcome:

The percentage of patients who were discharged were 93.2% in the patients who received Remdesivir within 10 days of onset of the symptoms and 75% in patients who received Remdesivir more than 10 days of onset of the symptoms. The death was significantly lower among those were received Remdesivir early (<10 days) i.e. 6.8%, while 25% among those who received the same treatment late (>10days). This observation was deemed significant with a p-value of 0.039.

Table 3: Patient's outcome

			Patient Outcome		Total
			Discharged	Expired	
Day of onset of Remdesivir from the onset of symptoms	<10 days	Count	82	6	88
	>11 days	Count	9	3	12
Total		Count	91	9	100

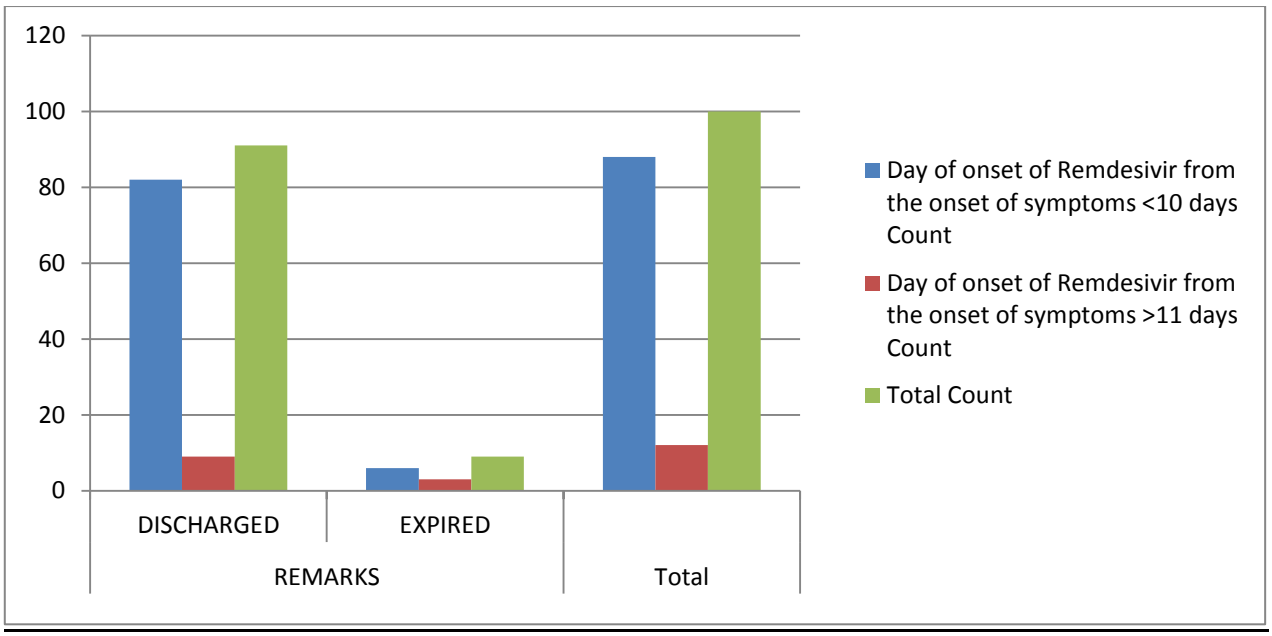

Figure 3: Patient's outcome

Discussion

Remdesivir (GS-5734), an inhibitor of the viral RNA-dependent, RNA polymerase with in vitro inhibitory activity against SARS-CoV-1 and the Middle East respiratory syndrome (MERS-CoV), was identified early as a promising therapeutic candidate for Covid-19 because of its ability to inhibit SARS-CoV-2 in vitro.

In our study, age ranges from 17 to 90 years, with a mean age of 55 (+/- 14.36), males constituted 49.6% and females constituted 50.4%. The percentage of patients who were discharged were 93.2% in the patients who received Remdesivir within 10 days of onset of the symptoms and 75% in patients who received Remdesivir more than 10 days of onset of the symptoms. The death was significantly lower among those were received Remdesivir early (<10 days) i.e. 6.8%, while 25% among those who received the same treatment late (>10days). This observation was deemed significant with a p-value of 0.039.

A study conducted by Emily Hillaker, Julie Belfer et al concluded that Late initiation of remdesivir may be effective in treating SARS-CoV-2, unlike antivirals utilized for different disease states, such as oseltamivir, that are most effective when started as soon as possible following symptom onset [10].

A study conducted by Ravindra M Mehta et al in November 2020 concluded that initiation of remdesivir ≤9 days from symptom-onset was associated with a significant mortality benefit and that these findings indicate a treatment window and reinforce the need for earlier remdesivir initiation in moderate to severe COVID-19 infection [11].

Conclusion

The study concludes that there is a significant improvement in the outcome of the patients who have received Remdesivir within 10 days of onset of symptoms in comparison to those who have received after 10 days of onset of symptoms. Thus, our study suggests the need for early initiation of Remdesivir from the onset of symptoms in moderate to severe COVID-19 infection.

Limitation

1. Retrospective study.
2. Sample size was a small and single-center study.

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