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A Case Series on the First Ten Covid-19 Patients Treated In ICU with Remdesivir in Rgssh, Tahirpur, New Delhi

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Abstract
Severe Acute Respiratory Syndrome Corona Virus 2 (SARS CoV2) is the virus responsible for the COVID 19 disease, which has evolved into a pandemic. Various parallels have been made between SARS CoV2 and other corona viruses as data is scarce. Remdesivir, a broad spectrum antiviral, is a prodrug which has shown efficacy in vitro against SARS CoV2. But the same is questionable in patients with severe COVID 19 disease. Among the 10 patients treated with Remdesivir, 8 patients got discharged from the ICU and 2 patients required mechanical ventilation. All 10 patients became plasma negative for SARS CoV2 after 10 days. The treatment duration was a period of 5 days as per the Emergency Use Approval (EUA), Experimental by the Indian Council for Medical Research (ICMR). Also it is noted that the patients were on concurrent therapy with corticosteroids, anti coagulants and antibiotics as well. Around 7 patients had an increase in their alanine aminotransferase levels (3 to 5 times). 6 patients developed maculopapular rash, which receded after stoppage of remdesivir. 4 patients had increased serum creatinine levels. This case series aims to describe the clinical outcomes of the first 10 COVID patients in Rajiv Gandhi Super Speciality hospital. This study also highlights the complexity of Remdesivir, when used in severe COVID 19 patients.

Key Words: *Remdesivir, macular rash, COVID 19, aminotransferase,*

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I. Introduction

In 2019 December, Severe Acute Respiratory Syndrome Corona Virus-2 (SARS CoV-2) was identified as responsible for COVID 19 outbreak. Many treatment options were investigated, especially during SARS and MERS (Middle East Respiratory Syndrome epidemic), which were caused by Beta coronavirus genus (SARS-CoV-1) and MERS-Cov respectively. The various agents include Ribavirin and Interferon alpha-2beta, Lopinavir/Ritonavir and Hydroxychloroquine.

Remdesivir is a nucleotide analogue and a prodrug with broad spectrum antiviral activity against SARS CoV-2 in vitro. Two case reports (Hol Shue et al 2020 and Keyauski et al 2020) and a recent clinical study of 54 patients (Grein et al) also showed encouraging reports.

Ten (10) patients were treated with compassionate use of Remdesivir in Rajiv Gandhi Super Speciality hospital, New Delhi.

CASE PRESENTATION

All patients were admitted to Rajiv Gandhi Super Speciality hospital and treated with Remdesivir (Gilead Sciences) were enrolled. The indication criteria for the compassionate use of the novel antiviral Remdesivir is defined by the ICMR(Indian Council for Medical Research). Also there was absence of identifying images or personal/ clinical details that could compromise anonymity.

PROCEDURE

All 10 patients were given Remdesivir infusion of 200mg loading dose followed by 100mg for a maximum duration of 5 days. The WHO 6 point criteria was used and the course of illness monitored. A decrease in 2 points was considered significant.

The 6 point score included:

1. Not hospitalised
2. Hospitalised
3. Hospitalised + requiring supplemental O2
4. Hospitalised + requiring high flow nasal O2 (NIV)
5. Hospitalised + requiring invasive mechanical ventilation or ECMO or both
6. Death

II. Results

CASE 1

A 54 year old Indian from the state of Uttar Pradesh reported flu like symptoms for 6 days and was diagnosed with COVID 19. The standard RTPCR was done. He was hospitalised immediately as he had mild hypopnea and thrombocytopenia (1,46,000). No abnormalities on chest X ray. On day 7 of the illness, he was transferred to the Intensive Care Unit due to worsening of oxygen saturation. X ray chest PA view showed B/L growing glass opacities. Remdesivir was started on day 9 of the illness and was stopped on day 14. The dose given was 200mg iv bolus on day 14. The dose given was 200 mg iv bolus (over 20 min) on day 1 followed by 100mg iv bolus once daily for 4 days. Increase in Alanine Aminotransferase (ALT) 165 IU vs 46 IU was noted before and after Remdesivir administration. Also the patient developed macula papular rash. The skin and liver abnormalities improved within 3 days of discontinuing treatment. The patient was discharged on day 24.

CASE 2

A 76 year old tourist from Bangladesh. The patient had a past history of thyroid cancer. He presented with fever and diarrhoea of 4 days duration. x ray chest showed B/L alveolar opacities. Airborne and contact precautions were observed. His nasopharyngeal RTPCR was COVID 19 positive. He developed acute respiratory failure and multiple organ failure. He was shifted to the ICU. Broad spectrum antibiotics were started. Remdesivir was started on day 4. Total 5 days of Remdesivri with 200mg iv bolus over a period of 20 minutes on day 1 followed by 100mg iv for 4 days. A CT scan performed showed B/L alveolar consolidation, ground glass opacities and pulmonary cyst. The patient was eventually put on mechanical ventilation as his condition worsened. He developed multi organ dysfunction and had an episode of cardiac arrest. He died 14 days after admission.

CASE 3

A 40 year old female airport worker who was obese (BMI 33kg/m2) with obstructive sleep apnea syndrome was diagnosed with severe COVID 19 a. She had severe cough and fever for 6 days. She presented with acute respiratory failure (PaO2=74mmHg). She was initially kept on high flow nasal cannula 40L/min (40%). She had a drop in saturation and admitted to the ICU and was started on Remdesivir on day 7 of illness. The normal dosage of 200mg iv bolus on day 1 for 20 minutes followed by 100mg iv infusion once daily for 4 days was continued. The patient was found to have basal interstitial syndrome on chest X ray. The patient was weaned off oxygen on day 16 of illness. Remdesivir was discontinued after 5 days of treatment. ALT was found to be elevated (112 IU vs 40IU before Remdesivir). The ALT became normal after 6 days of stopping Remdesivir. Patient was discharged after 24 days of the initial illness.

CASE 4

A 79 year old Bangladesh national with a history of chronic kidney injury (creatinine 115 micromol/L, normal 50-70 micromol/L) was admitted with fever for 24 hours and cough for 48 hours duration. He was diagnosed with COVID 19 through RTPCR. The patient was shifted to the ICU with SpO2 88% (on nasal prongs at 5L/min). He showed posterior pulmonary ground glass opacities on chest CT. On day 7 of the illness, his O2 saturation worsened. He was kept on high flow nasal oxygen at 40L/min. He was started on Remdesivir at 200mg iv bolus on day 1 (infusion over 20 minutes in DNS) followed by 100mg iv infusion once daily for the next 4 days. Meanwhile, he developed dyspnea and severe tachypnea. His O2 saturation worsened. He was intubated and kept on ventilator. Patient deteriorated and had B/L ARDS and extensive pulmonary infiltrates. Patient had one episode of cardiac arrest. He could not be revived. He was declared dead 16 day post admission.

CASE 5

A 60 year old female with a history of hypertension and diabetes mellitus was diagnosed with COVID 19. She had cough and fever for 6 days. She was taking cough syrup and tablet Paracetamol 500mg sos. She was shifted to the ICU 3 days post admission due to tachypnea and fall in saturation (96% on admission on room air -> 88% on room air) . Remdesivir was started on second day of admission. It was given as 200mg iv bolus ninfusion over 20 minutes followed by 100mg once daily for 4 days. Her ALT was elevated (118 IU/L from 48 IU/L). She was also encouraged proning (16 hours a day). She developed maculopapular rash. After 4 days of remdesivir, patient's symptoms decreased and her ALT became normal and rash reduced. She was discharged on day 26 from hospital.

CASE 6

A 34 year old male from Uttar Pradesh, India reported flu like symptoms 4 days back. He was diagnosed with COVID 19 with RTPCR. He was shifted to the ICU when he started having respiratory distress. He was kept on high flow nasal O2 at 40L/minute. His chest CT showed B/L posterior lobe consolidation. He was

started on Injection Remdesivir 200mg iv bolus and followed by 100mg iv infusion once daily for a period of 4 days. His ALT increased mildly (108 IU/L from 44 IU/L before start of Remdesivir). On day 6 post stopping Remdesivir, his symptoms decreased. His breathing pattern improved. He was discharged from the hospital 16 days post admission.

CASE 7

An 84 year old female originating from Haryana with complaints of fever for 4 days and cough for 3 days. she was a known case of COPD and also had history of Tuberculosis in the past. She was admitted to the ICU when her saturation dropped from 92% on room air ->84% on room air. Chest X ray showed B/L basal ground glass opacities. She was started on Injection Remdesivir 200mg iv bolus as infusion over a period of 20 minutes followed by 100mg iv infusion for 4 days. Chest CT showed posterior lobe consolidation. Nevertheless, she developed multi organ failure and refractory acute respiratory distress syndrome despite proning and adapted mechanical ventilation. She was started on Dexamethasone and Low molecular weight heparin. She died 17 days post admission (21 days of illness).

CASE 8

A 69 year old male originating from Delhi with history of fever for 4 days and cough for 4 days. Chest X ray showed B/L alveolar opacities. Airborne and contact precautions were observed and diagnosis of COVID 19 was eventually made 2 days later by RTPCR. Patient was shifted to the ICU when she developed breathlessness and saturation dropped to 88% on room air. She was started on injection Remdesivir 200mg iv bolus on day 1 followed by 100mg iv infusion for 4 days. His ALT got elevated from 44IU/L to 134IU/L. His symptoms decreased on day 4 after stopping Remdesivir. He was shifted back to the ward. His ALT became normal. He was discharged on day 18 of illness.

CASE 9

An 84 year old tourist from Bangladesh got admitted with complaints of fever for 2 days and cough for 2 days. He was a known case of chronic renal failure on renal replacement therapy. He was confirmed COVID 19 positive through RTPCR and was shifted to the ICU when he had respiratory distress. Patient was started on Injection Remdesivir 200mg iv infusion boys on day 1 followed by 100mg iv infusion over a period of 20 minutes once daily for 4 days. The patient had B/L posterior lobe opacities in CT scan. On day 6, the patient developed macular rash on hands and face. His ALT increased from 48 IU/L to 168 IU/L. Despite prone position and adapted mechanical ventilation, he developed multi organ dysfunction. Also he developed sudden acute respiratory distress syndrome. The patient suffered cardiac arrest and succumbed on day 27 of illness.

CASE 10

A 46 year old male from Delhi presented with complaints of fever for 6 days and cough for 4 days. He was diagnosed as COVID positive on RTPCR. He was shifted to the ICU on day 6 of admission owing to breathlessness. He was started on Injection Remdesivir 200mg iv bolus on day 1 followed by Injection Remdesivir 100mg iv over a period of 20 minutes once daily for 4 days. Chest X ray showed B/L posterior lobular opacities. On day 2 of Remdesivir, he developed macular rash and his ALT increased 40IU/L to 155 IU/L. On day 6 post stoppage of Remdesivir, his symptoms decreased. He became symptom free post 8 days of stoppage of Remdesivir and was discharged on day 24 post admission in RGSSH.

III. Discussion

Of this case series 10 COVID 19 patients requiring ICU treatment for respiratory distress and treated with Remdesivir, 6 patients had a favourable outcome despite initial respiratory severity. They were weaned off oxygen between day 14 and day 19 of illness and discharged between day 20-day 30 of illness. Four patients died of multi organ failure and severe acute respiratory syndrome. While on Remdesivir, we observed the patients experienced major side effects. They suffered renal injury. 7 patients had macula papular rash. 3 patients had cytotoxic hepatitis. The renal injury could be related to both COVID 19 as well as Remdesivir. In a previous case report (Grein et al 2020) 53 patients of COVID 19 on Remdesivir treatment were described , of which 30 were on mechanical ventilation. After a median follow up of 18 days, after Remdesivir initiation, a total of 25 (47%) were discharged. Seven (13%) died and 10 were still on mechanical ventilation. No virological data was available on that report. Also in 12%, Remdesivir was discontinued due to adverse effects.

IV. Conclusion

In conclusion, the cases of 10 patients presented herein highlights some difficulties with Remdesivir infusion when administered in patients with advanced diseases. Particular attention should be paid to hepatic and renal functions when administering this treatment.

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CONFLICT OF INTEREST
The authors declare they have no competing interest.

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