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The Effect of Remdesivir in Patients with Severe COVID-19, Reporting Case Series

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Dear Editor,

The outbreak of SARS-CoV-2 in Wuhan, China, in December 2019, which causes COVID-19, has turned into a global health threat to human (1, 2). COVID-19 was declared a pandemic by the World Health Organization (WHO) in March 2020 (3). Numerous lives have been affected as a result of compulsory distancing/quarantine. The pandemic can overwhelm national healthcare systems and result in grave consequences for the world's economy if it spreads out of control, or if effective treatments are not used (4). Furthermore, it can incur more harm to people with underlying diseases, especially prevalent diseases such as diabetes and hypertension (5). Clinical trials are being carried out on a wide range of new treatment modalities, but no effective medication has yet been introduced for treating COVID-19 (6, 7). Remdesivir (code: GS-5734) is a prodrug monophosphoramidite nucleoside, which was first developed in response to the ebola outbreak in 2014 - 2016 in West Africa (7, 8). Remdesivir has shown a wide range of activities against human and zoonotic coronaviruses in preclinical models and proved promising for COVID-19 clinical trials (7, 8). This medication has also been assessed in clinical trials with COVID-19 patients (9, 10).

The present case series was conducted to assess and compare remdesivir with standard of care (SOC) in terms of effectiveness in patients with severe COVID-19.

This study used records of 60 eligible patients admitted to Shahid Mohammadi Hospital, Bandar Abbas, Iran, in early 2020. All patients underwent a WHO-approved treatment regimen for severe COVID-19. The inclusion criteria of the study consisted of presenting to acute respiratory diseases center in Shahid Mohammadi Public Hospital, definitive diagnosis of COVID-19 through positive PCR for SARS-CoV-2, and confirmed clinical and imaging evidence (spiral chest CT-scan). The exclusion criteria were AST or ALT, five times greater than normal, and creatinine clearance < 50 mL/min (9). Signs and symptoms required for inclusion (critical categories) (11): Tachypnea (respiratory rate > 30/min), Hypoxemia (PO_2 saturation $\geq$ 93, PaO_2 < 300), lung infiltration (< 50% of lung space in 24 to 48 hours), LDH > 245 U/L, progressive lymphopenia, CRP > 100. The study population was divided into two groups of 30 each: Group A receiving remdesivir plus SOC (as per records and treatment process), and group B receiving SOC alone. Remdesivir was administered at a dose of 200 mg on day one and then at 100 mg on days two to ten.

SOC included the following medications according to the treatment protocol of National COVID-19 Committee (9):

(1) Hydroxychloroquine/chloroquine phosphate as hydroxychloroquine sulfate 200 mg tablets or chloroquine phosphate 250 mg tablets (equivalent to 150 mg base value) two tablets bid on the first day, followed by one tablet bd for a minimum of seven days and maximum of 14 days.

(2) One of the following medications at the doctor's discretion:

(A) Two 200/50 mg kaletra (lopinavir/ritonavir) tablets bid after meals for a minimum of seven days and maximum of 14 days.

(B) One 300/100 mg (atazanavir/ritonavir) tablets daily with food or one 400 mg atazanavir daily for a minimum of seven days and a maximum of 14 days.

The primary objective was to assess the effectiveness of remdesivir + SOC and SOC alone on the patients' recovery and mortality rate. The secondary objective was to assess the difference between the two groups in terms of laboratory findings and hospital stay (Table 1).

Table 1. Difference Between the Two Groups in Terms of Laboratory Findings and Hospital Stay [a]

Variables	A (N = 3)	B (N = 3)	P-Value [b]
Gender (male)	17 (56)	17 (56)	1
Age (y)	50 ± 15	51 ± 13	0.7
WBC ($\times 10^9$/L)	9000 ± 2100	9800 ± 2500	0.34
Hb g/dL	11.1 ± 3.1	11.4 ± 2.8	0.22
LDH (U/L)	370 ± 72	384 ± 90	0.27
CRP (mg/dL)	17 ± 12	19 ± 14	0.18
Hospital stay (day)	9 ± 4	12 ± 5	0.031
Mortality rate	6 (20)	10 (33)	0.002

[a] Values are expressed as No. (%) or mean ± SD.
[b] $P < 0.05$ was significant.

The present study showed that mortality rate as one of the main outcomes was significantly lower in the group A. Moreover, the mean hospital stay was also significantly less in the group A than that in the group B.

Various studies have reported contradictory results (9, 12, 13). Thus, further studies are needed to increase scientific, credible, and reliable data. Yet, in agreement with most other studies, the results of the present study confirmed the relationship between administration of interferon and patient recovery. In comparison, considering the effects of different medication groups such as nonsteroidal anti-inflammatory medications like ibuprofen, or medications such as famotidine or N-acetylcysteine, which are effective in managing the inflammatory phase in patients with moderate to severe COVID-19, paying particular attention to the effect of antivirals (with virus-specific action) is highly important in patients with COVID (14-16).

This case series showed that administration of remdesivir in patients with severe COVID-19 has positive effects on reducing the mortality rate and duration of hospital stay. However. Further studies and clinical trials are recommended to confirm these results.

Footnotes

Authors' Contribution: HR.S and M.KJ contributed to conception, design, and statistical analysis. Other authors contributed to data collection and manuscript drafting. M.KJ supervised the study. All authors approved the final version of the manuscript.

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