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Archives of Pharmacology and Therapeutics Letter to the Editor

Remdesivir in COVID-19 Patients with End Stage Renal Disease on Hemodialysis

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Abstract

To date, only glucocorticoids have been shown to reduce mortality in COVID-19. Use of remdesivir was associated with reduced length of stay in hospitalized COVID-19 patients. A deadly second wave in Asian countries has caused increased demand and usage of remdesivir in these countries. However, there is limited data about its efficacy in patients with severe renal dysfunction or end-stage renal disease on dialysis.

COVID-19, a global pandemic caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) has resulted in hospitalization in many cases. The pathophysiology involves an initial viral response phase where patients mostly have mild constitutional symptoms, followed by a pulmonary and then a hyperinflammatory phase where patients have shortness of breath, hypoxemia, abnormal chest imaging and elevated inflammatory markers [1].

Current treatment for COVID-19 includes dexamethasone and remdesivir, besides supportive care and supplemental oxygen [2,3]. Recently, the RECOVERY study group also reported positive results with tocilizumab when used in combination with dexamethasone [4]. Initial trials on remdesivir excluded patients with CrCl<30 ml/min/1.73m^2. Evidence suggests that acute kidney injury is present in >20% of hospitalized patients and >50% of patients in the ICU [5]. In addition, mortality rates are much higher (between 26 and 35%) in this high risk, vulnerable population [6].

Remdesivir is a broad-spectrum anti-viral drug and inhibits viral RNA-dependent RNA polymerase. Intracellularly, remdesivir prodrug is rapidly converted into its metabolite GS-704277 and subsequently into GS-441524, which becomes the main circulating metabolite. The metabolites compete with adenosine triphosphate for incorporation into viral RNA, causing premature chain termination and inhibition of viral replication [7,8]. The other component of remdesivir includes SBECD, which helps in increasing the solubility of remdesivir. Concerns about safety data for SBECD carrier's accumulation should be allayed by the available data on voriconazole [9]. Remdesivir is renally excreted approximately 10% as unchanged drug and 49% as GS-441524. GS-441524 is removed by hemodialysis, with post-dialysis concentrations 45%–49% lower than pre-dialysis levels [10].

We conducted a retrospective study on all hospitalized patients at our institution with a diagnosis of COVID-19 and end stage renal disease on hemodialysis between April 1 and December 31, 2020. A total of 52 charts were reviewed, of which 28 met the inclusion criteria. 14 patients received remdesivir, and 14 patients did not receive remdesivir. Primary endpoints were length of stay, mortality, maximum oxygen requirements along with escalation of care needing mechanical ventilation. Secondary endpoints included change in CRP, d dimer levels and disposition. A two-sample t-test was used to compare means. Z-test and chi-square analysis were used to compare proportions. Type 1 error (alpha) was set at 0.05. Statistical analysis was performed using 'R' programming software.

	NON REMDESIVIR (n=14)	REMDESIVIR (n=14)	P Value
Mean Age – yr.	66.6 (± 14.94)	64.0 (± 13.80)	0.640
Females – no. (%)	7 (50)	8 (57)	0.704
White Race or ethnic group– no (%)	6 (43)	7 (50)	0.461
Tobacco use – no. (%)	6 (43)	7 (54)	0.704
Diabetes mellitus – no. (%)	10 (71)	9 (64)	0.685
Hypertension – no. (%)	14 (100)	13 (93)	0.308
Obesity (BMI>30 kg/m²) – no. (%)	4 (28)	5 (36)	0.685
Dexamethasone – no. (%)	6 (43)	14 (100)	<0.001
Antibiotics	7 (50)	9 (64)	0.445
Disposition – Home - no. (%)	3 (38)	5 (62)	0.723
Disposition- Died – no. (%)	6 (60)	4 (40)	0.751
Peak CRP levels (Mean ± SD)	176 ± 80.3	174 ± 80.5	0.944
Peak d dimer levels (Mean ± SD)	896 ± 585	1453 ± 1529	0.227
LOS in days (Mean ± SD)	10.4 ± 6.4	14.1 ± 9.23	0.228
Max O_2 requirement (L/min)	18 ± 20.6	15.5 ± 19.9	0.751

Table 1: Baseline, clinical and laboratory characteristics of patient population.

Most of our patients were Caucasians, females and had diabetes and hypertension. The mean length of stay in the remdesivir group was 14.1 days compared to 10.4 days in the non-remdesivir group. Maximum oxygen requirement in the remdesivir group was 15.5 L/min compared to 18 L/min in the non-remdesivir group. There was no statistical difference in mortality, length of stay or maximum oxygen requirement. There was no difference in CRP levels, d dimer levels and rates of mechanical ventilation between the two groups [11] (Table 1).

Our study had some limitations. Firstly, the sample size was small and may not have been powered adequately to detect a difference. To detect statistical significance with 5% sampling error, we would have needed approximately 85 patients. Secondly, being a retrospective study, the study design has inherent biases such as selection and confounding biases. Our patient population was derived through convenience sampling. This increases the probability of sampling error and reduces generalizability. Lastly, it is unclear if the higher concomitant use of dexamethasone in the remdesivir group eclipsed potential differences in any of the outcomes despite using multivariate analysis.

The ACTT-1 trial showed that the median time to recovery was 10 days in the remdesivir group compared to 15 days in the placebo group [2]. However, remdesivir failed to provide a survival benefit. Despite having a limited sample size, our results in this population subgroup were consistent with ACTT-1 study results. In addition, there was no difference in length of stay or inflammatory marker levels. Large scale studies are needed to further elucidate the benefit of remdesivir in this population subgroup and also patients with chronic kidney disease stage 4 or 5 that are not on hemodialysis.

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