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RESEARCH LETTER

Safety profile and clinical results of Remdesivir in Hemodialysis patients infected with SARS-CoV-2. A single-center Spanish cohort study

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Since its outbreak in March 2020, COVID-19 has disrupted the world. Hemodialysis patients are susceptible to the development of severe disease due to their immunocompromised state [1].

A variety of treatment regimens for COVID-19 have been tested. In May 2020, remdesivir was the first antiviral drug to be approved by the US Food and Drug Administration (FDA) for emergency use in moderate-to-severe COVID-19. Its mechanism of action consists in inhibiting the viral RNA-dependent RNA polymerase (RdRp) [2]. Remdesivir is not recommended in patients with an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2 due to the presumed toxicity of the drug itself and the accumulation of its solubilizing excipient sulfobutyl ether β-cyclodextrin (SBECD) [2]. Initially, this drug was associated with a reduction in morbidity and mortality. Later, through two larger clinical trials (Solidarity and ACTT-1), it was found only to improve recovery times and shorten hospital stays [3]. Moreover, a prospective, double-blind trial conducted in China found no difference between remdesivir and placebo in early recovery [2]. More data regarding the safety profile and use of remdesivir in end-stage kidney disease (ESKD) have emerged [3, 4].

This retrospective cohort study of 36 hemodialysis patients infected with SARS-CoV-2 between December 2021 and March 2022 aims to report our single-center experience using remdesivir. Patients had a median age of 71.4 ± 14.6 years, and most were males (72.2%). Thirty-five (97.2%) had hypertension, 13 (36.1%) type 2 diabetes, 17 (47.2%) dyslipidemia, 1 (2.7%) hepatopathy, and 4 (11.1%) had chronic obstructive pulmonary disease, with a mean Charlson's comorbidity index of 6.63 ± 2.41. The mean dialysis vintage was 58.03 ± 92.64 months. Thirty-four patients (94.4%) had been previously vaccinated with two doses of a SARS-CoV-2 mRNA vaccine.

Twenty-one patients (58.3%) completed five days of treatment with remdesivir, receiving the first dose within the first 48 h of diagnosis. No statistically significant differences were found between treated and control groups in any of the previously mentioned variables. Remdesivir was started at diagnosis in all patients who accepted, at a dosage of 200 mg on the first day, followed by four doses of 100 mg every 24 h. The medication was administered in the hospital setting if hospital admission was needed or at home if they could be discharged. On days coinciding with hemodialysis, the treatment was administered immediately after the session. Liver function was monitored daily during treatment.

In addition to remdesivir, each patient also received 40 mg of enoxaparin subcutaneously (or intravenously during the dialysis sessions). Patients with bilateral pneumonia on chest x-ray and C-reactive protein (CRP) above 7 mg/dL also received 6 mg of intravenous dexamethasone every 24 h for seven days. If the patient had mucopurulent sputum with leucocytosis and neutrophilia, a third-generation cephalosporin was added to treat a possible bacterial superinfection. Nasopharyngeal swabs for SARS-CoV-2 by reverse transcription-polymerase chain reaction were repeated seven days after admission and then every 72 h afterwards until obtaining a negative result.

Patients were classified as having mild/moderate disease if oxygen saturation on room air was ≥ 94% or < 94%

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requiring nasal prongs or facemasks and a chest x-ray with no or unilateral involvement. Severe infection was defined as having oxygen saturation on room air < 90% requiring high flow oxygen therapy or a chest x-ray with bilateral involvement. Thirty-two patients (88.8%) suffered a mild infection, and among them, 10 (27.7%) did not require hospital admission and were therefore sent home. None of the patients required invasive ventilation, though nine (25%) needed oxygen supplementation (seven by nasal prongs and two by facemask).

During follow-up, three patients (8.3%) died. Only one of these deaths was related to COVID-19; the other two were due to an endovascular bacterial infection and decompensated heart failure, respectively. Liver function remained stable in all patients, with no abnormalities observed before or after treatment, and none of the patients required discontinuation due to side effects. There were no differences in biochemical markers (CRP or serum ferritin) between the two groups, or with regard to days of hospitalization or amount of time before testing negative for COVID-19.

Unlike other published studies in which remdesivir correlated with a decrease in hospital stay and shortened recovery time [2–5], its use, despite being well-tolerated and not having shown any adverse effects, did not seem beneficial in our population. Our main limitation is the small sample size that may have caused a Type II error (false-negative results) to surface; however, our study differs from the previously published ones in other relevant aspects. The most important one is the difference in the remdesivir administration method since most studies administer it 4 h before the hemodialysis session. In our institution, the drug was administered at the end of the session to avoid its elimination during dialysis and with a loading dose on the first day[3–5]. Although this would not explain the results obtained either, we might have expected a greater number of significant adverse effects, yet these were not seen. In addition, it should be borne in mind that we administered remdesivir to all patients who accepted the treatment regardless of infection severity.

Based on these results, remdesivir would not appear to be to be cost-effective in the vaccinated hemodialysis population, although further studies-analyses with larger cohorts are needed to gather more evidence.

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Declarations

Conflict of interest The authors have nothing to disclose nor relevant financial interests.

Ethical statement The Local Clinical Research Ethics Committee has approved this study. Data collection has followed the Regulation (EU) 2016/679 (General Data Protection Regulation), its subordinate national and regional laws, and the Declaration of Helsinki principles.

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