Iranian Journal of Pharmaceutical Sciences
2024: 20 (1): 69- 79
https://journals.sbmu.ac.ir/IJPS

Original Article

Evaluation of Clinical Outcomes in COVID-19 Patients Receiving Remdesivir in Outpatient Setting

Forough Goudarzi[a], Behnam Behnoush[b], Elahe Hesari[a], Saeed Nateghi[c], Majid Akrami[d], Nafisehsadat Alizadeh[e], Mohammad Arefi[f], Mohammad Vaseie[g], Arezoo Khosravani[h], Roya Sani[h], Mahbobeh Alizadeh[i*]

[a]Department of Epidemiology Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran., [b]Department of Forensic Medicine, Tehran University of Medical Sciences, Tehran, Iran, [c]Department of Cardiology, Development and Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran, [d]Department of Anesthesiology, Development and Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran, [e]Department of Clinical Pharmacotherapy, Development and Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran, [f] Department of Gastroenterology, Development and Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran, [g]Department of Emergency Medicine, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran, [h]Department of Nursing, Nursing School of Tehran University of Medical Science, Tehran, Iran, [I]Department of Infectious Diseases, Nosocomial Infections fellowship, Development and Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Remdesivir (RDV) is one of the drugs that showed beneficial effects in treating Coronavirus disease in 2019 (COVID-19). We performed the present study to evaluate the safety of Remdesivir administration in the outpatient setting. In this study, 512 patients with COVID-19 participated. When selected patients came to the hospital for the drug injection on the appointed day, the vital signs and the percentage of oxygen saturation were measured before Remdesivir administration. During and after the injection, if any drug side effects occurred, it was recorded. Laboratory tests, including Complete blood count differential, C-reactive protein, Liver function tests, Blood urea nitrogen, and creatinine, were checked before and between the treatment courses. The mean age of participants was 46.19±14.20 years, and 46.9% were men. 97.4 percent of patients did not experience any side effects following Remdesivir administration. The amounts of laboratory components like White blood cells, Platelet, Alanine aminotransferase, and Blood urea nitrogen were significantly increased. In contrast, Hemoglobin, C-reactive protein, Aspartate aminotransferase, Alkaline phosphatase, and Creatinine levels were significantly decreased following the administration of Remdesivir compared to baseline values.

In the current study, there were no severe side effects of taking Remdesivir, so RDV can be used safely to treat COVID-19 in the outpatient setting.

Keywords: Remdesivir, RDV, Adverse effects, Side effects, Outcome, Outpatient, COVID-19.

Corresponding Author: Mahbobeh Alizadeh, Department of Infectious Diseases, Nosocomial Infections fellowship, Development and Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran. E-mails: mahbobeh.alizadeh.mg@gmail.com

Cite this article as: Goudarzi F, Behnoush B, Hesari E, Nateghi S, Akrami M, Alizadeh M, et al. *Evaluation of Clinical Outcomes in COVID-19 Patients Receiving Remdesivir in Outpatient Setting*, Iran. J. Pharm. Sci., 2024, 20 (1): 69- 79.
DOI: https://doi.org/10.22037/ijps.v20i1.42191

1. Introduction

Coronavirus disease in 2019 (COVID-19) is an infectious and inflammatory disease caused by the SARS-CoV-2 virus. Until January 15, 2024, more than 700 million people have been infected

with COVID-19, of whom nearly 7 million have died from the disease. In Iran, more than 7.5 million people were infected with the virus; of them, almost 1.9% died [1]. Everyone at any age is susceptible to the disease, so it is important to pay attention to the prevention and treatment of this disease [2]. No definitive antiviral treatment has been identified for COVID-19 [3]. According to the guidelines, several antivirals treat this disease, including Remdesivir (RDV), Molnupiravir, and Paxlovid [4].

Remdesivir is an adenosine analog nucleotide prodrug that inhibits virus replication. The drug is Food and drug administration (FDA) approved to treat COVID-19 either in hospitalized adult patients as well as in pediatric patients (older than 28 days and over 3 kg) for five days or mild to moderate patients but at high risk for progression to severe disease for three days [5]. It is injected intravenously and is approved by the US Food and Drug Administration [6]. RDV has previously been used to treat Ebola. It is effective against SARS CoV-2 in vitro; viral levels were lower in the animals' lungs treated with RDV, and their lungs were less damaged than those in the control group [7, 8].

In a study after a ten-day treatment course of RDV, 68% of patients with COVID-19 experienced clinical improvement, but it should be noted that there was no control group in the study [9]. According to the results of a review study, treatment with RDV was associated with an increase in clinical improvement of 21% and 29% on days 7 and 14, respectively. Patients treated with RDV showed a 39% reduction in mortality on day 14, but there was no significant difference on day 28 compared to the control group. Also, serious side effects were significantly less in patients treated with RDV [10]. During medical treatment, RDV can cause kidney or liver problems, and in patients with liver and kidney disorders, medical evaluations should be performed [11]. However, in another study, RDV was significantly associated with a reduced risk of Acute kidney injury (AKI) [12].

In the studies and clinical trials performed so far, different results have been reported regarding the effectiveness and side effects of RDV in non-hospitalized COVID-19 patients. Furthermore, since the issuance of the outpatient use of RDV in Iran, limited studies have specifically examined the clinical outcomes of patients receiving RDV. Therefore, this study was performed to evaluate the safety of outpatient administration, the drug side effects, and possible implementation problems of the project in a university hospital for three months.

2. Materials and Methods

This cohort study with a 2-week follow-up period was performed in 2021 at Baharloo Hospital of Tehran University of Medical Sciences in Iran.

2.1. Study Population and Data Collection

In the present study, a sample of 512 patients with COVID-19 was enrolled using the convenience sampling method. The sample size was calculated using the following formula:

$$n = \frac{z^2_{1-\frac{\alpha}{2}}\, p(1-p)}{d^2}$$

Considering an acceptable error level of 5% and clinical improvement of 68% in a similar study [9] and $\alpha = 0.05$, a sample size of 335 people was obtained. Due to more patient access, 512 people were included in the study.

They came to the Baharloo emergency department during the fifth peak of the disease in IRAN. Patients entered the study with personal consent and could withdraw from the study at any time.

In addition to the physician's clinical diagnosis, the following criteria were considered in selecting the patients for outpatient treatment with Remdesivir:

- Based on World health organization (WHO) definitions for the severity of COVID-19 [2], patients with mild disease plus at least one risk factor for COVID-19 progression or moderate disease without any predisposing factors **(**Age ≥65, BMI ≥30, Pregnancy or Post-partum, Diabetes Mellitus, Cardiovascular diseases (Ischemic Heart Disease, Cardiac Heart Failure, Cardiomyopathy), Hypertension, Chronic lung diseases (Interstitial Lung Disease, Pulmonary Embolism, Pulmonary Hypertension, Chronic Obstructive Pulmonary Disease/Asthma, Cystic Fibrosis), Tuberculosis, Chronic liver diseases (Cirrhosis, Autoimmune Hepatitis, Alcoholic liver disease, NASH), Chronic kidney diseases, Cerebrovascular Accident, Severe neuro-psychiatric disorders (Dementia, Depression, Schizophrenia), Genetic disorders (such as Down's syndrome), Hemoglobinopathies (Thalassemia, Sickle cell anemia), Malignancies, Organ transplantation, Taking immunosuppressive drugs, Alcohol or Drug abuse, Smoking**)**.
- Availability of proper conditions for home care and having immediate access to medical centers; also, if there was hypoxia and need for oxygen support at home, it could be prepared.
- Patient's Age, Equal to or more than 18 years.
- The patient's weight, equal to or more than 40 kilograms.
- Non-pregnant women.
- Absence of severe anorexia and/or nausea/vomiting.
- Equal to or less than 7-10 days after the onset of the symptoms.
- In the presence of underlying disease, it should be under control, such as the absence of pulmonary edema in Cardiac heart failure (CHF), Diabetic ketoacidosis (DKA).
- No possibility of secondary severe pulmonary infection, active infection in other parts of the body, or systemic infection.
- Relatively stable in terms of hemodynamic status.
- The percentage of O2 saturation in room air, at least ≥90 (in chronic cardiopulmonary diseases, without respiratory distress ≥88).
- No organ dysfunction (liver enzymes less than five times the upper limit of normal and Glomerular filtration rate (GFR) ≥30 ml/min/1.73 m^2).
- No electrolyte disturbances (if the abnormal findings were mild and can be corrected with oral treatment, it was not prohibited).
- Without QT prolongation and other significant acute changes on the Electrocardiogram (ECG).
- In the chest Computed tomography (CT) scan, the lung involvement, less than 50%.
- According to paraclinical findings, a COVID-19-positive Polymerase chain reaction (PCR) test and/or CT scan consistent with COVID-19 lung involvement.

Patients who did not answer phone calls (at least two times during 2-3 days) and the participants with incomplete laboratory results were excluded from the study.

The patients were not asked about their history of receiving the COVID-19 vaccine

because, at the time of this research (2021), less than six months had passed since the start of vaccination in the general population in Iran. At that time, less than 10% of the population had received one dose and less than 5% two doses.

On admission day, the patient was visited by an emergency medicine specialist, and if he/she was a candidate for Remdesivir administration, required laboratory tests, according to the national guidelines for outpatient COVID-19, were checked. If there was no contraindication for receiving RDV, the loading dose (200 mg) was infused in the emergency department. Afterward, the patient was introduced to the Remdesivir department for the following doses.

Each patient came for a drug injection on the appointed day. The Remdesivir brands used were Actoverco and Ronak (made in IRAN). After diluting the lyophilized powder vial with serum, the drug was infused during 30-120 minutes.

At discharge, patients were educated about warning signs and symptoms.

If the baseline tests were normal, Liver function tests (LFT) and Blood urea nitrogen (BUN) and Creatinine (Cr) were rechecked before the third or fourth dose, and if the baseline tests were abnormal, they were repeated every day or every other day.

The nurses were trained to record the following data in admission forms:

- The patient's demographic characteristics.
- The total number of RDV injection days (depending on clinical response and physician's decision, might be 3-5 days).
- The disease improvement/progression status (if the patient worsens clinically, the physician must be informed).
- The patient's vital signs prior to RDV infusion, as required, up to one hour after that.
- O2 saturation at each visit (the patient's physician was notified if it decreased compared to the previous day).
- Results of the basic and repeated laboratory tests (if necessary, any new tests of the patient were reported to the physician in charge of the RDV injection unit).
- Any adverse events due to the drug infusion.

In the next stage, 10-14 days after the completion of the treatment period (the length of time that non-severe COVID-19 patients are expected to recover), one of the researchers called the patients by phone and their outcomes (complete recovery, partial recovery, hospitalization, death) and incidence of the disease complications and/or the drug side effects were recorded. It should be noted that the meaning of complete recovery is the improvement of all the initial signs/symptoms of the disease, and the meaning of partial recovery is the improvement of the acute phase of the disease and the remaining one or more signs/symptoms of the disease with less intensity than the onset of illness.

2.2. Data analysis

After completing the data collection process, the data were analyzed with SPSS V22 software, and the significance level was considered to be 0.05. The normality of data was assessed using the Kolmogorov–Smirnov test; data followed a normal distribution. Descriptive statistics are used to describe the characteristics of the patients. Mean and standard deviation were used to describe

continuous variables, and frequency and percentage were used to describe two-state or multi-state variables. An Independent T-test was used to compare numerical variables between different groups, or a Mann-Whitney test was used if the variable distribution was abnormal. The Chi-square or Fisher exact test was used to compare the qualitative variables.

3. Results and Discussion

Of 799 selected patients, in 287 cases, the information forms, which had been designed for collecting data, could not be completed because 199 patients did not respond to the phone calls; in 16 cases, the recorded phone numbers were not correct; in 70 patients, before and between treatments, biochemical laboratory tests were not complete or were not available and two patients did not collaborate for participating in the study.

Finally, the data collected from 512 participants was analyzed. The patients were between 18 to 84 years of age (mean age 46.19±14.20); 46.9% of them were male; the mean weight of study participants was 73.76±12.62; 41% of the study population had positive, and 5% had negative PCR test; for other participants, COVID-19 PCR test was not available or was not checked due to the patient's financial constraints. The mean number of outpatient RDV injections was four doses. The most common underlying diseases were hypertension (11.3%) and diabetes mellitus (9.8%). Most patients had no history of any drug use; the most common drugs that patients used were losartan (8.8%) and metformin (8%). (**Table 1**)

Table 1: Patients' characteristics.

Variable	**Frequency (n=512)**
Age (Mean ± SD)	46.19±14.20
Sex (n, %)	
- Male	240 (46.9)
- Female	272 (53.1)
weight (Mean ± SD)	73.76 (12.62)
Underlying diseases (n, %)	
- Anemia	3 (0.6)
- Asthma	1 (0.2)
- Cancer	2 (0.4)
- CVA	4 (0.8)
- Diabetes mellitus (DM)	50 (9.8)
- Fatty liver Disease	2 (0.4)
- Hypertension (HTN)	58 (11.3)
- Hyperthyroidism	1 (0.2)
- Hypothyroidism	6 (1.2)
- IHD/MI	10 (2)
- Migraine	2 (0.4)
- Parkinson's disease	1 (0.2)
- Rheumatoid Arthritis	3 (0.6)
- No disease	438 (85.5)
History of drug use (n, %)	
- Acarbose	1 (0.2)
- Amlopres	1 (0.2)
- ASA	10 (2)
- Atenolol	1 (0.2)
- Atorvastatin	3 (0.6)
- Calcium/vitamin D	3 (0.6)
- Carvedilol	2 (0.4)
- Cinnora	1 (0.2)
- Citalopram	5 (1)
- Glibenclamide	1 (0.2)
- Gliclazide	1 (0.2)
- Insulin	2 (0.4)
- Livergol (a kind of herbal drug)	1 (0.2)
- Levothyroxine	5 (1)
- Losartan	45 (8.8)
- Metformin	41 (8)
- Methimazole	1 (0.2)
- Nitrocontin	3 (0.6)
- Osvix	1 (0.2)
- Propranolol	4 (0.8)
- Zipmet	2 (0.4)
- No drug use	442 (86.3)
PCR (n, %)	
- Positive	210 (41)
- Negative	26 (5)
- Not available*	276 (54)
Number of RDV injected (n, %)	
- Four doses	486 (95)
- Five doses	26 (5)

Complications during RDV injection were rare, and 97.4% of patients did not experience any side effects after treatment with RDV. Only three patients were referred to a physician due to RDV complications: one patient because of

high blood pressure, another patient due to chest discomfort, and another one due to muscle cramps/spasms. (**Table 2**)

Table 2: RDV complications.

Complications during RDV injection (n, %)	
- Chest discomfort/ Breath shortness	1 (0.2)
- Dyspnea and high blood pressure	1 (0.2)
- Flushing	1 (0.2)
- Genital burning	2 (0.4)
- Headache	2 (0.4)
- Itching	1 (0.2)
- Muscle cramps	1 (0.2)
- Nausea	1 (0.2)
- Stomachache	1 (0.2)
- Tenesmus/Abdominal cramps	1 (0.2)
- Weakness and drowsiness	1 (0.2)
- No complication	499 (97.4)
Refer to a physician due to some of the above complications (n, %)	
- Yes	3 (0.6)
- No	509 (99.4)

81.6% of patients were satisfied about RDV injection services in the hospital. 84.4% of patients reported that the nurses checked and recorded their vital signs before RDV injection. Also, the nurses checked 84.8 % of patients for oxygen saturation, 98% for baseline and new laboratory results, and 84.4% for general conditions. Most patients (99.6%) reported that the RDV injection process lasted 30-60 minutes. Acute complication during RDV injection was rare (2.6%).

Only in three patients, due to acute complications, RDV injection was transiently discontinued; the patients were referred to an emergency medicine specialist; one of them was also referred to a cardiologist (after more evaluation of these three patients by specialists, none had important side effects). At the end of the RDV treatment period, 87.9% of patients completely recovered, 11.5% partially recovered, 0.6% revisited and hospitalized, and no patient died. (**Table 3**)

Table 3: Patients' satisfaction with RDV injection.

Variable	**Frequency (n=512)**
Satisfaction with RDV outpatient injection department services (n, %)	
- Satisfied	418 (81.6)
- Approximately Satisfied	73 (14.3)
- Never Satisfied	15 (2.9)
- No response	6 (1.2)
Items performed and recorded by the nurse before injecting the drug (n, %)	
Vital signs assessment	
- Yes	432 (84.4)
- No	80 (15.6)
Oxygen Saturation*	
- Yes	434 (84.8)
- No	78 (15.2)*
Baseline and during the treatment laboratory results	
- Yes	502 (98)
- No	10 (2)
General condition of the patient	
- Yes	432 (84.4)
- No	80 (15.6)
Duration of RDV injection/infusion (n, %)	
- Between 30 min and one hour	510 (99.6)
- More than one hour	2 (0.4)
Acute complication during RDV injection (n, %)	
- Yes	13 (2.6)
- No	499 (97.4)
Discontinue drug injection due to acute complications (n, %)	
- Yes	0 (0)
- No	512 (100)
The patient's outcome at the end of the treatment (n, %)	
- Complete recovery	450 (87.9)
- Partial recovery	59 (11.5)
- Hospitalization	3 (0.6)
- Death	0 (0)

*In this group, oxygen saturation had checked in triage by nurse or at home by one of the family members and, if the patient's report was reliable, O2 sat did not check again in the RDV injection department because sometimes the ward was too crowded.

Mean counts of White blood cells (WBC) and mean levels of Platelet (PLT), Alanine aminotransferase (ALT), and BUN increased during outpatient treatment with RDV. Of these laboratory factors, mean levels of Hemoglobin (Hb), C-reactive protein (CRP), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), and Cr decreased after the treatment. Of these laboratory factors, changes were significantly different before and during the treatment, except for Cr. **(Table 4**).

When Remdesivir was introduced as a drug for COVID-19 treatment in protocols, it was criticized by some experts [13]. Since then, many studies have been performed to evaluate the potential effects of this drug on COVID-19 and to identify its side effects.

However, not all studies have the same results; even the results obtained from different studies were completely different. In addition, resources in referral hospitals for COVID-19, especially during the peaks of the disease, have been limited, and now it seems necessary to introduce effective oral antivirals and perform more assessments about the safety and side effects of RDV administration in the outpatient setting; therefore, we conducted this study to evaluate these issues.

Table 4: Laboratory result alternation after RDV injection (Total=512).

Laboratory results (Mean ± SD)	Before injection	After injection	Mean difference	P value
WBC	6.51 ±11.56	8.71 + 9.85	2.16	**0.001**
Male	6.29±3.13	9.65+14.03	3.26	**0.000**
Female	6.70±15.52	7.89+3.14	1.19	0.195
Hb	13.76+2.01	13.38+1.80	-0.38	**0.000**
Male	14.69+2.21	14.34+1.49	-0.36	**0.006**
Female	12.95 (1.37)	12.54(1.63)	-0.41	**0.000**
PLT	208.89+83.32	267.44+102.11	58.36	**0.000**
Male	194.13+83.84	257.21+107.56	63.08	**0.000**
Female	221.69+80.25	275.45+96.07	54.21	**0.000**
CRP	36.00+36.30	21.06+34.23	-14.85	**0.000**
Male	40.98+34.07	21.93+27.37	-19.05	**0.000**
Female	31.85+37.88	20.87+39.89	-11.17	**0.000**
AST (SGOT)	43.88+31.82	39.86+29.69	-4.12	**0.001**
Male	45.42+29.19	43.80+29.20	-2	0.326
Female	42.54+33.94	36.44+29.74	-6.24	**0.001**
ALT (SGPT)	42.90+ 36.50	49.13+42.13	6.06	**0.000**
Male	44.46+35.84	54.67+42.77	10.21	**0.000**
Female	41.50+37.29	43.99+40.96	2.42	0.184
ALP	162.59+73.49	148.13+57.76	-14.48	**0.000**
Male	157.75+68.70	144.95+57.89	-12.8	**0.001**
Female	166.79+77.01	151.17+57.71	-15.94	**0.000**
BUN	28.21+10.43	35.02+12.51	6.56	**0.000**
Male	32.461+2.26	38.95+14.14	6.49	**0.000**
Female	25.24+9.56	31.91+10.78	6.6	**0.000**
Cr	0.99+0.20	0.91+ 0.17	-0.08	**0.000**
Male	1.10+ 0.19	1.00+ 0.19	-0.12	**0.000**
Female	0.89+0.15	0.84+0.14	-0.06	**0.000**

WBC, White blood cells; HB, Hemoglobin; PLT, Platelet; CRP, C-reactive protein; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; ALP, Alkaline phosphatase; BUN, Blood urea nitrogen; Cr, Creatinine

In our study, most patients who received RDV recovered, and only 3(0.6%) were hospitalized. However, it should be noted that most enrolled patients had no severe illness or underlying disease at the beginning of the study, which is an important issue that might impact the improvement results.

Many studies have been done on the effectiveness of Remdesivir and the side effects caused by this drug in inpatient settings. However, only a few studies evaluated its safety in terms of its side effects on liver and kidney tests in outpatient settings. Our study could add scientific evidence to fill a gap in this area of research.

In the Pasquini [14], Gupta [15], and Diaz [16] studies, mortality was significantly lower in the RDV group than in the control group. In these cohort studies, patients were followed for at least ten days. In the studies of Wong [17] and Olender [18], in addition to the fact that mortality was significantly lower in the RDV group comparing the control group, more clinical improvement was seen in the RDV group. In the WHO Solidarity Trial [19], Ruso [20], Due [7], Ohl [21], and Almaghlouth [22] studies, no significant difference was found between the mortality of patients taking RDV and other patients. In Beigel's [23] and Joo's [24] studies, the difference in mortality between the groups was insignificant. However, the recovery time, the proportion of patients who needed mechanical ventilation support, and the viral load in the treatment group were significantly lower than in the control group.

Remdesivir may cause serious side effects, including allergic reactions and elevated liver enzymes. The most common side effect of RDV is nausea [15]. In our study, a small number of patients had complications during or immediately after receiving the drug (2.6%). Complications such as chest discomfort, dyspnea, flushing, genital burning, headache, itching, muscle cramps, nausea, stomachache, tenesmus, weakness and drowsiness were each seen in one or two patients. Most of these side effects were not distinguishable from COVID-19 symptoms or adverse reactions of other medications (like dexamethasone), which might be used concomitantly with Remdesivir. In the Spinner [25] study, nausea, hypokalemia, and headache were more common in patients treated with RDV than in controls. In some studies, chest discomfort, diarrhea, insomnia, rash, hepatic failure/hepatitis, renal impairment/and acute kidney injury were adverse effects reported in the groups taking RDV [9, 26-30]. In Flisiak's [31] study, side effects, e.g., diarrhea, nausea, and vomiting, were less severe in the treatment group than in the control group. However, in Mahajan's [32] study, there was no significant difference between side effects in the treatment and control groups.

In the current study, several laboratory components were measured before and between the treatments. In the laboratory findings, except for the WBC, ALT, and AST, the variables were statistically significant both in general and in men and women. WBC, PLT, ALT, and BUN significantly increased after receiving the drug, and Hb, CRP, AST, ALP, and Cr levels significantly decreased after receiving the drug compared to the baseline values. In the Mahajan's [32] study, AST, ALT, and Cr elevated. In another meta-

analysis study, RDV was associated with a reduced risk of elevated ALT and AST [10]. An article published in 2022 and a review article published in 2023 concluded that in COVID-19 patients at high risk for disease progression and receiving Remdesivir for up to 3 days in an outpatient setting, the drug is safe, effective, and generally well tolerated [33, 34].

Our study had some limitations. First, there was a lack of cooperation in some patients to obtain an accurate history of current and previous disease information and medication use; in such cases, after the patient's general condition improved, we tried to get a history from the patient or get help from his/her companions by phone. Second, some patients did not answer the phone for the first time, and if they did not answer, we would call them at another time.

Regarding the strength of our study, since the oral antiviral drug for the treatment of COVID-19 is still not available in some countries, if the patient needs to receive outpatient Remdesivir, he/she could receive this drug more easily and at a lower cost, because based on the results of this study, in patients without Liver and/or kidney disorders, does not seem to be necessary to repeat the tests during the period of receiving RDV.

4. Conclusion

In the present study, severe adverse effects were not found following taking Remdesivir in the outpatient setting; therefore, it seems that RDV can be used to treat non-hospitalized COVID-19 patients safely without the need to repeat kidney and liver function tests during treatment. In order to achieve more reliable results, more studies should be performed with a larger sample size in multicenter trials.

Conflict of interest

The authors declare to have no conflict of interest.

Acknowledgment

The authors would like to thank Dr. Elham Bazmi, epidemiologist, and Mohsen Aramideh, emergency medicine specialist, for their kind cooperation, and they also want to thank the lab technicians and nurses who helped them accomplish this work.

References

[1] worldometers. COVID-19 CORONAVIRUS PANDEMIC 2022 [cited 2024 January 15]. Available from: https://www.worldometers.info/coronavirus/.

[2] who. Coronavirus disease (COVID-19) 2022. https://www.who.int/health-topics/coronavirus#.

[3] Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, evaluation, and treatment of coronavirus (COVID-19). Statpearls [internet] (2022).

[4] Health NIo. Coronavirus disease 2019 (COVID-19) treatment guidelines. 2020. Available form: https://www covid19treatmentguidelines nih gov/,(Accessed on 16 September, 2021) (2021).

[5] Veklury® (Remdesivir) is First and Only Approved Treatment for Pediatric Patients Under 12 Years of Age with COVID-19 [cited 2022 April 25]. Available from: https://www.gilead.com/news-and-press/press-room/press-releases/2022/4/veklury-remdesivir-is-first-and-only-approved-treatment-for-pediatric-patients-under-12-years-of-age-with-covid19.

[6] Srivastava K, Singh MK. Drug repurposing in COVID-19: a review with past, present and future. Metabolism Open (2021) 12:100121.

[7] Barratt-Due A, Olsen IC, Nezvalova-Henriksen K, Kåsine T, Lund-Johansen F, Hoel H, Holten AR, et al. Evaluation of the effects of remdesivir and hydroxychloroquine on viral clearance in COVID-19: A randomized trial. Annals of internal medicine (2021) 174(9):1261-9.

[8] Williamson BN, Feldmann F, Schwarz B, Meade-White K, Porter DP, Schulz J, Van Doremalen N, et al. Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2. Nature (2020) 585(7824):273-6.

[9] Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, Feldt T, et al. Compassionate use of remdesivir for patients with severe Covid-19. New England Journal of Medicine (2020) 382(24):2327-36.

[10] Angamo MT, Mohammed MA, Peterson GM. Efficacy and safety of remdesivir in hospitalised COVID-19 patients: a systematic review and meta-analysis. Infection (2021):1-15.

[11] Mohamad Rahimi M, Jahantabi E, Lotfi B, Forouzesh M, Valizadeh R, Farshid S. Renal and liver injury following the treatment of COVID-19 by remdesivir. Journal of Nephropathology (2021) 10(2):1-4.

[12] Kuno T, Miyamoto Y, Iwagami M, Ishimaru M, Takahashi M, Egorova NN. The association of remdesivir and in-hospital outcomes for COVID-19 patients treated with steroids. Journal of Antimicrobial Chemotherapy (2021) 76(10):2690-6.

[13] Lamb YN. Remdesivir: first approval. Drugs (2020) 80:1355-63.

[14] Pasquini Z, Montalti R, Temperoni C, Canovari B, Mancini M, Tempesta M, Pimpini D, et al. Effectiveness of remdesivir in patients with COVID-19 under mechanical ventilation in an Italian ICU. Journal of Antimicrobial Chemotherapy (2020) 75(11):3359-65.

[15] Gupta V, Ingawale S, Bhondve A, Khot W, Salagre S, Sonawale A, Joshi K, et al. Clinical Study of Use of Remdesivir and Tocilizumab in Severely Ill COVID-19 Patients. The Journal of the Association of Physicians of India (2021) 69(7):14-9.

[16] Diaz GA, Christensen AB, Pusch T, Goulet D, Chang S-C, Grunkemeier GL, McKelvey PA, et al. Remdesivir and Mortality in Patients with COVID-19. Clin infect dis (2021).

[17] Wong CK, Lau KT, Au IC, Xiong X, Chung MS, Lau EH, Cowling BJ. Optimal timing of remdesivir initiation in hospitalized COVID-19 patients administered with dexamethasone. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America (2021).

[18] Olender SA, Walunas TL, Martinez E, Perez KK, Castagna A, Wang S, Kurbegov D, et al., editors. Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection: An Analysis of 28-Day Mortality. Open forum infectious diseases; 2021: Oxford University Press US.

[19] Consortium WST. Repurposed antiviral drugs for Covid-19—interim WHO solidarity trial results. New England journal of medicine (2021) 384(6):497-511.

[20] Russo A, Binetti E, Borrazzo C, Cacciola EG, Battistini L, Ceccarelli G, Mastroianni CM, et al. Efficacy of remdesivir-containing therapy in hospitalized COVID-19 patients: a prospective clinical experience. Journal of clinical medicine (2021) 10(17):3784.

[21] Ohl ME, Miller DR, Lund BC, Kobayashi T, Miell KR, Beck BF, Alexander B, et al. Association of remdesivir treatment with survival and length of hospital stay among US veterans hospitalized with COVID-19. JAMA network open (2021) 4(7):e2114741-e.

[22] Almaghlouth NK, Anyiam FE, Shah S, Haq S, Attia MJ, Guevara R, Antony S. The Use of Single Therapy With Tocilizumab Versus Combination Therapy With Remdesivir and Tocilizumab in SARS-CoV-2 Patients in El Paso, Texas. Cureus (2021) 13(7).

[23] Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, Hohmann E, et al.

Remdesivir for the treatment of Covid-19—preliminary report. New England Journal of Medicine (2020) 383(19):1813-36.

[24] Joo E-J, Ko J-H, Kim SE, Kang S-J, Baek JH, Heo EY, Shi HJ, et al. Clinical and virologic effectiveness of remdesivir treatment for severe coronavirus disease 2019 (COVID-19) in Korea: a nationwide multicenter retrospective cohort study. Journal of Korean medical science (2021) 36(11).

[25] Spinner CD, Gottlieb RL, Criner GJ, López JRA, Cattelan AM, Viladomiu AS, Ogbuagu O, et al. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. Jama (2020) 324(11):1048-57.

[26] Antinori S, Cossu MV, Ridolfo AL, Rech R, Bonazzetti C, Pagani G, Gubertini G, et al. Compassionate remdesivir treatment of severe Covid-19 pneumonia in intensive care unit (ICU) and Non-ICU patients: Clinical outcome and differences in post-treatment hospitalisation status. Pharmacological research (2020) 158:104899.

[27] Lee C, Ahn MY, Byeon K, Choi J-P, Hahm C, Kim H, Kim S, et al. Clinical experience with use of remdesivir in the treatment of severe acute respiratory syndrome coronavirus 2: a case series. Infection & chemotherapy (2020) 52(3):369.

[28] Dubert M, Visseaux B, Isernia V, Bouadma L, Deconinck L, Patrier J, Wicky P-H, et al. Case report study of the first five COVID-19 patients treated with remdesivir in France. International journal of infectious diseases (2020) 98:290-3.

[29] McCoy JA, Short WR, Srinivas SK, Levine LD, Hirshberg A. Compassionate use of remdesivir for treatment of severe coronavirus disease 2019 in pregnant women at a United States academic center. American journal of obstetrics & gynecology MFM (2020) 2(3):100164.

[30] Montastruc F, Thuriot S, Durrieu G. Hepatic disorders with the use of remdesivir for coronavirus 2019. Clinical Gastroenterology and Hepatology (2020) 18(12):2835-6.

[31] Flisiak R, Zarębska-Michaluk D, Berkan-Kawińska A, Tudrujek-Zdunek M, Rogalska M, Piekarska A, Kozielewicz D, et al. Remdesivir-based therapy improved recovery of patients with COVID-19 in the SARSTer multicentre, real-world study. medRxiv (2020).

[32] Mahajan L, AP Singh G. Clinical outcomes of using remdesivir in patients with moderate to severe COVID-19: A prospective randomised study. Indian Journal of Anaesthesia (2021) 65(Suppl 1):S41.

[33] Gottlieb RL, Vaca CE, Paredes R, Mera J, Webb BJ, Perez G, Oguchi G, et al. Early remdesivir to prevent progression to severe Covid-19 in outpatients. New England Journal of Medicine (2022) 386(4):305-15.

[34] Blair HA. Remdesivir: a review in COVID-19. Drugs (2023) 83(13):1215-37.