Evaluating The Effect Of Remdesivir On The Mortality Rate And Recovery Of COVID-19 Patients In The Intensive Care Units Of Shohdaye Ashayer Hospital In Khorramabad In The First Half Of 2020

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Abstract

Title: Evaluating the effect of remdesivir on the mortality rate and other outcomes of COVID-19 patients in the intensive care units of Shohdaye Ashayer Hospital in Khorramabad in the first half of 2020

Introduction: Researchers are looking for safe and effective treatment methods Due following the emergence of SARS-CoV-2. Remdesivir is currently being evaluated for clinical efficacy and safety in COVID-19 patients. The present study evaluates the effect of remdesivir on the mortality rate and other outcomes of covid-19 patients in the ICUs of Shohdaye Ashayer Hospital in Khorramabad in the first half of 2020.

Methods: In this retrospective cross-sectional descriptive study, 35 patients' medical records in each group were reviewed. Patients were divided into two remdesivir and control groups. In this regard, 35 subjects in the remdesivir group received remdesivir in addition to the standard diet, and 35 people in the control group received only the standard diet. The two groups were compared regarding the frequency distribution of underlying characteristics, the effect of the drug on the length of stay in the hospital and ICU, the effect of the drug on mechanical ventilation, and the recovery and mortality rate.

Results: In the remdesivir group, 18 were male and 17 were female. In the control group, 22 were male and 13 were female. In both groups, cardiovascular diseases were identified as the most frequent underlying diseases. There was a significant difference between the groups regarding weakness and lethargy and respiratory distress ($P<0.05$). There was no significant difference between the two groups regarding the mean length of stay in the hospital and ICU, the duration of recovery and mechanical ventilation, and the recovery and mortality rate of the studied patients ($P>0.05$).

Conclusion: according to the results, remdesivir did not have any positive effect on the clinical outcomes of the remdesivir group compared to the control group. The results of the present study did not consider the use of this drug as an effective treatment in covid-19 patients.

Keywords: Covid-19, Coronavirus, Remdesivir, Mortality rate.

Introduction

Coronaviruses belong to the Coronaviridae family (1, 2). They are enveloped RNA viruses that cause infection in humans (3). A new strain of coronavirus, SARS-CoV-2, the causative agent of Covid-19 emerged in Wuhan, China in December 2019. Since then, the rate of mortality caused by this virus has

increased dramatically worldwide. Coronavirus causes lower pulmonary respiratory symptoms. It has been isolated from animals such as cats and dogs and has recently been identified in bats (4). It can be transmitted through nasal drops, direct contact, urine, and feces. About 70% of patients show signs of shortness of breath and resistant fevers, 30% of patients show signs of recovery after one week, and about 20-30% of patients require mechanical ventilation. Pathological findings in these patients suggest extensive lung damage. This severe lung damage in corona patients is either due to the direct invasion of the virus or due to immune-pathological effects. However, many of its pathological aspects have not yet been identified (5). Older patients and those with respiratory or cardiovascular diseases have the highest rate of involvement and severe complications (6). In the absence of a proven effective treatment, current treatments include supportive care, invasive and non-invasive oxygen therapy, and off-label drugs such as antivirals, anti-parasites, and steroidal anti-inflammatory drugs (7). Remdesivir is one of the drugs used widely in this regard. It is a prodrug of adenosine analog mono-phosphoramidite, which has a wide range of viruses, including filoviruses, paramyxoviruses, pneumoviruses, and coronaviruses (8). Remdesivir is a viral RNA polymerase inhibitor that has an inhibitory effect on MERS and SARS-CoV.

A study by Huang et al. on 41 confirmed cases of infection with the new coronavirus SARS-CoV-2 admitted to a Wuhan hospital showed that fever (98%), cough (76%), shortness of breath (55%), and muscle pain and fatigue (44%), respectively, were the most common clinical symptoms of this infection (9). Another study conducted in China also confirmed these results (10). Loss of the sense of smell in adults after infection with viruses infecting the upper respiratory tract is called "anosmia after viral infection". It accounts for almost 40% of anosmia cases (11). Studies conducted on the Covid-19 patients have reported the incidence of common gastrointestinal symptoms such as diarrhea, nausea, and vomiting (12). Skin rash is one of the rare symptoms reported in Covid-19 patients. The reported skin rashes are in the form of erythematous, extensive hives, and chickenpox-like blisters that occur without itching or with slight itching in the trunk area of the patients (13).

Acute heart damage, defined by a significant increase in the level of cardiac troponins in a blood test, has been reported as the most common cardiac abnormality in Covid-19. Other reports suggest the presence of myocarditis and cardiac arrest (14). Blood in urine, blood urea nitrogen, and high serum creatinine have been recently reported in these patients (15). This virus can create a severe inflammatory state that disrupts the capability of the pancreas to release insulin and reduces the ability of the liver and muscles to recognize the hormone (16). In a clinical trial in 2018 on Ebola patients, remdesivir was compared with other drug combinations including monoclonal antibodies. The highest mortality rate was observed in the remdesivir group (higher than the control group). For this reason, this drug was excluded from the study in the middle of the study (17). Following the emergence of the SARS-CoV-2 virus, the hope for the effectiveness of the remdesivir drug increases again. Some studies, including the study by Wang et al., showed that this drug has a significant effect in controlling viral infection in cultured cells in the laboratory environment (18).In the absence of an approved drug for the treatment of patients with Covid-19, remdesivir was given to patients without approval and in compassionate use in January 2020. The results showed that the symptoms of recovery were observed in 36 out of 53 patients (68%) who received the drug (19). Accordingly, clinical trials began in patients with mild, moderate, and severe covid-19 at the beginning of February 2020.

In a randomized, double-blind, placebo-controlled trial, Biegle et al. (2020) examined 1063 COVID-19 patients with lower respiratory tract infections. The results showed that the mean time to recovery was 10 days in those who received remdesivir and 15 days in

those who received a placebo. Serious side effects were reported in 131 of 532 patients who received remdesivir (24.6%) and in 163 of 516 patients who received a placebo (31.6%) (20). Chen-Yang et al. (2020) examined the effectiveness of remdesivir in COVID-19 patients in a two-arm controlled simulated study. The results did not confirm the effectiveness of remdesivir and contributed greatly to the design of a large-scale randomized controlled trial (21). In their clinical trial, Goldman et al. (2020) treated patients with covid-19 with remdesivir in 2 treatment periods of 10 days and 5 days. In their clinical trial, Goldman et al. (2020) treated covid-19 patients using remdesivir in 2 treatment periods of 10 days and 5 days. The results showed that clinical symptoms in the patients worsened during 5 days (short term). However, in the long term, it improved the symptoms and caused side effects such as nausea, respiratory failure, and elevated ALT (22). Several studies have revealed that it is useful in patients with severe COVID-19. However, the clinical and antiviral effect of remdesivir in COVID-19 is unclear. In this regard, the present study evaluated the effectiveness of the remdesivir drug on the mortality rate of COVID-19 patients.

Materials and Methods

This study was a retrospective, cross-sectional, and descriptive study. The statistical population of the study consisted of covid-19 patients referred to Shohdaye Ashayer Hospital in the first half of 2020 in Khorramabad. In this study, out of 70 patients, 35 patients were in the control group and 35 were in the remdesivir group. Inclusion criteria of the study included having age over 18 years, severe pulmonary involvement, oxygen saturation less than 94% while receiving oxygen support, and a positive PCR test. The data collection tool was a researcher-made questionnaire. It included demographic characteristics, clinical results, and laboratory findings. The disease severity was defined as death or hospitalization in the ICU. The recovery status was defined as discharge from the hospital or death. After collecting the data, the frequency distribution of underlying characteristics (age, gender, disease type, and underlying disease), the effect of the drug on the mortality of patients, and the effect of the drug on mechanical ventilation were evaluated.

After collecting the data and entering them into the SPSS-21 statistical software, appropriate central and dispersion indices and ratios were obtained. To investigate the relationship between the independent variables and the recovery rate of the patients, multiple logistic regression was used. The results were reported at a significance level of 5%. Also, two scoring systems, including Sofa Score and APACHE II Score, were used to predict the mortality rate in the studied patients hospitalized and referred to the intensive care units. This study was conducted in the Ethics Committee of Lorestan University of Medical Sciences and with the Code of Ethics of IR. LUMS. REC. 1400. 013.

Results

In the present study, out of 70 eligible patients, 35 patients were included in the remdesivir group (receiving remdesivir in addition to receiving standard diet), and 35 patients were included in the control group (receiving standard diet). The results revealed that 22 people (62.86%) in the control group were male and 13 (37.14%) were female with a mean age of 66.37±18.14. Among them, 28 (80%) had a history of drug use, 4 (11.43%) had a history of smoking or other addictions, and 30 (85.71%) had an underlying disease. In the remdesivir group, 17 (48.57%) were male, and 18 (51.43%) were female with a mean age of 65.54±12.54. Among them, 28 (80%) had a history of drug use, 3 (8.57%) had a history of smoking and other addictions, and 28 (80%) had an underlying disease. There was no significant difference between the intervention and control groups regarding the demographic and clinical parameters (P>0.05). In the control group, out of 35 patients, 16 (45.71%) had cardiovascular diseases, 9 (25.71%) had diabetes, 4 (11.43%) had respiratory diseases, and 3 (8.57%) had kidney diseases. In the remdesivir group, out of 35 patients, 22 (62.86%) had cardiovascular diseases, 14 (40%) had diabetes, 4 (11.43%) had respiratory diseases, and 1 (86 2.2%) had kidney diseases. There was no significant difference between the two control and remdesivir groups

regarding the underlying diseases (P>0.05).

Concerning the frequency of primary symptoms in covid-19 patients when they visit referred to the hospital, the highest frequency was related to shortness of breath, fever and chills, cough, weakness and lethargy, myalgia, loss of appetite, nausea, and vomiting, respectively, in the control group. They also included shortness of breath, weakness and lethargy, cough, fever and chills, myalgia and nausea, and vomiting, respectively, in the remdesivir group. There was a significant difference between the control and remdesivir groups regarding two variables of weakness and lethargy and respiratory distress (P<0.05). However, there was no significant difference between the two control and remdesivir groups regarding the number of days between the onset of symptoms and treatment and other variables (P>0.05).

In the control group, the mean body temperature was 37.18±0.49, the mean heart rate was 87.59±15.06, the mean respiration rate was 87.37±3.2, the mean systolic blood pressure was 119.06±28.95, the mean diastolic blood pressure was 74.31 ± 16.96, and the mean blood oxygen level was 81.53±11.81. In the remdesivir group, the mean body temperature was 37.09 ± 0.57, the mean heart rate was 86.33 ± 12.86, the mean respiratory rate was 20.34 ± 3.98, the mean systolic blood pressure was 123.40±19.73, the mean diastolic blood pressure was 76.48±17.46, and the mean blood oxygen level was 85.94±8.60. Statistically, there was no significant difference between the two groups (P>0.05).

By comparing the information predicting the progress of the disease, including INR, LDH, Troponin C, CPK, and CRP in the control and remdesivir groups in the baseline, Table 1 shows that there is a statistically significant difference between the two control and remdesivir groups regarding the ESR factor (P<0.05). However, this difference was not significant regarding other variables (P<0.05).

Table 1: Factors predicting disease progression in the two control and intervention groups in the baseline

Clinical indices and laboratory findings	Control group (Mean ± Std)	Remdesivir group (Mean ± Std)	P
INR	1.2 ± 0.37	1.07 ±0.14	0.08
LDH (U/liter)	870.44 ± 269.34	743.36 ± 281.62	0.09
Troponin C (ng/ml)	0.05 ± 0.02	0.05 ± 00	0.9
CPK (U/liter)	129.28 ± 90.90	184.06 ± 140.56	0.1
CRP(qualitative)	+2.07 ± 0.73	+1.83 ± 0.94	0.47
ESR (mm/hr)	36.58 ± 27.46	54.89 ± 31.02	0.03

As shown in Table (2), there was a statistically significant difference in the magnesium variable at the beginning of the study (P<0.05). However, there was no significant difference at the end of the study in this regard. Examining other laboratory data showed no significant difference between the mean changes in the control and remdesivir groups (P>0.05).

Table 2- Comparison of the mean laboratory indices of the covid-19 patients in the control and remdesivir groups at the admission and discharge times

Variable	Group	Admission (Mean ± Std)	Admission P	Discharge (Mean ± Std)	Discharge P
WBC (×10^3/Ul)	Control	12.31 ± 13.97	0.23	11.84 ± 9.86	0.95
	remdesivir	9.11 ± 5.49		11.99 ± 7.45	
Lamphocyte (%)	Control	11.53 ± 8.25	0.64	5.18 ± 4.84	0.08
	remdesivir	12.50 ± 8.64		7.81 ± 5.92	
Hb (g/dl)	Control	13.93 ± 2.45	0.45	11.70 ± 2.62	0.44
	remdesivir	13.49 ± 2.16		11.23 ± 1.94	

Platelet (×10^3)	Control	193.88 ± 101.09	0.99	102.62 ± 95.39	0.21
	remdesivir	194.06 ± 96.66		131.19 ± 69.23	
Creatinine (mg/dl)	Control	1.14 ± 0.46	0.61	1.57 ± 1.05	0.56
	remdesivir	1.08 ± 0.46		1.40 ± 1.14	
Urea (mg/dl)	Control	50.96 ± 32.16	0.23	126.54 ± 89.31	0.17
	remdesivir	50.38 ± 24.58		93.85 ± 74.03	
Total Bilirobin (mg/dl)	Control	0.92 ± 0.49	0.61	5.27 ± 5.57	0.22
	remdesivir	0.83 ± 0.31		2.75 ± 2.85	
Sodium(meq/liter)	Control	140.03 ± 5.88	0.13	141.68 ± 9.31	0.9
	remdesivir	138.03 ± 4.51		141.41 ± 5.94	
Potassium (meq/liter)	Control	3.90 ± 0.5	0.07	4.5 ± 0.77	0.9
	remdesivir	4.12 ± 0.46		4.53 ± 0.89	
Calcium (mg/dl)	Control	8.50 ± 0.92	0.15	8.06 ± 1.44	0.38
	remdesivir	8.20 ± 0.63		7.60 ± 1.05	
Phosphor(mg/dl)	Control	2.73 ± 0.52	0.20	3.78 ± 1.01	0.71
	remdesivir	3.12 ± 0.91		3.43 ± 1.95	
Magnesium (mg/dl)	Control	1.98 ± 0.44	0.01	2.16 ± 0.55	0.82
	remdesivir	1.71 ± 0.30		2.27 ± 0.71	
AST (U/liter)	Control	49.07 ± 29.15	0.43	57.4 ± 66.06	0.93
	remdesivir	43.90 ± 21.31		55.08 ± 36.77	
ALT (U/liter)	Control	40.8 ± 26.31	0.24	68.25 ± 46.72	0.88
	remdesivir	33.66 ± 19.58		73.28 ± 60.19	
ALP (U/liter)	Control	214.6 ± 106.83	0.68	235.33 ± 113.62	0.96
	remdesivir	203.07 ± 109.47		231.38 ± 129.63	

Based on Table 3, in the control group, the mean length of stay in the hospital was 12.97 ± 9.65, the mean length of stay in ICU was 11.05 ± 9.1, the mean duration of mechanical ventilation was 4.62 ± 5.24, and the mean recovery time was 0.2 ± 1.18. In the remdesivir group, the mean length of stay in the hospital was 16.11 ± 11.52, the mean length of stay in ICU was 14.03 ± 11.55, the mean duration of mechanical ventilation was 7.03 ± 8.92m and the mean recovery time was 0.43±1.65 days. Thus, no significant difference was found between the two control and remdesivir groups in this regard (P>0.05).

Table 3- Comparison of the mean length of stay in hospital and ICU and the duration of recovery and mechanical ventilation in covid-19 patients in the control and remdesivir groups

Variable	Group	N	Mean±Std	P
mean length of stay in hospital (day)	Control	35	12.97 ± 9.65	0.22
	remdesivir	35	16.11 ± 11.52	
Mean length of stay in ICU(day)	Control	35	11.05 ± 9.1	0.23
	remdesivir	35	14.03 ± 11.55	
Mean duration of mechanical ventilation (day)	Control	35	4.62 ± 5.24	0.18
	remdesivir	35	7.03 ± 8.92	
mean recovery time (day)	Control	35	0.2 ± 1.18	0.5
	remdesivir	35	0.43 ± 1.65	

In Table 4, the information related to the sofa score and the mortality rate of the studied patients with covid-19 based on Sofa Score showed that in the control group, 23 people (65.71%) had a mortality of less than 33%, 6 people (17.14%) 50% mortality and 6 people (17.14%) mortality above 95% and in remdesivir group 27 people (77.14%) mortality less than 33%, 4 people (11.43%) 50% mortality and 4 people (43 11.0% had mortality above 95%. Also, the mean SOFA score in the control group was 8.37±3.18 and in the remdesivir group was 8.31±2.50, and there was no statistically significant difference between the two control and remdesivir groups (P>0.05).

Table 4. Comparison of the prediction of the mortality rate of the Covid-19 patients based on Sofa Score in the control and remdesivir groups in the baseline

Sofa Score		Control group	Remdesivir group	P
Mortality (%)	Less than 33%	23 (65.71)	27 (77.14)	0.29
	50%	6 (17.14)	4 (11.43)	0.49
	More than 95%	6 (17.14)	4 (11.43)	0.49
Point (Mean ± Std)		8.37 ± 3.18	8.31 ± 2.50	0.93

As shown in Table 5, the information related to the Apache 2 score and the mortality rate of the Covid-19 patients based on the APACHE II Score showed that in the control group, 23 people (65.71%) had mortality less than 20%, 10 people (28.57%) had mortality between 20 and 40%, and 2 people (5.71%) had mortality between 40 and 60%. Also, in the intervention group, 24 people (68.57%) had a mortality rate lower than 20%, 10 people (28.57%) had a mortality rate between 20 and 40%, and 1 person (2.86%) had a mortality rate between 40 and 60%. Also, the mean APACHE II Score was 13.31 ± 6.29 in the control group and 12.14 ± 5.94 in the remdesivir group. There was no statistically significant difference between the two groups in this regard (P>0.05).

Table 5. Comparison of predicting the mortality rates in the covid-19 patients based on APACHE II Score in the control and remdesivir groups in the baseline

APACHE II Score		Control group	remdesivir group	P
Mortality (%)	Less than 20%	23 (65.71)	24 (68.57)	0.79
	20-40%	10 (28.57)	10 (28.57)	> 0.99
	40-60%	2 (5.71)	1 (2.86)	0.55
Point (Mean±Std)		13.31 ± 6.29	12.14 ± 5.94	0.42

In the control group, out of 35 patients, 5 people (14.28%) were discharged and 30 people (85.71%) died. In the remdesivir group, out of 35 patients, 4 people (4.4%) were discharged and 31 people (34.06) %) died. There was no statistically significant difference between the control and remdesivir groups regarding recovery and mortality rates (P>0.05).

Table 6: Table of recovery and mortality rates in the covid-19 patients in the control and remdesivir groups

Recovery status	Group		P
	Control N (%)	Remdesivir N (%)	
discharged	5 (14.28)	4 (11.43)	0.72
Died	30 (85.71)	31 (88.57)	

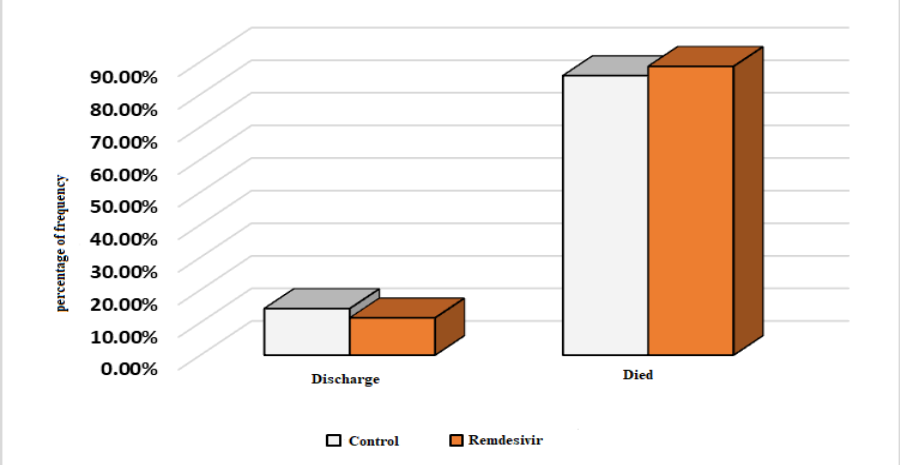

Chart 1: Recovery and mortality rates in the covid-19 patients in the control and remdesivir groups

Discussion

Remdesivir was one of the first treatments allowed for emergency use through the processes related to the US Food and Drug Administration and the European Medicines. Studies based on molecular dynamics simulations and free energy perturbation methods identify SARS-CoV-2 Rd as the target of remdesivir. In vitro and in vivo studies have shown that remdesivir inhibits the replication of SARS-CoV-2 in human airway epithelial cells. Also, its clinical and virological effects have been proven in mammalian models. In the present study, 22 subjects were male 13 were female in the control group and 17 subjects were male, and 18 were female in the remdesivir group. Most of the previous studies have shown that the number of males infected with Covid-19 was more than the number of females. The study by Chen et al. (2020) showed that among the 249 patients studied, 126 (50.6%) were male (23) in the control group, which is in line with the results of the present study. In explaining this result, it can be stated there is a possibility that the gender imbalance only reflects travel and contact patterns that make males more exposed to virus carriers than females. The mean age of the people was 65.54±12.54 in the remdesivir group and it was 66.37±18.14 in the control group. The difference was not statistically significant. A study by Ohl et al. (2021) investigated the association of remdesivir treatment with survival and length of stay in hospital among US disabled people who were hospitalized due to COVID-19. The mean age of remdesivir and control groups was homogenous (66.6 years vs. 67.5 years), and gender differences (1101 male (93.9%) vs. 1101 male (93.9%)) were obtained (24).

In the study entitled "Remdesivir for Treatment of Severe COVID-19: A community hospital experience", Lee et al. (2020) examined 76 patients who received remdesivir. In their study, the mean age was 63 years (59.8-66.2), and 36 (47.4%) male and 40 (52.6%) female subjects participated (25). Regarding drug use, 28 people from each group had a history of drug use. There was no significant difference between the two remdesivir and control groups in this regard. Three (8.57%) and four (11.43%) subjects in the remdesivir and control groups were smoking and no significant difference was seen in this regard. Sheikhi et al. (2021 investigated the clinical and demographic characteristics of Covid-19 patients in Iranshahr Hospital in 2020. Their study showed that 11 people (6.5%) had a history of smoking (26). Also, 28 people (80%) in the remdesivir group and 30 people (85.71%) in the control group had an underlying disease. The observed difference was not statistically significant. Generally, people with underlying diseases are more likely to suffer from serious diseases caused by Covid-19. A study by stud Lee et al. (2020) showed that most of the 54 patients (71.1%) had at least one comorbidity. Hypertension was the most common comorbidity (43 (56.6)) (25). However, in the study by Ohl et al. (2021), 889 people (37.4%) had lung diseases (24). In the study by Grein et al., the most comorbidities were hypertension (26% in the intervention group and 21% in the control group), diabetes (24% in the intervention group and 5% in the control group), hyperlipidemia (15% in the intervention group and 5% in the control group), and asthma (15% in the intervention group and 5% in the control group) (27). Cardiovascular diseases, hypertension, diabetes, and pulmonary insufficiency are involved in the infection of covid-19 and the spread of this disease.

In the present study, the most frequent primary symptoms in the remdesivir group were shortness of breath, weakness and lethargy, cough, fever and chills, myalgia, nausea, and vomiting and the least frequent symptoms were headache and sore throat. Also, in the control group, the most frequent primary symptoms were shortness of breath, fever and chills, cough, weakness and lethargy, myalgia, loss of appetite, nausea and vomiting, and the least frequent symptoms were respiratory distress and sore throat. In the study by Sheikhi et al. (2021), shortness of breath (71.6%) and cough (69.8%) were the most frequent symptoms, and chest pain (7.7%) was the least symptom in the covid-19 patients (26).

In the study by Talebi et al. (2020), investigating the baseline clinical symptoms in

all patients showed that shortness of breath (72.5%) was the most common symptom, followed by cough (61.8%) and fever (48.9%), respectively. The cough symptom was significantly higher in patients who recovered (28). In the study by Long, the cough was the most common symptom (66%) (29). In the study by Chen, fever (81.7%) and cough (36.5%) were the most common symptoms in Covid-19 patients (23). The mentioned study also compared the mean baseline clinical indices of patients infected with covid-19 in the control and remdesivir groups. The mean baseline body temperature was 37.09 ± 0.57 in the remdesivir group and 37.18 ± 0.49 in the control group. Thus, the difference between the two groups was not statistically significant.

The study by Antinori et al. (2020) investigated the clinical and laboratory outcomes of treatment with remdesivir in two groups of patients hospitalized in ICU and non-ICU units. The mean body temperature was 0.37 C (36.0-37.6) in the ICU group and 0.37 C (36.0-38.0) in the non-ICU group (30). ESR was the only measured index its mean was statistically significant between the two study groups. Its mean was 54.89 ± 31.02 in the remdesivir group and 36.58 ± 27.46 in the control group. The study by Jalali Farahani et al. (2021), which compared clinical, laboratory, and radiological findings in elderly and non-elderly patients infected with covid-19, reported that the number of neutrophils, ESR, AST, LDH, and CRP increased in all elderly and non-elderly patients (31).

In the retrospective cohort study by Stoeckle et al. (2021) on 55 patients hospitalized due to Covid-19, C-reactive protein (CRP), D-dimer, and lactate dehydrogenase levels were significantly higher in patients who progressed to intubation or death within 14 days compared to those who remained stable. CRP levels were significantly reduced after prescribing remdesivir in patients who were not intubated during the study (32). The present study data are consistent with those of previous studies and show that elevated levels of CRP and LDH might be predictors of poor clinical outcomes including mechanical ventilation and death in patients with severe COVID-19 pneumonia.

In the present study, the mean laboratory indices were compared in the covid-19 patients in the control and remdesivir groups at the admission and discharge times. None of the differences were statistically significant. In the remdesivir and control groups, an increase in the mean number of white blood cells was observed at the end of the study. However, these differences were not statistically significant. The mean of white blood cells in the study by Ohl et al. (2021) was 7.3 (x 103) in the group that received remdesivir and 7.1 (x 103) in the control group (24). In both remdesivir and control groups, a decrease in the mean number of lymphocytes was observed at the discharge time compared to the beginning of the study. However, the difference was not statistically significant. The results of the study by Antinori et al. (2020) revealed a significant increase in the number of lymphocytes and a significant decrease in C-reactive protein levels after 10 days of remdesivir treatment in both groups (30). The results of the mentioned study were not in line with those of our study.

The mean AST in the remdesivir group was 43.90 ± 21.31 and 49.07 ± 29.15 in the control group at the beginning of the study. It was 55.08 ± 36.77 in the remdesivir group and 57.4 ± 66.06 in the control group at the discharge time. An increase in mean AST was observed in both remdesivir and control groups. The mean ALT was 33.66 ± 19.58 in the remdesivir group and 40.8 ± 26.31 in the control group at the beginning of the study. The mean ALT was 73.28 ± 60.19 in the remdesivir group and 68.25 ± 46.72 in the control group at the end of the study. In the study by Ohl et al. (2020), the mean AST was 55.5 in the control group and 123.8 in the remdesivir group. Moreover, the mean ALT was 46.3 in the remdesivir group and 118.9 in the control group (24). In the study by van Laar et al. (2021), liver and kidney functions were investigated in 103 patients with Covid-19 treated with remdesivir for 15 days. In total, 11% of the patients showed a decrease in estimated glomerular filtration rate greater than 10 ml/min/1.73 m2.

Additionally, the levels of alanine transaminase and aspartate transaminase increased by 25% and 35%, respectively (33). The mean ALP was 203.07 ± 109.47 in the remdesivir group and 214.6 ± 106.83 in the control group at the time of the study. It was also found at 231±129.63 in the remdesivir group and 235.33 ± 113.62 in the control group at the end of the study. No statistically significant difference was observed between them in this regard. The observed increase in the mean ALP in both groups after receiving the drug was not statistically significant.

Based on the results, the mean length of stay in the hospital was 16.11 ± 11.52 days in the remdesivir group and 12.97 ± 9.65 days in the control group. The length of stay in the hospital for the participants in the intervention group was longer than the participants in the control group. However, this difference was not statistically significant. The mean length of stay in the ICU was 14.03 ± 11.55 in the remdesivir group and 11.05 ± 9.1 days in the control group. The mean length of stay in the ICU for the remdesivir group is higher than the control group. However, this difference is not statistically significant. The results indicate that the treatment with remdesivir has can reduce the length of stay in the hospital. However, the shorter length of stay in the ICU in patients who received remdesivir suggests that it may have an impact on reducing the risk of nosocomial infections, thrombotic events, and an error in prescribing drugs. Also, a faster recovery reduces the burden on the healthcare system and potentially increases its capacity, which is a critical factor.

The results of a study by Biegle et al. (2020) showed that the mean recovery time was 10 days for those who received remdesivir and 15 days for those who received a placebo. In contrast to the results of the present study, in the study by Chen-Yang et al. (2020), the remdesivir group showed a 33% higher chance of discharge from the hospital compared to the control group (20). In the study by Lee et al. (2020), the mean length of stay in the hospital was 10.09 days (8.6-11.6) for 76 patients who received remdesivir. In total, 14 (18.4%) of the patients who received remdesivir were admitted to the ICU with a mean length of stay of 9.29 days (5.6-13) (23). The results of a study by Abd-Elsalam et al. (2021) revealed that the remdesivir group had a significantly shorter mean stay in the hospital (10 days) than the control group (16 days) (34). The mean duration of mechanical ventilation for the remdesivir and control groups was 7.03 ± 8.92 and 4.62 ± 5.24 days, respectively. Although its mean was higher in the group that received remdesivir than the group that only received the standard diet, no significant difference was found in this regard. However, it seems that treatment with the standard diet combined with remdesivir did not have a positive impact on reducing the duration of mechanical ventilation compared to the standard diet alone.

In the study by Lee et al. (2020), among 76 patients receiving remdesivir, the mean duration of mechanical ventilation for patients was 9.42 days (10.8-8.0), which is more than the mean obtained for the intervention group in our study (25). The recovery time was 0.43 ± 1.65 for the group that received remdesivir and 0.2 ± 1.18 for the group that received the standard diet. The difference was not statistically significant. The results of the present study indicate that remdesivir significantly shortens the recovery time compared with the placebo. Concerning the recovery time, the results of this meta-analysis were not numerically in favor of remdesivir and were not statistically significant (35).

In the study by Grein et al. (2020), 30 of 53 patients (57%) received mechanical ventilation at the beginning. After a 10-day course of remdesivir treatment, 17 out of the 30 patients (57%), who received mechanical ventilation, were extubated (19). The mortality rates of the covid-19 patients were examined and compared based on Sofa Score and APACHE II Score in the control and remdesivir groups in the baseline. The results revealed that the Sofa and APACHE II scores were slightly lower in the group that received remdesivir plus standard diet than the group that did not receive remdesivir. However, this difference was not statistically significant. In the present study, remdesivir treatment was not considered a strong predictor of mortality. In this regard, the

study by Abd-Elsalam et al. (2021) revealed that remdesivir treatment did not affect the mortality rate of Egyptian covid-19 patients (34).

Our results were in line with the results of the Solidarity therapy trial, which showed that remdesivir did not affect mortality. In the study by Grein et al (2020), the mortality rate was 18% (6 of 34) among those who were treated with remdesivir and received invasive ventilation and it was 5% (1 of 19) among the patients who did not receive invasive ventilation (19). A meta-analysis by Yokoyama et al. (2020), which included 4 randomized controlled trials, showed that clinical recovery in the remdesivir group was significantly higher compared to the standard diet group (36). The results of the mentioned study did not confirm the results of the present study.

Conclusion

The results revealed that remdesivir did not cause any statistically significant difference between the remdesivir group and the control group regarding the variables of mortality rate, the length of stay in the hospital, the length of stay in the ICU, and the duration of mechanical ventilation. The results did not consider the use of this drug as an effective treatment in covid-19 patients. However, randomized controlled trials are needed to evaluate the safety and effectiveness of remdesivir and any other research agents in the treatment of SARS-CoV-2 patients.

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