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Evaluation of Outcome Parameters of Using Remdesivir in Patients with SARS-COV-2 Infection

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Abstract

Background: To assess outcome parameters of using Remdesivir in patients with SARS- COV-2 infection. **Methods:** A total of 62 patients (males- 38, females- 24) were assigned into two groups – group 1 (Remdesivir group (31) who received intravenous (IV) remdesivir for 5 days along with standard care (SC) and group 2 (SC group (31) who did not receive remdesivir, but received SC. Patient's clinical status was assessed by estimating serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels and serum creatinine level were estimated in all patient. **Results:** The mean number of admission days in group 1 was 11.2 days and in group 2 was 12.6 days. AST level in group 1 patients was 37.5 U/litre and in group 2 patients was 38.9 U/litre. ALT level in group 1 patients was 38.1 U/litre and in group 2 patients was 35.4 U/litre. Serum creatinine level was 0.97 and 1.05 in group 1 and 2 respectively. Low flow supplemental oxygen requirement was 80% in group 1 and 72% in group 2, non-invasive ventilation or high-flow oxygen requirement was 21% in group 1 and 28% in group 2 and both groups did not require invasive mechanical ventilation. **Conclusions:** Remdesivir therapy for 5 days did not produce improvement in clinical outcomes in moderate to severe COVID-19 cases.

Keywords:- Remdesivir, Severe Acute Respiratory Coronavirus, Covid-19, Invasive Ventilation

INTRODUCTION

The first cases of severe acute respiratory coronavirus 2 (SARS-CoV-2) was reported in December 2019 and later on this infection became worldwide pandemic. Covid-19 is the illness caused by SARS-CoV-2.[1] The symptoms in patients vary extensively, from asymptomatic disease to pneumonia and life-threatening complications, including acute respiratory distress syndrome, multisystem organ failure, and ultimately, death.[2]

Geriatric population especially having pre-existing respiratory or cardiovascular conditions are more prone to greatest risk for severe complications. Most of the patients are treated symptomatically with the use of antipyretic, analgesics, multivitamin, anti-inflammatory compounds, convalescent plasma, invasive and non-invasive oxygen support etc.[3]

Remdesivir is a nucleotide prodrug whose active metabolite inhibits viral RNA-dependent RNA polymerases, structurally conserved

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enzymes that play a key role in the replication of a broad range of viruses, including Coronaviridae.[4] Remdesivir has broad-spectrum activity against members of several virus families, including filoviruses and coronaviruses (e.g., SARS-CoV and Middle East respiratory syndrome coronavirus [MERS-CoV]) and has shown prophylactic and therapeutic efficacy in nonclinical models of these corona viruses.[5] A first randomized, placebo-controlled trial of remdesivir among patients with COVID-19 conducted in Wuhan, China, could not complete enrollment to meaningfully assess efficacy.[6]

In a rhesus macaque model of SARS-CoV-2 infection, remdesivir treatment was initiated soon after inoculation; the remdesivir-treated animals had lower virus levels in the lungs and less lung damage than the control animals.[7] The United States Food and Drug Administration issued Emergency Use Authorisation on May 1, 2020 to permit the use of remdesivir for treatment in adults and children hospitalised with suspected or laboratory-confirmed COVID-19.[8] There has always been a lack of confirmed guidelines whether remdesivir should be used in the management of COVID-19. Its benefit in severe COVID-19 cases has been debated.[9] Considering this, we attempted present study with the aim to assess outcome parameters of using Remdesivir in patients with SARS- COV-2 infection.

MATERIAL AND METHODS

This prospective cross- sectional trial was initiated after ethical clearance committee approved our study. All recruited patients had SARS-CoV-2 infection confirmed by polymerase-chain-reaction assay (PCR) within the last 4 days. Written consent from each participant was obtained. Our study had total of 62 patients (males- 38, females- 24).

Following simple random sampling technique, patients were assigned into two groups – group 1 (Remdesivir group (31) who received intravenous (IV) remdesivir for 5 days along with standard care (SC) and group 2 (SC group (31) who did not receive remdesivir, but received SC. In both groups, patients received IV 200 mg remdesivir on day 1, followed by 100 mg of remdesivir once daily for the next 4 days. Patients had respiratory rate >24/min and oxygen saturation of 94% or less. Radiographic exercise comprised of CT scan which confirmed existence of pneumonia. physical examination was carried out. Patient's clinical status was assessed by estimating serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels and serum creatinine level were estimated in all patient. Co- morbidities such as diabetes, hypertension, hyperlipidaemia, CAD, CKD, asthma and hypothyroidism etc. were recorded. Oxygen support requirements and adverse events were recorded.

RESULTS

The mean number of admission days in group 1 was 11.2 days and in group 2 was 12.6 days. AST level in group 1 patients was 37.5 U/litre and in group 2 patients was 38.9 U/litre. ALT level in group 1 patients was 38.1 U/litre and in group 2 patients was 35.4 U/litre. Serum creatinine level was 0.97 and 1.05 in group 1 and 2 respectively. Group 1 had 18 patients of diabetes, 16 patients of hypertension, 4 patients of hyperlipidaemia, 3 patients of CAD, 2 patients of CKD, 1 patient of asthma and 4 patients of hypothyroidism while group 2 had

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16 patients of diabetes, 17 patients of hypertension, 3 patients of hyperlipidaemia, 5 patients of CAD, 1patients of CKD and 2 patients of hypothyroidism. A non- significant difference existed between both groups [Table 1].

Table 1: Baseline clinical and laboratory characteristics.

Characteristics	Group 1	Group 2	P value
Mean no. admission days	11.2	12.6	>0.05
AST level (U/litre)	37.5	38.9	>0.05
ALT level (U/litre)	38.1	35.4	>0.05
Serum creatinine level (mg/dl)	0.97	1.05	>0.05
Diabetes	18	16	>0.05
Hypertension	16	17	>0.05
Hyperlipidaemia	4	3	>0.05
CAD	3	5	>0.05
CKD	2	1	>0.05
Asthma	1	0	>0.05
Hypothyroidism	4	2	>0.05

Table 2: Clinical management

Characteristics	Group 1	Group 2	P value
Low flow supplemental oxygen	80%	72%	>0.05
Non-invasive ventilation or high-flow oxygen	21%	28%	>0.05
Invasive mechanical ventilation	0	0	0

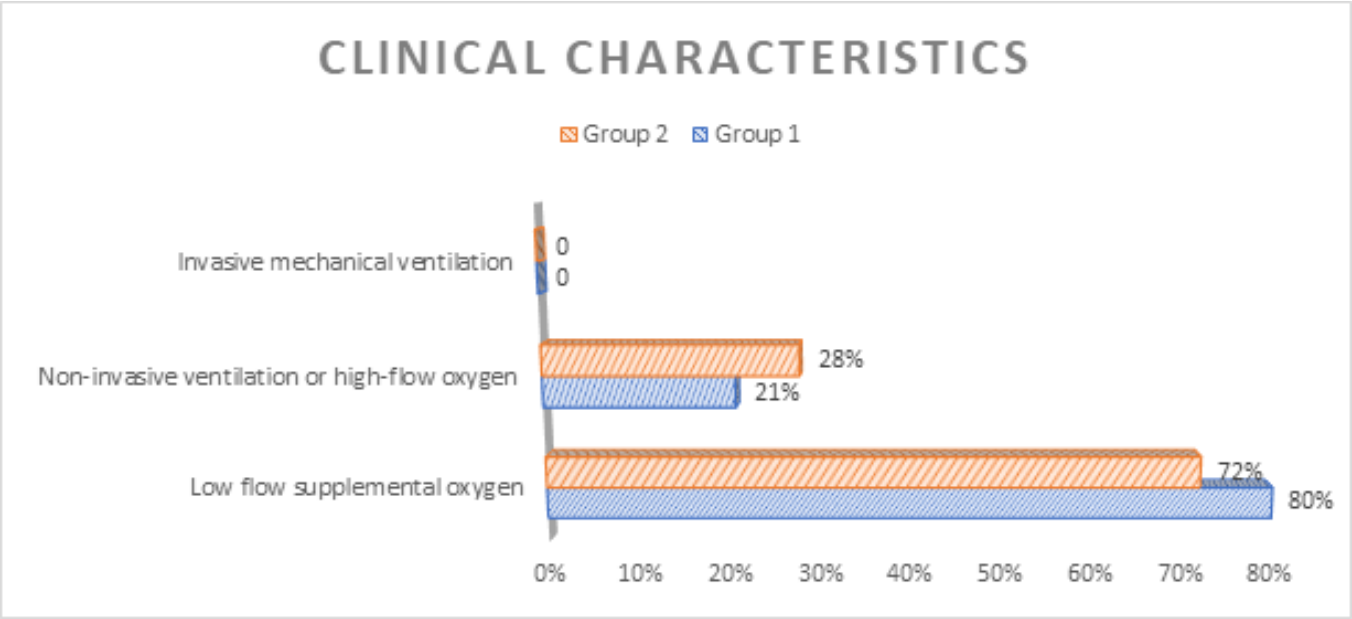

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Table 3: Alteration in Enzymes Level During Remdesivir Treatment

Enzyme level	Group 1		Group 2		P value
	Baseline	After treatment	Baseline	After treatment	
Increase in AST	37.4	38.8	38.0	39.4	>0.05
Increase in ALT	38.0	39.4	35.2	36.7	>0.05
Increase in creatinine	0.97	1.14	1.02	1.58	>0.05

Low flow supplemental oxygen requirement was 80% in group 1 and 72% in group 2, non-invasive ventilation or high-flow oxygen requirement was 21% in group 1 and 28% in group 2 and both groups did not require invasive mechanical ventilation. A non-significant difference existed between both groups [Table 2, Figure 1].

The mean AST level at baseline in group 1 was 37.4 and after treatment was 38.8. In group 2, at baseline was 38.0 and after treatment was 39.4. The mean ALT level at baseline in group 1 was 38.0 and after treatment was 39.4. In group 2, at baseline was 35.2 and after treatment was 36.7. The mean creatinine level at baseline in group 1 was 0.97 and after treatment was 1.14. In group 2, at baseline was 1.02 and after treatment was 1.58. A non- significant difference existed between both groups [Table 3].

DISCUSSION

We assessed outcome parameters of using Remdesivir in patients with SARS- COV-2 infection. Our study had total of 62 patients which comprised of 38 males and 24 females. Coronavirus disease-2019 (COVID-19) is a contagious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[10] The global pandemic of SARS-CoV-2 has produced a protracted medical, five days years old social, and economic crisis all over the world.[11] In the first 6 months of the pandemic, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread worldwide and has infected nearly 20 million people.[12] As of August 10, 2020, coronavirus disease 2019 (COVID-19), the disease caused by SARS-CoV-2, resulted in more than 163 000 deaths in the United States and more than 730 000 worldwide.[13] Many infected people are asymptomatic or experience mild symptoms and recover without medical intervention. However, older people and those with comorbid hypertension, diabetes, obesity, and heart disease are at higher risk of life-threatening illness. The search for the 'right' drug to treat COVID-19 is not yet over.[14] Many drug trials have taken place, but they have not provided any real-time therapeutic solutions. The search for different therapeutic strategies to combat COVID-19 is going on and is in different phases of completion Mortality from COVID-19 is particularly high among patients with coexisting conditions, including hypertension, diabetes, and cardiovascular disease, and in those who reach the point of requiring invasive mechanical ventilation. Safe and effective treatment options are needed to reduce the burden of COVID-19.[15]

Our study showed that mean number of admission days in group 1 was 11.2 days and in group 2 was 12.6 days. AST level in group 1 patients was 37.5 U/litre and in group 2 patients was 38.9 U/litre. ALT level in group 1 patients was 38.1 U/litre and in group 2 patients was 35.4 U/litre. Serum creatinine level was 0.97

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and 1.05 in group 1 and 2 respectively. Mahajan et al,[16] evaluated improvement in clinical outcomes with remdesivir treatment for five days. Patients above 40-years old and with moderate to severe COVID-19 but not on mechanical ventilation were randomly assigned into two groups-remdesivir group (34 cases) to receive the study drug intravenous (IV) remdesivir for five days plus the standard care (SC) and non-remdesivir group (36 cases) to receive the SC but not to receive the study drug. High-flow oxygen support and non-invasive ventilation was required at baseline by lesser patients in the remdesivir group. In the end, both groups had similar outcomes after adjustment for baseline clinical status. There was no statistical difference in mortality between the two groups (p = 0.749). Patients in both groups had an equal time to recovery. There was no difference in the occurrence of adverse effects of remdesivir between the two groups.

Our results revealed that group 1 had 18 patients of diabetes, 16 patients of hypertension, 4 patients of hyperlipidaemia, 3 patients of CAD, 2 patients of CKD, 1 patient of asthma and 4 patients of hypothyroidism while group 2 had 16 patients of diabetes, 17 patients of hypertension, 3 patients of hyperlipidaemia, 5 patients of CAD, 1patients of CKD and 2 patients of hypothyroidism. Spinner et al,[17] determined the efficacy of 5 or 10 days of remdesivir treatment compared with standard care on clinical status on day 11 after initiation of treatment. Patients were randomized in a 1:1:1 ratio to receive a 10-day course of remdesivir (n = 197), a 5-day course of remdesivir (n = 199), or standard care (n = 200). Median length of treatment was 5 days for patients in the 5-day remdesivir group and 6 days for patients in the 10-day remdesivir group. On day 11, patients in the 5-day remdesivir group had statistically significantly higher odds of a better clinical status distribution than those receiving standard care. The clinical status distribution on day 11 between the 10-day remdesivir and standard care groups was not significantly different. By day 28, 9 patients had died: 2 (1%) in the 5-day remdesivir group, 3 (2%) in the 10-day remdesivir group, and 4 (2%) in the standard care group. Nausea (10% vs 3%), hypokalemia (6% vs 2%), and headache (5% vs 3%) were more frequent among remdesivir-treated patients compared with standard care.

Our study showed that the mean AST level at baseline in group 1 was 37.4 and after treatment was 38.8. In group 2, at baseline was 38.0 and after treatment was 39.4. The mean ALT level at baseline in group 1 was 38.0 and after treatment was 39.4. In group 2, at baseline was 35.2 and after treatment was 36.7. The mean creatinine level at baseline in group 1 was 0.97 and after treatment was 1.14. In group 2, at baseline was 1.02 and after treatment was 1.58. In the study by Beigel et al,[18] 957 severe disease stratum patients in the remdesivir group had a shorter time to recovery (median 11 days) than placebo group patients (median 18 days). Also, 5% patients in remdesivir group were readmitted to hospital compared with 3% in placebo group.

CONCLUSIONS

Remdesivir therapy for 5 days did not produce improvement in clinical outcomes in moderate to severe COVID-19 cases.

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