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Original Research Article

A comparative study to see the result of remdesevir in moderate and severe patients of covid 19

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ABSTRACT

Introduction: Till date for covid 19 infection no specific drug has been developed. This study was taken up to see the effect of remdesevir in moderate and severe covid cases.
Materials and Methods: 22 diagnosed patients of covid 19 in moderate and severe category were included in the study and divived in two groups of 11 patients each. Group a received only symptomatic treatment and other group B received injection remdesevir for 5 days along with symptomatic treatment.
Results: Total 13 male (7 in group A; 6 in group B) and 9 female (4 in group A; 5 in group A) patients were included in the study. Patients in group B receiving injection remdesevir had shortened hospital stay, early symptom improvement and less mortality than those receiving only symptomatic treatment.
Conclusion: With no definite drug till date we conclude that remdesevir could be used as a good alternative treatment in moderate and severe category patients of covid 19.

1. Introduction

Till date COVID 19 has involved the entire world and killed almost a million of patients around the globe, and till date the numbers are increasing. Lack of specific medicine is the most important reason for the uncontrolled expansion of the disease. Although for the treatment of Covid 19 medications have been proposed but none is being proven very effective and Search for a curative medication is still ongoing.

Remdesivir is an experimental drug having broad spectrum antiviral activity. It has been used previously for treatment of Ebola which is a viral haemorrhagic fever.

It is a prodrug of nucleotide analog. On first of May 2020, it was approved by US FDA for use in severe confirmed or suspected cases of covid 19 in both adults and children as emergency drug.[1,2] Later on, it was given authorization for emergency use by US FDA on 28 of august 2020 for use in moderate disease.[3]

Another trial was initiated in June 2020 to determine whether remdesevir can be used in nebulized form in early stage of disease on outpatient basis.[4]

2. Materials and Methods

This was prospective case control study done in the department of TB and Respiratory Diseases of a tertiary care hospital in Uttar Pradesh from 15 August 2021 to 15 September 2021. Ethical clearance was obtained from institutional ethical committee.

2.1. Inclusion criteria

Patients presenting to emergency department with symptoms of covid 19 diagnosed by RT PCR of

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nasopharyngeal sample and falling into moderate and severe category according to WHO criteria were included in the study.[5]

2.2. Exclusion criteria

1. Patients diagnosed as case of covid 19 by RT PCR of nasopharyngeal sample but falling into mild catergory according to WHO classification.
2. Patients of moderate and severe category not giving consent for injection remdesevir.

2.3. Methodology

This was a prospective study done to see the result of remdesevir in covid 19 patients of moderate and severe category respectively. A total of 22 patients were included in the study which were divided into two groups of 11 patients each .one group did not receive injection remdesevir and other group received 5 days of injection remdesevir.

Upon presenting to emergency department with symptoms suggestive of covid 19 nasopharyngeal sample was sent for investigation and blood investigations like complete haemogram, renal function test, liver function tests, arterial blood gas analysis , D-dimer values, chest x-ray and saturation at room air by pulse oximeter were done.

On being diagnosed as a case of covid 19 patients were shifted to dedicated covid 19 ward of the hospital where there were PPE adorned doctors and paramedical staff to take care of the patients and multispeciality team of doctors were in touch with the patients through telemedicine and video calls from control room. Daily progress of the patients in terms of vital conditions were recorded three times.

Patients of both the groups were matched for age group and presenting complains and classified as moderate or severe case according to WHO criteria[5]

Primary outcome of this study was seen in terms of:

1. Effect of remdesevir in symptom improvement and reducing duration of hospital stay of the patients receiving remdesevir.
2. Mortality in two groups.
3. Requirement of oxygen at discharge in two groups.

3. Result

A total of 22 patients were included in this study divided into two groups of 11 patients each.

Group A did not receive injection remdesevir while Group B received 5 days of injection remdesevir.

Group A had 7 males and 4 females while group B had 6 males and 5 females. All the patients in both the groups were in age group 40-70 years.

Most common presenting symptom in both the groups was shortness of breath with 9 patients in group A and 11 patients in group B. next common symptom was fever with 6 patients in group A and 8 patients in Group B. 5 patients in group A had dry cough while 4 patients in group B had dry cough. Cough with expectoration at presentation was seen 3 and 1 patient in group A and B respectively. Two patients in group B had gastrointestinal symptoms of nausea, vomiting and pain abdomen.

Common Comorbidities seen in both the groups were type 2 diabetes mellitus with 4 and 3 patients in each group respectively, systemic hypertension in 2 and 3 patients in each group respectively.one patient in group A was diagnosed as a case of type 2 diabetes mellitus during hospital stay. Other comorbidities in group A were bronchial asthma in two patients and old pulmonary Koch in one patient whereas two patients of group B were on treatment for coronary artery disease.

Base line blood investigations were normal of all the patients except for D-dimer values. D-dimer values were raised in all the patients of both the groups.in group B D-dimer value was raised twice the normal in 1 patient, thrice the normal in 3 patients and >10 times normal 7 patients. In group B It was seen D-dimer was raised twice normal value in 2 patient , thrice normal value in 3 patients, four times normal value in 3 patients , more than 5 times in 2 patients and more than six times in 1 patient.

In group A 4 male patients had smoking history while 3 were non-smokers and while three females had history of exposure to biomass fuel while one female patient had no history of smoking. In group B among male patients only one patient was a current smoker rest five were non-smokers. Among female patients In group B all had history of exposure to bio mass fuel.

Chest x-ray of all the patients in both the groups had bilateral pneumonic infiltrates.

Patients having symptoms of pneumonia and room air saturation by pulse oximeter between 90-94% were classified as moderate case and patients having symptoms of pneumonia and room air saturation was <90% were classified as severe case. Group A had 4 patients in moderate category and 7 patients in severe category whereas group B had 3 and 8 patients respectively in moderate and severe category according to WHO classification.

4 patients of group A in moderate category were given only supplemental oxygen therapy while 7 patients in severe category were given non-invasive ventilator support and one patient among them later on underwent endotracheal intubation. Patients in group A were managed symptomatically and were given drugs according to their symptoms and for their associated comorbidities. However, they were also given tablet doxycycline 100mg BD and tablet ivermectin 6mg BD for5 days after diagnosis of COVID 19 along with symptomatic treatment.

Patients of moderate category improved symptomatically and were maintaining saturation >94% at room air and were

discharged after testing negative of RT PCR sample. Mean duration of hospital stay of patients in GROUP A moderate category was 14.5 days. Out of 7 patients in severe category three patients expired and rest 4 patients of severe category were shifted to TB and Respiratory Department ward and were managed accordingly. Mean duration of hospital stay of patients in severe category was 28 days. One patient out of these 4 patients expired in the ward ICU after 14 days of testing negative for COVID 19. Remaining 3 patients of severe category of group A were advised home based oxygen therapy as they were not maintaining saturation on room air and were discharged.

Patients in group B were also given symptomatic treatment and treatment of associated comorbidities along with 5 days of tablet doxycycline 100mg and tablet ivermectin 6mg twice daily. They were given injection remdesevir according to current dose schedule as:

Day 1: 200mg IV OD

Day 2-5: 100mg IV OD

It was administered as slow infusion over 30-60 minutes.

There was no side effect reported from any patient.

Informed consent was taken from either patient or patient's attendants.

Three patients in moderate category of group B improved on supplemental oxygen and were maintaining saturation >94% on room air. Mean duration of hospital stay was 9.3 days for patients of moderate category. 7 Patients of severe category were given non invasive ventilator support and one patient underwent endotracheal intubation and was later extubated and given non-invasive ventilator support. Mean duration of hospital stay of patients of severe category who received 5 days of injection remdesevir was only 11.3 days. Only one patient of this group has prolonged hospital stay of 28 days and was discharged on home based oxygen therapy rest all patients of severe category too were maintaining saturation >94% at room air and were discharged. No mortality was seen in group of patients receiving injection remdesevir.

These findings have been summarized in Table 1.

Table 1: Summary of results of study group

	Moderate category	Severe category
Only supplemental oxygen	3	0
Only NIV	0	11
NIV + ET intubation	0	1
Mean duration of hospital stay	9	16
Mean duration of supplemental oxygen requirement	7	14
Mean duration of niv requirement	-	14
Mortality	0	0
Discharged on home based oxygen therapy	0	2

4. Discussion

COVID 19 was officially recognized by WHO as a pandemic, on 11 of March 2020. It was caused by severe acute respiratory syndrome corona virus-2 (SARS-CoV 2) which is an enveloped beta corona virus.

A specific antiviral treatment for COVID-19 is yet to be identified;[6] therefore, several strategies have been proposed to treat patients, including the use of convalescent plasma and interferon (IFN), as well as interleukin 6 receptor inhibitors since they have the potential to inhibit the cytokine storm.[7]

Remdesevir is adenosine nucleotide prodrug which gets metabolized to its active form, nucleoside triphosphate, in the cells. And acts as a competitive inhibitor of RNA-dependent RNA polymerase of the virus. It has a broad antival spectrum and is effective against filoviruses, paramyxoviruses, pneumoviruses, and coronaviruses.[8,9]

Remdesivir inhibits the replication of SARS-CoV-2 in human nasal cells and bronchial airway epithelial cells.[10] It has also been found that nuclear transport of vial proteins is inhibited by ivermectin.[11,12]

Historically, remdesivir was tested in the treatment of Ebola patients in 2018 in Democratic Republic of the Congo.[13] World Health Organization included remdesevir in clinical trial in order to find an effective treatment for COVID-19. A 35-year-old patient from Washington was the first to be treated with remdesevir who improved after 7 days of treatment.[14] Remdesivir was also used to treat seven patients in Seattle, USA, who were critically ill.[15] A larger study by Grein J et al found that clinical improvement was shown in 68% of patients (36 out of 53 patients), following a 10-day course of treatment with remdesevir (200 mg on day 1, followed by 100 mg daily intravenously).[16]

Similarly in a study done by Beigel et al they found that patients receiving remdesevir had earlier recovery time and less mortality than the patients of COVID19 not receiving remdesevir.[17]

Wang Y et found in their study that patients treated with remdesevir showed clinical improvement earlier than those receiving placebo presenting with symptom duration of 10 days or less.[18]

Few other studies done by Oleander SA et al, they found that by day 14 of remdesivir treatment recovery was significantly improved and odds of death were reduced by 62% as compared with standard treatment of severe covid 19.[19] Spinner CD et al observed in their study that Patients receiving a 5-day course of remdesivir had a statistically significant improvement in clinical status compared with standard care.[20]

Indications of remdesevir:

1. Confirmed case of covid 19 by RTPCR.
2. Moderate and severe covid 19 patients with room air saturation </= 94% or requiring supplemental oxygen or mechanical ventilation at presentation.

3. Radiographic infiltrates.

Contraindications of remdesevir

1. Known hypersensitivity to drug.
2. Hepatic dysfunction: ALT/AST > 5 times upper limit of normal Or ALT elevation accompanied by signs and symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase or INR.
3. GFR <30ml/min or renal replacement therapy.
4. Pregnant or breast feeding female.

Patients should be monitored with daily LFT and drug should be stopped if ALT >5 times ULN.

Patient should also be monitored for any infusion related side effects like diaphoresis, hypotension, nausea, shivering and vomiting.

Concomitant use of Hdroxychloroquine may decrease antiviral effect of remdesevir, so it is not recommended.[21]

5. Conclusion

In this study we saw that remdesevir reduces duration of hospital stay, increases recovery time and decreases mortality in both moderate and severe category of covid 19 patients. Thus, we conclude that remdesevir should be given to moderate and severe patients of covid 19 however further larger studies are required for the same.

6. Limitations of Study

Number of patients included in the study were too small to give the proper evaluation of outcome.

7. Conflict of Interest

None.

8. Source of Funding

None.

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