Use of Remdesivir in The Treatment of COVID-19 Infection Among Sudanese Patients - Case Series

Maysoun Ahmed Awad Yousif

Imperial Specialized Hospital

Ghada Omer Hamad Abd El-Raheem (✉ ghadaomer90@gmail.com)

Imperial Specialized Hospital

Doaa Salih Ibrahim Mohamed

Imperial Specialized Hospital

Research Article

Keywords: COVID-19, treatment, corona virus, Remdesivir, hypotension, Imperial Hospital, Sudan, Sudanese patients

Posted Date: February 8th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-153556/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Introduction: COVID-19 infection is a viral pandemic started in 2019, all societies have the susceptibility of getting infected. Remdesivir is an anti-retroviral agent, with a broad spectrum of activity. Remdesivir activity against COVID-19 had been studied in both *in vitro* and *in vivo*, but still considered new for COVID-19 treatment and not available in all countries. The aim of our study was to report the use of remdesivir among Sudanese population and report the adverse events related to the course of treatment.

Methods: case series study was conducted in Imperial Hospital reporting the three cases who received Remdesivir for treating COVID-19 infection.

Cases presentation: Three cases had received remdesivir for treating COVID-19 infection, side effects reported were elevated liver enzymes, profound hypotension and hypoalbuminemia.

Discussion: All three patients were severe cases of COVID-19 admitted to the ICU. Unexpectedly, severe resistant hypotension was the cause of death in 2 cases who received remdesivir. Increased liver enzymes was noticed in one case. In the other hand, hypoalbuminemia was noticed in one case as well.

Introduction

COVID-19 infection is a viral pandemic started in 2019, all societies have the susceptibility of getting infected; especially health care personnel and elderly population. Concomitant comorbid conditions, such as diabetes mellitus (DM), are related to the severity of COVID-19 infection [1, 2]. Remdesivir is an anti-retroviral agent, with a broad spectrum of activity. It is a pro-drug, which was firstly developed to be used for the treatment of the Ebola outbreak [3]. Recently, it was proposed to treat COVID-19 infection [4, 5]. Remdesivir activity against COVID-19 had been studied in both *in vitro* and *in vivo*, but still considered new for COVID-19 treatment and not available in all countries [6, 7]. Although, some remdesivir trials had no enough power [8], other large scale clinical trials were done [9]. The aim of our study was to report the use of remdesivir among Sudanese population and report the adverse events related to the course of treatment.

Methods

Case series study design was implemented. All cases were described in details. The data were collected retrospectively from the medical records. Confidentiality of participants was assured through the use of an anonymous research tool. Informed consents from surrogate decision makers were obtained, voluntary, by contacting them through their registered phone numbers. The collected data were used strictly for the purpose of the study objectives.

Case-1 Presentation

63 years old male was presented to the Emergency Isolation room at Imperial hospital on November the 26th complaining of cough, shortness of breath and fatigue. The symptoms started 2 weeks ago with dry cough only. The patient's co-morbid conditions were hypertension and renal transplant 10 years ago with no other co-morbidity. Oxygen therapy was initiated through a non-rebreathing mask by a rate of 15 litre/minute, oxygen saturation was 97% with the mask. The patient was transferred for dialysis on day 2, the 28th of November. On day 4, the 29th of November, the patient started being anxious with oxygen drop to 88%, then immediately transferred to the isolation ICU. Table 1. below illustrates the medications received by the patient.

Chest computed tomography was done for the patient on the first day of hospital arrival, shown in figure 1. below.

On day 2 of the ICU, day 5 of hospital admission, the patient was on and off CPAP mask ventilation. Remdesivir was started on the 4th of December, day 5 of the ICU, with a loading dose of 200 mg in 250 mL normal saline intravenously followed by a maintenance dose of 100 mg in 250 mL normal saline daily, planned for 10 days. The patient was stable with mildly elevated serum creatinine, 1.7 mg/dl, and adequate urine output. The patient was seen by a nephrologist. On the 6th of December, the dose of enoxaparin was switched to the therapeutic dose, 80 mg B.D. On the 4th day of the remdesivir treatment, profound hypotension occurred and vasopressors were started. Despite the maximum dose of noradrenaline and dopamine along with normal saline, the hypotension persisted. Profound bradycardia occurred with a pulse rate of 36 bpm, and marked drop of oxygen saturation to 52% on CPAP mask. The patient was deceased 35 minutes later on the 7th of December, 2020.

Table 1: COVID-19 treatment medications administered to the patients

Medications	Medications
Remdesivir 200 mg I.V. LD, 100 mg I.V. O.D	Vitamin C 1000 mg daily
Meropenem 1 gm I.V B.D.	Zinc sulphate 15 mg daily
Enoxaparin 40mg S.C. B.D.	Azithromycin 500 mg daily
Dexamethasone 6 mg daily	Salbutamol nebulized solution 6 Hourly
Paracetamol 1gm I.V on need	Ipratropium nebulized solution 6 Hourly
Pantoprazole 40 mg I.V daily	Pulmicort 0.5 gm nebulized solution 6 Hourly

LD=Loading dose, I.V.= Intravenously, O.D.= Once daily, B.D.= Twice daily

Case-2 presentation

78 years old male was presented to the Emergency Isolation room at Imperial hospital on December the 8th with a positive PCR test for COVID-19. The swab was taken on the 4th of December, 2020 and the

result was received on the 5th of December. SARS- COV-2 RNA by PCR was detected, while, SARS- COV-2 antibody was negative. The patient was complaining of shortness of breath for 3 days. His comorbidities were, diabetes mellitus (DM) on insulin treatment, and a history of Ca colon operated 2 years ago and he was on oral chemotherapy. The patient had no other co-morbid conditions. A confirmatory test by using RT-PCR was done on the 10th of December (IgG 12.04, IgM 0.243). The medications in table 1. above, were given to the patient since day 1 and planned for 10 days, besides 1.5 litres of fluids. The patient was admitted to the isolation ICU on the same day of hospital arrival. Remdesivir was started on day 1, the 8th of December 2020. A loading dose of 200 mg was given in 250 mL of normal saline followed by a maintenance dose of 100 mg I.V in 250 mL of normal saline daily, planned for 10 days. On admission, the SPO₂ was 92%, CPAP was applied. Table 2. below illustrated the daily vital signs of the patient.

Table 2: Daily vital signs of the patient (Case-2)

Vital signs	Day 1 8/12/2020	Day2 9/12/2020	Day 3 10/12/2020	Day 4 11/12/2020	Day 5 12/12/2020	Day 6 13/12/2020
SPO₂	92%	94%	95%	94%	90%	83%, 80%
RR	30	35	33	30	32	34
HR	100 109 bpm	128 115 bmp	122 130 bpm	130 bpm	132 bpm	125 bpm
B.P.	130/70 140/80	139/87 133/85	149/92 168/100	170/83	155/83	99/56 Undetectable 84/40
GCS	15/15	15/15	13/15	10/15	10/15	3/15
RBG	233 402	343 230	300 370	350 310	369 368	268 280
Temp.	37.3	36.0	36.4			

Laboratory examinations were done daily starting from day 3, the 10th of December. The results were presented in table 3 below.

Table 3: Results of laboratory examinations of the patient (Case-2)

Laboratory tests	Day 3	Day 5	Laboratory tests	Day 3	Day 5
Blood Urea	121		pH		7.347
Serum creatinine	1.2 mg/dl		SO2%		97.50%
Na+ (Sodium)	153 mmo/L	165.2 mmol/L	HCO3		27
K+ (Potassium)	5.3 mmol/L	4.66 mmol/L	Hct		49.50%
D-dimer	5		Cl		114.5
CRP	215		Total protein	7.5 g/dL	7.6 g/dL
TWBCs	17.7		Serum albumin	2.4 g/dL	2.6 g/dL
RBCs	5.7		ALP	97 U/L	111 U/L
Neutrophis	88		ALT (GPT)	288 I.U/L	142 I.U/L
Lymphocytes	7		AST (GOT)	431 I.U/L	70 I.U/L
PLts	351		Prothrombin time	65 Sec.	24 Sec.
PCO2		50.6 mmHg	INR	>10	1.8
PO2		105.4 mmHg	APTT	49 Sec.	

Chest computed tomography was done for the patient on the first day of hospital arrival, the 8th of December, shown in figure 2. below.

On day 2 in the ICU, the patient started doing better and getting stable. On day 3, the GCS was reducing and the patient started deteriorating. Nasogastric feeding was started and I.V fluids were increased to 3 litters per day alongside the same plan. On day 6, severe hypotension had occurred to the patient, to an extent that blood pressure was undetectable on any monitor or manual devices. Hypotension was resistant to fluids and vasopressors which eventually lead to the death of the patient. The patient was deceased on day 6, the 13th of December, as a result of severe refractory hypotension..

Case-3 presentation

75 years old male was presented to the Emergency Isolation room at Imperial hospital on the 18th of December 2020, with generalized fatigue and fever for 1 week, and hemiparesis. Co-morbid conditions of the patient were pacemaker device and BPH condition, which was operated 5 years ago. Oxygen saturation with CPAP mask was 87%. The patient was diagnosed with COVID-19 pneumonia and sepsis which were confirmed by PCR and CT-Chest. An incidence of haemorrhagic stroke was confirmed through brain imaging. The patient was admitted to the Isolation ICU immediately, with reduced GCS (9/15). Respiratory support was initiated with physiotherapy and prone positioning for 16 hours per day. 3 units of fresh frozen plasma (FFP), platelet concentrate 50 U/Kg and vitamin K 10 mg I.V. were administered. The patient developed hypernatremia (Serum Na⁺ 153), INR (2.8). Remdesivir was initiated on day 1 of

admission, the 18th of December and stopped on day 5, the 23rd of December. Hypoalbuminemia was noticed on the 24th of December (2.2 g/dl), albumin 20% infusion was given twice daily for 4 days. On the 27th of December, the 10th day of hospital admission, the patient was transferred to a different healthcare facility. The medications in table 1, were given to the patient during the hospital stay.

Discussion

Our patients were aged between 62 and 78 years, as in published studies [9, 10]. All our study cases were males, as COVID-19 infection was more prevalent in males [10,11, 12]. In our study, Case-2 was diabetic, diabetes is known to be associated with COVID-19 severity of infection [2]. This comorbidity was reported for 25% and 16% of patients who received remdesivir [9, 10]. Remdesivir is considered a viable treatment option in severe infections [13, 14]. Cases were put on non-invasive ventilation, in contrast with study [10] reporting that non-invasive ventilation was less common. Remdesivir doses administered for our patients were, 200 mg intravenously loading dose followed by 100 mg daily dose, which were the recommended doses [9, 15]. All cases had received antibiotics and steroids along with remdesivir, this was in line with [9]. Hypoalbuminemia was reported in patients taking remdesivir [9], as in, case-3 of our study. But case-2 had hypoalbuminemia on presentation. Case-1 and 2 patients had 4 and 6 treatment days with remdesivir respectively, with no improvement, in contrast to published trials in which remdesivir treatment course of 5 days had shown significant improvements [16, 17]. Our second case patient received remdesivir after 4 days of presentation of COVID-19 symptoms, which is consistent with published literature reporting that the efficacy of remdesivir is higher in patients who received it within 10 days of symptoms presentation [18]. While another study concluded that delayed treatment initiation with remdesivir was beneficial as well [19]. In the other hand, our first case had symptoms for more than 10 days before remdesivir treatment. Liver enzymes abnormalities had been reported among patients who received remdesivir [4, 10, 20]. For such cases, treatment course should be stopped [14]. In our second case, liver enzymes were extremely elevated since day 3 of treatment, but remdesivir course had not been discontinued. Two of our cases were deceased and that was expected, as per a case series study in US, in which 50% of patients with severe COVID-19 infection on remdesivir were deceased [21]. Also, in a clinical study only 3% of patients on remdesivir had clinical improvement on day 7 [9]. In another study, compassionate use of remdesivir resulted in improvements in 69% of patients [10]. The cause of death for both cases was severe resistant hypotension, which was reported as a serious event in remdesivir use [10, 20]. The limitations of our study were the observational nature of case series that cannot establish direct cause-effect relationships. Also, the data were collected retrospectively from the medical records of the patients which had some missing medical results.

Conclusion

All three patients were severe cases of COVID-19 admitted to the ICU. Unexpectedly, severe resistant hypotension was the cause of death in 2 cases who received remdesivir. Increased liver enzymes was noticed in one case. In the other hand, hypoalbuminemia was noticed in one case as well.

Recommendations

Wider studies regarding remdesivir use among patients in Sudan must be conducted extensively in order to study this unexpected fatal event and assess the association of this event to remdesivir use, as well as, to report the frequency of the side effects.

Abbreviations

CPAP: Continuous Positive Airway Pressure

CT: Computed Tomography

DM: Diabetes Mellitus

FFP: Fresh Frozen Plasma

GCS: Glasgow Coma Scale

ICU: Intensive Care Unit

IgG: Immunoglobulin G

IgM: Immunoglobulin M

I.V: Intravenously

MOH: Ministry of health

PCR: Polymerase Chain Reaction

RNA: Ribonucleic Acid

RT-PCR: Reverse Transcription Polymerase Chain Reaction

SARS-COV-2: Severe Acute Respiratory Syndrome

SP_O₂: Oxygen Saturation

Declarations

Ethical approval and consent to participate

Approval was firstly obtained from the Medical administration of Imperial Hospital. The study proposal was then submitted to the Administration of Innovation and Scientific Research at the State Ministry Of

Health (MOH), Khartoum. Expedited review was conducted by the IRB of the MOH and approval was granted. Another copy of the proposal was submitted to the Administration of Private Medical Facilities.

Consent for publication

All authors have read the final manuscript and gave their consent for the article to be published. No clinical details of participants that might compromise their anonymity were used in the development of this manuscript titled “ **Use of Remdesivir in the treatment of COVID-19 infection among Sudanese patients- Case series** ”.

Availability of supporting data

All supporting data are available. Adjustments of brightness and contrast were done to the entire images without misrepresentation of any features of the original images. No images had been duplicated or published elsewhere.

Competing interests

The authors declared no competing interest.

Funding

No funding was applied for this study.

Authors' contributions

All authors have read the final manuscript and gave their approval for publication.

MAAY: Collected the data, assisted in getting the ethical approval, read the first draft of the manuscript and proof read the final manuscript prior to submission.

GOHA: Assisted in the data collection, got the ethical approval, wrote the first draft and the final manuscript.

DSIM: Facilitated the administrative arrangements at Imperial Hospital and read the final manuscript prior to submission.

Acknowledgments

The authors are grateful to the departments of Imperial Hospital whose participation enabled this study to be completed.

References

1. Tu H, Tu S, Gao S, Shao A, Sheng J. Current epidemiological and clinical features of COVID-19; a global perspective from China. *J Infect.* 2020 Jul;81(1):1-9. doi: 10.1016/j.jinf.2020.04.011. Epub 2020 Apr 18. PMID: 32315723; PMCID: PMC7166041.
2. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, Khare S, Srivastava A. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. *Diabetes Metab Syndr.* 2020 Jul-Aug;14(4):535-545. doi: 10.1016/j.dsx.2020.04.044. Epub 2020 May 6. PMID: 32408118; PMCID: PMC7200339.
3. Jorgensen SCJ, Kebriaei R, Dresser LD. Remdesivir: Review of Pharmacology, Pre-clinical Data, and Emerging Clinical Experience for COVID-19. *Pharmacotherapy.* 2020 Jul;40(7):659-671. doi: 10.1002/phar.2429. Epub 2020 Jun 28. PMID: 32446287; PMCID: PMC7283864.
4. Davies M, Osborne V, Lane S, Roy D, Dhanda S, Evans A, Shakir S. Remdesivir in Treatment of COVID-19: A Systematic Benefit-Risk Assessment. *Drug Saf.* 2020 Jul;43(7):645-656. doi: 10.1007/s40264-020-00952-1. PMID: 32468196; PMCID: PMC7255634.
5. Al-Tawfiq JA, Al-Homoud AH, Memish ZA. Remdesivir as a possible therapeutic option for the COVID-19. *Travel Med Infect Dis.* 2020 Mar-Apr;34:101615. doi: 10.1016/j.tmaid.2020.101615. Epub 2020 Mar 5. PMID: 32145386; PMCID: PMC7129391.
6. Frediansyah A, Nainu F, Dhama K, Mudatsir M, Harapan H. Remdesivir and its antiviral activity against COVID-19: A systematic review. *Clin Epidemiol Glob Health.* 2020 Aug 7. doi: 10.1016/j.cegh.2020.07.011. Epub ahead of print. PMID: 32838064; PMCID: PMC7410793.
7. Musa A, Pendi K, Hashemi A, Warbasse E, Kouyoumjian S, Yousif J, Blodget E, Stevens S, Aly B, Baron DA. Remdesivir for the Treatment of COVID-19: A Systematic Review of the Literature. *West J Emerg Med.* 2020 May 20;21(4):737-741. doi: 10.5811/westjem.2020.5.47658. PMID: 32726230; PMCID: PMC7390571.
8. Norrie JD. Remdesivir for COVID-19: challenges of underpowered studies. *Lancet.* 2020 May 16;395(10236):1525-1527. doi: 10.1016/S0140-6736(20)31023-0. Epub 2020 Apr 29. PMID: 32423580; PMCID: PMC7190306.
9. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, Fu S, Gao L, Cheng Z, Lu Q, Hu Y, Luo G, Wang K, Lu Y, Li H, Wang S, Ruan S, Yang C, Mei C, Wang Y, Ding D, Wu F, Tang X, Ye X, Ye Y, Liu B, Yang J, Yin W, Wang A, Fan G, Zhou F, Liu Z, Gu X, Xu J, Shang L, Zhang Y, Cao L, Guo T, Wan Y, Qin H, Jiang Y, Jaki T, Hayden FG, Horby PW, Cao B, Wang C. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet.* 2020 May 16;395(10236):1569-1578. doi: 10.1016/S0140-6736(20)31022-9. Epub 2020 Apr 29. Erratum in: *Lancet.* 2020 May 30;395(10238):1694. PMID: 32423584; PMCID: PMC7190303

10. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, Feldt T, Green G, Green ML, Lescure FX, Nicastrì E, Oda R, Yo K, Quiros-Roldan E, Studemeister A, Redinski J, Ahmed S, Bernett J, Chelliah D, Chen D, Chihara S, Cohen SH, Cunningham J, D'Arminio Monforte A, Ismail S, Kato H, Lapadula G, L'Her E, Maeno T, Majumder S, Massari M, Mora-Rillo M, Mutoh Y, Nguyen D, Verweij E, Zoufaly A, Osinusi AO, DeZure A, Zhao Y, Zhong L, Chokkalingam A, Elboudwarej E, Telep L, Timbs L, Henne I, Sellers S, Cao H, Tan SK, Winterbourne L, Desai P, Mera R, Gaggari A, Myers RP, Brainard DM, Childs R, Flanigan T. Compassionate Use of Remdesivir for Patients with Severe Covid-19. *N Engl J Med*. 2020 Jun 11;382(24):2327-2336. doi: 10.1056/NEJMoa2007016. Epub 2020 Apr 10. PMID: 32275812; PMCID: PMC7169476.
11. Li LQ, Huang T, Wang YQ, Wang ZP, Liang Y, Huang TB, Zhang HY, Sun W, Wang Y. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol*. 2020 Jun;92(6):577-583. doi: 10.1002/jmv.25757. Epub 2020 Mar 23. PMID: 32162702; PMCID: PMC7228329.
12. Fang X, Li S, Yu H, Wang P, Zhang Y, Chen Z, Li Y, Cheng L, Li W, Jia H, Ma X. Epidemiological, comorbidity factors with severity and prognosis of COVID-19: a systematic review and meta-analysis. *Aging (Albany NY)*. 2020 Jul 13;12(13):12493-12503. doi: 10.18632/aging.103579. Epub 2020 Jul 13. PMID: 32658868; PMCID: PMC7377860.
13. Davies M, Osborne V, Lane S, Roy D, Dhanda S, Evans A, Shakir S. Remdesivir in Treatment of COVID-19: A Systematic Benefit-Risk Assessment. *Drug Saf*. 2020 Jul;43(7):645-656. doi: 10.1007/s40264-020-00952-1. PMID: 32468196; PMCID: PMC7255634.
14. Spinner CD, Gottlieb RL, Criner GJ, Arribas López JR, Cattelan AM, Soriano Viladomiu A, Ogbuagu O, Malhotra P, Mullane KM, Castagna A, Chai LYA, Roestenberg M, Tsang OTY, Bernasconi E, Le Turnier P, Chang SC, SenGupta D, Hyland RH, Osinusi AO, Cao H, Blair C, Wang H, Gaggari A, Brainard DM, McPhail MJ, Bhagani S, Ahn MY, Sanyal AJ, Huhn G, Marty FM; GS-US-540-5774 Investigators. Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. *JAMA*. 2020 Sep 15;324(11):1048-1057. doi: 10.1001/jama.2020.16349. PMID: 32821939; PMCID: PMC7442954.
15. Hashemian SM, Farhadi T, Velayati AA. A Review on Remdesivir: A Possible Promising Agent for the Treatment of COVID-19. *Drug Des Devel Ther*. 2020 Aug 6;14:3215-3222. doi: 10.2147/DDDT.S261154. PMID: 32821086; PMCID: PMC7425093.
16. McCreary EK, Angus DC. Efficacy of Remdesivir in COVID-19. *JAMA*. 2020 Sep 15;324(11):1041-1042. doi: 10.1001/jama.2020.16337. PMID: 32821934.
17. Yokoyama Y, Briassoulis A, Takagi H, Kuno T. Effect of remdesivir on patients with COVID-19: A network meta-analysis of randomized control trials. *Virus Res*. 2020 Oct 15;288:198137. doi: 10.1016/j.virusres.2020.198137. Epub 2020 Aug 19. PMID: 32827627; PMCID: PMC7437510.
18. Edwards JK, Cole SR, Adimora AA. Remdesivir and COVID-19. *Lancet*. 2020 Oct 3;396(10256):953. doi: 10.1016/S0140-6736(20)32020-1. PMID: 33010832; PMCID: PMC7529398.

19. Hillaker E, Belfer JJ, Bondici A, Murad H, Dumkow LE. Delayed Initiation of Remdesivir in a COVID-19-Positive Patient. *Pharmacotherapy*. 2020 Jun;40(6):592-598. doi: 10.1002/phar.2403. Epub 2020 May 20. PMID: 32281114; PMCID: PMC7262085.
20. Goldman JD, Lye DCB, Hui DS, Marks KM, Bruno R, Montejano R, Spinner CD, Galli M, Ahn MY, Nahass RG, Chen YS, SenGupta D, Hyland RH, Osinusi AO, Cao H, Blair C, Wei X, Gaggar A, Brainard DM, Towner WJ, Muñoz J, Mullane KM, Marty FM, Tashima KT, Diaz G, Subramanian A; GS-US-540-5773 Investigators. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. *N Engl J Med*. 2020 Nov 5;383(19):1827-1837. doi: 10.1056/NEJMoa2015301. Epub 2020 May 27. PMID: 32459919; PMCID: PMC7377062.
21. Singh AK, Singh A, Singh R, Misra A. Remdesivir in COVID-19: A critical review of pharmacology, pre-clinical and clinical studies. *Diabetes Metab Syndr*. 2020 Jul-Aug;14(4):641-648. doi: 10.1016/j.dsx.2020.05.018. Epub 2020 May 12. PMID: 32428865; PMCID: PMC7214279.

Figures

Figure 1

Chest computed tomography of case-1 on hospital arrival

Figure 2

Chest computed tomography of case-2 on hospital arrival