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Impact on Early Remdesivir Therapy in High Risk Patient with Sars-Cov-2 Diagnosis: Importance of Immediate Treatment Strategy in the Covid-19 Era

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Abstract

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS Cov2), is a viral respiratory infection that varies from asymptomatic to severe illness and death .At June 2021,has resulted in 176 million infections and 3.8 million deaths, globally [1]. High Risk patients with hypertension, obesity, diabetes, cardiovascular disease, chronic lung disease, and cancer predict a severe course, risk of hospitalization, and death [2]. On 22 October, 2020, the US Food and Drug Administration was approved Remdesivir, a nucleoside analogue and RNA polymerase inhibitor, for the treatment of COVID-19 patients requiring hospitalization [3]. In patients with COVID-19, peak SARS-CoV-2 concentrations occur on Day 5 and most active replication in the throat during the first 5 days of symptoms onset [4]. In rhesus macaques infected with SARS-CoV-2 and Middle East respiratory syndrome coronavirus, best outcomes were obtained when remdesivir was started early, at 12 h of inoculation [5]. These observations suggest that inhibiting viral replication with remdesivir would be more effective if started early after symptoms development. We report a High Risk patient with Sars-Cov-2 diagnosis and co-morbidities, using an early treatment strategy with remdesivir.

Keywords: Early remdesivir; High risk patient; Sars-Cov-2

Introduction

Our Italian patient 60-year-old , male , developed fever up to 38.5 degrees C, asthenia, myalgia, difuse arthromyalgia, dysgeusia, anosmia, general malaise on 22 April 2021. In the Hospital she was admitted immediately after computed tomography (CT) imaging of her chest showed over the entire lung area, but more extensively on the right, several tenuously hyper dense "ground glass" areas, with peripheral subpleural arrangement more represented at the lung bases and discrete thickening of interlobular septa and fibrotic striae. The image is compatible with a phlogistic condition such as SARS-CoV-2 related early interstitial pneumonia. Nasopharyngeal swab specimens were collected to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid. The swab specimens were tested by real-time reverse transcriptase–polymerase chain reaction; a positive result was received 1 days later on 23 April 2021. Emogasanalysis at admission (Fi02 21% AA pH 7.45, pO2 45mmHg, pCO2 32mmHg P/F 214). Our patient was diagnosed with COVID-19 (early stage) and on 24 April 2021 (one day after diagnosis) your therapy is remdesivir (Veklury) 200 mg e.v. first day and 100 mg e.v. from second to five day. She received Proton Promp Inhibitor (pantoprazole 40 mg), hypocolerolemizing (simvastatin 20 mg), Methimazole 5 mg and Monday-Wednesday-Friday, insulin with pump, rehydration therapy,EBPM at prophylactic dosage (enoxaparin 4000 IU), steroid (dexamethasone 6 mg). The patient had a history of

Diabetes mellitus type I insulin-dependent with pump, Basehor's disease, Hypercholesterolemia, BMI=25 (normal weight). Biochemistry test indicated leucocytes 9.58 × 10 3c/µl (reference 4–11 × 103c/µl), D-dimer 3.3 µg/ml (reference 0.1–0.5 µg/ml), C-reactive protein 329 mg/l (reference 0–5 mg/l), procalcitonin 6.72ng/ml (reference 0–0.1 ng/ml), lactate dehydrogenase 316u/l (reference 135–225 u/l) and lactic acid 3.6 mmol/l (reference 0.5–1 mmol/l). At day 3 Second Emogasanalysis (nasal cannulae O2 2l/min Fi02 28% pH 7.47, pO2 109mmHg, pCO2 41 mmHg P/F 389). The response to treatment with Remdesivir (early stage) was favourably. The patient's haemodynamic status was satisfactory. Fortunately, after 5 day of treatment our patient progressively improved to total recovery. Emogasanalysis at 5 day (Fi02 21% AA pH 7.46, pO2 102mmHg, pCO2 42 mmHg P/F 486). On May 17, 2021, our patient was negative and she has after computed tomography (CT) imaging of her chest a complete resolution of bilateral areas of altered density a ground glass after treatment (Figure 1).

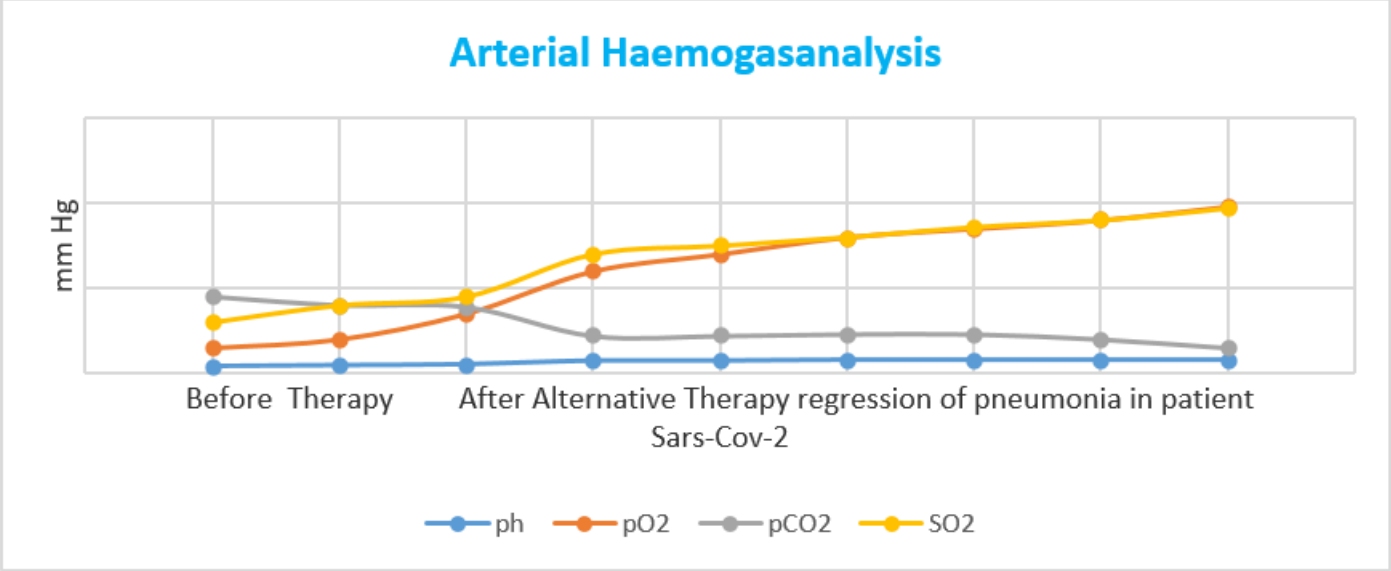

Figure 1: *This figure show arterial haemogasanalysis before early treatment strategy with remdesivir and during therapy with regression of pneumonia.*

Discussion

Any antiviral agent will be most effective when applied early in SARS-CoV2 infection, as it can interfere with multiple cycles of virus replication. During the first year of the pandemic, the majority of COVID-19-related deaths resulted from large outbreaks in residential care homes. These were commonly associated with death rates of 10–20% and higher [6]. Due to their age and comorbidities, the elderly commonly succumb to COVID-19 within two weeks. However, when such outbreaks were detected, many infected individuals were still asymptomatic or within the first 1–2 days of symptoms. The rapid provision of intravenous remdesivir for 3–5 days by medical intervention teams to all PCR-positive residents could have drastically reduced mortality rates. Rapid initiation of antiviral treatment with remdesivir in high-risk individuals, defined as those aged > 70 years, immediately upon qRT-PCR-based confirmation of infection could potentially have saved many lives. Importantly, remdesivir has shown an excellent side effect profile and can thus be employed without major risk, even in the elderly. However, remdesivir has not yet been tested or licensed to treat asymptomatic or early-stage SARS-CoV-2 infections in individuals who are at >10% risk of COVID-19-related. Treatment initiation within 48 h of the onset of symptoms may be responsible for the excellent response to remdesivir. Failure to inhibit viral replication at its peak time may allow disease progression, where virus-induced tissue damage, abnormal immunomodulation and inflammation, become determinants of the patient outcomes. We propose that delayed treatment initiation is at least partly responsible for the reported modest therapeutic response of remdesivir [7].

Conclusion

To ensure effective control of future pandemics, any new antiviral agent entering human trials should be tested in a post-exposure setting, i.e., in PCR-positive individuals before the onset of symptoms. Future studies comparing the effect of treatment time from disease onset to the first dose of remdesivir are needed. Until then, early administration of remdesivir among high-risk patients should be considered and recommended.

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