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Case Report

The Cardiotoxic Effects of Remdesivir Administered to the Patients with SARS-CoV Infection

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ABSTRACT

Coronavirus has become a pandemic without a reliable treatment since December 2019. The antiviral medication remdesivir, which also inhibits one of the most powerful viral RNA enzymes, RNA dependent RNA polymerase, prevents the SARS-CoV virus from reproducing. Cardiomyocytes can experience substantial cytotoxic effects from remdesivir. Remdesivir binds to human mitochondrial RNA polymerase, which causes cardiotoxicity. A prolonged QT interval and the emergence of torsade de pointes could result from lengthening the field potential duration while lowering the amplitude of the Na+ peak and the pace of spontaneous beating in a dose-dependent way. The current safety profile of Remdesivir is not yet completely established, and it is necessary to evaluate the safety profile and any potential adverse cardiovascular consequences by conducting additional clinical trials. In this case report, adverse effects of remdesivir to assess its safety profile in Covid-19 patients is reviewed.

Keywords: SARS-CoV, Remdesivir, Adverse effect, QT prolongation, Cardiotoxicity, Bradycardia.

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INTRODUCTION

Despite having an effective cure, the corona virus disease is still spreading around the world. The upper respiratory tract was primarily affected by the pandemic's medical complications, which spread around the world. Many medications, including lopinavir, hydroxychloroquine, chloroquine, Remdesivir, and azithromycin, were demonstrated to have beneficial effects during the clinical trial. Remdesivir was the only drug authorised to treat COVID-19 in an emergency.[1]

Originally designed for treating the Ebola virus, Remdesivir is a prodrug of adenosine nucleotide. Its active metabolite inhibits the viral replication enzymes categorised as RNA-dependent RNA polymerases.[2,3]

Although being used successfully to treat the SARS 2 corona virus infection, the medication has some notable side effects, including hypotension, sinus bradycardia, and QTc wave lengthening. Remdesivir's IV infusion has been associated with some extremely serious side effects, including cardiac arrest and total heart block.[1,4]

CASE PRESENTATION

An elderly woman without any prior medical history, has been complaining about body ache, dry cough, shortness of breath, and fever for seven days arrived at the emergency room. Following encounter with a COVID-19 positive patient in her family, she was found to be positive. She does not smoke or consume alcohol, and deep vein thrombosis, breast cancer, type 2 diabetes, and hypertension run in her family without any negative results.[5]

She was afebrile, vitally stable, and sustaining 100% oxygen saturation on room air at the time of presentation. Her pulse rate was 70 bpm. Her primary ECG revealed a normal sinus rhythm and the physical examination revealed nothing unusual. Her baseline blood tests revealed that she had the following values: WBC less than 4.0g/dl haemoglobin less than 12 g/dl, CRP more than 5 mg/dl, lactate dehydrogenase (LDH) more than 214 U/L, Ferritin more than 307 ng/dl, and normal ALT and AST levels.[5]

Following the discovery of infiltrates in the right lower zone on a chest X-ray, she was hospitalised after receiving a mild COVID-19 pneumonia diagnosis. According to the national COVID-19 treatment protocol, she got oral treatment with Favipiravir and Amoxicillin-clavulanic acid. Throughout her course of treatment in hospital, she continued to have fever spikes, which required a change in her medication from Amoxicillin-clavulanic acid

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to Ampicillin-sulbactam Intravenous (IV), as well as a septic work-up, which ultimately came back negative.[5]

Azithromycin was added after ten days, when the patient's fever still persisted. She rapidly lost her saturation, and to maintain it, she needed oxygen. In order to complete the full five-day course, she started Remdesivir with a loading dose of 200 mg and continued with daily doses of 100 mg for an additional four days. She began taking two units of convalescent plasma and Anakinra as her inflammatory marker began to rise. Her CRP increased to 88 mg/dl, her ferritin increased to 955 ng/mL, and she had a high level of interleukin 6. The patient was diagnosed with sinus bradycardia a few days after using Remdesivir, and her heart rate dropped to 37 bpm during the next few days (Figure 1). Her baseline heart rate was 60–70 bpm.[5]

Azithromycin was withdrawn since it can lengthen QTc intervals and because her ECG also revealed QT prolongation. The patient was sent to the Intensive Care Unit (ICU) for continuous cardiac monitoring a few days later when she began to experience symptoms of bradycardia (dizziness and weariness). A cardiologist was contacted in the ICU, and she began receiving a 3 microgram/min dopamine infusion and atropine as needed (if her bradycardia was less than 35/min). The findings of the cardiac biomarker test were negative, and she underwent an unremarkable echocardiography. Additionally, holter monitoring revealed an atrial fibrillation event lasting for an hour and 12 min, which was reversed by amiodarone IV.[5]

Remdesivir was decided to stop being administered before the third dose. After that, throughout the following days, her heart rate began to increase, fluctuating between 45 and 50 beats per minute. After her heart rate returned to normal (over 60 beats per minute) and her ECG was also normal, the patient was sent home.[5]

Effect of remdesivir on the cardiovascular system

Chow *et al.* reported on a male, aged 16, who was overweight and suffering from COVID-19. He exhibited symptoms of fever, breathing difficulties, a persistent dry cough, headache, and abdominal discomfort while being treated at the hospital. At rest, the heart rate of the patient was greater than 90 bpm. The medical staff decided against administering corticosteroids because of the patient's moderate hypoxia. On the second day of hospitalisation, the remdesivir course of treatment was begun. Over the next 4 days, there was a drop-in pulse rate. The patient had normal systolic function and left ventricular size, and did not exhibit any signs of hypotension. Pulse rate returned to normal for the patient, two days after Remdesivir was stopped.[6]

Sanchez-Codez *et al.* reported on a teenager with bronchial asthma who also had a history of severe hypoxemia, bilateral pneumonia, and a resting pulse rate of 80 to 90 beats per minute upon admission for COVID-19. He was given remdesivir (200 mg/day for a loading dose and 100 mg/day thereafter), ceftriaxone, dexamethasone, and oxygen therapy. The patient's pulse rate was went down following the third Remdesivir dose as a result of non-hemodynamically relevant sinus bradycardia. Discontinuing the Remdesivir infusion resulted in the patient's pulse rate returning to normal the next day. Both the cardiac biomarker levels and Echo scan parameters were within standard values. They asserted that the patient's bradycardia was caused by remdesivir, a drug that has the propensity to impede the AV node.[7]

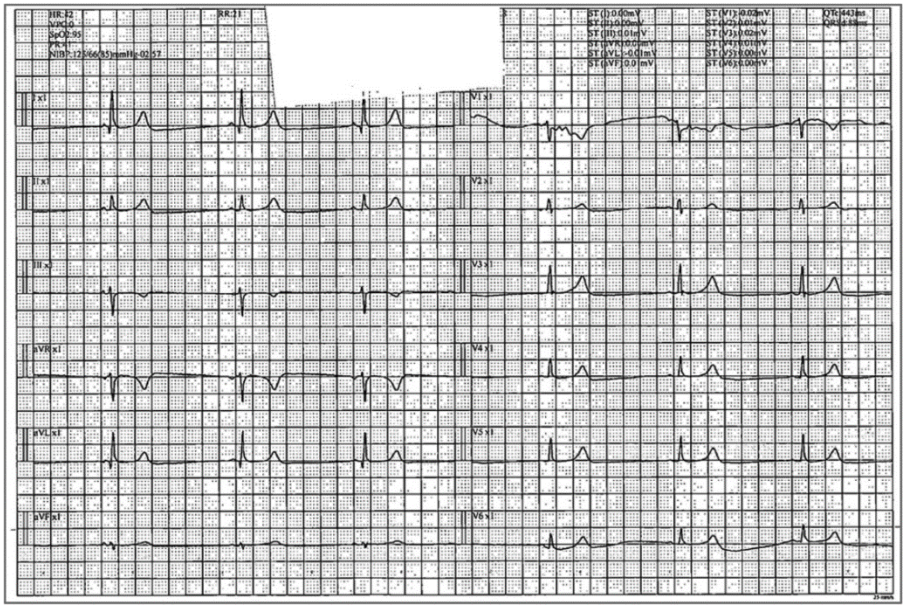

Figure 1: Electrocardiogram for Case presentation 1 few days after starting Remdesivir therapy.[5]

DISCUSSION

Remdesivir is a nucleoside triphosphate metabolite (GS443902) that is activated from a nucleotide analogue prodrug. This metabolite is an adenosine analogue, although it has a much longer elimination half-life than adenosine, at 11 hr.[1]

By causing transitory AV nodal block, adenosine also shows to have antiarrhythmic properties in Supraventricular tachycardia. However, in people with structural cardiac disease, it might be proarrhythmic.[8]

Although it has a longer half-life, remdesivir and adenosine share a similar structural makeup. Its harmful cardiovascular effects are therefore expected.[9]

Human embryonic stem cells and human induced pluripotent stem cells were used to create human pluripotent stem cell-derived cardiomyocytes (hPSC-CMs), which were then used by Choi *et al*. to study the possible cardiovascular risk of remdesivir treatment in COVID-19-infected hPSC-CMs. According to this research, remdesivir can be much more severely cytotoxic to cardiomyocytes than chloroquine.[10]

Remdesivir decreased spontaneous beating rates and Na+ peak amplitudes, which at higher dosages completely stopped spontaneous beating. Remdesivir also increased the duration of the field potential in a dose-dependent way. These findings showed that medication accumulation or overdose could have serious negative effects on the heart. This suggests that remdesivir concentrations above the anticipated peak plasma concentration (C_{max} 9) may provide a risk of QT prolongation. As a result, it is recommended to carefully monitor the ECG and QT interval while using remdesivir, especially in individuals with structural cardiac issues or those who have a severe COVID-19 infection.[10]

CONCLUSION

The morbidity and death burden of COVID-19 is substantial. The risk of death is increased in people with pre-existing cardiovascular illness or those who acquire cardiac dysfunction as a result of COVID-19 infection. Remdesivir can cause sinus bradycardia and a longer QT interval in some COVID-19 patients. As the safety of remdesivir is still largely unknown, appropriate caution and continuing EKG monitoring should be used in all patients participating in ongoing trials for COVID-19.

After receiving remdesivir, there have also been a few documented cases of cardiopulmonary arrest and third degree Artrioventricular (AV) block. Patients who have a history of heart problems may see Remdesivir's proarrhythmic and cardiotoxic side effects more obviously.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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