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RESEARCH ARTICLE

"REMDESIVIR INDUCED SINUS BRADYCARDIA IN A 53-YEAR-OLD WOMAN DURING THE TREATMENT OF COVID-19 INFECTION: A CASE REPORT"

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Abstract

We report a case of a 53-year-old woman with severe COVID-19 infection. On the second day of her treatment with Remdesivir and other standard therapies, sinus bradycardia was noted, requiring atropine and dopamine. Workup excluded the secondary causes. A probable diagnosis of Remdesivir-induced bradycardia was made and thus, Remdesivir was discontinued. Her condition normalized after four days of discontinuing Remdesivir. Hence, the treating physicians must be aware of the cardiac adverse effects of Remdesivir.

Introduction:-

Food and Drug Administration (FDA) approved the emergency use of Remdesivir for the management of severe Coronavirus Disease 2019 (COVID-19) infection[1]. Common adverse events for Remdesivir (1%–10% incidence) include rash, headache, nausea, diarrhoea, and moderate to severely elevated transaminases[2]. Although it has been widely used during the pandemic COVID-19, there is limited evidence regarding its cardiac side effects[3].

Case Report:-

A 53-year-old diabetic and hypertensive woman presented to the Emergency Room of Hospital for Advanced Medicine and Surgery (HAMS), Kathmandu with complaints of fever (maximum temperature: 101 F) and dry cough for a week. She also developed acute shortness of breath, even on mild exertion for four days, with loss of smell and taste for the same duration. Polymerase Chain Reaction (PCR) for the nasopharyngeal sample was positive for COVID-19 infection. Hence, she was admitted to the COVID-19 isolation ward.

On initial assessment, her physical examinations and vitals were within normal limits. Oxygenation was maintained with supplemental oxygen 2L /min via nasal prongs. Chest X ray showed moderate haziness at left lower zone. An Electrocardiogram (ECG) at the time of admission showed normal sinus rhythm with heart rate of 78 bpm.She was treated with antibiotic therapy (Inj. ceftriaxone 2 g twelve hourly), steroid (Inj. dexamethasone 6 mg six hourly), Inj. Remdesivir (an intravenous loading dose 200 mg on day 1 followed by 100 mg once a day), low molecular weight heparin (Inj. enoxaparin 60 mg subcutaneous twice a day), Insulin- Inj. Lantus 10 U subcutaneous once a day, and Tab. amlodipine-losartan (5/25 mg) once a day. Lab investigations are mentioned in Table 1.

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Table 1:- Laboratory Investigations on Admission and Day 2.

Investigations	On Admission	Day 2	Reference range
Hemoglobin (g/dL)	13.8	14.2	13.5–17.5
White cell count (per microL)	4300	5900	4500–11,000
Platelet count (per micrpL)	118000	178000	150,000–400,000
Potassium (mmol/L)	4.5	4.8	3.5–5.3
Sodium (mmol/L)	137	139	136-146
Magnesium (mmol/L)	1.70	1.68	1.3-2.1
Alanine aminotransferase (U/L	26	45	10-35
Aspartate aminotransferase (U/L)	37	61	10-35
Creatinine kinase (U/L	50	25	25-160
Troponin (pg/mL)	3.4	4.3	0.1-11.6
Thyroid-stimulating hormone	-	0.47	0.38–5.33
Interleukin-6 (pg/mL)	2.67		0.0–6.4

One the second day of admission, bradycardia was noted on the monitor ECG (lowest reading of 35/min). A 12-lead ECG showed sinus bradycardia with a heart rate of 38 bpm(Figure 1).

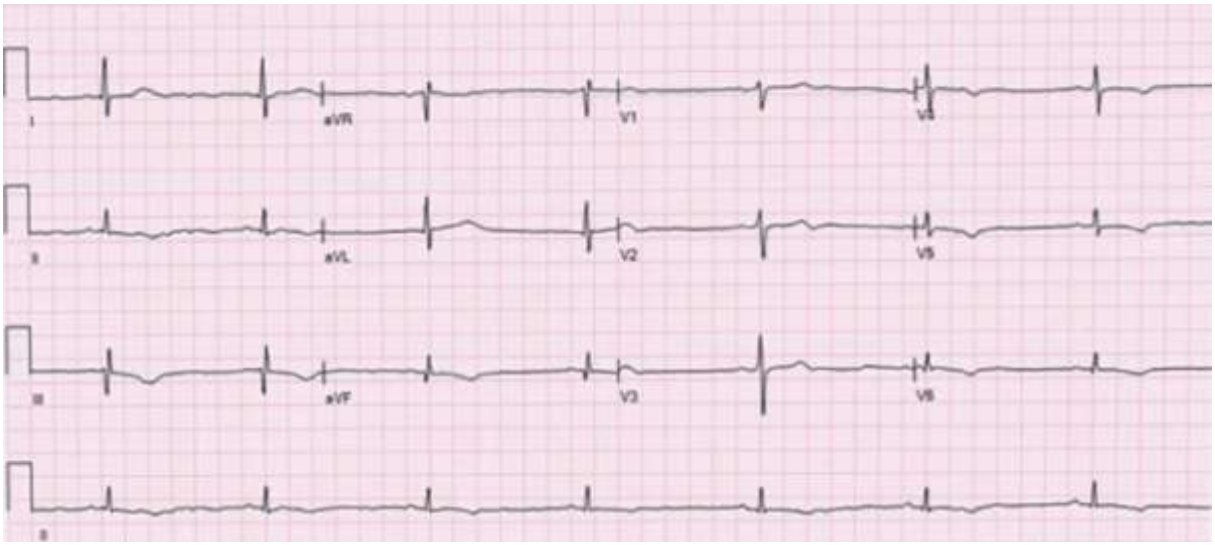

Figure 1:- ECG showing Sinus Bradycardia on day 2 of admission.

She was asymptomatic, however, her heart rate was persistently below 40/min. Two doses of Inj. Atropine 0.6 mg IV stat were given. Due to no improvement in the heart rate, Inj. Dopamine infusion was started at 5 mcg/kg/min and titrated accordingly. She was immediately transferred to the Intensive Care Unit (ICU) for further monitoring and management with probable differential diagnosis including: Myocardial Ischemia, Myocarditis, Hypothyroidism, Electrolyte Disorders, Massive Pulmonary embolism**.**

During her ICU stay, the physical examinations were unrevealing. The laboratory investigations were within normal limits (Table 1). Echocardiogram was normal with Left Ventricular Ejection Fraction (LVEF)-65%. Other causes of sinus bradycardia were ruled out through the extensive workup (Table 1).

Consequently, a provisional diagnosis of Remdesivir-induced bradycardia was made. Thus, Remdesivir was discontinued. Other treatments were continued as previously. Inj. Dopamine infusion was gradually tapered and was stopped by the fourth day when her heart rate was completely stabilized. She was then transferred back to the ward and was discharged after a week.

Discussion:-

To our best knowledge, there are very few cases of reported cardiac side effects of Remdesivir during the COVID-19 pandemic. Previous studies during the Ebola pandemic reported the incidence of cardiac side effects of

Remdesivir including cardiac arrest, hypotension, bradycardia, and atrial fibrillation[4]. COVID-19 infection has been associated with cardiovascular complications, including myocardial infarction, myocarditis and rhythm abnormalities[5]. Myocarditis, myocardial ischemia and strain, electrolyte disturbances, intravascular volume imbalances, drug side effects, severe hypoxia or inflammatory damage of cardiac pacemaker cells could be the probable causes of arrhythmia in COVID-19 infection[6, 7].

Remdesivir, a nucleoside analogue pro-drug acting as an RNA polymerase inhibitor, has been shown to shorten the time to recovery in hospitalized adults with severe COVID-19 requiring low-flow supplemental oxygen[2, 3]. There could be several mechanisms of bradycardia due to Remdesivir. The resemblance of Remdesivir with adenosine triphosphate may lead to inhibition of the atrioventricular node by binding to the A1 receptor on cardiac cells[8]. Also, a potential drug-induced mitochondrial dysfunction caused by the strong affinity of Remdesivir for human mitochondrial RNA polymerase (h-mtRNAP) has also been proposed mechanism[8].

In our case, the patient was not under other medications that would account for the bradycardia. Clinical features neither were suggestive of heightened vagal tone. Thus, after excluding all the possible secondary causes of bradycardia with the extensive workup, and returning of the heart rate to the baseline normal after stopping Remdesivir, it can be agreed that there is a reversible association of Remdesivir with sinus bradycardia. However, a more reassuring pathophysiological mechanism of sinus bradycardia due to Remdesivir is yet to be well established.

Conclusion:-

In light of the increasing use of Remdesivir for COVID-19 therapy, our case highlights the incidence of sinus bradycardia as one of the serious adverse effects. Thus treating physicians should be aware of these events and need to monitor patients to avoid fatal outcomes. Also, it warrants a need for further large-scale studies to better understand the association.

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Conflict of Interest:

None.

References:-

1. Veklury summary review. Silver Spring (MD): US Food and Drug Administration, Center for Drug Evaluation and Research Pharmacovigilance Memorandum. U.S. Food and Drug Administration, Center for Drug Evaluation and Research; 2015. Available: www.accessdata.fda.gov/drugsatfda_docs/nda/2020/214787Orig1s000SumR.pdf(accessed 2022 Sep. 10).
2. Beigel JH, Tomashek KM, Dodd LE, et al.; ACTT-1 Study Group Members. Remdesivir for the treatment of COVID-19: final report. N Engl J Med 2020;383:1813-26.
3. Gordon, C.J.; Tchesnokov, E.P.;Woolner, E.; Perry, J.K.; Feng, J.Y.; Porter, D.P.; Götte, M. Remdesivir is a direct-acting antiviral that inhibits RNA-dependent RNA polymerase from severe acute respiratory syndrome coronavirus 2 with high potency. J. Biol. Chem. **2020**, 295, 6785–6797.
4. Mulangu S, Dodd LE, Davey RT. A randomized, controlled trial of Ebola virus disease therapeutics. N Engl J Med 2019;381:2293–303.
5. Wu, Z.; McGoogan, J.M. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72,314 Cases From the Chinese Center for Disease Control and Prevention. JAMA **2020**, 323, 1239–1242
6. Dherange, P.; Lang, J.; Qian, P.; Oberfeld, B.; Sauer, W.H.; Koplan, B.; Tedrow, U. Arrhythmias and COVID-19. JACC: Clin. Electrophysiol. **2020**, 6, 1193–1204.
7. Amaratunga, E.A.; Corwin, D.S.; Moran, L.; Snyder, R. Bradycardia in PatientsWith COVID-19: A Calm Before the Storm? Cureus**2020**, 12, e8599.
8. Gubitosa, J.C.; Kakar, P.; Gerula, C.; Nossa, H.; Finkel, D.;Wong, K.; Khatri, M.; Ali, H. Marked Sinus Bradycardia Associated With Remdesivir in COVID-19. JACC Case Rep. **2020**, 2, 2260–2264.