

RAAS Inhibitors and Statins in COVID-19 Pandemic -A Perspective

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ABSTRACT

Novel Corona virus (COVID-19) caused global outbreak and affected the health of many individuals and caused millions of death worldwide. World health organisation announced this disease as pandemic virus. This disease was first reported in Hubei Province on December at Wuhan, China. Within a short span the disease spread across 177 countries across the globe and World health organisation reported 16,755,633 confirmed cases and 661,244 deaths as on 29th July 2020. Respiratory illness and mild flu like symptoms are mostly common symptoms of COVID-19. It also affects the cardiovascular status especially the individual with pre-existing cardiovascular disease. Direct myocardial injury is observed and appearance of inflammation is the primary mechanism involved for Cardiac injury. This review enlightens the role of RAAS Inhibitors like ACE-Is, ARBs and statins in COVID-19 pandemic.

Keywords: Novel Corona virus, COVID-19, Cardiovascular, RAAS inhibitors, Statins

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INTRODUCTION

Novel Coronavirus (COVID-19) discovered in China, Wuhan province caused a major global outbreak and increased the mortality rate when compared to SARS CoV and MERS CoV-2. The World Health Organisation (WHO) announced this COVID-19 as a pandemic virus and as an international public health emergency. Novel Coronavirus disease (COVID -19) is an infectious disease with an increase in mortality amongst the older population and in patients with an underlying disease like diabetes, cardiovascular, hypertension, cancer. Lung lesions are reported as severe damage in SARS CoV-2 infections. ¹ COVID-19 viral infection is predominantly observed in those with existing cardiovascular disease (10.8%) and diabetes (7.3%).

The situation reports in the WHO among south-east Asia, confirmed cases reported as 1,949,850 the Mortality rate is found to be 43117 as on July 2020. The COVID-19 status in India is quite alarming. There is no specific vaccine or drug therapy available for this deadly virus as on date, which is infecting over one million people and increasing death toll rate every day. A lot of research is underway with around 100 trails to discover a vaccine. Similarly, efforts are ongoing to evaluate the effectiveness of antiviral and other antimicrobial drugs in the treatment of the disease.

Literature review on RAAS inhibitors

The results published by the experts in JAMA cardiology states that the novel coronavirus severely causes cardiovascular symptoms. The damage to the heart muscle is observed even in patients who did not previously report any cardiovascular disease. And, the risk is even higher in those with pre-existing cardiovascular problem² SARS-CoV, and MERS-CoV infections cause acute respiratory illness, cardiac arrhythmias, acute myocardial ischemia.

Serious cardiac complications like elevated troponins and cardiac muscle injuries were observed in patients affected with COVID-19.³ Article published in the economic times stated that COVID-19 affects cardiovascular patients (CAD, Hypertensive) in older adults and requires intensive medical

intervention. In MERS-CoV, fulminant myocarditis has been reported: the same can be expected to occur in SARS-CoV-2.

In anecdotal reports, it was observed that the fatality rate in CVD patients will rise to 30 % roughly. Similar to experience from Italy, India has also reported two-fold increases in the fatality rate in cardiac disease and diabetes. Human receptor ACE₂ is found to be the entry for the COVID -19 virus as reported for SARS-CoV. Angiotensin receptor blockers have a similar mechanism of action like Angiotensin-converting enzyme inhibitors. Based on the clinical perspective, ARBs were found to be an effective drug compared to ACE-Is as ARBs produce few side effects. Recently, Sommerstein and Grani *et al*,⁴ reported that the Angiotensin-converting enzyme inhibitors (ACE-Is) could be a potential risk for COVID-19 patients with the underlying cardiac disease by the concept of up-regulating ACE₂.

A recent study published in European Society of Cardiology by Kuster *et al* ⁵ states inhibition of renin-angiotensin-aldosterone system (mineral corticosteroid antagonist) ACE inhibitors (ACE I₂) Angiotensin receptor blockers (ARB) which are Antihypertensive drugs primarily used in the management of hypertension and Post Myocardial infarction (MI) could be protective in COVID-19 infection. However, the underlying mechanism is not very clear that this drug inhibits or beneficial in the management of COVID-19. Discontinuing these drugs may result in heart failure thereby increases the mortality rate.

Statins role in Cardiovascular disease

Pre-existing cardiovascular disease is the more common risk factor for COVID -19. Studies published by Ruan *et al* ⁶ based on the analysis of 150 patients in Wuhan province, China reported marked elevations in mortality of COVID-19 patients with underlying cardiac manifestations. Few observations published on the web in recent days indicates the use of statins in the treatment of COVID-19, but there is no clinical evidence available for this.

In general, Statins are considered to be a safer drug. Theoretically, statins protect the innate immune response in

COVID-19 patients. A study published by Totura *et al* showed that Signalling of TL3 Toll like receptor 3 found to protect innate immune response to SARS-CoV infection.⁷ Similarly, TL4–Toll like receptor 4 have emerged to prevent damaging inflammatory response in SARS-CoV.⁸ Shu Yuan demonstrated the use of statins in regulating the innate immune response to MERS- CoV infection, MYD88, a Toll-like receptor that plays a vital role in the management of acute respiratory infections. Deficiency of MYD88 resulted in higher death rates in MERS- CoV. MYD88 level remains unaffected with the use of statins.⁹ Atorvastatin, commonly available OTC drug maintains the MYD88 at a normal level in severe acute respiratory infections.

Hepatic considerations of Statins

SARS- CoV used ACE 2 receptor for cell entry which is found in the Liver. Liver injury is also observed in SARS CoV2 severely infected patients than with milder ones. The same was earlier reported in SARS-CoV and MERS-CoV infections. Studies showed that in COVID-19 patients elevations in the ALT /AST bilirubin, a decrease in the albumin level. Studies in the mechanism of the hepatic injury are limited in COVID 19 patients. However, the autopsy of COVID -19 patients revealed steatosis, mild lobular, portal activity.¹⁰ This cause is known to be unclear as it may be caused by drugs used in the treatment of COVID-19 or any other reason. According to a recent review by Gupta et al, hypertension and elevated troponin levels are associated with increased severity of disease and risk of death. And, a high inflammatory burden associated with COVID-19 may cause myocarditis or arrhythmias due to increased metabolic demand, hypoxia or sympathetic stimulation in patients with and without pre-existing cardiovascular disease.¹¹

CONCLUSION

In conclusion, COVID-19 pandemic has infected millions of patients putting unprecedented strain on the healthcare system around the world. Based on the current literature and available data, the mortality rate is found to be significantly higher in cardiovascular patients. Therefore, we would like to raise the awareness that the utmost care must be given to cardiovascular patients affected by COVID-19. Usage of ACEIs, ARB and statins as prescribed by the physicians to prevent cardiac muscle injury and innate immune response in COVID-19 affected patients. As currently there is no clear evidence about the mechanism of these drugs on COVID-19 infection, caution must be taken into consideration while treating the cardiovascular patients affected with COVID-19 pandemic. Hepatic considerations are important while initiating statin therapy. Statin therapy must not be considered if the patients have elevations in the ALT /AST /Bilirubin levels two-three-fold rise than the normal levels.

CONFLICT OF INTEREST

Nil

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