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An Arterial Hypertension Diagnosis And Its Treatment During Covid-19

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Abstract

SARS-CoV-2-infected As a result of the new corona virus infection's quick spread, COVID-19 has now developed into a pandemic that has affected people all across the world. Because of the high fatality and morbidity rates associated with the virus, additional research is being conducted to uncover potential risk factors for the outcomes of patients. Patients diagnosed with COVID-19 are more likely to suffer from hypertension, a condition that has been associated with an increased risk of death as well as hospitalisation. When a pilot investigation indicated that rennin angiotenin aldosterone system inhibitors could potentially raise the risk of viral infection and aggravate the severity of illness, medical professionals all over the world expressed alarm. This was due to the high prevalence of hypertension. Antihypertensive drugs, on the other hand, have been demonstrated to have a beneficial effect on COVID-19 infection in people who have hypertension. This is the case despite earlier research predicting that antihypertensive medicines would have the opposite effect. At the time that this article was written, it was not known how patients infected with COVID-19 would be affected by hypertension (high blood pressure). In this mini-review, which discusses the etiology of SARS-CoV-2 infection and hypertension, we find that alterations in Angiotensin converting enzyme 2 (ACE2) and RAAS play dual roles in COVID-19 and hypertension. Their individual functions are essential to the whole. There is a connection between the release of pro inflammatory chemicals and the immune response as well as gastrointestinal issues caused by COVID-19.

Keywords: COVID-19, Hypertension, Anti-inflammatory, ACE2.

Introduction

Corona virus disease (COVID-19) was discovered for the first time in December 2019 in Wuhan. The disease is caused by SARS-CoV, which stands for severe acute respiratory syndrome coronavirus [1,2.] (SARS-CoV-2). The following pandemic, which has already infected over 200 countries and territories, has now reached China as well as the rest of the world. As of the 22nd of March, 2021, there have been over 120 million cases and 2,711,071 deaths around the world; in the United States of America alone, it is estimated that there have been 29,497,998 cases and 537,781 deaths. Transmission of SARS-CoV-2 from human to human is an extraordinarily prevalent occurrence. Transmission of the virus can occur through a variety of different channels, including droplets, faeces, [3]and direct skin contact with contaminated surfaces. The majority of instances of COVID-19 are mild to moderate in severity; however, approximately 15 percent of older people or those with chronic illnesses may progress to severe pneumonia, septic shock, and/or organ failure, all of which can be potentially fatal. Patients who have COVID-19 have an increased likelihood of

having hypertension as a comorbidity. Hypertension is a prominent risk factor that has been identified as contributing to the disease's increased severity and mortality rate.[4,5,6]

It was discovered that persons in China infected with COVID-19 had hypertension at rates ranging from 15% to 25%. In the meantime, hypertension was present in 49.7 percent of COVID-19 patients admitted to hospitals in the United States.[7] It was discovered that hypertension is a substantial risk factor for the development of critical illness or mortality in the general population, and its prevalence has increased anywhere from two to three times during the past century. In patients who were infected with COVID-19, Pranata and colleagues discovered that[8,9] hypertension increased the probability of unfavourable outcomes such as the severity of the infection, acute respiratory distress syndrome (ARDS), and death.

At this time, there is no licenced drug that can be used to treat COVID-19. Even though antivirals, glucocorticoids, and interferons have all been examined for other conditions but have not been successful in treating those conditions, the only treatment option for COVID-19 at this time is symptomatic care alone. Patients who are severely ill receive treatment that focuses on bringing the infection under control, providing supportive care, and addressing COVID-19's sequelae and consequences. Additionally, the management of COVID-19 patients with hypertension is difficult. In earlier studies conducted on animals, the level of expression of the angiotensin-converting enzyme 2 (ACE2) was found to be elevated in cardiac tissue. [10,11] This finding raises the idea that hypertension could stimulate viral interaction with host cells and worsen COVID-19. There has been a lot of discussion on whether or not RAAS inhibitors can actually make it more difficult to control the SARS-CoV-2 infection. Patients diagnosed with COVID-19 who also have hypertension have a significantly increased risk of having a worse outcome than those who do not have hypertension. It is a distinct possibility that hypertension played a part in the onset or course of either of these conditions.

Management of hypertension in COVID-19

The coronavirus known as COVID-19 has emerged as a major source of death and sickness around the globe. According to the most recent data, illnesses caused by SARS-CoV-2 have now been reported in more than 500,000 persons around the world. The search for a vaccine or a treatment that is effective has turned into a worldwide arms race. The vast majority of experts believe that it will be at least 18 months before a vaccination is ready, and a pharmacological treatment has not even been devised yet. As a consequence of this, it appears that COVID-19 will be an indispensable component of contemporary medicine for a considerable amount of time. [12]

Patients diagnosed with COVID-19 should have a high priority placed on the management of their chronic diseases. Hypertension affects people all across the world, and researchers have found a correlation between it and the large rise in morbidity and mortality that occurred during the COVID-19 epidemic. Antihypertensive medications such as ACEIs and ARBs are among the blood pressure-lowering drugs that are prescribed most frequently for the treatment of high blood pressure in industrialised countries all over the world. As initial therapies, they do not pose any health risks, are generally well tolerated, and are effective. Patients who take ACEIs or ARBs have a higher risk of SARS-CoV-2 infection, according to recent research, and the reason for this is that these medications increase the viral binding site of angiotensin-converting enzyme 2. (ACE2).[13,14,15]

It has been demonstrated that the SARS-CoV-2 virus enters the body through ACE2. ACE2 was detected in the heart, kidney, and testis; nonetheless, it is the only human ACE homolog that has ever been

discovered. [17,18] The discovery of ACE2 occurred in the year 2000. According to more investigation, it was then determined that it existed in the lungs, blood vessels, the small intestine, and the brain of the individual. According to the most recent studies, the basal level of ACE2 mRNA in the respiratory system is significantly lower than in the levels found in the other organs. [19] When ACE2 expression is low, the SARS-CoV-2 infection and replication process is the only one that can take place. To start, the infection does not simply have an effect on cells that have the ACE2 gene expressed in them. In bioinformatics research based on human-virus protein interactions, human dipeptidyl peptidase [4] and the spike receptor–binding domain of SARS-CoV-2 revealed substantial affinity for one other. This suggests that SARS-CoV-2 may use dipeptidyl peptidase 4 as a coreceptor to enter host cells[16]. Additionally, NRP1 has been identified as a potential coreceptor in studies. In vitro, NRP1 knockdown resulted in a decreased incidence of SARS-CoV-2 infection, and the incubation of patient-derived SARS-CoV-2 with monoclonal anti-NRP1 resulted in a lower infection efficiency of cells expressing ACE2. Coreceptors including CD147 and GRP78, which have been the subject of research, are utilised by SARS-CoV-2 infected cells. As a direct consequence of this interaction, the SARS-CoV-2 virus is ingested by the membrane receptor for ACE2 and endocytosed together with it. This is how viruses multiply; they move from one cell to another and spread from there. [20]

It can have a wide variety of effects on both the physiological and pathological systems. ACE2 In addition to this, not only does ACE2 perform the role of the cellular receptor for the SARS-CoV-2 infection, but it is also an essential regulator of the RAAS signalling pathway. Angiotensin II, often known as Ang II, is frequently regarded as a potent hypertensive hormone in the field of hypertension research.[21,22] Figure 1 demonstrates that the ACE/Ang II/Ang II type 1 receptor (AT1R) axis plays a significant role in the control of the RAAS. Because ACE, which is a chemical messenger, is responsible for the conversion of Ang I to Ang II, this causes the release of aldosterone and an increase in blood pressure. AT1R is activated by Ang II, which in turn causes vasoconstriction to occur. On the other hand, ACE2 acts in a manner that is antagonistic to ACE. The ACE2/Ang (1-7)/AT2R axis is responsible for the inhibition of RAAS activity. I and II are disassembled into their constituent parts, which are then transformed into the angiotensin-converting enzymes that are more typically put to use (ACEs). [23]Vasodilation and a decrease in blood pressure are both side effects of Ang II type 2 receptor (AT2R) activation and binding, which occurs when Ang 1-7 and Ang 1-9 are present in the body. It also inhibits hypertrophic and pathological cardiac remodelling, prevents the development of heart failure as a result of a myocardial infarction, and lessens damage to lung tissue and inflammation in order to prevent severe acute lung failure. All of these benefits are combined to prevent severe acute lung failure. [24,25] Because there is a paucity of evidence, it is not suggested that people with COVID-19 be prevented from using ACEIs and ARBs. According to the American Heart Association and the European Society of Cardiology, patients with COVID-19 hypertension should continue their treatment with ACEI or ARB. On the other hand, if a patient has been given a diagnosis of COVID-19 as well as a new diagnostic of hypertension, we advise that they be treated with a different drug. [26]

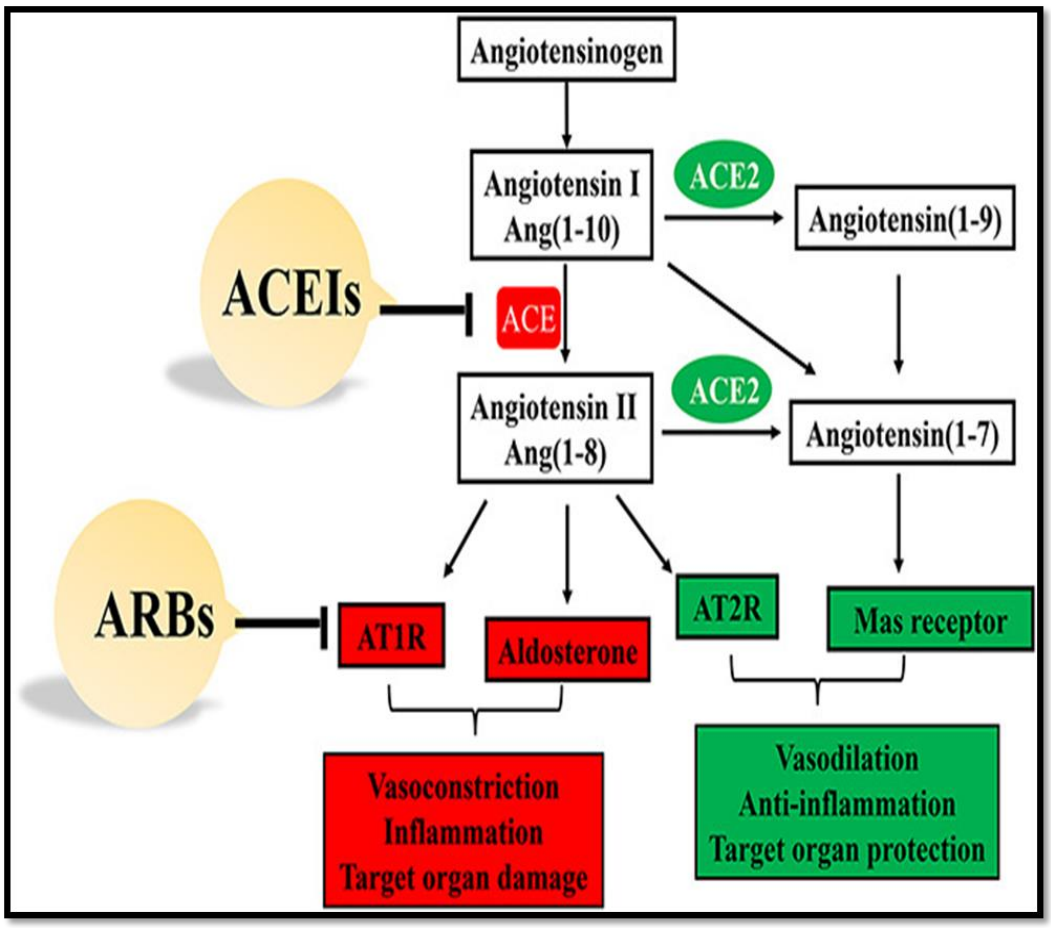

Fig: 1 ACE and ACE2 proteins in RAAS are crucial. ACEIs and ARBs decrease blood pressure by targeting the organ-protecting RAAS[5].

Up until very recently, verapamil was a common medication for the treatment of hypertension. Verapamil has been largely replaced by ACEIs, ARBs, and calcium channel blockers; however, it is still widely used in the treatment of supraventricular tachycardia (SVT), migraine prophylaxis (MPP), and hypertension with co-morbid atrial fibrillation. Despite this, verapamil is still used in these ways. According to our findings, patients with COVID-19 who have hypertension may benefit from taking this medicine as a primary method of treatment for the condition. In animal experiments, verapamil did not seem to have any influence on the expression of the ACE2 enzyme. It has also been established that the administration of this medicine improves the symptoms of viral myocarditis when tested on mouse models. There is evidence to suggest that this is the case, as researchers have detected considerably less cardiac damage in mice treated with verapamil prior to and/or during an encephalomyocarditis virus injection than in a control group that was not treated with any medication at all. In particular, COVID-19 can cause a severe condition known as SARS-CoV-2-associated myocarditis, which has the potential to be fatal. It makes perfect sense to treat hypertension with a medicine that, in addition to not encouraging the growth of COVID-19, has the potential to reduce inflammation in viral myocarditis. This will allow patients to experience an improvement in their overall health. [28,29]

In the context of treating COVID-19, the hypertension medicine carvedilol, which is a 1-adrenergic blocker, is another promising antihypertensive medication. Carvedilol, like verapamil, can be used to treat rat models of acute viral myocarditis to achieve the same anti-inflammatory effects. The mice that were given carvedilol instead of metoprolol after being infected with the coxsackie B3 virus had a better prognosis than the animals that were given metoprolol. Although it is not understood how carvedilol works, one theory suggests that it decreases inflammation in the heart by preventing the creation of peroxidants. [30] Carvedilol's exact mechanism of action is not known. In cases of myocarditis, carvedilol's ability to slow the heart rate may result in less myocyte destruction and less ventricular remodelling than would otherwise be the case.

It has been demonstrated that increasing ACE2 levels can reduce inflammation in the body. In the context of COVID-19, there is evidence to suggest that taking medicine that contains either ACEI or ARB can improve pulmonary function. Despite the purported benefits of ARBs and ACEIs, there is a possibility that they play a part in the progression of viral illnesses. This has not been demonstrated as of yet.[31,32]

Patients' blood pressure and cardiovascular risk profiles were examined after COVID-19.

People who suffered from hypertension in various regions of the world went without regular care as a direct result of the COVID-19 epidemic and the restrictions imposed as a result of it. During the pandemic, the number of patients treated per week decreased from a median of 50 before the outbreak to a median of 5 during the survey of the 52 excellence centres (ECs) of the European Society of Hypertension. This was a significant drop from the median number of patients treated per week before the outbreak, which was [25] (ESH). 60 percent of patients reported having restricted access to medical consultations, and 85 percent of ECs indicated that their service was closed for nine weeks. Patients who have limited access to emergency room visits and hospital admissions may have a greater chance of being diagnosed with high blood pressure and receiving treatment for it in primary care settings over the long term. Patients who are hypertensive may suffer as a result of this, and this may contribute to poorer blood pressure management in the years after the COVID-19 epidemic. Home blood pressure readings and telemedicine consultations are becoming increasingly used in outpatient clinics across the world as a response to the shortage of general practitioners in many countries. [33]

Having high blood pressure is a condition that develops over time and worsens with age. It increases the risk of developing heart disease and renal illness. The percentage of adults suffering from high blood pressure rose from 26.4 percent in the year 2000 to 31.1 percent in the year 2010. [33]

Managing one's blood pressure in an appropriate manner can lower one's chance of having a stroke, a heart attack, or heart failure. There is a wide variety of antihypertensive medication that can be utilised for the treatment of hypertension as well as the prevention of its occurrence. ACE inhibitors, ARBs, diuretics, calcium channel blockers, and beta blockers are the most common antihypertensive drugs that are prescribed to patients. However, there are many other types of antihypertensive medications.

This year, in the month of December, the first cases of SARS-CoV-2, the virus that causes COVID-19, a new respiratory infectious disease, were discovered in Wuhan, China, which is the capital of the province of Hubei. The clinical manifestations of COVID19 are quite varied, spanning the spectrum from a condition with no discernible symptoms to potentially fatal lung infections.

Patients who have high blood pressure have a higher risk of developing an infection caused by COVID-19. This leads one to believe that chronic arterial hypertension may have a substantial role in the worsening of COVID-19 symptoms, as has been reported in other investigations. Patients with hypertension who were infected with COVID-19 had a higher mortality risk compared to patients with the same condition who were not infected with the virus. Because high blood pressure is a key contributor to the risk of contracting COVID-19, it is extremely important to find a drug that effectively lowers blood pressure. [34,35]

Alpha Blocker

Patients who have high blood pressure often take a number of drugs, including ABs, in order to bring it under control. We examined the risk of hypotension and concomitant adverse events associated with the use of AB in comparison to the use of other blood pressure (BP) lowering drugs by conducting a population-based, retrospective cohort study in the province of Ontario, Canada, between the years 1995 and 2015. The Cox proportional hazards model was used to analyse the link between the use of AB and hypotension-related events (syncope, fall, and fracture) in contrast to the use of other drugs. The high-dimensional propensity score served as the basis for this assessment. The primary outcome was the number of hospitalizations within a year that were caused by hypotension (including syncope, fractures, and falls). AB was prescribed to 14,106 women out of a total of 734,907 women who were eligible for the study (mean age: 75.7; standard deviation: 6.9 years; median follow-up: one year), and then these women were matched with 14,106 other women who were also prescribed BP-lowering drugs. It was discovered that the crude incidence rate of hypotension and related events was 95.7 percent when AB was used (95 percent confidence interval [CI], 90.4-101.1, events 1214 [8.6 percent]), whereas the crude incidence rate of hypotension and related events was 79 percent when other BP-lowering medications were used (95 percent confidence interval [CI], 74.9-84.7 per 1000 person years, 1025 [7.3 percent]) (incident rate ratio, 1.20; 95 percent CI, 1.10-1.30). The risk of hypotension and syncope was higher (hazard ratio, 1.71; 95 percent confidence interval [CI], 1.33-2.20), but there was no difference between the groups in terms of the incidence of falls, fractures, cardiac events, or overall mortality. When compared to other drugs that lower blood pressure, the use of ABs to treat hypertension in women is associated with an increased risk of hypotension and events related to hypotension. Even when used in combination with other therapies to manage hypertension, our research indicates that ABs should be taken with extreme caution. [36,37]

Beta- Blocker

One hundred thirty-three RCTs met the requirements to be eligible. There were a total of 23,613 people who participated in the comparison with a placebo across the four randomised controlled trials. Additionally, 18,241 people participated in the comparison with diuretics, a CCB, and a RAS inhibitor (3 RCTs, 10,828 participants). In several of these randomised controlled trials (RCTs), there was a considerable risk of bias due to errors in the research design, the way the research was carried out, and the way the data was processed. Atenolol was the beta-blocker of choice for the vast majority of the study's 40,245 participants, making it the most often used medicine. We were unable to locate any outcomes studies for any of the more recent vasodilating beta-blockers (e.g. nebivolol). [38]

When compared to diuretics and RAS inhibitors, however, beta blockers were shown to be more effective at reducing overall mortality than CCBs (RR 0.99, 95 percent CI 0.88 to 1.11). (Relative risk = 1.07, 95% confidence interval = 1.00 to 1.14). In terms of mortality, each comparison produced data

consistent with a level of moderate certainty. The risk ratio for total cardiovascular disease was lower for beta-blockers (RR 0.88, 95 percent confidence interval [CI] 0.79 to 0.97; low-certainty evidence) than it was for placebo, despite the fact that there was no difference in coronary heart disease (CHD) between the two groups (CHD: RR 0.93, 95 percent CI 0.81 to 1.07; moderate-certainty evidence). It was discovered that beta-blockers had a bigger influence on the risk of cardiovascular disease than CCBs (RR 1.18, 95 percent CI 1.08 to 1.29; moderate-certainty evidence), however, beta-blockers were not different from diuretics or RAS inhibitors (low-certainty). [39] When compared to CCBs and RAS inhibitors, beta-blockers were found to carry a higher risk of stroke than the other two classes of drugs (RR 1.24, 95 percent CI 1.11 to 1.40; moderate-certainty evidence). CCBs showed a moderate degree of certainty, RAS inhibitors showed a low degree of certainty, while beta-blockers and diuretics showed little to no change in CHD. When compared to diuretics, atenolol was found to be associated with a higher risk of cardiovascular disease (CVD) in a single trial that involved individuals who were 65 years of age or older (RR 1.63, 95 percent CI 1.15 to 2.32). Those who were given beta-blockers were more likely to stop treatment due to adverse events than those who were given RAS inhibitors (relative risk = 1.41, 95% confidence interval = 1.29 to 1.54; evidence of moderate certainty), whereas there was little or no difference with those who were given a placebo, diuretics, or CCBs (low-certainty evidence). [40]

Calcium channel blocker

The use of efficient medications for high blood pressure can lead to a significant reduction in the risk of cardiovascular and renal diseases that are caused by hypertension (BP). Despite the fact that these fundamentals are common knowledge, hypertension is still not controlled sufficiently all over the world. The extensive use of rational, integrated, and synergistic combination therapies, even as a first-line strategy, has been proposed as a way to achieve the recommended blood pressure targets for patients who have hypertension. This has been suggested as a way to improve adherence to prescribed medications and ensure that the antihypertensive drugs used are effective, long-lasting, and well-tolerated. Among the antihypertensive drug classes that are currently available for the clinical management of hypertension, those that inhibit the renin-angiotensin system and calcium channel blockers (CCBs) have been shown to be effective and safe in lowering blood pressure and in achieving the recommended blood pressure targets with a good tolerability profile. [41] This makes them stand out as some of the best antihypertensive drug classes. Because of their effectiveness in lowering blood pressure levels, good tolerability, and abundant evidence that they reduce the effects of hypertension on the cardiovascular system and the kidneys, CCBs have become one of the antihypertensive medications that have seen the greatest amount of use over the past 20 years. This page contains an update to the data that supports the use of antihypertensive regimens based on CCBs. These regimens can be used either as monotherapy or in combination therapies with other classes of antihypertensive medications.[42]

Diuretic

When it comes to the treatment of hypertension, diuretics are among the medications that are recommended the most frequently.[43,44] Researchers have established a connection between the use of diuretics and a variety of unfavourable side effects, such as hyperuricemia, hyponatremia, and hypokalemia. In contrast to other antihypertensive drugs, diuretics have the potential to have a negative impact on the cardiopulmonary interactions of COVID-19 patients who are undergoing mechanical ventilation. Additionally, it has been shown that the use of diuretics is associated with a higher risk of heart injury in COVID-19. [45]

Conclusion

According to the information that is currently available, patients who have both COVID-19 and hypertension have to keep taking their antihypertensive medication as prescribed. In addition, it is possible that RAAS inhibitors are more effective than other medications in controlling hypertension in this particular group. To substantiate the findings of this analysis, additional research on both women and men is required. It would appear from the outcomes of ongoing clinical trials that antihypertensive medications are not connected in any way to the results of COVID-19 in individuals who have hypertension. Even in conditions in which mortality is lower, there is a possibility that ACEIs and ARBs will be beneficial. It is for this reason that we need to conduct additional research to determine exactly how ACEIs/ARB medication affects COVID-19 persons who have high blood pressure and how this affects the overall health outcomes of such individuals. People who have hypertension need to work on improving their autoimmunity and reducing chronic inflammation in order to be successful in fighting off the SARS-CoV-2 virus.

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