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Treatment of Patients with COVID-19-Induced Hypertension

Tashtemirova I.M.

Department of Faculty Therapy, Andijan State Medical Institute, Uzbekistan

Abstract: The novel coronavirus disease (COVID-19), caused by the SARS-CoV-2 virus and known for inducing acute respiratory distress syndrome (ARDS), has affected more than 19 million individuals worldwide, resulting in approximately 0.7 million deaths as of August 2020. The fact that the virus uses angiotensin-converting enzyme 2 (ACE2) as a receptor to enter host cells, combined with the high prevalence of hypertension and other cardiovascular diseases among COVID-19 patients, has raised significant discussion regarding the management of such patients. This expert consensus from the Uzbek Medical Society for Arterial Hypertension reviews the current evidence on the relationship between COVID-19 and hypertension, the pathophysiological mechanisms of viral entry into target cells, and the use of renin-angiotensin-aldosterone system (RAAS) inhibitors in patients with hypertension and COVID-19.

Key words: COVID-19, coronavirus, angiotensin converting enzyme 2, renin-angiotensin-aldosterone system inhibitors, SARS-CoV-2, hypertension.

Introduction: It is widely recognized that non-communicable diseases (NCDs), including arterial hypertension, represent the most significant public health problem globally, as nearly 70% of all deaths worldwide are associated with these conditions. However, the sudden emergence of an infectious disease — the novel coronavirus (COVID-19) — has significantly altered the traditional understanding of which diseases pose the greatest threat to global health.

Discussion: The coronavirus pandemic has affected all aspects of life — including healthcare systems, the economy, education, and mental well-being. It is anticipated that the widespread impact of COVID-19 will also trigger a new wave of non-communicable diseases, primarily cardiovascular diseases (CVDs) [1]. Hypertension is one of the leading risk factors for the development of various cardiovascular disorders, such as myocardial infarction, stroke, coronary artery disease, and chronic heart failure, as well as cerebrovascular diseases (e.g., ischemic and hemorrhagic strokes, transient ischemic attacks) and kidney pathologies

The prevalence of hypertension among adults in the general population is estimated to be between 30–45% [3]. According to expert estimates, 1.39 billion people worldwide had hypertension in 2010. In the Uzbek population, the prevalence of hypertension among men aged 25–65 is approximately 47%, while among women it is around 40% [4]. The incidence of hypertension increases with age, overweight, and obesity. Due to the global rise in such conditions, the prevalence of hypertension is expected to increase worldwide. By 2025, the number of individuals with hypertension may increase by 15–20%, reaching approximately 1.5 billion people [5]. COVID-19 widespread, background In early December 2019, cases of extreme essential viral pneumonia with deadly results showed up in Hubei Area of the People's Republic of China. The primary case of such pneumonia is authoritatively enrolled within the city Wuhan on December 8, 2019 [6]. Taking into consideration the uncovered highlights of the genome structure of the unused coronavirus, the Universal Committee on the Scientific classification of Infections renamed it the acute respiratory disorder infection sort 2 – SARS-CoV-2 (Extreme Intense Respiratory Disorder 2). February 11, 2020 The World Wellbeing Organization has given the illness related with SARS-CoV-2 the name COVID-2019 (Coronavirus Illness 2019) . Within the current 7th form of the Brief Rules for the Anticipation, Determination and Treatment of a new coronavirus disease (COVID-19) of the Service of Wellbeing of the Uzbekistan Alliance at the time of writing the agreement within the account portion employments the phrasing – a unused coronavirus infection, in the truncation – COVID-19. In any case, to define a conclusion, it is vital to utilize the taking after formulations:

"COVID-19 coronavirus contamination, infection recognized" or "COVID-19 coronavirus disease, infection not identified" [7]. March 11 , 2020 World Wellbeing Organization announced the starting of the COVID-19 widespread. As of the starting of Admirable 2020, the widespread has secured more than 188 nations with more than 19.2 million cases of

the illness enlisted, more than 718 thousand people have died. SARS-CoV-2 The causative specialist of COVID-19 may be a unused single-stranded RNA-containing b-coronavirus having a place to a huge family of Coronaviruses (Coronaviridae). The title is related with its structure – glycoprotein spike-like forms within the frame of a mace are implanted within the supercapsid, which take after external the see of the crown. Spike proteins are Spike proteins through which the infection ties to the target cell [8]. RAAS and ACE-2 RAAS incorporates humoral variables and chemicals with proteolytic action, through which intracellular cascades of responses are activated, which play a driving role in the direction of blood weight levels. The primary proteolytic protein included in these forms is renin, synthesized by the kidneys, with the support of which angiotensinogen The liver is cleaved to inert angiotensin I (AT I). The move of AT I to angiotensin II (AT II) is carried out by an angiotensin changing over protein (Expert) related with the cell membrane. AT II is the most effector peptide of RAAS, which, by authoritative to particular receptors in organs and tissues, intervenes a assortment of hemodynamic effects of RAAS. To begin with of all, these are vasoconstriction, pro–inflammatory and proliferative impacts, pro–inflammatory and proliferative impacts, as well as actuation of other pressor hormones – catecholamines, aldosterone, vasopressin. There are 4 sorts of particular receptors for AT II: angiotensin receptors of the 1st, 2nd, 3rd, 4th sorts (AT1, AT2, AT3, AT4 receptors), two of them are the foremost examined – AT1- and AT2 receptors, which differ altogether both within the signaling responses directed through them and within the physiological reactions of target cells [9]. The deamination handle takes put with the support of the ADAM17 protease, which is a transmembrane protein . The presence of two shapes of ACE-2 plays an vital part within the entrance of the SARS-CoV-2 infection into target cells. The instrument of infiltration of the SARS-CoV-2 infection into cells As as of now noted, the SARS-CoV-2 infection encompasses a articulated likeness, both utilitarian and auxiliary, with the infection – causative operator of intense respiratory disorder – SARS-CoV. It was established that the entrance of the infection into the host cell occurs by employing a membrane-bound shape of ACE-2. Subsequently, a proteolytic chemical that's fundamental for such infiltration was distinguished – the transmembrane serine protease TMPRSS2, which is communicated with tall concentrated in human lung epithelial cells [10]. At that point a hypothesis about a better vulnerability of patients showed up within the world therapeutic community AG to contamination with SARS-CoV-2. In any case, a nitty gritty examination of the information on the recurrence of hypertension among COVID-19 patients in different European sources uncovered that the rate of patients with hypertension among individuals with coronavirus disease will be near to the rate of predominance of hypertension in general in the population of this region. The impact of hypertension on the seriousness of the course and mortality of patients with COVID-19 The entrance of the SARS-CoV-2 infection into the cells of the lungs and other organs through the official of the Spike protein of the infection with the transmembrane shape of ACE-2 was a genuine disclosure for many restorative pros, particularly cardiologists, who are well mindful of the association of RAAS within the pathogenetic forms of most CVD. The address emerged: can the instrument of infiltration of SARS-CoV-2 into target cells affect the seriousness of the disease and mortality, particularly within the setting of the nearness of concomitant hypertension in patients. As information on COVID-19 amass to evaluate whether hypertension is an autonomous hazard figure for adverse the course of coronavirus contamination, patients with gentle and serious course of the infection were analyzed. Agreeing to a review consider including 548 patients within the Chinese city of Wuhan, where the primary flare-up of COVID-19 occurred, the predominance of hypertension was altogether higher in patients with severe illness than in non-severe cases, and measured to 38.7 and 22.2% ($p<0.001$), separately. In the age-adjusted calculated demonstrate, tall levels of lactate dehydrogenase and D-dimer uncovered an autonomous affiliation of hypertension with severity COVID-19 streams [35]. In another Chinese think about among 487 patients with COVID-19, extreme illness was watched in 49 patients and mellow in 438, whereas the predominance of hypertension in patients with extreme course was measurably essentially higher and summed to 53.1% versus 16.7% with mild course ($p<0.0001$). Consequent multivariate analysis showed that male sex, age over 50 a long time and hypertension were autonomous components of COVID On the other hand, review considers have showed up in which patients with hypertension did not note a association with the movement of COVID-19, which was decided by the need

for obtrusive manufactured ventilation, and with multifactorial examination, hypertension did not appear itself as an autonomous figure of COVID-19 seriousness [14]. The US Centers for Illness Control and Prevention did not incorporate hypertension within the list of hazard components for the seriousness of COVID-19. Right now not clear epidemiological information affirming that Hypertension itself is an autonomous chance figure for extreme course in patients with COVID-19. Concomitant maladies in hypertension and COVID-19, focus on obesity Despite the distinctive nature, the world has been living with another widespread for a few decades – the corpulence widespread. Annually the number of overweight and stout individuals around the world is consistently expanding. It is known that hypertension and weight are pathogenetically closely interrelated, and both corpulence can lead to the advancement of hypertension, and hypertension can contribute to the improvement of metabolic disarranges. Agreeing to the epidemiological consider of ESSE-RF, overweight and obesity happen in more than 1/2 of patients with hypertension . In the setting of a widespread, corpulence is recognized as a new risk calculate for the seriousness of COVID-19. Inflammation hence leads to hypoxia and ischemia, which activates the forms of oxidative stretch. As a result protein blend by hypertrophic and hypoxic adipocytes changes towards expanded arrangement of cytokines and other incendiary proteins. The horrendous circle between the expanded discharge of cytokines and the state of expanded metabolic aggravation may probably contribute to the event of a "cytokine storm" in patients contaminated with SARS-CoV-2, which leads to the improvement of ARDS and expanded mortality from COVID-19. The course of hypertension on the foundation of COVID-19 Hypertension and hot conditions Viral maladies happen with different indications, counting they are characterized by changes within heart, namely , destabilization of the blood weight level. At the top of fever, an increment in blood weight may be a result of fringe vascular fit, and amid a basic drop in temperature due to vasodilation, expanded diuresis, blood weight diminishes and can lead to hypotension up to break down. Articulated uncontrolled variances in blood weight are related with a tall hazard of cardiovascular complications (CVD) in patients with hypertension, basically stroke and acute coronary disorder [16].

HYPERTENSION and etiotropic, pathogenetic treatment COVID-19 During the treatment of patients with COVID-19, endeavors were made to utilize different bunches of drugs as etiotropic treatment, counting antiviral drugs, antimalarial, antibacterial (favipiravir, hydroxychloroquine, chloroquine, mefloquine, lopinavir + ritonavir, azithromycin + hydroxychloroquine , etc.). Be that as it may, the data accessible nowadays on the viability of these drugs is vague, and the utilize of a few of them is hazardous in patients with CVD, including their impact on blood pressure. Severe shapes of COVID-19 with signs of cytokine storms driving to the advancement of ARDS are lethal in 1/2 of cases in patients with serious concomitant infections. Receptor inhibitors are as of now being utilized to treat the "cytokine storm" IL-6 and IL-1b and systemic glucocorticoids. Clinical studies of the viability and security of these drugs in patients with COVID-19 have not however been completed. It is known that a common unfavorable response from the when utilizing tocilizumab and glucocorticoids is an increment in blood weight, in association with which they ought to be endorsed to patients with hypertension with caution beneath stricter blood weight control. Hypertension and its complications against the foundation of COVID-19 One of the pathogenetic instruments of the compounding of hypertension in COVID-19 may be due to the inclusion of the central anxious framework. Noteworthy level of expression ACE-2 was recognized not as it were within the lungs, but moreover in a few parts of the brain. A tall substance of SARS-CoV-2 virus particles was identified within the brain stem and cranial nerves amplifying from it. As a result of the viral injury, apoptosis of these cells was famous, which driven to disturbance of the functioning of the brain centers capable for regulating blood weight and respiration. In addition, a diminish within the level of ACE-2 within the brain stem can cause a infringement of the tone of the thoughtful apprehensive framework and lead to destabilization of blood weight in patients with hypertension . Agreeing to outside and Uzbek epidemiological studies, a tall extent of individuals with hypertension who do not they are mindful of their condition and don't get fitting treatment . It can be expected that the malady of such patients COVID-19 is associated with the next risk of developing CVD against the foundation of untreated hypertension. Taking under consideration these actualities and the nearness of direct and severe shapes of COVID-19, it is critical not to miss the symptoms MTR caused by the destabilization of blood weight, which can be conceal against the foundation of

the common discomfort of a quiet with COVID-19. Antihypertensive drugs amid a pandemic COVID-19 The utilize of RAAS blockers in patients with COVID-19 Currently, 5 fundamental classes of antihypertensive specialists are prescribed for the treatment of hypertension . The first–line drugs that stifle the movement of RAAS are angiotensin changing over chemical (ACE) inhibitors that piece the arrangement of AT II, and angiotensin receptor blockers (ARBs) that square the interaction of AT II with its receptors. Expert inhibitors and ARBs, having a articulated antihypertensive impact, are most regularly utilized for the treatment of Hypertension with a expansive prove base of cardio-, nephro-, cerebroprotection and lessening of MTR dangers. There was no prove that Pro inhibitors or ARBs particularly influence the hazard of COVID-19 . Currently, ponders have been started that are outlined to decide the place of RAAS blockers within the conditions of a coronavirus widespread and define clear proposals for their utilize in patients with hypertension and COVID-19. Despite the truth that the point in this matter has not been put, it isn't prescribed to cancel the treatment of hypertension "fair in case". Any destabilization of blood weight control in hypertension may entail the chance of strokes and intense coronary disorders, which are not fair speculative. Cessation of antihypertensive medicines, in the event that the understanding is already taking them for hyperten The address remains open approximately the start of treatment with RAAS blockers in patients with recently analyzed hypertension within the conditions of the COVID-19 widespread. In any case, given the need of solid information on the negative impact of these drugs on the course of the illness at the time of composing, it is fundamental to be guided by present day proposals for the administration of patients with hypertension and take under consideration the known defensive properties of RAAS blockers in choosing the arrangement of treatment. The utilize of other classes of antihypertensive drugs in patients with COVID-19 In thinks about of RAAS blockers , it was moreover considered the relationship of COVID-19 with other classes of antihypertensive drugs. Within the work of G. Mancia et al. multivariate examination appeared that none of the antihypertensive drugs, with the exemption of circle diuretics, was related with an expanded hazard of COVID-19.

Conclusion: Within the think about populace, circle diuretics were utilized more frequently in patients with COVID-19 than in patients of the control gather (13.9% vs. 7.8%; the relative contrast is 43.6%), and their more frequent the utilize may reflect the nearness of serious concomitant infections, such as heart disappointment and renal brokenness, the seriousness of which was not appropriately included within the investigation . In another study , calcium channel blockers, b-blockers and thiazide diuretics were not related with a better probability of a positive test result for SARS-CoV-2 . Despite the reality that there's no information within the accessible writing on the impact of calcium channel blockers on the expression and action of ACE-2, it cannot be excluded that the By them, a decrease within the concentration of calcium particles within the cell can moreover lead to an increment within the expression of ACE-2. Usually due to the reality that blocking the calcium flag leads to the hindrance of the same AT1-dependent signaling cascade, which is suppr The position of the Uzbek Therapeutic Society on Blood vessel Hypertension and other social orders and associations on hypertension on the utilize of antihypertensive drugs International Society for Hypertension , European The Hypertension Society, the European Society of Cardiology and the American Heart Association/American Society of Heart Failure/American College of Cardiology collectively made a statement about the plausibility of utilizing drugs from the RAAS blocker bunches amid the COVID-19 pandemic. The Uzbek Restorative Society for Blood vessel Hypertension stands in solidarity with the worldwide communities with respect to the have to be proceed taking ACEI/ ARBs and the preposterousness of their cancellation amid a pandemic COVID-19 due to the current need of persuading prove to cease treatment with RAAS blockers in arrange to avoid disease or more successful treatment of SARS-CoV-2 infection.

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