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ASSESSING THE IMPACT OF ANTIHYPERTENSIVE DRUGS ON THE CLINICAL PICTURE AND COURSE OF HYPERTENSION IN ELDERLY PATIENTS WHO HAVE HAD COVID-19

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ABSTRACT

The severe acute respiratory syndrome (SARS)-CoV-2 novel coronavirus (CoV) outbreak began in late 2019 in Wuhan, China, and has spread to more than 200 countries. We receive in this information the databases and archives of Fergana branch of the republican specialized scientific-practical medical center of cardiology. In a retrospective study, we identified 80 adult patients who had COVID-19 with laboratory confirmed tests. Multivariate logistic regression was performed in patients with comorbid hypertension to examine the potential association between clinical outcomes, disease severity, and clinical characteristics using ACEIs, ARBs, calcium channel blockers (CCBs), beta blockers (BBs), and thiazides. Clinical outcomes, shortness of breath, and fatigue were significantly reduced in patients, especially adult patients over 65 years of age, who were taking an ARB before hospitalization compared with patients who were not taking medication. Reduced disease severity in older patients with COVID-19 was associated with users of CCBs and ACEIs. Clinical parameters including CRP, lymphocyte count, D dimer, procalcitonin, and hemoglobin were significantly improved in older ARB users.

Key words

(SARS) -CoV-2 new coronavirus infection, antihypertensive drugs, ARBs, BB, CCB, acute respiratory distress syndrome, RAAS.

Introduction.

At the end of 2019, several cases of deadly pneumonia were reported in Wuhan, China. Soon, a coronavirus (SARS-CoV) was isolated from the respiratory tract of patients and the viral genome was sequenced; it was later named SARS-CoV. In severe cases of COVID-19, patients develop acute respiratory distress syndrome (ARDS) and often die with multiple organ dysfunction syndrome (MODS). By March 11, 2020, the viral infection had spread to more than 100

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countries, and the World Health Organization declared SARS-CoV-2 infection a global pandemic.

There is growing concern about the use of antihypertensive drugs in patients with COVID-19, largely because angiotensin-converting enzyme 2 (ACE2), a negative regulator of the renin-angiotensin-aldosterone receptor system (RAAS), is a coreceptor for viral entry into human cells using SARS-CoV-2. ACE breaks down angiotensin I to form angiotensin II, while ACE2 converts angiotensin II to angiotensin. By counteracting the effects of ACE, ACE2 plays a critical role in maintaining blood pressure homeostasis and fluid and salt balance. ACE inhibitor (ACEI) and angiotensin receptor blockers (ARB) are the most commonly prescribed antihypertensive drugs. The viewpoint, "COVID-19 and Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers: What is the Evidence," published March 24, 2020 in JAMA, points to a lack of clinical data. In a special report, "Renin -angiotensin-aldosterone system (RAAS) inhibitors in patients with COVID-19," published March 30, 2020 in the New England Journal of Medicine, the authors discussed the potential benefits rather than harms of RAAS blockers in COVID-19, but also indicated that insufficient data are available to determine whether these observations easily translate to humans, and no studies have assessed the effect of RAAS inhibitors on COVID-19.

A previous study from this research group examined the role of the RAAS in acute pulmonary failure caused by SARS-CoV-222 infection. SARS-CoV-2 infection and the SARS-CoV-2 spike protein reduce ACE2 expression, increase angiotensin II signaling through the angiotensin II type 1a (AT1a) receptor, contribute to disease pathogenesis, cause pulmonary edema, and impair respiratory function. We demonstrated that the ARB losartan can attenuate acute lung failure in a mouse model that worsened after injection of the SARS-CoV-29 spike protein. We have also shown an imbalanced RAAS in many conditions predisposing to ARDS, including sepsis, acid aspiration, bacteria, SARS-CoV-2, avian influenza (H5N1 and H7N9) infections, and nanoparticle aspiration. These studies showed that blocking the RAAS pathway and reducing angiotensin II levels may improve lung injury. Observational studies have associated the use of ACEIs and ARBs with improved outcomes in patients with pneumonia24. Our previous study reported a significant increase in plasma angiotensin II levels in patients with COVID-19, again indicating RAAS imbalance in COVID-19. Other studies of ACEIs/ARBs associated with COVID-19 mortality and morbidity have recently reported different results. Here, we conducted a retrospective study to examine the potential association between antihypertensive drug use and COVID-19 disease severity.

Materials and methods.

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Study design and participants. In this retrospective study, we identified all adult patients (age ≥ 18 years) with laboratory-confirmed COVID-19 pneumonia.

The diagnosis was based on the prevention and control program for new coronavirus pneumonia published by the Uzbekistan healthcare system. The final analysis included only patients with comorbid hypertension diagnosed using the criteria of the National Guidelines for the Treatment of Arterial Hypertension in Uzbekistan and the ESC/ESH 2018 Guidelines for the Treatment of Arterial Hypertension. Verbal informed consent was obtained from patients or family members if available.

Results.

Clinical characteristics of participants This study cohort included 80 patients who had recovered from COVID-19 and were hospitalized in the FF RSNPMCC. Subsequent analyzes included 65 participants with hypertension, and 9 cases were excluded due to missing medication information (Figure 1). The mean age (± standard error) was 64.6 ± 11.8 years, 51.25% of patients were male, and 29 patients were older than 65 years. The age and gender distribution of patients with severe (21, 26.25%) and non-severe (59, 73.75%) COVID-19 varied significantly. Patients with severe COVID-19 were older (69.6 ± 11.0 years vs. 62.9 ± 11.5 years, $P < 0.001$). Additionally, nonsurvivors were significantly older than survivors (71.0 ± 10.9 years vs. 64.2 ± 11.7 years, $P < 0.001$). No association was found between death and gender ($P>0.05$). Among older patients (>65 years), older patients are more likely to develop severe COVID-19 and die. Men were more likely to develop severe COVID-19, but this did not have a statistically significant effect on mortality.

ARBs and CCBs are associated with reduced mortality in older patients with COVID-19. Using multivariate logistic regression, we assessed the effect of patients with concomitant hypertension who were taking antihypertensive drugs before hospitalization. In the subgroups of ARBs, ACEIs, CCBs, thiazide and beta blockers, in terms of mortality and disease severity compared with a group of patients with concomitant hypertension who were not taking medications. Clinical outcomes of patients taking ARBs were statistically significantly improved by adjusting for age, sex, baseline blood pressure, and associated health variables among all patients (adjusted OR = 0.421, 95% CI: 0.19–0.934, P = 0.033) and in elderly patients who were over 65 years of age (adjusted OR = 0.202, 95% CI: 0.055–0.745, P = 0.016). Clinical outcomes among CCB users were statistically significantly improved in older patients (adjusted OR =0.22, 95% CI: 0.062–0.778, P = 0.019). Our data suggest that ARBs and CCBs may be beneficial for patients with COVID-19.

CCBs and ACEIs are associated with reduced disease severity in older patients with COVID-19. OR = 0.472, 95% CI: 0.257–0.865, P = 0.015), especially in older patients (adjusted OR = 0.287, 95% CI: 0.114–0.723, P = 0.008). Disease severity

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among ACEI users was statistically significantly reduced in older patients (adjusted OR = 0.156, 95% CI: 0.036–0.67, P = 0.013). A statistically significant reduction in the odds of developing severe disease among ARB users compared with nonusers was not observed without adjustment. Thus, CCBs and ACEI antihypertensive drugs may be associated with disease severity in patients with COVID-19.

ARBs help reduce shortness of breath and fatigue in patients with COVID-19 Shortness of breath and fatigue are characteristics of COVID-19. In particular, respiratory dyspnea, which is defined by peripheral oxygen saturation (SPO2) <93% and respiratory rate >30 times per minute. Using multivariate logistic regression estimated in Cohort C, in which some clinically detailed presentations were recorded, we found that ARB users compared with non-users. Antihypertensive drug users were associated with decreased dyspnea (adjusted OR = 0.4, 95% CI: 0.236–0.678, P = 0.001) and less fatigue (adjusted OR = 0.643, 95% CI: 0.457–0.906, P = 0.012). Similar results were observed in older patients with COVID-19. BB and CCB users were also associated with a significant reduction in shortness of breath in patients with COVID-19. These data suggest that an ARB may improve respiratory syndromes in patients with COVID-19.

Using the Mann-Whitney U test, we found that clinical parameters related to infection and inflammation, including CRP, lymphocyte count, and procalcitonin, were significantly improved to normal levels in older patients with COVID-19 who took an ARB before treatment.

Hospitalization versus non-antihypertensive drug users. Blood clots have been reported in patients with COVID-19. D dimer, a biomarker of blood clots, was significantly reduced in older adults taking ARBs compared with those taking non-antihypertensive medications. Levels of hemoglobin, which carries oxygen from the lungs to the rest of the body, were also significantly increased, returning to normal levels in older adults taking ARBs. In older patients with COVID-19, those who received a thiazide, beta-blocker, or CCB before hospitalization were also associated with these improved clinical measures, with the exception of blood clot biomarker. Taken together, these data suggest that older COVID-19 patients with concomitant hypertension who were taking an ARB before hospitalization may have fewer clinical syndromes compared with those not taking antihypertensive drugs.

Discussion.

In this retrospective study, we found an association between ARB use and reduced mortality in COVID-19 patients with comorbid hypertension (compared with those not taking antihypertensive medications). We also noticed a decrease in disease severity in older patients with COVID-19. There are 18 reports examining the association of ARBs and ACEI drugs with COVID-19. Eleven of the 18 articles

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reported analysis of mortality. The results are somewhat inconsistent due to the different methodologies used and the nature of the cohorts. Eight of the eleven articles did not separate ARB and ACEI users and combined them into one study group. Although both ARBs and ACEIs are RAAS blockers, they target different genes. A more rigorous analysis would be to calculate the association of ARBs and ACEIs between COVID-19 separately. The remaining three articles are included separately. The EPIRB User Group, one of three reports published in Hypertension, shows a similar conclusion to our report here. However, this study is short communication with only 1 figure without detailed methodology. Two reports published in JAMA and JAMA Cardiology and one NEJM closed paper found that ARBs were not statistically significantly associated with death from COVID-19. One of the main differences is that their control group was completely different from our control group. The JAMA article used CCB users as the control group 42. The remaining articles (published in JAMA Cardiology and the retracted NEJM article) used all hypertensive patients except the drug users studied (Non-ARB users) as the control group. It is noteworthy that them. The control group of ARB users included ACEI users. ACE inhibitors, such drugs of the RAAS system may have an effect similar to ARBs. We used our method (i.e., all hypertensive patients excluding ARBs, and including ACEIs in the control group) on our data: adjusted results showed that ARBs were not statistically significantly associated with COVID-19 mortality. However, ARB drugs statistically significantly improved mortality in patients with COVID-19 when users of ACEI drugs were excluded from the control group. Thus, this may partially contribute to the other finding of this article that ARBs/ACEI drugs did not statistically reduce mortality in patients with COVID-19.

In our study, ARBs and ACEIs showed different effects related to mortality and morbidity in patients with COVID-19, although both are RAAS blockers. Previous literature has reported that ARBs can effectively block AT1R, the stimulation of which is implicated in multiorgan injury 28,49,50, suggesting that ARBs may be more effective in treating mods. In addition to their antihypertensive effects, ARBs may directly reduce pulmonary edema, epithelial and endothelial cell damage, proinflammatory cytokines and chemokines, reduce apoptosis and fibrosis, protect mitochondrial function, support insulin and lipid metabolism, and normalize the coagulation cascade. These reports may provide mechanisms that ARBs were associated with significant improvements in clinical characteristics of COVID-19 patients in this study. Our unpublished data demonstrated that ARBs, especially losartan, prolong survival more than ACEIs in a mouse model of avian influenza A H5N116. Subsequent education is necessary to elucidate the mechanisms involved in both ACEIs and ARBs.

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Although a wide range of conditions, including SARS-CoV, sepsis, acid aspiration, bacteremia, and avian influenza (H5N1 and H7N9) infections, predispose patients to ARDS, the common mechanism appears to be an imbalance of the RAAS. Our previous studies in mice showed that ACE, angiotensin II, and angiotensin II receptor type 1a are involved in disease pathogenesis, whereas ACE2 and angiotensin II receptor type 2a can protect mice from severe acute lung injury. Increased levels of angiotensin II in the blood have been reported in patients with COVID-19. Interventions that restore the balance of the RAAS, for example, thus antihypertensive drugs ARBs may be useful. A trial of losartan, a member of the ARB, as a treatment for COVID-19 is currently ongoing at TMA.

We noted the limitations of this study. The number of patients taking ACE inhibitors and thiazide was too small and may cause statistical error. Outcomes of hypertensive patients and patients with nonhypertensive COVID-19 were not compared. However, the uniqueness of our study lies in the statistical adjustment for all combined factors of age, gender, baseline blood pressure (including SBP and DBP) and comorbidities (including chronic diseases of the heart, lungs, kidneys, liver and cerebral vessels, diabetes, etc.) and cancer), although BB was not statistically significant before adjustment. In summary, the results of this statistical human study link RAAS blockers to patients with COVID-19 and show that the use of ARBs in patients with hypertension is associated with reduced mortality in patients with COVID-19. Therefore, patients with hypertension should continue to take ARBs and ACEIs during the current COVID-19 pandemic. Our study also suggests that antihypertensive drugs ARBs, ACEIs, CCBs and beta-blockers may also be potentially cost-effective and effective treatments for patients with COVID-19, especially older patients calling for clinical trials to directly test this.

Conclusion.

Clinical outcomes were statistically significantly improved in patients treated with antihypertensive drugs ARBs, beta blockers, and CCBs after statistical adjustment for all ages, sex, baseline blood pressure, and comorbidities. Our data suggest that the hypertension drugs ARBs, ACEIs, CCBs, and beta-blockers may be beneficial for patients with COVID-19.

LITERATURE:

1. Chan, J. F.-W. et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 395, 514–523 (2020).

2. Huang, C. et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395, 497–506 (2020).

3. Zhang, N. et al. Recent advances in the detection of respiratory virus infection in humans. J. Med. Virol. 92, 408–417 (2020).

4. Hui, D. S. et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — the latest 2019 novel coronavirus outbreak in Wuhan, China. Int. J. Infect. Dis. 91, 264–266 (2020).

5. Wang, C., Horby, P. W., Hayden, F. G. & Gao, G. F. A novel coronavirus outbreak of global health concern. Lancet 395, 470–473 (2020).

6. Zhu, N. et al. A novel coronavirus from patients with pneumonia in China, 2019. N. Engl. J. Med. 382, 727–733 (2020).

7. Liu, Y. et al. Elevated levels of plasma cytokines in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection reflect viral load and lung injury. Natl Sci. Rev. (2020).

8. Liu, Y. et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci. China Life Sci. 63, 364–374 (2020).

9. Cuba, K. et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nat. Med. 11, 875–879 (2005).

10. Xu, Z. et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet. Resp. Med. 8, 420–422 (2020).

11. Huang, F. et al. Angiotensin II plasma levels are linked to disease severity and predict fatal outcomes in H7N9-infected patients. Nat. Commun. 5, 3595 (2014).

12. Imai, Y. et al. Angiotensin-converting enzyme 2 protects from severe acute lung failure. Nature 436, 112–116 (2005).

13. Zou, Z. et al. Angiotensin-converting enzyme 2 protects from lethal avian influenza A H5N1 infections. Nat. Commun. 5, 3594 (2014).

14. Forrester, S. J. et al. Angiotensin II signal transduction: an update on the mechanisms of physiology and pathophysiology. Physiol. Rev. 98, 1627–1738 (2018).

15. Lin, Y. C. et al. Effects of calcium channel blockers comparing to angiotensinconverting enzyme inhibitors and angiotensin receptor blockers in patients with hypertension and chronic kidney disease stage 3 to 5 and dialysis: asystematic review and meta-analysis. PLoS ONE 12, e0188975 (2017).

16. Умаров , З. . (2023). РЕВМАТОИД АРТИТ МАВЖУД БЕМОРЛАРДА СУТКАЛИК АРТЕРИАЛ ҚОН БОСИМ ТИПЛАРИ. Евразийский журнал медицинских и естественных наук, 3(5), 185–190.

17. Умаров Зоҳиджон Асқарали ўғли. (2023). ТУРҒУН ЗЎРИҚИШ СТЕНОКАРДИЯСИ СУРУНКАЛИ ПАНКРЕАТИТ БИЛАН БИРГА КЕЧГАНДА ЮРАК РИТМИ БУЗИЛИШЛАРИНИ СОЛИШТИРМА ТАҲЛИЛИ. Scientific Impulse, 1(10), 652–656.