

COVID-19 and the use of angiotensin-converting enzyme inhibitors and receptor blockers

Scientific brief

7 May 2020



Background

Concerns exist that angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs) increase susceptibility to coronavirus SARS CoV-2 (the viral agent that causes the disease COVID-19) and the likelihood of severe COVID-19 illness.¹ These concerns are based on considerations of biological plausibility,² and the observation that there is an overrepresentation of patients with hypertension and other cardiovascular comorbidities among patients with COVID-19 who have poor outcomes.³ Millions of people around the world are on treatment with ACE-Is and ARBs for hypertension, heart failure, coronary artery disease, or kidney disease. Speculation about worse outcomes among patients on these medications during the COVID-19 pandemic has caused widespread anxiety among patients and their care providers. On the other hand, the harms of indiscriminate withdrawal of these medications on cardiovascular outcomes are well documented.⁴ There is also widespread speculation about the potential benefits of ACE-Is and ARBs, based on biological plausibility arguments and animal data and small clinical studies on patients with other viral respiratory infections.⁵

This brief summarizes the current evidence on the impact of ACE inhibitors or angiotensin receptor blockers on severe acute respiratory illness due to SARS CoV-2.

Methods

A rapid review was carried out using Ovid MEDLINE and the Cochrane Database of Systematic Reviews from 1 January 2003 to 24 April 2020 as well as the World Health Organization database of COVID-19 publications, clinicaltrials.gov, and medRxiv.org from inception to 17 April 2020 using terms for COVID-19, SARS virus, Middle East Respiratory Syndrome, angiotensin-converting enzyme inhibitors, and angiotensin receptor antagonists. Additional citations were identified from hand-searching reference lists. Studies in all languages were included. Study quality was assessed using the Newcastle-Ottawa Quality Assessment Scale.

Review of the evidence

The rapid review identified 11 observational studies,⁶⁻¹⁶ eight of which were conducted in China,^{8-10, 12-16} along with single studies from Italy,¹¹ the United Kingdom,⁷ and the United States.⁶ Nearly all studies included only patients with lab-confirmed COVID-19. No studies were found that were designed to directly assess whether ACE inhibitors or ARBs increase the risk of acquiring COVID-19. After adjustment for confounders, history of ACE inhibitor or ARB use was not found to be associated with increased severity of COVID-19 illness. There were no studies that address the potential benefits and harms of initiating ACE inhibitors or ARBs as treatment for patients with COVID-19.

Conclusion

There is low-certainty evidence that patients on long-term therapy with ACE inhibitors or ARBs are not at higher risk of poor outcomes from COVID-19.

References

1. Watkins J. Preventing a covid-19 pandemic. *BMJ*. 2020;368:m810.
2. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *Journal of virology* 2020;94(7).
3. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. *China CDC Weekly*. <http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>. In.
4. Gilstrap LG, Fonarow GC, Desai AS, Liang L, Matsouaka R, DeVore AD, et al. Initiation, Continuation, or Withdrawal of Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers and Outcomes in Patients Hospitalized With Heart Failure With Reduced Ejection Fraction. *Journal of the American Heart Association* 2017;6(2).
5. Kuster GM, Pfister O, Burkard T, Zhou Q, Twerenbold R, Haaf P, et al. SARS-CoV2: should inhibitors of the renin-angiotensin system be withdrawn in patients with COVID-19? *Eur Heart J* 2020.
6. Rentsch CT, Kidwai-Khan F, Tate JP, et al. Covid-19 Testing, Hospital Admission, and Intensive Care Among 2,026,227 United States Veterans Aged 54-75 Years. *medRxiv*. 2020:2020.2004.2009.20059964.
7. Bean D, Kraljevic Z, Searle T, et al. Treatment with ACE-inhibitors is associated with less severe disease with SARS-Covid-19 infection in a multi-site UK acute Hospital Trust. *medRxiv*. 2020.
8. Liu Y, Huang F, Xu J, et al. Anti-hypertensive Angiotensin II receptor blockers associated to mitigation of disease severity in elderly COVID-19 patients. *medRxiv*. 2020:2020.2003.2020.20039586.
9. Feng Y, Ling Y, Bai T, et al. COVID-19 with Different Severity: A Multi-center Study of Clinical Features. *American Journal of Respiratory and Critical Care Medicine*. 2020.
10. Meng J, Xiao G, Zhang J, et al. Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension. *Emerging Microbes & Infections*. 2020;9(1):757-760.
11. Rossi, GP, Marino M, Formisano D, Venturelli F, Vicentini M, Grilli R. Characteristics and outcomes of a cohort of SARS-CoV-2 patients in the Province of Reggio Emilia, Italy. *medRxiv*. 2020:2020.2004.2013.20063545.
12. Yang G, Tan Z, Zhou L, et al. Angiotensin II Receptor Blockers and Angiotensin-Converting Enzyme Inhibitors Usage is Associated with Improved Inflammatory Status and Clinical Outcomes in COVID-19 Patients With Hypertension. *medRxiv*. 2020:2020.2003.2031.20038935.
13. Peng YD, Meng K, Guan HQ, et al. [Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV]. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2020;48(0):E004.
14. Zeng Z, Sha T, Zhang Y, et al. Hypertension in patients hospitalized with COVID-19 in Wuhan, China: A single-center retrospective observational study. *medRxiv*. 2020:2020.2004.2006.20054825.
15. Li J, Wang X, Chen J, Zhang H, Deng A. Association of Renin-Angiotensin System Inhibitors With Severity or Risk of Death in Patients With Hypertension Hospitalized for Coronavirus Disease 2019 (COVID-19) Infection in Wuhan, China. *JAMA Cardiology*. 2020.
16. Zhang P, Zhu L, Cai J, et al. Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19. *Circulation Research*.0(0).

WHO continues to monitor the situation closely for any changes that may affect this scientific brief. Should any factors change, WHO will issue a further update. Otherwise, this scientific brief document will expire 2 years after the date of publication.

© World Health Organization 2020. Some rights reserved. This work is available under the [CC BY-NC-SA 3.0 IGO](https://creativecommons.org/licenses/by-nc-sa/3.0/) licence.

WHO reference number: [WHO/2019-nCoV/Sci_Brief/ACE-I/2020.1](https://www.who.int/publications/iitem/WHO/2019-nCoV/Sci_Brief/ACE-I/2020.1)