Topic Brief: COVID-19 Treatment with Angiotensin or Recombinant Human Angiotensin Converting Enzyme

Date: 4/20/2020
Nomination Number: 901

Purpose: This document summarizes the information addressing a nomination submitted on 3/21/2020 through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: The nominator is interested in research about whether angiotensin could be an effective treatment for COVID-19.

Assessment: Primary research outside the scope of the AHRQ Evidence-based Practice Center Program. We found an in-process systematic review and two in-process clinical trials related to this topic. This is a rapidly growing area of research and much is yet unknown.

Background

- There is widespread ongoing transmission of a respiratory illness caused by a novel (new) coronavirus called SARS-CoV-2. The disease has been named "coronavirus disease 2019" (abbreviated "COVID-19").
- This is a rapidly growing area of research, and evidence being added daily to aid our understanding of how to treat COVID-19.
- Recent studies have shown that Angiotensin converting enzyme 2 (ACE2) receptors are an entry point into human cells for SARS-CoV-2. In animal studies, angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) have been shown to upregulate ACE2 expression in the heart. [1]
- Angiotensin-2 has been shown to downregulate ACE2 in both mouse and human models. It is unknown whether exogenous angiotensin-2 has the same effect on ACE2 and modulate the rate of COVID-19 cell entry and viral replication.[2]
- Another treatment pathway could be through blocking the interaction of virus the receptor. Exogenous supplement of recombinant human ACE2 might be a treatment of COVID-19, especially for those patients with cardiovascular diseases. Researchers found that injecting exogenous rhACE2 protein could relieve lung injuries in several acute pneumonia experimental models.[3]

Summary of Selection Criteria Assessment

Primary research is outside the scope of the EPC Program. While this is an important area with the potential for high impact, we found too few studies for an evidence review at this time. This is an active area of research, and additional studies are in-progress.

We identified one completed and one ongoing systematic review that might include angiotensin or and/or recombinant human ACE2.

- Sanders et al. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19)A Review. JAMA. April 13, 2020.[4]
    - This review concluded that current evidence does not support stopping angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in patients with COVID-19. No mention was made of angiotensin or recombinant human ACE2, though the search was broad.
- Yasin Khan, Kali Barrett, Stephen Mac, Raphael Ximenes, Marina Englesakis, David Naimark, Beate Sander. Pharmacologic and non-pharmacologic interventions for the management of hospitalized patients with coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. PROSPERO 2020 CRD42020173774 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020173774
    - We confirmed with the authors that they will include recombinant human angiotensin converting enzymes.

We identified two ongoing studies on angiotensin or angiotensin converting enzyme.

- Angiotensin Treatment in COVID-19: the ATCO Trial. NCT04332666
- Recombinant Human Angiotensin-converting Enzyme 2 (rhACE2) as a Treatment for Patients With COVID-19. NCT04335136

Resources

Selected resources for research studies

- LitCovid. This is a curated literature hub hosted by the US National Library of Medicine on research about Covid-19. https://www.ncbi.nlm.nih.gov/research/coronavirus/
- EPPI-Centre evidence map. This is a visual display of completed research studies on COVID-19. http://eppi.ioe.ac.uk/COVID19_MAP/covid_map_v3.html
- Oxford COVID-19 Evidence Service https://www.cebm.net/covid-19/
- COVID-19 Open Research Dataset https://pages.semanticscholar.org/coronavirus-research

References

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2. Chow JH, Mazzeffi MA, McCurdy MT. Angiotensin II for the Treatment of COVID-19-Related Vasodilatory Shock. Anesth Analg. 2020 Mar 23. doi: 10.1213/ANE.0000000000004825. PMID: 32209811. https://www.ncbi.nlm.nih.gov/pubmed/32209811

3. Guo J, Huang Z, Lin L, et al. Coronavirus Disease 2019 (COVID-19) and Cardiovascular Disease: A Viewpoint on the Potential Influence of Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers on Onset and Severity of Severe Acute Respiratory Syndrome Coronavirus 2 Infection. J Am Heart Assoc. 2020 Apr 7;9(7):e016219. doi: 10.1161/JAHA.120.016219. PMID: 32233755. https://www.ncbi.nlm.nih.gov/pubmed/32233755

4. Sanders JM, Monogue ML, Jodlowski TZ, et al. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review. JAMA. 2020 Apr 13. doi: 10.1001/jama.2020.6019. PMID: 32282022. https://www.ncbi.nlm.nih.gov/pubmed/32282022

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