Rapid response to:

Editorials

Preventing a covid-19 pandemic

BMJ 2020; 368 doi: https://doi.org/10.1136/bmj.m810 (Published 28 February 2020) Cite this as: BMJ 2020;368:m810

- Article
- Related content
- Article metrics
- Rapid responses
- Response

Rapid Response:

Re: Preventing a covid-19 pandemic: ACE inhibitors as a potential risk factor for fatal Covid-19

Dear Editor,

The coronavirus disease 2019 (Covid-19) outbreak from Wuhan, China, is spreading worldwide and is a major international concern as it has the potential to become pandemic [1].

The largest Chinese study with 44,672 confirmed cases of Covid-19 shows a high overall case fatality rate (CFR) of 2.3% [2]. Important co-morbidities are hypertension (CFR 6.0%), diabetes (CFR 7.3%), cardiovascular disease (CFR 10.5%) and age >70 (CFR 10.2%) [2]. Similar co-morbidities were noted for the SARS outbreak in 2003.

It is widely unclear what the commonality of these risk factors is. This is somehow surprising as compared to for example the 2009 pandemic H1N1 influenza outbreak, immunosuppressant patients were primary affected. Cardiac patients seem to be at higher risk in Covid-19. One possible answer could be the following: Patients with the comorbidities of hypertension, diabetes and cardiovascular disease might fulfil the indication for the use of angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists [3].

The question is, does there exist a connection between the use of these drugs and severe sequela of Covid-19? While the epidemiological association has not been investigated yet, several indicators underline the hypothesis of the link between ACE inhibitors and Covid-19:

On the one hand, it has been shown that the Covid-19 agent (also known as SARS-CoV-2), uses the SARS-COV receptor angiotensin converting enzyme (ACE) 2 for entry into target cells [4]. The interface between ACE2 and the viral spike protein SARS-S has been elucidated and the efficiency of ACE2 usage was found to be a key determinant of SARS-CoV transmissibility [4].

On the other hand, it could be shown in animal experiments that both the ACE-inhibitor lisinopril and the angiotensin-receptor blocker losartan can significantly increase mRNA expression of cardiac ACE2 (5-fold and 3-fold, respectively) [5]. Further, losartan also significantly increases cardiac ACE2 activity [5].

Is a link between these observations possible? Is the expression of ACE2 receptor in the virus targeted cells increased by the use of ACE-inhibitor/angiotensin-receptor blocker and is the patient therefore more at risk for a severe course? We need rapid epidemiological and preclinical studies to clarify this relationship. If this were the case, we might be able to reduce the risk of fatal Covid-19 courses in many patients by temporarily replacing these drugs.

References

1. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020.
2. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020[J]. China CDC Weekly, 2020, 2(8): 113-122.
3. Jackson, Edwin K. (2006). "Chapter 30. Renin and Angiotensin". In Brunton, Laurence L.; Lazo, John S.; Parker, Keith (eds.). Goodman & Gilman's The Pharmacological Basis of Therapeutics (11th ed.). New York: McGraw-Hill. ISBN 978-0-07-142280-2.
4. Hoffmann M, Kleine-Weber H, Krüger N, Müller M, Drosten C, Pöhlmann S. The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. bioRxiv 2020:2020.01.31.929042.
5. Ferrario CM, Jessup J, Chappell MC, et al. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. Circulation 2005;111:2605-10.

Competing interests: No competing interests

03 March 2020

Rami Sommerstein
Infectious Diseases Physician and Hospital Epidemiologist
Christoph Gräni, Department of Cardiology, Bern University Hospital, Switzerland
Department of Infectious Diseases, Bern University Hospital, Switzerland
Bern, Switzerland
@chrisgraeni