



Medications that could affect COVID19

Should patients continue to take an ACEI/ARB during the COVID19 pandemic?

BOTTOM LINE: Patients should continue taking their ACEI/ARB unless there is another reason to stop them. Patients with cardiovascular disease/diabetes should take extra precautions to avoid contracting COVID19.

Hypertension Canada statement: no evidence that patients with hypertension or those treated with ARB or ACE inhibitor antihypertensive therapy are at higher risk of adverse outcomes from COVID-19 infection, patients with hypertension to continue with their current blood pressure treatment.

These recommendations are echoed by the Canadian Cardiovascular Society, European Society of Cardiology, UK Renal Association, International Society of Hypertension, American College of Physicians, American Heart Association, American College of Cardiology, European Renal Association, and many others

What is the link with COVID19 and ACEI/ARBs?

- COVID19 uses Angiotensin Converting Enzyme 2 (ACE2) to gain cell entry
- In animal studies, cardiac ACE2 levels were increased with ACEI/ARB therapy. However, this may not correlate to tissue levels in the lungs, and human data shows no change in circulating ACE2 levels
- In a mouse trial with SARS coronavirus, the use of losartan (ARB) reduced lung injury
- It is not clear how ACE2 upregulation affects COVID19 at this time, and we do not know if there is benefit or harm from the use of ACEI/ARB use. There is currently a registered trial looking at losartan and COVID19

Are patients with hypertension/diabetes at a higher risk for COVID19 mortality?

- The data currently available is inconclusive as it is not adjusted for co-founders such as age or other co-morbidities
- Early data suggests that the most frequent comorbidities of patients with COVID19 are hypertension, CV diseases, and diabetes (all often treated with ACEi/ARB)
- It is currently unclear whether these patients are at higher baseline risk, higher risk due to the pathophysiology of their comorbidities or age, or higher risk due to treatments for these comorbidities
- COVID19 can sometimes present with cardiovascular symptoms and hypokalemia, with a large proportion of ICU admissions experiencing acute myocardial injury. These patients have a poor prognosis

Paper	Study Population	Proportion with HT?	Association of HT with outcomes?	Adjusted analysis?
Guan et al NEJM Jan 29 2020	N = 1099 552 Hospitals 30 Regions in China	165 (15%)	HT: 24% in those w/ severe dz vs 14 % among those w/ non-severe dz HT: 36% w/ 1 outcome* vs 14 % w/out 1 outcome	Not done
Huang et al Lancet Jan 22 2020	N = 41 Jinyintan Hospital Wuhan	6 (15%)	NR	
Wang et al JAMA Feb 3 2020	N = 138 Single centre Zhongnan Hospital Wuhan	43 (31%)	NR	
Zhang et al Allergy Feb 13 2020	N = 140 No. 7 Hospital Wuhan	42 (30%)	HT: 38% with severe dz 24% with non severe dz	Not done
Zhou et al Lancet March 9 2020	N = 191 Jinyintan and Wuhan Hospitals	58 (30%)	48% HT among died vs 23% HT among survived HR 3.05 (1.6 - 5.9)	HT not included in multivariable model
Wu et al JAMA IM March 13 2020	N = 201 Jinyintan Hospital Wuhan	39 (19.4%)	ARDS: HR 1.82 (95% CI 1.13 - 2.95) Mortality HR 1.70 (95% CI 0.92 - 3.13)	Bivariate cox regression; not multivariable adjusted for age and other factors

Table from Sparks MA, Hiremath S et al. "The Coronavirus Conundrum: ACE2 and Hypertension Edition" NephJC



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Should NSAIDs be avoided in patients with potential COVID19?

BOTTOM LINE: It is reasonable to avoid NSAIDs and consider acetaminophen as first line due to its safety profile when compared to NSAIDs. The impact of NSAIDs on the course of COVID19 is currently not known, and it appears safer to avoid using NSAIDs until more is known.

- The French health minister has advised against the use of NSAIDs, citing “serious adverse events related to the use of nonsteroidal anti-inflammatory drugs (NSAIDs) have been reported in patients with COVID19 or suspected cases”. This appears to stem from reports of 4 otherwise healthy young people who were taking NSAIDs and developed serious symptoms in the early stages of COVID19 infection.
- Several groups (Canadian Pharmacists Association, European Medicines Agency, Royal Pharmaceutical Society) highlight that there is little to no scientific evidence that NSAIDs increase the risk of complications in COVID19 at present
- There are many hypotheses surrounding how they may influence the course of disease (e.g. reduced antibody production, fluid/sodium dysregulation among others)
- NSAIDs have been linked with poorer outcomes for lower respiratory tract infections/pneumonia: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6617416/>
- Indomethacin has actually been found to have antiviral activity against the SARS coronavirus: <https://www.ncbi.nlm.nih.gov/pubmed/17302372>
- Confounding by indication: it is difficult to say whether the use of NSAIDs leads to increased susceptibility to COVID19, worse outcomes for COVID19, or if patients with more severe COVID19 infection are more likely to take NSAIDs
- Drugs that are cardiotoxic or that worsen cardiovascular disease (such as NSAIDs or certain antivirals) may precipitate poor outcomes in COVID19 infection
- Regardless of COVID19-status, NSAIDs should be used with caution in older adults or in patients with cardiovascular or renal disease.

Expert commentaries on the subject:

<https://www.sciencemediacentre.org/expert-reaction-to-reports-that-the-french-health-minister-recommended-use-of-paracetamol-for-fever-from-covid-19-rather-than-ibuprofen-or-cortisone/>

<https://twitter.com/DavidJuurlink/status/1239552349804339202>

<https://www.bmj.com/content/368/bmj.m1086>

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