EMA advice on renin-angiotensin system medicines during covid-19 pandemic

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Key learning points

- The European Medicines Agency (EMA) has responded to reports questioning whether use of angiotensin converting enzyme inhibitors (ACEI) or angiotensin II receptor antagonists (AIIRA) could worsen disease caused by coronavirus (covid-19).
- No clinical or epidemiological evidence has established that treatment with ACEI or AIIRA worsens covid-19.
- It is important that patients do not interrupt their treatment with ACEI or AIIRA inappropriately.

The European Medicines Agency (EMA) has issued advice on the use of ACEI and AIIRA medicines during the covid-19 pandemic.[1]

EMA advice

Following on from its statement on the use of NSAIDs in people with covid-19, the EMA has issued a response to reports that have questioned whether use of medicines that act on the renin-angiotensin-aldosterone system could worsen covid-19 disease.[1] The EMA is not aware of any evidence from clinical or epidemiological studies that has established a link between ACEI and AIIRA medicines and worsening of covid-19. The EMA has stated that patients should not stop taking their ACEI or AIIRA and that there is no need to switch to other medicines. The EMA statement cites guidance from the European Society of Cardiology's council on hypertension, which strongly recommends that patients continue treatment with their usual antihypertensive medication 'because there is no clinical or scientific evidence to suggest that treatment with ACEI or AIIRAs should be discontinued because of the covid-19 infection'.[2] The American College of Cardiology, the American Heart Association and the Heart Failure Society of America have also stated that there are no research or clinical data showing either beneficial or adverse effects of ACEI or AIIRAs in covid-19 or in patients with covid-19 with cardiovascular disease who have been treated with these medicines.[3] It advises that treatment should be continued for those patients 'who are currently prescribed such agents for indications for which these agents are known to be beneficial'. The British and Irish Hypertension Society advises that all patients taking ACEI and AIIRA should continue to do so during the covid-19 pandemic.[4] The EMA is monitoring the situation and collaborating to coordinate epidemiological studies on the impact of ACEI and AIIRAs in people with covid-19.[1]

Context

Covid-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and human pathogenic coronaviruses (SARS-CoV-1 and SARS-CoV-2) bind to their target cells through ACE2.[1 5 6] It has been suggested that the interaction between the SARS virus and ACE2 may play a role in its infectivity and disease virulence.[6] Although it has been hypothesised that medicines that increase expression of ACE2 may increase the risk of developing severe and fatal covid-19, this hypothesis requires further study and investigation and 'does not constitute a recommendation to use certain drugs or not'.[5 7]

A New England Journal of Medicine article discusses the complex role of ACE2 in animals and humans and the effect of medicines that act on the renin angiotensin system.[6] The authors note that there is a lack of data showing the effects of such medicines on lung-specific expression of ACE2 and no studies have evaluated their effect in covid-19. Of concern is the impact that stopping ACEI and AIIRA treatment might have on patients with heart failure, hypertension or ischaemic heart disease. The authors conclude that until further data are available, medicines that act on the renin angiotensin aldosterone system 'should be continued in patients in otherwise stable condition who are at risk for, being evaluated for, or with covid-19'.[6] A *British Medical Journal* editorial suggests that doctors advise patients taking ACEI/AIIRA for long-term benefits (eg, well controlled mild hypertension) to consider stopping ACEI/AIIRA if there is a high risk of infection and to stop ACEI/AIIRA if positive for covid-19.[8] However, the practicality of implementing such advice and the risks of stopping treatment are not clear.

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Provenance and peer review Commissioned; internally peer reviewed.

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DOI: 10.1136/dtb.2020.000026