NICE advice

COVID-19 rapid evidence summary: angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in people with or at risk of COVID-19

Evidence summary
Published: 21 May 2020
www.nice.org.uk/guidance/es24

Key messages

The content of this evidence review was up-to-date on 1 April 2020. See summaries of product characteristics (SPCs), British national formulary (BNF) or the MHRA or NICE websites for up-to-date information..

Angiotensin-converting enzyme 2 (ACE2) is abundant in the epithelial cells of the lung where it acts as a cell receptor and forms part of the renin-angiotensin pathway. Both angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) act on the renin-angiotensin pathway and are thought to upregulate ACE2 expression. ACE2 has 2 possible roles in COVID-19:

- Coronaviruses, including those responsible for Middle East respiratory syndrome (MERS), severe acute respiratory syndrome (SARS), and coronavirus disease (COVID-19), bind to ACE2 to gain access to the epithelial cells. Therefore, upregulation of ACE2 could theoretically increase a person's risk of COVID-19 or developing more severe COVID-19.
- Upregulation of ACE2 has been shown to be protective in acute respiratory disease and downregulation of ACE2 has been implicated in lung injury.

The purpose of this review is to assess the best available evidence to determine:

- If there is any increased risk of developing COVID-19 due to ACEIs or ARBs
- If ACEIs or ARBs can lead to an increased risk of developing more severe symptoms of COVID-19.

This review identified 2 retrospective observational studies that met the inclusion criteria. One paper reported no statistically significant difference in the proportion of patients using an ACEI or an ARB who had critical and non-critical COVID-19 (3/16 [18.8%] compared with 19/96 [19.8%] respectively, p=1.00) (Peng et al 2020).

Alburikan et al 2020 reported that, in patients tested for MERS-CoV, ACEI or ARB prescribing was not associated with an increase or decrease in the likelihood of testing positive for MERS-CoV. ACEIs or ARBs were prescribed in 16% of suspected cases and 15% of confirmed cases, p=0.40.

Whilst no increase in risk of developing COVID-19 or more severe disease was found in the 2 observational studies included, the studies were of poor quality and subject to bias and confounding. Therefore, conclusions cannot be drawn on whether ACEIs or ARBs increase the risk of developing COVID-19 or developing more severe COVID-19.

Factors for decision making

Discussion and limitations of the evidence

The studies included in this evidence review are observational studies, which can be subject to bias and confounding and have many limitations affecting their application to clinical practice. Retrospective observational studies are subject to data being recorded accurately, completely and consistently. This type of study cannot reliably answer the research questions: the results can only be considered hypothesis generating and cannot support any definitive conclusions.

As SARS-CoV-2 (the virus that causes COVID-19) is a novel virus and new data are emerging every day, the search was expanded to include indirect evidence to inform the background. In addition to the 2 studies presented, this summary reviews letters published in peer-reviewed journals on the biological plausibility of the role of ACEIs and ARBs in COVID-19.

The conclusions of these letters were primarily based on data from in-vitro and animal models. Furthermore, the correspondence is conflicting and puts forward arguments for both stopping and using ACEIs and ARBs in COVID-19. Some letters also referenced epidemiological data in which conditions commonly treated with ACEIs or ARBs, (such as hypertension, diabetes and coronary heart disease), were shown to be associated with an increased risk of COVID-19 and more severe COVID-19. Such extrapolation is subject to bias and there are many known confounders associated with ACEI and ARB prescribing, developing COVID-19 and severity of COVID-19 (such as age, diabetes, hypertension, obesity and smoking).

Conclusion

Despite biological plausibility for the role of ACEIs and ARBs in both increasing and decreasing the risk of COVID-19 and its complications, this evidence review has not found any observational or experimental data to support these hypotheses. However, the risks of stopping treatment with an ACEI or an ARB, such as worsening heart failure or hypertension, are well understood.

See the full evidence review for more information.

Commissioned by NHS England

ISBN: 978-1-4731-3764-6