Renin–angiotensin–aldosterone system inhibitors and severe outcomes in patients with COVID-19

Synopsis

Use of angiotensin converting enzyme inhibitors (ACE-Is) and angiotensin II type-I receptor blockers (ARBs) may increase the risk of developing severe or fatal corona virus disease 2019 (COVID-19) by upregulating expression of the ACE2 enzyme, which is known to facilitate viral entry into cells. Case series have reported a high prevalence of hypertension, cardiovascular disease, and diabetes among patients hospitalized with severe COVID-19 – conditions often associated with prescription of ACE-Is/ARBs. This has sparked concerns among physicians and patients if ACE-Is and ARBs should be withdrawn in patients with COVID-19.

The European Medicines Agency and the European Society of Cardiology and other authorities have recommended that based on the available evidence, ACE-Is and ARBs should be maintained in patients with cardiovascular disease or hypertension, irrespective of SARS-CoV-2 infection, but called for additional research. Potential for benefit rather than harm of ACE-Is/ARBs in COVID-19 has also been hypothesized, as these drugs may protect against lung injury and have cardioprotective effects.

The health impact of discontinuing ACE-Is and ARBs in patients with COVID-19 is huge, as the drugs are indicated for their pre-existing medical conditions. There is therefore an urgent need to determine the impact of ACE-Is and ARBs on the prognosis of COVID-19. We therefore propose to determine the association between ACE-Is/ARBs use and severe outcomes following hospitalization for COVID-19.

The study population includes hospitalised patients with verified COVID-19. We will investigate the association between current use of ACE-Is/ARBs and the risk of severe outcomes including admission to an intensive care unit, mechanical ventilation, dialysis, and death.

Priority

The research project will address several of the prioritized research aims including addressing an acute research question with limited preexisting evidence, providing evidence on rational use of drugs during COVID-19, and being of public health importance because of the prevalent use of ACE-I/ARBs and potential severe adverse outcomes.

Research group

The research group consists of researchers from the Department of Clinical Epidemiology at Aarhus University, from the pharmacoepidemiology unit at Clinical Pharmacology and Pharmacy at University of Southern Denmark, from Statens Serum Institut, and from Aarhus and Aalborg University Hospitals. Other potential collaborators may be included in the research group if they fulfil the ICMJE criteria for authorship. The research project will be led by professor Henrik Toft Sørensen on behalf of the above research group, together with professor Hans Erik Bøtker on behalf of the cardiological chairs at the Danish universities. The group has documented substantial research experience in academic, industry, and regulatory pharmacoepidemiological drug-safety studies, including in the areas of cardiovascular disease and infections.

Conflicts of Interest

Henrik Toft Sørensen reports that the Department of Clinical Epidemiology is involved in studies with funding from various companies as research grants to (and administered by) Aarhus University. None of these studies are related to the current study.

Conflict of interest statement from other researchers involved in the project will be identified and submitted as soon as possible.