

Impact of use of proton pump inhibitors on susceptibility to infection and risk of severe outcomes in patients with COVID-19

Synopsis

Since the COVID-19 epidemic was introduced in Denmark, measures have been taken to contain the spread and fight the disease. Studies from China and Italy describe that risk of severe or fatal COVID-19 disease increase with age, male sex and certain comorbid disease^{1,2}. The observed risk varied in the populations implying that the results are not necessarily transferable to other countries. This poses a great need to confirm known risk factors and identify unknown risk factors in a Danish population.

Concern has been raised regarding antihypertensives and non-steroidal anti-inflammatory drugs (NSAIDs) via their suspected upregulation of ACE-2 receptors, but international recommendations have not yet been modified due to limited scientific evidence^{3,4}. Other medication possibly related to the host's susceptibility to pneumonia include proton pump inhibitors (PPIs) that reduce the protective stomach acid production.

Proton pump inhibitors have previously been associated with increased risk of infection in a meta-analysis from 2015 which showed that the risk of acquiring pneumonia and being admitted to hospital due to pneumonia was increased in persons receiving PPI⁵.

This project thus seeks to clarify susceptibility to infection and risk of severe outcomes in patients with COVID-19 when using proton pump inhibitors. Severe outcomes include hospitalization, intensive care unit (ICU) admission, mechanic ventilation, and death.

Perspective

This project could possibly fulfill several of the research aims as positive findings may form the basis for considerations of revised use of proton pump inhibitors by particular risk groups during epidemics with COVID-19. Proton pump inhibitors are widely prescribed medication in Denmark with almost 600.000 individually redeemed prescriptions in 2018⁶. Furthermore, association between use of the specific medications and the presence of COVID-19 or the risk of severe course of the disease will assist healthcare professionals in identifying patients at particular risk. Finally, both positive and negative outcomes of this project will contribute to the overall international and national knowledge of risk factors for developing severe COVID-19 disease.

Project group description

The project group consists of researchers from the Department of Infectious Diseases at Hvidovre Hospital and is led by professor Thomas Benfield, MD DMSc. The group members include a PhD-student, a postdoctoral fellow and a biostatistician. The group has substantial documented research experience in epidemiology and pharmacoepidemiology.

Conflict of interest statement

None.

References

1. Zhou, F. *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* **395**, 1054–1062 (2020).
2. Yang, X. *et al.* Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* (2020) doi:10.1016/S2213-2600(20)30079-5.
3. Dansk Cardiologisk Selskab. *Behandling med ACE-I og ARB i forbindelse med COVID-19.*
<https://www.cardio.dk/covid-19-position-statement-regarding-ace-i-and-arb> (2020).
4. European Medicines Agency. EMA gives advice on the use of non-steroidal anti-inflammatories for COVID-19. (2020).
5. Lambert, A. A. *et al.* Risk of community-acquired pneumonia with outpatient proton-pump inhibitor therapy: a systematic review and meta-analysis. *PLoS ONE* **10**, e0128004 (2015).
6. Sundhedsdatastyrelsen. *Medstat.dk (Antal personer i primærsektoren med brug af ATC-kode A02BC 'Protonpumpe-hæmmere').*
https://medstat.dk/da/viewDataTables/medicineAndMedicalGroups/%7B%22year%22:%5B%222018%22%22,%22region%22:%5B%220%22%22,%22gender%22:%5B%22A%22%22,%22ageGroup%22:%5B%22A%22%22,%22searchVariable%22:%5B%22people_count%22%22,%22errorMessagees%22:%5B%22%22,%22atcCode%22:%5B%22A02BC%22%22,%22sector%22:%5B%220%22%22%7D (2018).