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

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Study Finalised

Administrative details

EU PAS number

EUPAS35835

Study ID

41088

DARWIN EU® study

No

Study countries

☐ Denmark

Study description

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. 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. Other medications 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 PPI. This study is a Danish nationwide registry-based study. We aim to examine the association between current use of PPI and risk of SARS-CoV-2 infection in patients tested for SARS-CoV-2 (in a case-control design) and risk of hospitalisation, mechanical ventilation, intensive care unit admission and death among patients with confirmed COVID-19 (in a cohort design), respectively. All individuals tested positive for SARS-CoV-2 will be followed from the date of positive test until hospital admission, date of death, or for up to 90 days. Current use of PPI is defined as redeemed prescription for PPI within the prior 90 days. Odds ratios will be estimated for both the primary outcome (hospital admission) and the secondary outcome (SARS-CoV-2 infection, severe outcomes).

Study status

Finalised

Research institutions and networks

Institutions

Pharmacoepi center, University of Southern Denmark

Denmark

First published: 22/04/2010

Last updated: 27/07/2023

Institution | Educational Institution | ENCePP partner

Center of Research & Disruption in Infectious Diseases (CREDID), Department of Infectious Diseases, Amager Hvidovre Hospital Denmark

Contact details

Study institution contact

Simone Bastrup Israelsen

simone.elisabeth.bastrup.israelsen.02@regionh.dk

Study contact

simone.elisabeth.bastrup.israelsen.02@regionh.dk

Primary lead investigator

Simone Bastrup Israelsen

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 22/04/2020

Study start date
Actual: 27/02/2020

Data analysis start date
Planned: 16/07/2020

Date of final study report
Planned: 01/10/2020

Actual: 07/05/2021

Sources of funding

- Other

More details on funding

Erik and Susanna Olesen's Public Charity Fund

Study protocol

Impact of use of proton pump inhibitors on susceptibility to infection_v1.4_15.07.2020.pdf (322.14 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

The main objective of the study is to examine the association between concomitant use of PPI and risk of SARS-CoV-2 infection in patients tested for

SARS-CoV-2 and risk of hospitalisation, intensive care unit (ICU) admission, mechanical ventilation and death among patients with confirmed COVID-19, respectively.

Study Design

Non-interventional study design

Cohort

Case-control

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A02BC) Proton pump inhibitors

Proton pump inhibitors

Medical condition to be studied

COVID-19

Suspected COVID-19

Population studied

Short description of the study population

The study population consists of all patients tested for SARS-CoV-2 in the case-control design investigating the risk of infection. In the cohort design, the study population comprises patients with a positive test for SARS-CoV-2 examining the risk of hospitalisation and severe outcomes.

Age groups

- Term newborn infants (0 – 27 days)
- Infants and toddlers (28 days – 23 months)
- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)
- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

Estimated number of subjects

230000

Study design details

Outcomes

The primary outcome is hospital admission within 30 days after positive test for SARS-CoV-2 or a positive test for SARS-CoV-2 within 48 hours of hospital admission in patients already admitted before the date of the test, Secondary outcomes comprise ICU admission, mechanical ventilation and death within 30 and 90 days after positive SARS-CoV-2 test. In the risk of infection analysis, the outcome is a positive SARS-CoV-2 test among all patients tested during the study period, and where the negative tests are included as potential controls.

Data analysis plan

We will estimate odds ratios for hospital admission and severe outcomes in patients with positive SARS-CoV-2 test for the exposed group (current PPI use) relative to the unexposed group by using logistic regression. In the case-control

design, we will perform conditional logistic regression to examine a possible association between current PPI use and COVID-19 susceptibility, and results will be presented as odds ratios with 95% confidence intervals. In the nested case-control study, confounding by age, sex and calendar time will be handled by virtue of the risk set sampling and the matched analysis. Other potential confounders will be handled by multivariable modelling. In the cohort analysis, we will apply matching to adjust for pre-existing differences in significant risk factors between the exposed and unexposed groups. Matching will be performed by use of propensity scores. Sensitivity analysis will be performed on patients with current vs. past vs. never PPI use.

Documents

Study publications

Israelsen SB, Ernst MT, Lundh A, Lundbo LF, Sandholdt H, Hallas J, Benfield T. ...

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

Danish registries (access/analysis)

Data source(s), other

The Danish Microbiology Database Denmark

Data sources (types)

Disease registry

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No