USE OF DRUGS ACTING ON RENIN-ANGIOTENSIN SYSTEM (RAS) AND RISK OF COVID-19: A CASE-POPULATION STUDY (SRAA-COVID19)

First published: 31/03/2020

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Study Ongoing

Administrative details

PURI

https://redirect.ema.europa.eu/resource/34501

EU PAS number

EUPAS34437

Study ID

34501

DARWIN EU® study

No

Study countries

Spain

Study description

The coronavirus SARS-CoV-2 uses the protein ACE2 (angiotensin converting enzyme 2) as the receptor binding domain for its protein S (spike) to gain entry into cells and replicate. Blockers of the renin-angiotensin system (RAS) have been reported to upregulate the expression of ACE2 and this observation has raised the hypothesis that the use of these drugs could facilitate COVID-19 infection and/or make it more serious. Yet, the epidemiological evidence is lacking. The aim of this project is to carry out a quick case-population study using patients admitted to hospital with a diagnosis of COVID-19 as cases and a random sample of patients from a primary care database as the control series matched with cases for exact age, sex, and month-day (10 controls per case). Information on comorbidities and drugs used in the last month (current use) will be extracted from the clinical records in both cases and controls. We will examine the association of COVID-19 with the current use of RAS blockers as compared to non-use and as compared to current use of other antihypertensive drugs by computing the adjusted Odds Ratio through a conditional logistic regression model. The feasibility of selecting a secondary series of COVID-19+ cases who were not admitted to hospital (milder cases) will be assessed.

Study status

Ongoing

Research institutions and networks

Institutions

Hospital Universitario Príncipe de Asturias

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Puerta de Hierro-Majadahonda University Hospital

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Hospital Clinico San Carlos

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency for Medicines and Medical Devices, AEMPS)

Spain

First published: 01/02/2024

Last updated: 04/09/2024

Institution | EU Institution/Body/Agency | Not-for-profit | Regulatory Authority | ENCePP partner

Hospital Universitario Ramón y Cajal Madrid, Hospital Central de la Defensa Madrid, Hospital Clínico San Carlos Madrid, Hospital Universitario de la Princesa Madrid, Hospital Universitario Puerta de Hierro-Majadahonda Madrid, Hospital Universitario de Getafe Madrid

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Francisco José de Abajo Iglesias

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 18/03/2020

Actual: 18/03/2020

Study start date
Planned: 18/03/2020

Actual: 18/03/2020

Data analysis start date
Planned: 13/04/2020

Date of interim report, if expected
Planned: 06/04/2020

Date of final study report
Planned: 30/04/2020

Sources of funding

- Other

More details on funding

Instituto de Salud Carlos III

Study protocol

ACE2_COVID-19_V5_2.pdf(440.28 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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Main study objective:

To assess the association of renin-angiotensin system (RAS) blockers and non-steroidal anti-inflammatory drugs (NSAIDs) with hospital admission due to COVID-19 infection adjusted for age, sex, and cardiovascular risk factors.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Case-population study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(C03DA) Aldosterone antagonists

Aldosterone antagonists

(C09) AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

(M01AA) Butylpyrazolidines

Butylpyrazolidines

(M01AB) Acetic acid derivatives and related substances

Acetic acid derivatives and related substances

(M01AC56) meloxicam, combinations

meloxicam, combinations

(M01AE01) ibuprofen

ibuprofen

(M01AE02) naproxen

naproxen

(M01AG) Fenamates

Fenamates

(M01AH) Coxibs

Coxibs

(M01AX) Other antiinflammatory and antirheumatic agents, non-steroids

Other antiinflammatory and antirheumatic agents, non-steroids

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Medical condition to be studied

Coronavirus infection

Additional medical condition(s)

COVID-19

Population studied

Age groups

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

11000

Study design details

Outcomes

- Hospital admission due to COVID-19- Hospital admission to the intensive care unit (ICU) due to COVID-19- In-hospital death after admission due to COVID-19- Admission to ICU or in-hospital death (combined)

Data analysis plan

Main analysis:Crude odds ratios (ORs) and their 95% confidence intervals (CIs) will be computed through univariate conditional logistic regression to assess the association of current use of RAS blockers with the outcome of interest as compared to non-use and as compared to other antihypertensive drugs. After that, we built a multivariate model including the potential confounders (other comorbidities and comedications) all at once. Intermediate analyses: Intermediate analyses will be performed at different points along the study

when the number of cases included are: 100, 500 and 750.Sensitivity analysis: Two sources of information from different years will be used (2020 for cases and 2018 for controls). To correct for a secular trend in the prevalence of antihypertensive drugs, we will estimate the prevalence for 2020 and we will obtain a correction factor to adjust the odds ratios for.

Data management

Data sources

Data source(s)

BIFAP - Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)

Data sources (types)

Electronic healthcare records (EHR)

Other

Data sources (types), other

Electronic medical records from the participating Hospitals

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