ADDITION OF ANTIBIOTICS TO USUAL CARE MANAGEMENT OF ASTHMA EXACERBATIONS: A REALLIFE COMPARATIVE EFFECTIVENESS STUDY

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Last updated: 02/07/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/39106

EU PAS number

EUPAS12132

Study ID

39106

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

Asthma exacerbations are major contributors to asthma morbidity and mortality (and related costs). Their management presents a major clinical need that is not adequately met by current approaches. Respiratory viruses (especially rhinovirus) are the most common causes of asthma exacerbations and may be involved in the pathogenesis of chronic asthma in children, but there are other factors can increase the risk/severity of exacerbations. Recently evidence suggests atypical bacterial infections (such as Mycoplasma pneumonia and Chlamydophila) may also contribute to exacerbation severity. A recent randomised controlled (RCT) trial of telithromycin in adult patients (n=278) with acute exacerbations of asthma found a significant reduction in asthma symptoms among patients receiving add-on telithromycin compared with placebo. The mechanism or mechanisms of action was/were not determined. A second recent open-label randomised study, evaluating the effect of clarithromycin in children (n=40) with acute asthma suggests its use as add-on therapy may offer benefit over standard exacerbation treatment alone. Children in the trial were randomized to receive 15mg/kg of clarithromycin for 21 days in addition to their regular (GINA-guided) exacerbation treatment. Children were followed up with diary cards for 12 weeks, lung function was assessed at entry and at 3 and 12 weeks post exacerbation. Compared with controls, children receiving clarithromycin had an increase in their number of symptom-free days, a reduction in the number and severity of days with loss of control following index episode, and a decrease in the duration of the initial asthma exacerbation. Lung function did not differ between groups. These RCT findings warrant further exploration in larger more representative adult and paediatric routine care populations.

Study status

Finalised

Research institutions and networks

Institutions

Observational & Pragmatic Research Institute Pte (OPRI)

☐ United Kingdom

First published: 06/10/2015

Last updated: 19/08/2024

Institution | **Educational Institution** | **Laboratory/Research/Testing facility** | **ENCePP partner**

Networks

Respiratory Effectiveness Group (REG)

☐ Belgium
☐ Denmark
☐ France
☐ Germany
☐ Greece
☐ Hungary
☐ Italy

☐ Netherlands

☐ Spain

☐ Sweden

☐ United Kingdom

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Network | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 29/01/2016

Actual: 01/01/2017

Study start date

Planned: 15/02/2016

Actual: 01/07/2017

Date of final study report
Planned: 12/10/2016

Actual: 01/12/2020

Sources of funding

- Other

More details on funding

Respiratory Effectiveness Group

Study protocol

REG Study Protocol_Effect of Abx on Paeditric Asthma Exacerbation Outcomes.pdf(521.77 KB)

REG Study Protocol_Effect of Abx on Paeditric Asthma Exacerbation Outcomes_final version.pdf(505.87 KB)

Regulatory

Was the study required by a regulatory body?

Unknown

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

Not applicable

Methodological aspects

Study type

Study topic:

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The aim of the proposed study is to evaluate the comparative effectiveness of managing asthma exacerbations with oral steroids alone versus combination antibiotics and oral steroids in paediatric and adult asthma populations. Secondary objectives of the study will be to explore the differential usage and associated outcomes of different classes of antibiotics, as used in this context.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Observational, historical database study, Prospectively planned comparative effectiveness study drawing on retrospective EMRs from the OPCRD

Study drug and medical condition

Medical condition to be studied

Asthma

Population studied

Short description of the study population

To be eligible for inclusion in the study, patients must meet the following criteria:

• Be aged between 2–65 years at IPD.

• Have had ≥3 wheezing episodes ever

• Have:

o Patients ≥5 years: physician-diagnosed asthma (i.e. Read code for asthma)

o Patients <5 years: ≥1 coded asthma or wheezing episode in the baseline 6 months

• Received ≥1:

o Patients ≥5 years: inhaled corticosteroid (ICS) prescription in the baseline 6 months

o Patients <5 years: asthma or wheeze prescriptions in the baseline 6 months, where a “wheeze prescription” will be a maintenance/preventer therapy (e.g. ICS, LTRA, ICS/LABA). Releiver therapies (e.g. short-acting bronchodilators) will not be classified as “wheeze prescriptions”.

• ≥38 weeks continuous records: ≥26 weeks prior to IPD (baseline 6-months) and ≥12 weeks following IPD (12-week primary outcome).

Exclusion criteria

In order to provide the fullest picture of UK primary care prescribing practice possible, few patients will be excluded. The only exclusion that will be applied will aim to avoid confusion between index and outcome events associated with asthma and those associated with other chronic comorbidities:

Patients will be excluded if they meet the following criteria:

• Are receiving chronic antibiotics for other chronic respiratory conditions (e.g. cystic fibrosis, PCD, bronchiectasis)

• Are on maintenance oral steroids (for any reason)

Age groups

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Special population of interest

Other

Special population of interest, other

Asthma patients

Estimated number of subjects

50000

Study design details

Outcomes

1a. Primary care consultations coded for asthma / wheeze 1b. Primary care consultations coded for asthma / wheeze resulting in an antibiotic prescription1c. Primary care consultations coded for asthma / wheeze resulting in an oral steroid prescription1d. Primary care consultations coded for asthma / wheeze resulting in both an antibiotic and an oral steroid, 2a. Primary care consultations coded for asthma / wheeze resulting in a prescription for a short-

acting bronchodilator (SABA) 2b. Consultation for asthma / wheeze resulting in a SABA2c. Hospitalisations for lower respiratory complaints2d. Accident & Emergency (A&E) / Emergency Room (ER) attendance for lower respiratory complaints.

Data analysis plan

Matching, often used to minimise potential confounding by severity, will not be possible as it would required matching on multiple events per person. Three potential options have been identified:• Approach 1: a repeated measurements analysis • Approach 2: a survival analysis considering time to event following the index event, (for all events).• Approach 3: using each patient as their own control to evaluate different time to next event for patient depending on their index prescription (e.g. comparative time to next event for each patient when prescribed oral steroids only versus oral steroids + antibiotics).

Documents

Study publications

Murray CS, Lucas SJ, Blakey J, et al. A real-life comparative effectiveness stu...

Data management

Data sources

Data source(s)

Optimum Patient Care Research Database

Data sources (types)

Electronic healthcare records (EHR)

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