A strategy of bacterial eradication to prevent exacerbations of COPD in the frequent exacerbator phenotype population (GOAL study), a prospective randomized controlled pilot study

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Investigation of the impact of a treatment consisting of inhalation antibiotics and prolonged oral antibiotic course during a bacterial exacerbation on the prevention of further exacerbations.

Ethical review	Not approved
Status	Will not start
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON50113

Source
ToetsingOnline

Brief title
The GOAL Study

Condition

- Bacterial infectious disorders
- Bronchial disorders (excl neoplasms)

Synonym
chronic bronchitis, COPD

Research involving
Human

Sponsors and support

Primary sponsor: Amphia Ziekenhuis
Source(s) of monetary or material Support: Amphia + Chiesi,Chiesi Farmaceutici

Intervention

Keyword: COPD, Eradication, Exacerbations, Inhaled-antibiotics

Outcome measures

Primary outcome

time to next exacerbation, mean number of exacerbations in 6 month follow-up

Secondary outcome

Number of exacerbations

- Number of hospital admissions in 6 months

- Bacterial eradication measured by 3 different negative sputum cultures during

6 months

- Lung function: FEV1; FVC

- Quality of life

Study description

Background summary

Chronic obstructive pulmonary disease (COPD) is frequently aggravated by exacerbations (AECOPD)*short periods (at least 48 h) of increased cough, dyspnoea, and production of sputum. Exacerbations have a negative effect on disease prognosis. Therefore, a primary goal of treatment is to reduce the number of exacerbations. Until now long acting antimuscarinic agents (LAMAs), long acting * agonists (LABAs) and inhaled corticosteroid-LABA combination inhalers significantly reduced AECOPD. However, some patients remain experiencing 2 or more AECOPD (frequent exacerbator phenotype). Three prospective randomised double-blind studies showed that maintenance treatment with macrolides significantly decreased exacerbation rate. However, the development of macrolide resistance related to this treatment is a major

concern. Therefore, alternative strategies should be developed, which could prevent AECOPD.
One of these strategies could be directed at eradicating the bacterial causative agent of an exacerbation. It has been shown that in patients admitted to hospital for AECOPD, bacterial infections were detected in 54.7 % of cases and, more importantly, that the exacerbations were more severe than those in patients with non-infectious causes. It has also been demonstrated that patients with a positive sputum culture suffered more exacerbations per year than did patients with the same degree of lung function impairment but without a positive bacterial sputum culture. These findings emphasize the importance of intensive antibiotic treatment able to eradicate bacteria that causes the exacerbation, preventing further exacerbations.
Studies in Cystic fibrosis have shown, that intensive antibiotic therapy aimed at eradication of Pseudomonas aeruginosa was effective in preventing and delaying the onset of chronic infection.
In this study we hypothesize that an antibiotic treatment strategy consisting of 14 days of oral antibiotics during a bacterial AECOPD combined with 28 days of inhaled Levofloxacin could result in a delayed onset of a new exacerbation.
A bacterial exacerbation will be defined by the presence of an increased Procalcitonin (PCT) value >0.25 µg/L or CRP value > 50 mg/L.

Study objective

Investigation of the impact of a treatment consisting of inhalation antibiotics and prolonged oral antibiotic course during a bacterial exacerbation on the prevention of further exacerbations.

Study design

A prospective randomized controlled, open label, single center trial

Intervention

These patients will be randomized into:
1.Treatment with Levofloxacin inhalation twice daily 240 mg for 28 days administered via PARI LC PLUS jet nebuliser and oral antibiotics during 7 days
Or
2.Standard treatment with 7 days of oral antibiotics

Added to the standard care for patients admitted with an AECOPD

Study burden and risks

A number of pulmonary adverse events such as coughing and bronchospasm can occur with outpatient use of aerosolized antibiotics. Benefit: possible reduction in exacerbations and admissions because of an AECOPD, improvement of

other important clinical outcome parameters and improved eradication of microorganisms.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- COPD patients, who were 18 years or older, hospitalized with an exacerbation for
which they need to receive corticosteroids and antibiotic treatment.
- COPD patients with 1 or more exacerbations in the previous year before admission
for which they received steroids and/or antibiotic treatment.
- FEV1 less than 80% of predicted, FEV1 to FVC ratio < 0.7 and a history of smoking

- Procalcitonin value >0.25 µg/L or CRP value > 50 mg/L

Exclusion criteria

- History of fluoroquinolon hypersensitivity or adverse reaction to inhaled fluoroquinolones
- A history of other significant respiratory diseases (e.g. asthma, cystic fibrosis), the
presence of bronchiectasis assessed by computed tomography (CT), pregnant or lactating women, malignancy of any kind for which the subject received treatment or was being monitored as part of follow up after treatment,

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Augmentin
Generic name:	Amoxicillin/clavulanic acid
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Quinsair
Generic name:	levofloxacin
Registration:	Yes - NL outside intended use

Ethics review

Not approved

Date:	15-02-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-003967-24-NL
CCMO	NL72084.078.20