Exhaled Markers in COPD during viral and/or bacterial induced Exacerbations

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Part I (cross-sectional study)1. To identify breathprints of VOCs by electronic nose in exhaled air that are associated with a bacterial origin of an exacerbation in COPD patients. 2. To examine the critical VOCs of these breathprints in exhaled air...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Respiratory disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON42952

Source
ToetsingOnline

Brief title
MACE study

Condition

- Respiratory disorders NEC

Synonym
COPD

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Biomarkers, COPD, Electronic nose, Exhaled breath analysis

Outcome measures

Primary outcome

Part I

Breathprints obtained by SpiroNose of patients during an exacerbation of COPD with or without bacterial infection. Bacterial infection will be defined as colony-forming units >107/mL sputum or >105/mL in S. pneumonia [36].

Part II

Changes in breathprints obtained by SpiroNose of patients during exacerbation and recovery with or without viral, bacterial, viral and bacterial, or absence of infection. A virus was deemed present when either the sputum or naso-pharyngeal swap tested positive by PCR [31].

Secondary outcome

Secondary study parameters (part I and II):

• Specific molecular components (VOCs), which are, associated with the different origins of exacerbation of COPD patients as determined by gas-chromatography and mass-spectrometry (GC-MS). We will determine: retention time, abundance and the mass-to-charge ratio.

• Individual cellular and molecular biomarkers in sputum and blood. We will determine CRP, a complete blood count including differentiation, inflammatory

markers, cytokines and chemokines.

Study description

Background summary

COPD patients frequently exacerbate. Consequently, clinicians often empirically prescribe broad spectrum antibiotics, which may or may not have been indicated. The origin of the exacerbation might indeed be bacterial but can also be viral, in which antibiotics are not useful. Currently, information on the underlying cause of an exacerbation can only be available after 3 days. Therefore, there is an urgent need for a quick and reliable test at point-of-care to assess the origin of an exacerbation. We hypothesize that comprehensive analysis of the mixture of volatile organic compounds (VOCs) in exhaled air (breathprints) qualifies for this.

The present study has two parts. Part I is clinically focused and is testing the accuracy of exhaled VOC analysis in relation to bacterial infection at single clinical presentation of a COPD exacerbation. Part II is pathophysiologically oriented, examining the longitudinal changes in VOCs at clinical recovery and the association of exhaled VOCs with respiratory virus infection.

Study objective

Part I (cross-sectional study)
1. To identify breathprints of VOCs by electronic nose in exhaled air that are associated with a bacterial origin of an exacerbation in COPD patients.
2. To examine the critical VOCs of these breathprints in exhaled air by gas chromatography and mass spectrometry (GC-MS).
3. To identify specific VOCs by GC-MS analysis of in vitro headspace samples obtained from expectorated sputum.
4. To identify individual biomarkers in sputum and blood that are associated with COPD exacerbations and electronic nose (eNose) and GC-MS breathprints to help unravel the underlying pathophysiological pathways.

Part II (longitudinal study)
1. To identify breathprints of VOCs by electronic nose in exhaled air that are associated with a viral, bacterial, viral and bacterial or other origin of an exacerbation in COPD patients.
2. To identify within-subject changes in these breathprints of VOCs by electronic nose in exhaled air between exacerbation and recovery.
3. Objectives 2, 3 and 4 described under part I also apply for the changes in

breathprints in part II.

Study design

Part I will be a cross-sectional, observational study, requiring 62 GOLD I-IV COPD patients presenting with an acute exacerbation at the two referral hospitals (MST and AMC). Part II will be a prospective follow-up study including an exacerbation- and a recovery visit, requiring another 334 COPD patients, adding up to 396 patients in total. Patients will be divided into a training cohort (allowing internal validation) and a validation cohort (for independent, external validation).

Study burden and risks

The burden of the study procedures can be considered minimal and without risks for all patients. Part I: Adult patients will be asked for a spontaneous sputum sample and venous blood sample (part of regular care) and an exhaled breath sample and nasal-pharyngeal swab during an unscheduled visit to AMC or MST for an exacerbation. Part II: During a second, regular monitoring visit (< 4 months after exacerbation) at clinical recovery exhaled breath sampling will be repeated, together with spontaneous sputum sample, a venous blood sample and a nasal-pharyngeal swab. When there is no regular monitoring visit planned within 4 months after exacerbation, the patient will be contacted to schedule an extra visit.

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

a. >= 40 years
b. Smoking history >=10 pack years
c. COPD patients (GOLD stage II-IV) according to GOLD guidelines
d. Meeting the criteria for an exacerbation at inclusion

Exclusion criteria

• History of other pulmonary disease
• Systemic steroid or antibiotic therapy for > 24 hours

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	396
Type:	Anticipated

Medical products/devices used

Generic name:	SpiroNose
Registration:	No

Ethics review

Approved WMO Date:	17-06-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
CCMO	NL57068.018.16