Volatile organic compounds as a biomarker in immune-mediated pulmonary arterial hypertension

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Primary Objective: 1. to determine unique inflammatory VOC profiles that distinguish patients with PAH-CTD, CTEPH and IPAH from SSc and SLE (CTD) patients without PAH. Secondary objectives:1. to test whether these unique inflammatory VOCs associates...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON52988

Source
ToetsingOnline

Brief title
Volatile organic compounds and pulmonary arterial hypertension

Condition

- Autoimmune disorders
- Vascular hypertensive disorders

Synonym
high blood pressure in the arteries from heart to lungs, Pulmonary arterial hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Guy Peeters fonds en de Stichting ter

bevordering onderzoek en onderwijs Klinische Immunologie (eigen afdeling)

Intervention

Keyword: Biomarker, Pulmonary arterial hypertension, Systemic sclerosis, Volatile organic compounds

Outcome measures

Primary outcome

Determining unique inflammatory VOC profiles in four different groups of

patients: PAH-CTD patients, CTEPH patients, IPAH patients and SSc/SLE patients

without PAH.

Secondary outcome

Unique inflammatory VOCs will be studied in relation to well-established

biomarkers of immune activation and inflammation in PAH-CTD and idiopathic PAH.

To this end, the selective inflammatory VOCs will be compared with baseline VOC

profiles after 3, 6 and12 months in all patients treated with PAH medication

and/or immunosuppressive therapy.

Study description

Background summary

Pulmonary arterial hypertension (PAH) is a progressive disorder involving the pulmonary vasculature that leads to right heart failure and death. In idiopathic PAH (IPAH) and connective tissue disease associated PAH (PAH-CTD) (including systemic sclerosis) has the role of altered immunity and inflammation increasingly been recognized in earlier studies. Recently also inflammatory factors are described in chronic thromboembolic PH (CTEPH).The role of immunosuppressive therapy is currently still unclear. Consequently, a better understanding of inflammatory pathways and their role in the pathogenesis of PAH may lead to targeted therapeutic approaches. In this study, the analysis of exhaled air will be used as a biomarker of inflammation and autoimmunity in patients with autoimmune PAH in systemic sclerosis, SLE

(together CTD-PAH), in CTEPH patients and in IPAH. The analysis of exhaled air is known to contain a complex mixture of volatile organic compounds (VOCs). The occurrence of inflammation, and subsequent oxidative stress, can result in the excretion of specific volatile compounds that generate unique VOC patterns. Our study uses VOC profiles of patients with CTD-PAH, CTPEH patients and patients with IPAH to investigate their role as a biomarker in immune-mediated PAH. Further, VOC profiles of PAH-CTD patients will be compared with those of SSc/SLE patients without pulmonary hypertension.

Study objective

Primary Objective:
1. to determine unique inflammatory VOC profiles that distinguish patients with PAH-CTD, CTEPH and IPAH from SSc and SLE (CTD) patients without PAH.

Secondary objectives:
1. to test whether these unique inflammatory VOCs associates with well-established serum biomarkers of inflammation and autoimmunity in PAH as was demonstrated earlier. Markers which will be used:
- pro-inflammatory biomarkers (hsCRP, IL-6, CCL2, CXCL4)
- vascular biomarkers (VEGF, von Willebrand factor)
- IgG auto-antibodies against endothelial cells (AECAs)
2. to investigate whether unique inflammatory VOC products in all four groups of patients are affected by PAH and/or immunosuppressive therapy during 12 months follow-up.

Study design

The study is performed in patients with PAH-CTD, CTEPH, IPAH and patients with SSc or SLE (CTD) without PAH.
The first baseline phase of two weeks is a cross-sectional study where baseline VOC profiles will be determined in patients with PAH-CTD, CTEPH, IPAH and patients with SSc or SLE (CTD) without PAH.
In the second follow-up phase, a explorative pilot study is performed to evaluate specific inflammatory VOC products of treated patients in all four groups. Treatment consists of PAH medication and/or immunosuppressive therapy.

Study burden and risks

Risks of the study are related to known complications of the performed diagnostic tests. However, blood sampling, echocardiography, six minute walking test, pulmonary function testing, HR CT thorax and if necessary a right heart catheterization is considered standard of care in the clinical follow up of patients at risk for pulmonary arterial hypertension. In the noninvasive collection of exhaled air we do not expect any adverse events.

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

1) PAH-CTD patients, inclusion criteria:
- classification as definite systemic sclerosis or systemic lupus erythematosus according to respectively the ACR-EULAR criteria and SLICC criteria
- minimal age of 18 year
- diagnosis of pulmonary arterial hypertension: mean pulmonary artery pressure (mPAP) of >=25 mmHg, pulmonary capillary wedge pressure (PCWP) <=15 mmHg, and a pulmonary vascular resistance (PVR) >=240 dynes.s.cm-5 measured by right heart catherization. , 2) IPAH patients, inclusion criteria:
- diagnosis of pulmonary arterial hypertension: mean pulmonary artery pressure (mPAP) of >=25 mmHg, pulmonary capillary wedge pressure (PCWP) <=15 mmHg, and a pulmonary vascular resistance (PVR) >=240 dynes.s.cm-5 measured by right heart catherization.

- no family history of PAH
- triggering factor is excluded: connective tissue disease, drugs or toxins, human immunodeficiency virus, congenital heart disease, portal hypertension, schistosomiasis
- minimal age of 18 year, 3) SSc and SLE patients without PAH, inclusion criteria:
- classification as definite systemic sclerosis or systemic lupus erythematosus according to respectively the ACR-EULAR criteria (16) and SLICC criteria (17)
- minimal age of 18 year
- no signs of PAH at screening visit
4) CTEPH patients, inclusion criteria:
- diagnosis of pulmonary hypertension: mean pulmonary artery pressure (mPAP) of >=25 mmHg, pulmonary capillary wedge pressure (PCWP) <=15 mmHg measured by right heart catherization.
- mismatched perfusion defects on V/Q lung scan

Exclusion criteria

- active or treated malignancy
- tuberculosis or hepatitis B/C infection in case of immunosuppressive medication
- need to start immediately with immunosuppressive therapy
- already use of immune suppression

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-02-2018

Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	01-11-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-07-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT03819777

Register	ID
CCMO	NL57351.068.17