Protocol Clinical Trial (21/11/2018)

Title of project

Blood eosinophil measurements in patients with Chronic Obstructive Pulmonary disease in stable state.

Objective

To determine the within-day variation of blood eosinophils in patients with Chronic Obstructive Pulmonary disease in stable state.

To determine if there is a correlation between the blood eosinophils and certain clinical parameters.

Investigators

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Departments involved in the trial

Department of Family Medicine and Chronic Care, Vrije Universiteit Brussel

Department of Internal Medicine, Division of Respiratory Disease, UZ Brussel

Department of Clinical Biology, UZ Brussel

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a disease which leads to serious morbidity and mortality and it is currently the 4th leading cause of death in the world. (1) It is characterised by airflow limitation caused by a mixture of small airways disease and parenchymal destruction, the relative contributions of which vary from person to person. (2) It is a heterogeneous disease, resulting in different phenotypes with varying clinical and pathophysiological characteristics. One of these pathophysiological features is chronic airway inflammation and, although eosinophilic inflammation is thought to be a typical characteristic of asthma, there is mounting evidence that eosinophilic inflammation can also be present in COPD. (3)

Blood eosinophils are an accessible biomarker for the eosinophilic inflammation in COPD (3). Literature suggests a potential theragnostic role for this biomarker, seeing that COPD patients with higher levels of blood eosinophils could exhibit a greater responsiveness to corticosteroid treatments (4-7) and probably also to anti–IL-5 therapy. (8) Evidence also suggests that this biomarker could have a prognostic use for establishing the risk of exacerbations although conflicting results are found. (9)

But before being able to make decisions in the clinical management of patients based on blood eosinophils, more needs to be known about the different confounding factors and sources of within-subject variability of this biomarker. (10) As described by Brusselle et al. eosinophil counts can fluctuate due to their short half-life in blood and due to a diurnal rhythm. (11) There is evidence that this diurnal variation exists in healthy individuals (12) but, to the best of our knowledge, this has never been investigated in COPD patients before.

Study design

Prospective interventional study

Subjects

Number and recruitment of subjects

50 COPD patients (GOLD A+B+C+D). All eligible COPD patients will be recruited at the respiratory unit of the UZ Brussel (included the patients admitted for nocturnal oximetry) or from family practices.

Inclusion criteria

Participant is willing and able to give informed consent for participation in the study. Patients are 18 years or older, with the diagnosis of COPD according to GOLD (post-bronchodilator Tiffeneau index <0.7), in stable state of the disease and with a smoking history of >10 pack-years.

Exclusion criteria

Clinical diagnosis of asthma

Use of systemic corticosteroids (oral, intravenous or infiltration up to six weeks before inclusion).

Pregnancy.

A recent exacerbation of COPD (<4 weeks ago).

Replacement of subjects
Inclusion of patients will continue until 50 patients have gone through the entire study protocol.

Restrictions and prohibitions for the subjects
None.

Procedures and collected variables

Upon admission a questionnaire is filled in by the investigator or his representative: age, gender, smoking habits, weight, height, current medication, pulmonary function test with bronchodilation, mMRC (Modified Medical Research Council) Dyspnea Scale, exacerbation history in the previous year.

Fractional Exhaled Nictric Oxide (FENO) measurement and blood sampling at 08h00, 12h00, 16h00 (total red blood cell count, total white blood cell count with formula in absolute count and percentage of total white blood cells, and platelet count).

Randomisation/blinding

Not applicable.

Prior and concomitant therapy

Medication prohibited before and during the trial are systemic corticosteroids (oral, intravenous or infiltration, up to six weeks before inclusion). All other medication use is allowed.

Study analysis

Sample size calculation
Due to the lack of previous research, a sample size calculation was impossible to perform and an arbitrary decision was made.

Analysis of the samples
The analysis of the blood samples will be done at the Department of Clinical Biology, UZ Brussel. The pulmonary function test will be performed at the Department of Internal Medicine, Division of Respiratory Disease, UZ Brussel.

Statistical analysis
Statistical analyses will be performed by the Department of Statistics and Data-analyses of the Vrije Universiteit Brussel.

Quality control and quality assurance

Quality control and quality assurance will be done according to guidelines of the Association for the Accreditation of Human Research Protection Programs.

Data Protection

Responsible for processing of personal data
Department of Family Medicine and Chronic Care, Vrije Universiteit Brussel
Contact person: Inès Van Rossem, Vakgroep Huisartsgeneeskunde en Chronische Zorg, Vrije Universiteit Brussel, Laarbeeklaan 103, 1090 Jette, tel: +32 2 477 43 11

Data Protection Officer (DPO)
Audrey van Scharen, DPO Vrije Universiteit Brussel (DPO@vub.be)

Goal of the processing
The gathered data will be used for the academic scientific research purposes described in this protocol. It will be processed according to the principles imposed by the European General Data Protection Regulation (GDPR), which has been in force since 25 May 2018.
The legal basis for the processing is permission. There is an explicit permission from the data subject for the processing of personal data through informed consent. Permission can be withdrawn by the participant at any time, for any reason and without having to state a reason.

Recipients of data
The prime investigator and the study nurse will be the only individuals with access to personnel data. Study data will not be transferred to other countries.

Storage
The study data will be stored in an excel file in a coded fashion with the encryption key held in a separate file. Both the data file and the encryption key will be password protected and saved in the one drive system of the Vrije Universiteit Brussel.
The gathered study data will be saved for a period of minimum 20 years. This in accordance with the Belgian law on experiments on the human person (7 May 2004).

Publication policy

All authors will contribute to publication and hold all publication rights.

Funding

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Dr. Inès Van Rossem