The effect of resveratrol on metabolism and cardiovascular risk profile in patients with chronic obstructive pulmonary disease (COPD)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON44730

Source
ToetsingOnline

Brief title
CARMENS-trial

Condition

- Cardiac disorders, signs and symptoms NEC
- Muscle disorders
- Bronchial disorders (excl neoplasms)

Synonym
Chronic Obstructive Pulmonary disease

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Longfonds (voormalig astmafonds)

Intervention

Keyword: cardiovascular disease, COPD, metabolism, resveratrol

Outcome measures

Primary outcome

Primary outcome of this study is:

High sensitivity systemic inflammation (CRP) as a clinical marker of systemic inflammation via blood sampling.

Secondary outcome

Secondary outcomes of this study are:

Proposed mechanisms of action:

1. Quadriceps metabolism and mitochondrial function via vastus lateralis muscle biopsy and muscle cross-sectional area;

2. Adipose tissue inflammation via abdominal subcutaneous adipose tissue biopsy (macrophage infiltration, adipocytes size, inflammatory and metabolic gene expression);

3. Systemic inflammatory (IL-6, TNF-α, leptin and adiponectin) and oxidative stress markers, cellular redox status and glutathionylation of haemoglobin via blood sampling;

4. Lipid profile (triglyceride, total cholesterol, HDL cholesterol, apoA1, apoB100) via blood sampling;

5. Insulin sensitivity: Homeostatis Model Assessment of insulin resistance

(HOMA-IR) index (blood);

General markers of body composition and health status known to be affected by

CRP:

1. Body fat mass and distribution: Whole-body fat mass (DXA scan and

anthropometric measurements) and visceral fat (DXA scan);

2. Quadriceps function by leg dynamometry (Biodex);

3. Blood pressure and heart rate (hematometer);

4. Physical activity level

Study description

Background summary

In the general population cardiovascular disease (CVD) is the leading cause of mortality and it is well established that obesity (body mass index >30 kg/m²) is an important determinant. The risk is even further increased in COPD due to smoking behaviour and accumulation of visceral fat combined with a decreased skeletal muscle oxidative capacity. Enhanced systemic inflammation is identified as important driver in recent epidemiological and translational research. Aerobic exercise training (AET) is an established way to improve metabolic health and decrease CVD risk in the overweight general population but modulating potential is limited in COPD due to ventilatory limitations and related disease symptoms. Interventions which mimic the effects of AET are therefore considered as unmet medical need. Evidence is emerging that the nutritional supplement resveratrol is an interesting candidate that requires further investigation in COPD.

Study objective

The overall objective is to investigate the efficacy of resveratrol in modulating metabolism and CVD risk profile in patients with COPD.

The primary objective is to investigate the effect of resveratrol on CRP as

clinical marker of low grade systemic inflammation.

The secondary objective is to investigate the effect of resveratrol on body composition, inflammatory status and mechanistic markers in blood, adipose and muscle tissue as well as a comprehensive assessment of metabolic and physical performance profile known to be affected by low grade systemic inflammation and by resveratrol.

Study design

The research aims will be addressed in a proof-of-concept randomized placebo-controlled double blinded clinical trial comparing 2 groups of 26 subjects each.

Intervention

Subjects will be randomized to one of the research groups. The groups will receive the following intervention:
- Group 1 will receive a dose of 150 mg of resveratrol for 4 weeks (2 capsules of 220 mg/day)
- Group 2 will receive a placebo for 4 weeks (2 capsules of 220 mg/day)

Study burden and risks

We will perform reversibility measurements for lung function. This includes the inhalation of a short acting bronchodilator. This is a standard procedure for the diagnose COPD. The inhalation of the bronchodilator may sometimes be associated with dizziness and palpitations. However, this will resolve shortly after inhalation. Furthermore, subjects will be asked to wear an accelerometer two times for one week. This is a small device which can be worn as a belt around the waist and it will not hinder any daily activities. However, because subjects are not used to wearing this small device they might experience this as uncomfortable. Some measurements we are performing are invasive and not without any risk. Venous blood will be drawn and muscle and fat biopsies will be taken which can cause a local haematoma. Subjects using anti-coagulants are excluded from this procedure for this reason. Infection or bleedings on the other hand are very rare. The subjects will be instructed to refrain from heavy physical labour and not to remove the pressure bandage from the leg where the biopsy was taken within the first 24h. The biopsies will be taken by a skilled medical doctor. Some subjects may also report pain during the sampling of muscle material.
DXA-scanning is a safe procedures, with no known health risk as long as none of the exclusion criteria is met. The radiation dose emitted during a DXA-scan is 0.001 mSv. This is a very low exposure compared to the total background radiation in The Netherlands, which is ~2.5 mSv/year. In total, subjects have to come once for a screening and two times two days for measurements to the

MUMC.

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 (GOLD I-IV);
- Current or ex-smoker;
- Age >18 years.

Exclusion criteria

- COPD patients planned for pulmonary rehabilitation or who recently participated in a

rehabilitation program in the previous 6 months;
- Investigator*s uncertainty about willingness or ability of the patient to comply with the protocol requirements;
- Participation in any other study involving investigational exercise training, nutritional or pharmacological intervention;
- Oral glucocorticoid use;
- Recent exacerbation (<4 weeks) that required oral steroids and/or hospital admission;
- Subject is pregnant, planning to be pregnant during the study period, lactating, or women who consider themselves to be of childbearing potential and who are engaged in an active sex life and are unwilling to commit to the use of an approved form of contraception throughout the study period. The method of contraception must be recorded in the source documentation;
- Diabetes mellitus (type 1 and 2);
- Active cardiovascular disease or a cardiovascular event (such as myocardial infarction, cerebrovascular haemorrhage/infarction) in the previous 6 months;
- Recent major surgery;
- Thyroid dysfunction, current hepatic or renal disorders;
- Current malignancy (except for dermal malignancies);
- Central or obstructive sleep apnea;
- Current alcohol consumption > 20 grams alcohol/day;
- Intake of resveratrol containing dietary supplements;

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2016
Enrollment:	52
Type:	Actual

Ethics review

Approved WMO Date:	10-09-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-12-2015
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
Other	ABR-49391
CCMO	NL49391.068.14

Study results

Date completed:	14-02-2018
Actual enrolment:	23

Summary results
Trial ended prematurely