Pilot study to investigate the anti-inflammatory effects of caffeine in subjects with chronic obstructive pulmonary disease (COPD)

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To evaluate the potential attenuating effects of a one-week supplementation with 2 x 250 mg caffeine per day on blood biomarkers of systemic inflammation in COPD patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON31548

Source
ToetsingOnline

Brief title
Anti-inflammatory effects of caffeine in COPD

Condition

- Respiratory disorders NEC

Synonym
chronic inflammation, chronic obstructive pulmonary disease (COPD)

Research involving
Human

Sponsors and support

Primary sponsor: Technologiestichting STW (NWO)
Source(s) of monetary or material Support: Technologiestichting STW

Intervention

Keyword: caffeine, COPD, Inflammation

Outcome measures

Primary outcome

The primary objective of the present study is to investigate the effects of a one-week daily supplementation of COPD patients with 2 x 250mg caffeine on biomarkers of systemic inflammation in blood such as C-reactive protein (CRP) and the cytokines TNF-a, IL-6, IL-8 and IL-10.

Secondary outcome

The secondary objectives of the study are

1) to investigate the effects of the one week caffeine supplementation on activation of poly-(ADP-ribose) polymerase I (PARP-I) and DNA-repair in peripheral blood lymphocytes by means of immune histochemical methods and the COMET assay. The COMET assay determines the level of DNA strand breaks, and is indicative for the amount of oxidative DNA lesions.

2) to investigate the effects of the one week caffeine supplementation on oxidative stress markers in urine such as the ratio of uric acid/allantoin (the oxidative metabolite of uric acid) and the creatinine levels

3) to determine the levels of caffeine and its metabolites in plasma and urine

4) to investigate the effects of the caffeine supplementation on organic volatiles (e.g. ethane, pentane and other (unknown) compounds that might be discriminatory for COPD patients) in exhaled air

5) to investigate the effects of the caffeine supplementation on the cytokine levels (TNF-a, IL-6, IL-8 and IL-10) in whole blood stimulated ex vivo with

LPS.

6) to investigate the effects of the caffeine supplementation on the gene

expression levels of cytokines, redox enzymes and other proteins involved in

the inflammatory and oxidative stress response

Study description

Background summary

Nowadays it has become evident that a chronic systemic inflammation is present in patients suffering from chronic obstructive pulmonary disease (COPD).
The role of the nuclear enzyme poly(adenosine diphosphate-ribose)polymerase (PARP) as a key mediator within these systemic inflammatory processes as well as in COPD associated exercise intolerance and muscle weakness could recently been identified. The attenuating effect of dietary ingredients with PARP inhibiting activity on systemic inflammation was supported by data from in vitro and in vivo studies, from other groups as well as from our own lab. We identified several caffeine metabolites as potent inhibitors of the most abundant PARP-isoform PARP-1 in-vitro, in animal models as well as in ex-vivo experiments with whole blood from COPD patients.
However, clinical data with respect to their anti-inflammatory effects in COPD patients are currently not available for none of these substances. Therefore, the current clinical pilot study is intended to establish for the first time clinical data (proof of principle) on the anti-inflammatory potential of caffeine (and its metabolites).

Study objective

To evaluate the potential attenuating effects of a one-week supplementation with 2 x 250 mg caffeine per day on blood biomarkers of systemic inflammation in COPD patients.

Study design

Double blind, randomised placebo controlled cross-over study

Intervention

According to the cross-over design, the study comprises two intervention periods of one week which are separated by a wash-out period of three weeks. Subjects will participate in a one-week run-in period preceding the two

intervention periods, during which they will be asked to replace their usual coffee consumed throughout the day by a decaffeinated coffee and tea provided by the investigators. Furthermore, they will be requested to abstain from any caffeine-containing foods and drinks. Maintenance of this dietary restriction is also required during both intervention periods.
Generally subjects will be asked not to change their usual dietary and lifestyle habits throughout the entire trial.
It will be determined by random in which order subjects will receive the verum and the placebo treatment. Caffeine will be applied in hard gelatine capsules containing 250 mg (plus an appropriate amount of bulking agent, ih required). The placebo capsules will solely contain the bulking agent of the verum medication.
Subjects will be instructed to take twice a day one capsule in the morning and at lunchtime.
Prior to the beginning of the study subjects will be invited for an initial visit with instructions on the implementation of a caffeine-free diet and the supply of the decaffeinated coffee and tea.
During the study subjects will attend four further visits at the investigational site, which take about 30 min. and will comprise an interview with the investigator about all study related issues. In addition, on these occasions 33 ml blood will be collected as well as a sample of exhaled air and freshly voided urine.
Including the screening subjects will be requested to attend six study visits at the investigational site.

Study burden and risks

No major risks will be associated with the intake of the investigational products. Caffeine is a compound of the normal diet and will be administered in a safe and responsible dose and manner.

There will be two periods each of two weeks during which the subjects will be requested to replace their usual consumed coffee and tea by decaffeinated coffee and tea provided by the investigator. However, subjects receive useful tips and instructions how to avoid caffeine intake from other dietary sources including caffeine-free alternatives. For this purpose they will be invited to participate in an additional visit prior to the start of the study.
Throughout the study period (six weeks) subjects will attend in total four visits at the investigational site of ca. 30 min. During these visits they will have an interview with the investigator about their well-being, the occurrence of any adverse events and any questions or problems related to their participation in the trial. Then heart rate and blood pressure will be controlled.
33 ml blood will be collected as well as a specimen of exhaled air and freshly voided urine. Over the entire study period (incl. the screening) subjects will attend six study visits. In total 138 ml blood will be collected per subject.
Altogether the investigators consider the burden of the subjects as low.

Whether the one-week consumption of caffeine may result in an improvement of any individual symptoms of the disease cannot be predicted. Participation is thus not related to any advantage or disadvantage for the individual subject's health.

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

Male subjects in an age of 40-70 years
BMI > 20 kg/m2 and < 30 kg/m2
Diastolic blood pressure (DBP)=60-90 mmHg, Systolic blood pressure (SBP)=100-150 mmHg
CRP-levels > 3mg/l
No acute and/or chronic inflammatory condition such as arthritis, arthrosis, chronic colitis, etc. during three months before entry of the study

No respiratory tract infection or exacerbation of COPD for at least 8 weeks prior to the start of the study
No change in treatment regime of the COPD subjects for at least 8 weeks prior to the start of the study
Normal constant dietary eating habits and a usual coffee consumption of at least 3 cups per day
Non-smokers and stopped smoking, respectively

Exclusion criteria

Women
age < 40 years or > 70 years old
BMI <= 20 kg/m2 and >= 30 kg/m2
Diastolic blood pressure (DBP) < 60 or > 90 mmHg, systolic blood pressure (SBP) <100 or >150 mmHg
Acute and/or chronic inflammatory condition such as arthritis, arthrosis, chronic colitis, etc. during three months before entry of the study
Respiratory tract infection or exacerbation of COPD during the last 8 weeks prior to the start of the study
Change in treatment regime of the COPD subjects during the last 8 weeks prior to the start of the study
Irregular eating habits, usual coffee consumption of less than 3 cups per day and current smoker

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-01-2009
Enrollment:	12

Type:	Actual

Ethics review

Approved WMO Date:	16-01-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-03-2008
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
CCMO	NL18785.068.07