The effects of plant sterols and stanol on cytokine production by mononucleair blood cells isolated out of blood from asthma patients

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

Summary

ID

NL-OMON33551

Source
ToetsingOnline

Brief title
Sterol, Stanol and Asthma Study (SSAS)

Condition

- Other condition
- Bronchial disorders (excl neoplasms)

Synonym
asthma

Health condition

astma

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,FHML (AIO salaris) + RAISIO (kosten van de studie),RAISIO, Finland

Intervention

Keyword: cytokines, plant stanols, plant sterols, T-helper cells

Outcome measures

Primary outcome

- differences in cytokine produktion by isolated PBMCs from asthma patients

versus healthy controls

- differences in cytokine produktion by exposing isolated PBMCs from asthma

patients versus healthy controls to

plant sterols and stanols

Secondary outcome

N.A.

Study description

Background summary

Western diets provide daily about 160 to 460 mg dietary plant sterols, of which campesterol, sitosterol and stigmasterol are the most common [1]. Plant stanols are the saturated derivatives of plant sterols. These sterols and stanols are structurally related to cholesterol, but have a different side-chain configuration. Additionally, plant stanols are lacking the double bond at C-5. Due to this structural similarity, these compounds lower intestinal cholesterol absorption. Although this reduction in cholesterol absorption induces endogenous cholesterol synthesis, the overall effect is that diets enriched with plant sterol or stanol esters lower fasting serum low-density lipoprotein

(LDL) cholesterol concentrations [2]. These effects have been found in many patient groups (e.g. slightly hypercholesterolemic people, subjects treated with statins, patients with familial hypercholesterolemia, and diabetic subjects), and do hardly depend on the composition of the food matrix or background [3]. As both plant sterol and stanol esters are generally recognized as safe (GRAS), these dietary agents have therefore a great potential in the prevention of coronary heart disease. In fact, functional foods enriched with plant sterol or stanol esters are nowadays widely available for the general population in many European countries, the U.S.A. and Australia.

Till now, there is little evidence for plant sterols and stanol effects other than improving lipid profiles. However, we have very recently found strong indications in ex vivo models using isolated human peripheral mononuclear blood cells (PBMCs) from healthy volunteers that plant sterols and stanols have the capacity to improve immune function. More into detail, plant stanols shifted the differentiation of naive T-cells into the Th1 direction. In our hands, this effect was mediated via activating a specific receptor present on the Antigen presenting cells (APCs) and T-cells both present in the PBMC mixtures. These in vitro effects are in line with findings presented in the literature in mouse models (4) and in human HIV patients (5). However, mice are not men and the study in HIV patients is not a real valid model since the cytokines used to determine the Th1/Th2 balance are in fact produced by CD4+ T-helper cells which are almost completely absent in HIV patients. Therefore, this finding needs to be confirmed in other patient groups, just like HIV patients characterized by a th2 skewing based on their cytokine profiles. Asthma is a typical example of a disease characterized by th2 skewing which in theory could benefit from Th1 activation to restore the th1/Th2 balance. However before starting a well-controlled intervention study providing plant sterol or stanol ester based products to asthma patients we here describe a pilot experiment to show that (1) asthma patients are indeed characterized by a th2 skewing, (2) that their PBMCs respond towards plant sterols or stanols by a th1 skewing and (3) we will compare different outcome parameters to find the parameters that is most responsive in this respect. We will use this parameter in an upcomming intervention study, which is now in development.
If true, the effect of plant sterols or stanols might ultimately be helpful in other situations in which the Th1/Th2 helper cell balance is disturbed into a Th2 over-responsiveness. By activating the Th1 response, the disturbed balance may be restored. This is for example a possibility in the treatment or prevention of asthma, food allergies or HIV in susceptible subjects.

Study objective

The major research objectives are (1) to prove that PBMCs isolated from asthma patients are indeed characterized by a Th2 phenotype and (2) that this disturbed balance can be restored by adding plant sterols or stanols during in vitro culturing and stimulation, and (3) which cytokine is most sensitive in

this response.

Study design

A pilot study using PBMCs isolated from 10 asthma patients and 10 matched controls. These cells will be cultured in vitro with and without plant sterols / stanols and cytokines produced will be evaluated. This will be done twice with 4 weeks interval to obtain information regarding reproducibility of the disturbed Th2 shift in asthma patients, the responsiveness of the PBMCs from these patients for plant sterols / stanols and the most sensitive parameter to evaluate this.

Study burden and risks

During the study, 2 blood samples (each 20 mL) will be taken. Total time investment for the subjects will be 80 min. Occasionally, a heamatoma or bruise can occur during venepuncture. The results of this study will show whether plant sterols and stanols have the capacity - at least in vitro - to restore the disturbed th1/Th2 balance seen in asthma patients. The ultimate aim is to test this effect - if present in this in vitro study - in an in vivo intervention study in asthma patients, which is however not part of this proposal.

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

- 18 to 70 years of age
- Men or women
- asthma patient or healthy volunteer

Exclusion criteria

- Current asthmatic exacerbations
- Other inflammatory based pathology like IBD, COPD, rheumatoid arthritis or HIV
- Autoimmune diseases like MS or Lupus
- Other conditions known to relate to Th1/Th2 balance disturbances like type II diabetes
- Any known (food) allergies
- Allergic asthma
- Retroviral infections with HTLV in the past
- Smoking
- Abuse of drugs and/or self-reported alcohol consumption of >2 drinks daily
- Pregnant or breast-feeding women
- Use of an investigational product containing plant sterols or stanols (benecol, becel pro-active or danacol) within the previous 30 days
- Having donated blood (as blood donor) within 1 month prior to the study or planning to do so during the study

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-03-2009
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	20-08-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-06-2009
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	NL24139.068.08