The effects of plant sterol and plant stanol ester enriched foods on liver inflammation in subjects at risk to develop NASH

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To assess the effect of consuming plant sterol or plant stanol esters (3 grams/day) for 6 months on ALT concentrations in subjects with elevated ALT concentrations, i.e. who are at risk to develop NASH.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55927

Source
ToetsingOnline

Brief title
NASH@risk

Condition

- Other condition

Synonym
fatty liver, Liver inflammation

Health condition

Leverontsteking

Research involving

Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: TKI funding,BASF,RAISIO,Unilever

Intervention

Keyword: Liver inflammation, Plant stanols, Plant sterols

Outcome measures

Primary outcome

The primary outcome parameter in this study is the change in plasma ALT concentration.

Secondary outcome

• liver function (AST, GGT, bilirubin CK18) and non-invasive plasma markers of liver inflammation (cathepsin-D and acid phosphatase)

• liver inflammation assessed by non-invasive volatile organic compounds (VOCs)

• liver fibroses assessed by the FibroScan

• body composition assessed by the BodPod

• microvascular function assessed by retinal images

• lipid and lipoprotein metabolism (cholesterol, triacylglycerol, (apo)lipoprotein and bile acid concentrations), glucose metabolism (glucose, insulin, HOMA index), non-cholesterol concentrations and plasma inflammatory markers

In a subgroup (n=30):

• liver inflammation and liver fat assessed by additional non-invasive magnetic

resonance spectroscopy (MRS)

Study description

Background summary

As the prevalence of obesity is reaching epidemic proportions, the prevalence of non-alcoholic fatty liver disease (NAFLD), including non-alcoholic steatohepatitis (NASH), increases concomitantly and becomes a major global health hazard. Successful pharmacological interventions to treat or prevent NASH are not available and so far only weight loss has clear benefits, but sustained weight-loss is difficult to achieve on the longer-term. We recently demonstrated in mice that plant sterol and stanol ester consumption inhibited the development of liver inflammation. Moreover, Javanmardi and co-workers recently observed reduced plasma concentrations of Alanine Transaminase (ALT) and Aspartate Transaminase (AST) after daily plant sterol consumption (1.6 g/d) for 6 weeks in a population of adult NAFLD patients. In the current study, we propose to evaluate the effect of long-term consuming plant sterol or plant stanol esters on ALT concentrations in subjects who are at risk to develop NASH. Furthermore, we want to demonstrate the effect of plant sterol and plant stanol consumption on other parameters reflecting liver health, such as cathepsin-D, liver fat and liver insulin sensitivity.

Study objective

To assess the effect of consuming plant sterol or plant stanol esters (3 grams/day) for 6 months on ALT concentrations in subjects with elevated ALT concentrations, i.e. who are at risk to develop NASH.

Study design

This study is a randomized, placebo-controlled, double blinded pilot study with a run-period of 2 weeks, an intervention period of 6 months and a wash-out period of 1 month.

Intervention

All subjects will start a run-in period of two weeks during which they consume daily 20 grams of control margarine after which they will be randomly allocated to consume 20 grams control margarine or plant sterol or plant stanol enriched margarine on a daily basis for a period of 6 months.

Study burden and risks

During a screening visit, body weight, body height and blood pressure are determined and a blood sample (5.5 mL) will be drawn. During the run-in period of two weeks, subjects will receive 20g control margarine and during the intervention period of 6 months they will be randomized to receive control, plant sterol ester or plant stanol ester margarine. On 7 occasions a fasting blood sample will be drawn (with a total of 195 mL) and at baseline and in week 26, samples for VOCs analysis will be taken, a FibroScan will be performed to measure liver fat and liver stiffness, body composition will be determined and retinal images will be taken. In a subgroup of 30 subjects, liver fat and liver inflammation will be measured with MRS imaging at baseline and at the of intervention in week 26. All subjects will be asked to fill out a food frequency questionnaire two times and to keep a diary throughout the study and body weight and blood pressure will be assessed on five occasions. Venipuncture and insertion of a cannula can cause discomfort and possibly a local haematoma or bruise. MRS and MRI are modern diagnostic tools that do not imply significant risks (no ionizing radiation). In principle, all measurements are routine in our metabolic research unit (MRUM) and are not expected to lead to physical side effects. Total time investment spread-out over the study participation will be approximately 6 hours or 34 hours (depending on the subgroup), excluding travel time. Plant sterol and plant stanol enriched products are commercially available and we therefore do not foresee any risks related to the consumption of these food products

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Be able to give written informed consent
2. Metabolic syndrome according to the NCEP ATP III definition (Grundy 2005)
3. Aged between 18 and 75 years
4. Willingness to consume 20 grams of margarine provided by us on a daily basis for a period of 6 months

Exclusion criteria

1. Are less than 18 years of age or over 75 years of age
2. Females who are pregnant, breast feeding or who may wish to become pregnant during the study
3. Have a significant acute or chronic coexisting illness such as cardiovascular disease, chronic kidney disease, gastrointestinal disorder, endocrinological disorder, immunological disorder, cancer or any condition which contraindicates, in the investigator*s judgement, entry to the study
4. Severe medical conditions that might interfere with the study such as epilepsy, asthma, chronic obstructive pulmonary disease, inflammatory bowel disease and rheumatoid arthritis
5. Use of diuretics or insulin therapy
6. History of illicit drug use
7. Consume more than the recommended alcohol guidelines i.e. >21 alcohol units/week for males and >14 units/week for females
8. Not willing to stop the consumption of plant sterol or plant stanol enriched products 1 month before the start of the study (wash-in period)
9. Use of an investigational product in another biomedical study within the previous month

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:	Recruiting
Start date (anticipated):	02-02-2021
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	19-12-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-02-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-07-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-06-2023
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	NL70963.068.19