The Role of microbial produced ethanol in etiology of non-alcoholic steatohepatitis

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20655

Source
Nationaal Trial Register

Brief title
ETHANASH trial

Health condition

NASH

Sponsors and support

Primary sponsor: Amsterdam UMC, locatie AMC
Source(s) of monetary or material Support: Amsterdam UMC, locatie AMC

Intervention

Outcome measures

Primary outcome

To investigate whether microbial produced ethanol plays a role in the development of NASH.

Secondary outcome

NA

Study description

Background summary

Changes in the composition of the gut microbiota have been associated with alterations in host metabolism and recent evidence suggest that gut microbiota might also be involved in the development of Non-Alcoholic Fatty Liver Disease (NAFLD) and subsequent Non-alcoholic steatohepatitis (NASH). So far, however, causality has not been demonstrated. Among many gut microbial metabolites, endogenous intestinally produced ethanol has gained interest in the past decade for its involvement in the development of NAFLD. Ethanol is produced by intestinal bacteria has been suggested that ethanol might play a role in the development of NAFLD, especially in the transition from NAFLD to NASH. When produced in significant amounts, hepatic ethanol metabolism inhibits beta-oxidation of fatty acids which will induce storage of lipids in the liver. Endogenously produced ethanol reaches the liver via the portal vein and is then rapidly removed from the circulation via extremely efficient hepatic mechanisms, leaving almost untraceable concentrations in the peripheral plasma if liver function is uncompromised. Several studies have however showed that subjects with NASH (known to have a compromised liver function) have increased peripheral concentrations of ethanol, however these concentrations are so low that one might argue whether this is clinical relevant regarding the development of NASH. The first step in ethanol catabolism is the oxidation of ethanol to acetaldehyde using NAD+, mainly via the hepatic enzyme alcohol dehydrogenase. Fomepizole (4-methylpyrazole) is a specific inhibitor of the enzyme alcohol dehydrogenase. In a previous study, a significant elevation of peripheral plasma ethanol concentrations were observed in lean subjects who were treated with fomepizole after intake of lingonberry juice. Since subjects with NASH might have more ethanol producing bacteria, we anticipate to find increased concentrations of ethanol in subjects with NASH compared to healthy control subjects during a mixed meal test after the infusion of fomepizole. Moreover, when intestinal microbiota is temporarily eradicated by a short term oral antibiotic course, we expect to see no increase in peripheral plasma ethanol levels upon fomepizole infusion in patients with NASH.

Study objective

We hypothesize that subjects with NASH produce more ethanol after a mixed meal tolerance test than subjects with a healthy liver after receiving a infusion with fomepizole.

Study design

baseline, visit 1, visit 2

Intervention

Subjects will undergo an ultrasonography of the liver to assess hepatic steatosis and will undergo a clinical mixed meal tolerance test and get an infusion with fomepizole or saline (placebo). Only NASH patients will also receive oral antibiotics course of 7 days followed by mixed meal test with fomepizole infusion.

Contacts

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Eligibility criteria

Inclusion criteria

- Diagnosis of NASH on liver biopsy taken on clinical grounds at the outpatient clinic, or healthy volunteer
- 18-65 years of age
- BMI > 25 kg/m2
- Subjects should be able to give informed consent

Exclusion criteria

- Primary lipid disorder
- Known genetic basis for insulin resistance or glucose intolerance
- Ethanol intake > 2 U/week
- Pregnancy, females who are breastfeeding
- Hepatitis B and/or C
- Liver cirrhosis
- Auto-immune hepatitis
- Wilson disease3/ alpha 1-antitripsine deficiency
- Hemochromatosis

- Use of drugs interacting with fomepizole (products requiring CYP2E1 for metabolizing).

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-04-2019
Enrollment:	20
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Plan description
We will not share IPD

Ethics review

Positive opinion

Date:	22-04-2019
Application type:	First submission

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
NTR-new	NL7693
Other	NA : METC Amsterdam UMC, lokatie AMC 2018_331

Study results