The use of 18F-fluorodeoxyglucose positron emission tomography and computed tomography imaging for the detection of inflammation in steatotic livers as an indicator of non-alcoholic steatohepatitis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational invasive

Summary

ID

NL-OMON32768

Source
ToetsingOnline

Brief title
The FLAME study: FDG detection of inflammation in steatosis

Condition

- Hepatic and hepatobiliary disorders
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
fatty liver, hepatic steatohepatitis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: betrokken afdelingen VUmc

Intervention

Keyword: Inflammation, Liver, NASH, PET

Outcome measures

Primary outcome

The primary outcome parameter is the level of hepatic FDG uptake in non-diabetic patients with biopsy-proven NASH and the level of hepatic FDG-uptake in non-diabetic patients with biopsy-proven non-inflammatory steatosis

Secondary outcome

FDG uptake levels will be studied in correlation with hepatic lipid content measured by 1H-MR-S, glucose tolerance status, determined by OGTT, transaminases and biochemical markers of inflammation.

Study description

Background summary

Non-alcoholic fatty liver disease (NAFLD) has been used as a general name for conditions ranging from simple steatosis through non-alcoholic steatohepatitis (NASH) to end-stage liver disease (cirrhosis). Simple steatosis is a rather benign condition as less then 5% shows progression to steatohepatitis. NASH proves to be more dangerous, as leads to cirrhosis in approximately 20% after 8-10 years of follow up. More then 30% of patients with end stage liver disease (cirrhosis) develop liver related morbidity and mortality. In spite of intense research, the mechanism that causes progression of simple steatosis to NASH

remains unclear. In 1998 Day launched the two-hit-theory, stating that two succeeding wallops have to be delivered to the liver to cause NASH. The first hit, development of hepatic steatosis, consists of the accumulation of triglycerides in the liver. Inflammation is the response to the second hit, formation of reactive oxygen species (ROS) and mitochondrial damage. The first step in establishing the diagnosis is physical examination and blood tests, directed to exclude other liver diseases: Increased waist-to-hip-ratio, mildly elevated transaminases and increased fasting glucose and hyperinsulinaemia should rise the suspicion of hepatic steatosis and it can be confirmed by radiologic imaging, with 1H-MR-spectroscopy as the most promising technique. Although a number of serological markers and imaging techniques can be helpful in distinguishing NASH from simple steatosis, a non-invasive tool to differentiate simple steatosis and NASH in an early stage is unavailable. To identify inflammation a liver biopsy still remains the gold standard.

Study objective

The primary objective is to study if non-diabetic patients with biopsy-proven NASH have higher hepatic FDG-uptake as compared to non-diabetic patients with biopsy-proven non-inflammatory steatosis?
Secondary Objectives are (1) to study the association between hepatic FDG-uptake and the degree of inflammation in the liver biopsies, (2) to study the association between hepatic FDG-uptake and 1H-MRS-measured hepatic fat content and (3) to study the association between the parameters measured by imaging (PET/1H-MRS) and circulating markers of metabolism, including insulin resistance and transaminases, and markers of inflammation?

Study design

Observational single center pilot study

Study burden and risks

Participating patients will have to bring 3 visits to the VUmc. Duration of these visits ranges from 45 minutes to a maximum of 4 hours. Subjects have to abstain from heavy physical activities (e.g. sports) 24-h prior to the visits and remain fasted as indicated. Visits will be scheduled in accordance with the participants schedule and preferably in the morning, so the fasting period can be at nights. FDG-PET CT-scan delivers an amount of approximately 4 milliSievert of ionizing radiation to the patient. Furthermore the contrast that is used may cause irritation at the injection place, nausea, minor allergic reaction and in rare cases severe allergic reactions. An oral glucose tolerance tests will be performed to determine glucose tolerance status (2* hours test time). Prior to and during the OGTT patients will be allowed a restricted regime of water intake. Participants will be presented with a light

meal and coffee/tea after testing.

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

* Men and women * 18 yrs of age
* Fasting plasma glucose *7.0 mmol/l
* Liver biopsy in the last 6 months prior to inclusion or existing medical indication indication for liver biopsy
* Written informed consent

Exclusion criteria

* Exclusion criteria for MR (claustrophobia, pacemaker, metal implants, etc)
* Exclusion criteria for liver biopsy (bleeding tendency, extended bile ducts etc)
* ALT levels * 150 IU/ml
* Creatinine levels * 120 IU/ml
* Present excessive alcohol use defined as > 2 units/day
* Present abuse of i.v. drugs (including methadon)
* Infection with HIV or Hepatitis B/C
* A psychiatric, addictive or any disorder that compromises the subjects ability to understand the study content and to give written informed consent for participation in 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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-01-2009
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO

Date:	08-08-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL23861.029.08