Metabolic and signaling pathways in steatosis and steatohepatitis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lipid metabolism disorders
Study type	Observational invasive

Summary

ID

NL-OMON31033

Source
ToetsingOnline

Brief title
steatosis and steatohepatitis

Condition

- Lipid metabolism disorders

Synonym
corpulence, obesity

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: BSIK

Intervention

Keyword: human, liver, NAFLD, obesitas, steatohepatitis, steatosis

Outcome measures

Primary outcome

1) Histopathological score in the different stages of NAFLD.

2) Gene expression profile in micro-array study.

Secondary outcome

not of application

Study description

Background summary

Obesity is presently an increasing problem. At this moment, almost half of the European citizens are overweight and a third of these people are obese. This increase in the number of overweight people is mainly due to the current sedentary lifestyle and the changes in food consumption. If more energy is taken up by the body than is consumed over a long period, the excess of energy is stored in the adipose tissue, and, to a lesser extent, in liver and muscle tissue. Once this fat is stored, it is not easily mobilized again. Because of this, obesity is defined as a chronic condition. Furthermore, obesity is associated with cardiovascular diseases, diabetes, etc.
The increased fat content in the liver and the muscle impairs mitochondrial function and, hence, the energy supply of these organs. Fat accumulation in the liver leads also without alcohol abuse to non-alcoholic fatty liver disease (NAFLD). NAFLD can be divided into different stages: fat accumulation (steatosis), fat accumulation and inflammation (steatohepatitis), formation of scar tissue (cirrhosis), and hepatocellular carcinoma. These different stages of NAFLD are characterized by a different degree of fat accumulation, cell death, inflammation, and scar tissue. We hypothesize that the disturbed energy production is caused by the inhibition of aconitase, which is an enzyme normally involved in energy production. As a consequence of the inhibition of aconitase, fat accumulation occurs.

Study objective

In this study we want to make an inventory of the metabolic and inflammatory

pathways which are significantly affected by the development of steatosis and steatohepatitis in human liver. We also want to relate these mechanisms with the different stages of NAFLD.

Study design

In this human study, a bank of liver biopsies of the entire spectrum of NAFLD, ranging from healthy to cirrhosis, will be generated. We will be collecting approximately 80 liver biopsies. In this manner we hope to be able to include at least 10 samples of each of the different stages of NAFLD. These liver biopsies will be acquired from partial hepatectomies that are performed to remove metastases of colon carcinoma and from liver biopsies of patients undergoing bariatric surgery for the treatment of morbid obesity. To classify the liver biopsies in one of the NAFLD stages the grading system developed by Kleiner et al. (Hepatology, 2005) will be used. The obtained liver biopsies will be subjected to micro-array analysis to identify the affected metabolic and inflammatory pathways in the development of steatosis and steatohepatitis. In this manner we want to correlate the staging system with these affected metabolic and inflammatory pathways.

Study burden and risks

The collection of liver biopsies for this study will be without any additional risks for the patients. In the patients with colon metastasis in the liver a liver specimen is taken as treatment of the disease. In this study we will use a liver biopsy from this liver specimen, and as a consequence no additional specimens need to be taken from the liver for this study. In the patients undergoing bariatric surgery a liver biopsy is taken as a standard for research. It is shown in previous studies that taking liver biopsies is without any risk for the patient (MEC 02-045.3).

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

adult women and men
partial hepatectomy or open liver biopsy

Exclusion criteria

alcohol abuse
drugs damaging the liver
hepatitis C and B

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-10-2007
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	04-09-2007
Application type:	First submission
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	NL16400.068.07