# Effects of omega-3 fatty acids on fatty liver and insulin sensitivity.

No registrations found.

| | |
|---|---|
| **Ethical review** | Not applicable |
| **Status** | Pending |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON26624

**Source**
NTR

**Brief title**
FAT trial (Fatty Acids Treatment trial)

**Health condition**

non-alcoholic fatty liver disease (NAFLD)
hepatic steatosis
insulin sensitivity
morbid obesity
omega-3 fatty acids

### Sponsors and support

**Primary sponsor:** Academic Medical Center, Amsterdam, The Netherlands.

### Intervention

### Outcome measures

**Primary outcome**

1. To assess the effects of omega-3 fatty acids on hepatic steatosis;

2. To assess the effects of omega-3 fatty acids on hepatic and peripheral insulin resistance.

**Secondary outcome**

1. Liver volume;

2. Fatty acids in the basal state and during hyperinsulinemia;

3. Plasma lipid profile;

4. Hepatic lipid profile;

5. Resting energy expenditure (REE);

6. Differences in expression profiles in liver tissue;

7. Histological classification of hepatic steatosis;

8. Changes in circulating inflammatory proteins.

# Study description

**Background summary**

Background of the study:

Hepatic steatosis is characterized by excessive triglyceride accumulation in the liver which is caused by either excessive import, diminished export and/or impaired beta-oxidation of fatty acids. Without treatment, simple steatosis (non-alcoholic fatty liver disease, NAFLD) may progress to an inflammatory state (non-alcoholic steatohepatitis, NASH) and ultimately fibrosis, cirrhosis and hepatocellular carcinoma (HCC). The prevalence of NAFLD in industrialized populations ranges from 20-40%. NAFLD is directly linked to obesity/the metabolic syndrome and with the epidemic growth of obesity, a higher incidence of NAFLD is expected.
Weight loss is the most effective treatment strategy for hepatic steatosis. Permanent weight loss in morbidly obese subjects can only be reached by bariatric surgery. However, enlarged steatotic livers may complicate surgery as in case of laparoscopic gastric bypass surgery it diminishes technical maneuverability in the gastroesophageal area. In addition, steatotic livers seem to be more vulnerable to complications caused by direct liver tissue damage when the liver is mobilized or retracted during operation. Therefore it may be of clinical benefit to reduce the degree of hepatic steatosis. In a rat model of hepatic steatosis, we recently showed that supplementation of

omega-3 fatty acids significantly reduced TG accumulation in the liver (Marsman et al, submitted). Fatty acids are activators of some nuclear receptors involved in beta-oxidation, but until now it is not completely unraveled whether and how omega-3 fatty acid supplementation affects hepatic steatosis in humans.

Objective of the study:

The aim of this study is to evaluate the effect of supplementation of a high oral dose of omega-3 fatty acids on hepatic steatosis and glucose metabolism in morbidly obese patients undergoing laparoscopic Roux-Y gastric bypass surgery (LRYGBP).

Study design:

Randomized controlled intervention study.

Study population:

Morbidly obese subjects scheduled for bariatric surgery, 18-65 years old.

Intervention:

Eucaloric diet with high dose omega-3 fatty acids (SupportanR) vs eucaloric diet without omega-3 fatty acids (FresubinR) 4 weeks prior to laparoscopic Roux-Y gastic bypass surgery.

Primary study parameters/outcome of the study:

1. To assess the effects of omega-3 fatty acids on hepatic steatosis;

2. To assess the effects of omega-3 fatty acids on hepatic and peripheral insulin resistance.

Secundary study parameters/outcome of the study:

1. Liver volume;

2. Fatty acids in the basal state and during hyperinsulinemia;

3. Plasma lipid profile;

4. Hepatic lipid profile;

5. Resting energy expenditure (REE);

6. Differences in expression profiles in liver tissue;

7. Histological classification of hepatic steatosis;

8. Changes in circulating inflammatory proteins.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

Biometric data such as waist circumference, BMI and blood pressure will be measured. During surgery biopsies will be taken from visceral and abdominal subcutaneous adipose tissue and the liver. The risks of bleeding from the biopsy sites during the bariatric surgery procedure are very small because the biopsy sites are completely visible to the surgeon and local hemostasis will be checked. Subjects will visit the research unit weekly during the study; total visit time will be about 34 hours. In addition an MRS of the liver will be performed to quantify liver fat content. The MRS-scan requires lying still as possible for 45 minutes. Subjects will undergo a 2-step hyperinsulinemic euglycemic clamp using stable isotopes before and after the diet period to study glucose metabolism. For the administration of the stable isotope, glucose and insulin and for blood sampling, intravenous canules will be inserted in the left and right antecubital vein. Stable isotopes are not harmful and hypoglycaemia will not occur because glucose is monitored every 5 minutes. Total clamping time on one day will be 7 hours.

**Study objective**

High dose of oral administration of omega-3 fatty acids ameliorates hepatic steatosis and insulin sensitivity in morbidly obese patients undergoing LRYGBP.

**Study design**

1. MRS liver + clamp pre-diet and post-diet;

2. Liverbiopsy post-diet during operation.

**Intervention**

Eucaloric diet with high dose omega-3 fatty acids (Supportan®) vs. eucaloric diet without omega-3 fatty acids (Fresubin®) 4 weeks prior to laparoscopic Roux-Y gastic bypass surgery.

# Contacts

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# Eligibility criteria

## Inclusion criteria

1. MRS suggesting NAFLD;

2. 18-65 years of age;

3. IFSO criteria;

4. Ability to provide informed consent;

5. Stable weight 2 months prior to inclusion.

### Exclusion criteria

1. Use of lipid lowering drugs (i.e., statins and fibrate drugs);

2. Any medication except anti-hypertensives, levothyroxine, OAC;

3. Any medical condition execpt for hypertension, dyslipidemia, glucose intolerance, treated hypothyroidism, coagulation disorders (increased bleeding time PT, aPTT);

4. Excessive alcohol intake - > > 14 units/week;

5. Contraindications to MR scanning - pacemaker or metallic foreign body, claustrophobia etc;

6. Use of n-3 PUFA supplements within the prior 4 months;

7. Current use of weight loss medication;

8. Pregnancy, females who are breastfeeding;

9. Renal insufficiency (creatinine > 150 umol/L);

10. History of jejunal-ileal bypass or extensive small bowel resection.

## Study design

### Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-05-2011 |

| | |
|---|---|
| Enrollment: | 20 |
| Type: | Anticipated |

## Ethics review

Not applicable
Application type: Not applicable

## 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 | NL2699 |
| NTR-old | NTR2836 |
| Other | : |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

## Study results

**Summary results**
N/A