A randomized double blind placebo controlled study on the effects of fenretinide Lym-X-Sorb on insulin sensitivity in obese insulin resistant subjects

Published: 22-02-2012
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Primary objective:To assess the effects of fenretinide on hepatic and peripheral insulin sensitivity in obese, insulin resistant subjectsSecondary objective:To assess the effects of fenretinide on hepatic steatosis, body weight and body fat...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON37344

Source
ToetsingOnline

Brief title
The effects of fenretinide on insulin sensitivity

Condition

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

Synonym
Insulin resistance; impaired glucose tolerance

Health condition

obesitas

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Metabole fonds

Intervention

Keyword: Fatty liver, Insulin resistance, Metabolic syndrome X, Obesity

Outcome measures

Primary outcome

Changes in hepatic and peripheral insulin sensitivity

Secondary outcome

Liver steatosis

Plasma retinol and RBP4 levels

Subcutaneous adipose tissue: concentrations of RBP4 and key proteins involved

in insulin signaling levels

Plasma HPR and its metabolites (MPR, 4-oxo-HPR) levels

Resting energy expenditure (REE) and body fat composition

Glucoregulatory hormones, adipokines and markers of inflammation

Safety and tolerability of HPR/LXS

Study description

Background summary

The prevalence of type 2 diabetes mellitus (T2DM) and obesity is increasing.
Recent studies have provided evidence that retinol binding protein 4 (RBP4) is

involved in the induction of insulin resistance (IR). Fenretinide is a synthetic retinoid found to lower RBP4 levels. Preliminary data show that it might improve insulin sensitivity, making it a promising new therapy for IR and T2DM.

Study objective

Primary objective:
To assess the effects of fenretinide on hepatic and peripheral insulin sensitivity in obese, insulin resistant subjects

Secondary objective:
To assess the effects of fenretinide on hepatic steatosis, body weight and body fat composition
To assess changes in RBP4 mRNA and protein levels as well as key proteins in the insulin signaling cascade in subcutaneous adipose tissue

Study design

Randomized double blind placebo controlled study

Intervention

Treatment arm: HPR/LXS 154 mg QD for 90 days; placebo arm: blank Lym-X-Sorb matrix (LXS) QD for 90 days

Study burden and risks

Biometric data such as waist circumference, BMI and blood pressure will be measured. Subjects will visit the research unit several times during the study; total visit time will be about 26 hours. 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 hyperinsulemic-euglycemic clamp using stable isotopes before and after the intervention 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. Fat biopsies, performed before and after the intervention period, will be used to investigate changes in insulin signalling pathways as a consequence of changes in insulin resistance. Subcutaneous fat biopsies will be taken from the periumbilical region and will take approximately 30 minutes. Biopsies will be preceded by local anesthesia with lidocain and will only cause minor discomfort.

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

Post menopausal female
Age 40-65 years
BMI * 30 kg * m-2
HOMA-IR * 2.7
Signed informed consent

Exclusion criteria

T2DM treated with medication other than metformin or sulfonylurea derivates
Any medical condition except for glucose intolerance, T2DM, hypertension and secondary dyslipidemia

Prolonged PTT/aPTT or thrombocytopenia
Retinol levels of < 1.8 uM

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	fenretinide/Lym-X-Sorb
Generic name:	fenretinide

Ethics review

Approved WMO Date:	22-02-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2012

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
EudraCT	EUCTR2011-006165-18-NL
CCMO	NL39363.018.12