pro-hepcidin and hepcidin levels in blood and urine of Gaucher patients in relation to iron homeostasis.

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Objectives Primary objective:- To determine if there is a difference in pro-hepcidin and hepcidin values in blood and urine between Gaucher patients and healthy controls, and between Gaucher patients and hemochromatosis patients. - To gain insight...

Ethical review	Approved WMO
Status	Pending
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON30063

Source
ToetsingOnline

Brief title
Iron homeostasis in Gaucher patients

Condition

- Metabolic and nutritional disorders congenital

Synonym
Gaucherdisease and glucocerebrosidase deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Gaucher, hepcidin, Iron, pro-hepcidin

Outcome measures

Primary outcome

Hepcidin in urine (SELDI-TOF MS)

Pro-hepcidin in blood (ELISA)

Secondary outcome

In blood: sedimentation rate of erythrocytes, C-reactive protein, white blood

count, creatinin, iron, ferritin, hemoglobin, erythrocyes MCV and

total-iron-binding-capacity.

In urine: hepcidin (SELDI-TOF MS) and creatinin.

Study description

Background summary

Gaucher disease type I (GD I) is the most common lysosomal storage disorder, with a prevalence of 1:50.000 in most countries 1. Gaucher disease type I is characterized by a deficiency of the lysosomal enzyme glucocerebrosidase (glucosylceramidase), which leads to the accumulation of glucocerebroside in macrophages. The lipid laden macrophages are called Gaucher cells. The Gaucher cells are mainly present found in liver, spleen and bone marrow, resulting in hepatosplenomegaly, skeletal disease and pancytopenia. Ironmetabolism is altered in Gaucher disease, with high levels of iron and ferritin (zimran 1992, nierau 1996)

One of the factors involved in iron metabolism and anemia is hepcidin. These 20 and 25 amino acid peptides are produced by the liver and kidney, and were initially described to be active against bacteria and fungi. Hepcidin is increased in inflammatory conditions. Their role in iron homeostasis was later discovered by the finding that mRNA was up-regulated upon iron overload and decreased by iron depletion in mice. Inappropriately low levels of hepcidin relative to body iron stores are associated with the abnormal iron homeostasis characteristic of hemochromatosis. Conversely, over expression of hepcidin

leads to severe iron deficiency and anemia in transgenic mice (ref. Nicolas et al. 2002).

It is unknown whether hepcidin levels in Gaucher patients are abnormal. In theory, hepcidin levels could be reduced as an adaptation to the anemia in Gaucher patients. However, it is also possible that hepcidin levels are increased due to the chronic low level pro-inflammatory state associated with Gaucher disease.
In order to gain more insight in iron-homeostais in Gaucher disease, hepcidine and pro-hepcidine (the inactive pro-peptide of hepcidin) levels in blood and urine of Gaucher type I patients will be measured and compared to those of healthy controls and patients with hemochromatosis.

Study objective

Objectives
Primary objective:
- To determine if there is a difference in pro-hepcidin and hepcidin values in blood and urine between Gaucher patients and healthy controls, and between Gaucher patients and hemochromatosis patients.
- To gain insight in fluctuations/changes in hepcidin values in time in healthy controls and in Gaucher patients receiving therapy.
Secondary objective:
- To see if the simple detection of pro-hepcidin values in blood can be used as a method to monitor circulating hepcidin levels. This will be achieved by determining the correlation of pro-hepcidin values in blood samples with hepcidin levels in urine monsters.

Study design

An observational pilot study will be performed in which hepcidine and pro-hepcidine will be measured in blood and urine from 20 hemochromatosis patients, 20 Gaucher patients and 20 healthy controls. If possible, blood and urine samples from Gaucher patients and healthy controls will be taken from stored samples. Additional samples from Gaucher patients and healthy controls will be sampled according to this study protocol. Healthy controls will be asked personally by the invesigator to participate in this study. The blood and urine samples of hemochromatosis patients will be taken during their regular visit for therapeutic phlebotomy.

Study burden and risks

From hemochromatosis patients a total of 35 ml blood will be obtained. Since blood will also be drawn for therapeutic phlebotolomy, no extra vena puncture will be performed, nor will extra blood be drawn. From healthy controls 42 ml blood will be obtained for which a vena puncture will be performed.

From hemochromatosis patients, Gaucher patients and healthy controls one specimen of mid-stream urine will be asked during a routine visit to the hospital.

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

-Patients, older than 18 years, with proven GD I, as evidenced by decreased plasma glucocerebrosidase activity or genotyping.
-Controls, older than 18 years with a normal total iron binding capacity in blood.
-Patients with proven Hematochromatosis as evidenced by total iron bindingcapacity of > 45% in blood or genotyping.
-Patients and controls have to provide written informed consent to participate in the study.

Exclusion criteria

none

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-09-2006
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

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	NL13723.018.06