Daily variation of serum hepcidin levels in healthy volunteers during a day of iron-free diet and a day of iron free diet + oral iron supplementation: a cross over study

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To gain better insights in mechanism of the biological variation of hepcidin. We investigate the role of iron in the diet, on the biological variation of hepcidin.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON34323

Source
ToetsingOnline

Brief title
Iron and diurnal rhythm of hepcidin

Condition

- Other condition

Synonym
Anemia/Iron overload

Health condition

IJzerstofwisselingsstoornis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,BV
www.hepcidinanalysis.com

Intervention

Keyword: Diet, Diurnal rhythm, Hepcidin, Iron

Outcome measures

Primary outcome

Hepcidin

Secondary outcome

Hemoglobin (Hb)

Mean Corpuscular Volume (MCV)

C-Reactive Protein (CRP)

Iron (Fe)

Total iron binding capacity (TIBC)

Tranferrin Saturation (TS) --> calculated from iron and total iron binding

capacity

Ferritin

Alanine Aminotransferase (ALAT)

Study description

Background summary

Hepcidin is a iron regulating hormone, that was first described in 2001.

Recently a serum assay for hepcidin was developed. Hepcidin is produced by hepatocytes in the liver en is excreted in the plasma Hepcidin is a negative regulator of iron-absorption. Hepcidin moldulates iron availability by promoting the internalization and degradation of ferroportin, which is essential for both iron absorption in the duodenum and recycling of iron/iron efflux by macrophages. Increased iron stores and inflammation induce hepcidin expression, whereas suppression occurs during hypoxia and anemia. The serum hepcidin assay is a promosing assay in the diagnosis of iron metabolims disorders. Previous research showed a daily variation in serum hepcidin levels. Following a normal diet, there is a significant increase of serum hepcidin levels during the day. However, the mechanism of this daily variation is unknown.

Study objective

To gain better insights in mechanism of the biological variation of hepcidin. We investigate the role of iron in the diet, on the biological variation of hepcidin.

Study design

Two weeks before the study starts:
To investigate if a volunteer can be included in the study, a pre-screening will be performed. 10 mL blood divided in two tubes will be sampled. Using this blood, hepcidin, CRP, ALAT, Fe, TIBC, ferritine and Hb will be measured. Further BMI will be calculated and the history of bloodtransfusion en chemotherapy was investigated.

Day 1:
Patients follow a iron-free diet. This diet is composed by the research-team using a nevotable. The diet contains the following products:

Drinks:
Black Tea
Coke

Cereal:
Cornflakes

Dairy:
Semi-skimmed milk
cottage cheese
Buttermilk

Other:
Sweetener

Liquorice

During the day, 1x 15mL en 3x 10mL blood will be sampled by this schedule:

8.00AM 10.30AM 1.00PM 4.00PM
Parameter
Hb x
MCV x
CRP x
Fe x x x x
TIBC x x x x
Ferritine x
ALAT x
Hepcidine x x x x
Buis
5ml EDTA (blood) x
10 ml tube (serum) x x x x

TS is calculated by the Fe/TIBC ratio.

The first serum sample (8.00u) should be taken fasted.

The volunteers could choose whether they want a peripheral cannula (blood will be drawn on the 4 time points) or whether they want four single blood samplings.

In the blood Hb, MCV, CRP, ALAT, Fe, TIBC and ferritin will be measured by routine measurement, to determine whether the volunteer has a healthy iron metabolism. Hepcidin levels will be measured by the Matrix Assisted Laser Desorption/Ionisation Time-of-Flight Massa Spectrometrische (MALDI-TOF MS) assay.

Day 2 (one week after day 1):
The volunteers follow the same iron-free diet as followed on day one supplemented with two tablets of 65mg ferrousfumarate. The ferrousfumarate tablets should be taken half an our before breakfast (65mg) and half an our before lunch (65 mg).

Bloodsampling and laboratory measurements follow the same protocol as the protocol on day one.

Intervention

Day 1: The volunteers follow an iron-free diet.
Day 2: The volunteers follow an iron-free diet, supplemented with tablets of 65mg ferrousfumarate.

9 samples of blood will be taken.

Study burden and risks

In the pre-screening, the participants will undergo 1 venepunction of 10 mL blood to test the fasted hepcidin level and iron parameters.
At study day 1, the participants will undergo 4 times a venepunction to draw a total of 45mL of blood or the participants get a peripheral cannula for one day to draw a total of 45mL of blood.
At study day 2, the participants will undergo 4 times a venepunction to draw a total of 45mL of blood or the participants get a peripheral cannula for one day to draw a total of 45mL of blood.

This puncture can be experienced as irritable for the volunteers.
The participant could develop a hematoma/bruise in the arm, but this risk is minimal for the information gained by this study about the biological variation of hepcidin.
If the participant choose a a peripheral cannula, there is a risk the cannula will clog. A new a peripheral cannula should be placed.

Taking 2 tablets of 65mg ferrufmaraat can, in a few cases, cause gastro-intestinal symptoms.

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

Between 20-60 years of age
Fasted hepcidin levels > detection limit (0.5 nM)
Hb within reference range
ferritin, TIBC, CRP and ALAT within reference range
BMI<30

Exclusion criteria

Red blood cell transfusions (> 2 units) in history
Chemotherapy in history

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-01-2011
Enrollment:	25

Type:	Actual

Ethics review

Approved WMO Date:	24-12-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL33198.091.10