Reference values of HEPcidin Plus other Iron paramEters in children

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Aim of the study* To determine age-and sex-dependent reference values of the iron regulatory hormone hepcidin.* To determine age-and sex-dependent reference values of newer parameters to determine iron deficiency, such as soluble Transferrin...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON42321

Source
ToetsingOnline

Brief title
HEPPIE study

Condition

- Haematological disorders NEC

Synonym
niet van toepassing: referentiewaardenstudie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: -child, -hepcidin, -iron parameters, -reference values

Outcome measures

Primary outcome

* To determine age-and sex-dependent reference values of the iron regulatory

hormone hepcidin.

* To determine age-and sex-dependent reference values of newer iron parameters,

such as soluble Transferrin Receptor (sTfR), reticulocyte hemoglobin content

(Ret-Hb), and Hb Erythrocytes (RBC Hb)

Secondary outcome

not applicable

Study description

Background summary

Iron plays an essential role in many biochemical processes, particularly in the production of heme for incorporation into Hb and myoglobin, and Fe-S clusters, which serve as enzyme cofactors. In iron deficiency, cells lose their capacity for electron transport and energy metabolism. Clinically, iron de!ciency causes anemia and may result in neurodevelopment deficits. Conversely, iron excess leads to complications such as endocrine disorders, liver cirrhosis, and cardiac dysfunction. Therefore, tight regulation of body iron homeostasis on both systemic and cellular levels is paramount. These processes comprise several proteins, most of which have been discovered in the last 20 years. Defects in these proteins lead to disorders of iron metabolism and heme synthesis that are characterized by iron overload, iron deficiency, or iron maldistribution. Cells involved in iron homeostasis are duodenal enterocytes, hepatocytes, macrophages, and erythroid precursors (Donker AE, 2014).

Hepcidin has emerged as the central regulatory molecule of systemic iron homeostasis. It is a 25-amino acid peptide hormone that is produced and secreted predominantly by hepatocytes, circulates in the bloodstream, and is excreted by the kidneys. By binding to the cellular iron exporter ferroportin

and inducing its internalization and degradation, hepcidin regulates cellular iron efflux. In this way, the absorption of dietary iron from the intestine and the release of recycled iron derived from senescent erythrocytes are controlled. (Galesloot TE, 2011; Kroot JJ, 2011).

Many diseases are associated with alterations in hepcidin concentrations (Kroot JJ, 2011; Donker AE, 2014).Disorders related to hepcidin deficiency are for example hereditary hemochromatosis and iron loading anemias due to an ineffective erythropoiesis like beta-thalassemia. On the other hand, hepcidin excess plays a critical role in anemia of chronic disease (ACD) and Iron Refractory Iron Deficiency Anemia (IRIDA), a disease characterized by resistance to oral iron supplementation due to a defect of the TMPRSS6 gene encoding matriptase-2. Loss of matriptase-2 activity results in an inability to reduce hepcidin synthesis during iron deficiency. Accordingly, patients have increased innate hepcidin concentrations resulting in microcytic hypochromic anemia with low transferrin saturation percentages.
Therefore, assessment of hepcidin concentrations can serve to exclude or raise the suspicion for disorders of iron metabolism.

Age and sex stratified reference ranges of hepcidin have been established for adults (Galesloot TE, 2011, www.hepcidinanalysis.com) and for children aged 0.5 -3 years (Uijterschoot, 2014, thesis). However, for children over 3 years no reference values are available yet. In this study we aim to obtain reference values of hepcidin and other iron parameters in children in order to get more insight in the (patho) physiology of iron metabolism in childhood, and to contribute to a better diagnosis and treatment of children with either an iron deficit or an iron surplus.

Study objective

Aim of the study
* To determine age-and sex-dependent reference values of the iron regulatory hormone hepcidin.
* To determine age-and sex-dependent reference values of newer parameters to determine iron deficiency, such as soluble Transferrin Receptor (sTfR), reticulocyte hemoglobin content (Ret-Hb), and Hb Erythrocytes (RBC Hb)

Study design

Patients and methods:

Patients:
Because this study aims to understand the iron metabolism of healthy children, it is important that the included patients do not suffer from a systemic underlying disease. Our group therefore consists of basically healthy children.
* who attend the out patient department of the Máxima Medisch Centrum Veldhoven

for minor health problems (eg abdominal pain, cardiac murmur, short stature) or
* who are hospitalized on the pediatric ward of the Máxima Medisch Centrum Veldhoven for surgery (eg inguinal hernia correction, circumcision, hypospadia correction, orthopedic surgery) and
* who need a venipunture of infusion drip for diagnostic reasons or for surgery respectively, in order to avoid extra blood withdrawal.

Study burden and risks

not applicable

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Inclusion criteria:
* Age 6 months to 18 years
* Western-European descent ((Non- Western European people may be a carrier of alpha or beta thalassemia, which may influence the results of serum hepcidin and other iron parameters)
* Infusion or venipuncture required for surgery or diagnostic
* Informed consent obtained from parents and from both parents and child in case the patient is (over)
12 years

Exclusion criteria

* Exprematurity (gestation <37 weeks), exdismaturity (birth weight * (status after) systemic underlying disease (malignancy, asthma, diabetes, congenital heart disease, kidney failure, congenital immunodeficiencies, etc.
* Known anemia
* Treatment with iron preparations
* Acute infection
* Trauma <48 hours ago
* Operation <48 hours ago
* Use of any medication
* If the laboratory results demonstrate increased inflammation parameters, the patient will be excluded afterwards

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-07-2016

Enrollment:	250
Type:	Actual

Ethics review

Approved WMO Date:	23-02-2016
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Not approved Date:	06-06-2017
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	NL53833.015.15

Study results

Date completed:	01-04-2018
Actual enrolment:	173