Iron and malaria: the central role of hepcidin and macrophage function

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anaemias nonhaemolytic and marrow depression
Study type	Observational non invasive

Summary

ID

NL-OMON32793

Source
ToetsingOnline

Brief title
iron and malaria

Condition

- Anaemias nonhaemolytic and marrow depression
- Ancillary infectious topics
- Iron and trace metal metabolism disorders

Synonym
malaria, Plasmodium falciparum infectie

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: NIH fonds.

Intervention

Keyword: hepcidin, iron, malaria, monocyte

Outcome measures

Primary outcome

- the change in mRNA expression of hepcidin and other iron regulating proteins

of the monocyte after incubation with several stimuli

-the change in mRNA expression and protein of cytokines in monocytes after

incubation with several stimuli

-the change in monocyte iron content

Secondary outcome

n.a.

Study description

Background summary

Malaria is a global health problem affecting 300 to 500 milj, cases each year. In malaria endemic areas anemia is an important public health problem leading to increased morbidity and mortality mainly in cildren and pregnant women. The anemia is mainly caused by malaria itself and iron deficiency. Treatment of iron deficiency is therefore a priority of the WHO micronutrient program and the efficacy of iron supplementation in the prevention and treatment of anemia in malaria endemic regions has been demonstrated in multiple studies. However, universal iron supplementation in settings with intense malaria transmission may not be without risk, since iron may stimulate the growth of malaria parasites and other microorganisms. So far, there is ongoing discussion on the risk-benefit ratio of iron supplementation in malaria endemic regions. A recent publication in the Lancet (Sazawal, 2006) showed the results of a large study in Zanzibar that *routine supplementation with iron and folic acid in preschool children in a population with high rates of malaria can result in an increased risk of severe illness and death*. These findings emphasize the complex web of serious interactions that exist between malaria, iron homeostasis, innate immunity and iron supplementation and the need to unravel the underlying mechanism of these interactions. The past decade has seen the identification

of new proteins involved in iron metabolism that has greatly increased the insight in iron uptake and distribution. Especially the identification of the central iron regulating hormone hepcidin has led to a shift in our perception of iron homeostasis. Moreover insight in the important role of the monocyte/macrophage in human iron homeostasis is increased.

Study objective

In the current proposal, we propose an in vitro study to explore the interaction of malaria infection, the parasitized erythrocyte, and monocyte iron metabolism. We aim to study the role of hepcidin and to explore a) the pathways involved in malaria induced alteration in monocyte hepcidin and b) the intracellular iron content. Also the role of other iron regulatory proteins are studied.

Study design

This proposol includes only in vitro experiments of (ex vivo) material of the voluntary donor. By venapuncture 4 tot 6 tubes of 10 ml are drawn. In the laboratory only monocytes are isolated and used for the experiments: stimulation of monocytes with several stimuli including malaria infected erythrocytes.

Study burden and risks

An once time only blooddonation, via a venapunction is asked from the volunteer and the associated health risks are limited. Because of the puncture local irritation, pain or hematoma can occur. Moreover 40 to 60 cc blood will be withdrawn, although minimal to the amount of circulating blood, short complaints of dizziness are light headiness can occur.
The volunteer has no contact nor any possibility of infection with the malaria parasite. Moreover the outcome of this in vitro reserach will not lead to any information about the volunteers healthstatus.

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

healthy, above 18 years

Exclusion criteria

use of iron supplementations (current or in previous 2 years)
vegan or vegetarian diet

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2010
Enrollment:	30
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	09-09-2009
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	NL29472.091.09