Thyroid hormone metabolism and innate immunity: the role of deiodinase type 3 in polymorphonuclear leukocytes

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The primary objective of the study is to assess the function and effect of deiodinase type 3 in PMN*s and the mechanisms behind its induction following activation of these cells.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	White blood cell disorders
Study type	Observational invasive

Summary

ID

NL-OMON44488

Source
ToetsingOnline

Brief title
The role of deiodinase type 3 in polymorphonuclear leukocytes

Condition

- White blood cell disorders
- Thyroid gland disorders
- Ancillary infectious topics

Synonym
Leukocyte function

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Polymorphonuclear leukocytes, Type 3 deiodinase

Outcome measures

Primary outcome

The main study parameters are changes in the amount of D3 protein, D3 activity,

bacterial killing capacity and subcellular localisation of D3 in activated

versus non-activated leukocytes.

Secondary outcome

n.v.t.

Study description

Background summary

Illness and infection are known to induce profound changes in thyroid hormone metabolism. These changes are collectively known as Non-Thyroidal Illness Syndrome (NTIS) and are characterized by a decrease in systemic thyroid hormone levels. NTIS occurs in a wide variety of diseases including myocardial infarction, acute stroke and critical illness. It is seen in 70% of hospitalized patients and is correlated with disease severity and outcome. Besides changes in systemic thyroid hormone levels, there is increasing evidence for local changes in thyroid hormone metabolism in specific tissues and cell types during illness. One of these cells is polymorphonuclear leukocytes (PMNs), one of the white blood cell subtypes. Activated leukocytes have long been known to degrade thyroid hormone. More recently, animal models have shown that in both acute infection and chronic inflammation, leukocytes express deiodinase type 3 (D3), an enzyme that inactivates thyroid hormone. D3 knock-out mice have impaired bacterial clearance compared to wildtype mice suggesting that D3 is a major determinant of the bacterial killing capacity of leukocytes during infection. The ability of leukocytes to phagocytose and kill pathogens is of paramount importance during infection and defects in this bacterial killing machinery can severely affect clinical outcome.

Study objective

The primary objective of the study is to assess the function and effect of

deiodinase type 3 in PMN*s and the mechanisms behind its induction following activation of these cells.

Study design

The study is an observational laboratory study on leukocytes isolated from venous blood of healthy volunteers

Study burden and risks

Vena puncture has a risk of mild local discomfort and bruising.

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 volunteers:
1. Aged >=18
2. Willing and able to provide signed informed consent prior to study-related procedures.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:;1. History of haematological diseases
2. Fever or other symptoms of infection during the past 7 days.
3. Use of medication that could affect haematological parameters or neutrophil function as specified by the Farmacotherapeutisch Kompas (http://www.fk.cvz.nl)

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):	08-05-2014
Enrollment:	38
Type:	Actual

Ethics review

Approved WMO

Date:	05-05-2014
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
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	NL48692.018.14