Immune regulation in Common Variable Immunodeficiency: the role of apoptosis and regulatory T cells.

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To gain insight in the regulation of immune responses in patients with CVID

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON32339

Source
ToetsingOnline

Brief title
Immune regulation in CVID

Condition

- Immunodeficiency syndromes

Synonym
defective antibody production of unknown cause, primary immunodeficiency

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Baxter,Baxter Bioscience

Intervention

Keyword: apoptosis, CVID, pathogenesis, regulatory T cells

Outcome measures

Primary outcome

1. Quantification and characterisation of apoptosis in T and B cells

2. Quantification and functional determination of regulatory T cells

3. Function of the thymus

Secondary outcome

1. The differences in the 3 abovementioned outcome parameters between healthy controls, CVID patients and XLA control patients for both the pediatric and adult population.

2. The differences in the 3 abovementioned outcome parameters between subgroups of CVID patients, namely patients with and without auto immune symptoms, also within the pediatric and adult population.

3. Correlation between the function of the thymus and the amount of regulatory T cells.

4. Correlation between regulatory T cells and apoptosis.

Study description

Background summary

CVID (Common Variable Immunodeficiency, a primary immune disease) is an immune disease with an unknown cause. Although the disease is relatively rare (incidence of some tens per year in the Netherlands), CVID remains important, due to the life-long duration, high morbidity and possible mortality. The hallmark of CVID is an impaired antibody production, as a result of functional B cell defects. This makes patients prone to infections and most research

therefore focusses on those B cells.
Additionally, a significant part of the CVID population suffers from a distorted immune regulation, leading to auto immune disease. Platelets and red blood cells can be attacked by auto-antibodies, causing potentially severe disorders such as anemia and an increased risk of bleedings.
It is difficult to understand why patients on one hand cannot produce sufficient antibodies to fight infections, while on the other hand they are able to produce antibodies against their own cells. One explanation could be that the programmed cell death or apoptosis of B cells (or of the T cells that help them) is disturbed. It is possible that self-reactive cells are not cleared properly, or that other cells die too easily, for example the regulatory T cells. These T cells are able to suppress immune responses. When there function is impaired, an uncontrolled immune response perpetuates, eventually causing autoimmunity. Another possibility is that the thymus does not produce enough regulatoy T cells, also leading to insufficient suppression of immune responses.

Study objective

To gain insight in the regulation of immune responses in patients with CVID

Study design

Cross-sectional patient control study

Study burden and risks

Minimal burden and risks: Of the patients and healthy controls, 20ml (children) or 40ml (adults) blood will be taken only at the moment when venipuncture has to be performed already, namely to supplete immunoglobulins or for routine blood controls (patients) and prior to surgical procedure that is not related to immune disease (pediatric controls).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Diagnosis of CVID; based on recurrent respiratory tract infections, decreased total serum IgG (<-2SD) and impaired specific antibody production after vaccination. Both patients with and without auto immune phenomena will be included.
Diagnosis of XLA; based on the (almost complete) absence of B cells and a mutation in the Btk gene.

Exclusion criteria

Both patients groups: uncertainty about the diagnosis. Acute and/or severe infections at the moment of inclusion.
XLA patients: existence of auto immune symptoms

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:	Recruitment stopped
Start date (anticipated):	31-07-2009
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO

Date:	23-09-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL22095.041.08