An observational study of immuneregulatory mechanisms in Juvenile Dermatomyositis

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to investigate the role of regulatory T cells in response to heat shock proteins in muscle and peripheral blood of patients with juvenile dermatomyositis. To identify patterns in T-cell responses and cytokineprofiles, in relation with clinical...

Ethical review	Approved WMO
Status	Completed
Health condition type	Muscle disorders
Study type	Observational invasive

Summary

ID

NL-OMON57213

Source
ToetsingOnline

Brief title
Immuneregulation in JDM

Condition

- Muscle disorders
- Skin vascular abnormalities

Synonym
juvenile dermatomyositis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,een aanvraag wordt

ingediend bij het Prinses Beatrix Fonds

Intervention

Keyword: cytokines, HSP70, juvenile dermatomyositis, regulatory T cells

Outcome measures

Primary outcome

The main objectives of the mechanism of disease part of study are:

- establish the role of regulatory T cells (Treg cells) in muscle and in peripheral blood of JDM patients in active disease and in remission compared to children with non-inflammatory muscle neuromuscular disorders

- responsiveness of Tregs to HSP60 and HSP70

- investigate the expression of HSP60 and HSP70 in muscle of JDM patients, compared to children with non-inflammatory neuromuscular disorders

Secondary outcome

- to investigate the homing of Treg cells to the site of inflammation (muscle)

- to assess the local suppressive capacity of Treg cells in muscle tissue

- to investigate the factors influencing the suppressive capacity of Treg cells

- expression of cytokines in muscle of JDM patients

- correlation between cytokine levels in serum and expression in muscle by multiplex assay

- to correlate the cytokine levels to disease activity parameters (CMAS and myometrie, plus labresults)

- compare these data to controls with other neuromuscular disorders than dermatomyositis.

Study description

Background summary

Juvenile dermatomyositis (JDM) is a rare chronic inflammatory disease of childhood, in which the immune system targets the microvasculature of the skeletal muscle and skin, leading to myopathy and a typical skin rash. The exact etiopathogenesis is unknown. In our previous studies we have shown the regulation of the immune respons by regulatory T-cells (T-regs) in peripheral blood is different in JDM compared to healthy controls. Furthermore it has been shown that in the muscle of JDM patients, where the inflammation takes place, the expression of heat shock proteins (HSP) is increased compared to muscle biopsies of healthy controls. We want to investigate whether regulatory T cells respond towards HSP in peripheral blood samples and the muscle tissue, in order to establish whether heat shock proteins can be used to induce tolerance in JDM. Also, we aim to establish whether T cell responses relate to clinical disease activity to identify markers to predict disease activity.

Study objective

to investigate the role of regulatory T cells in response to heat shock proteins in muscle and peripheral blood of patients with juvenile dermatomyositis. To identify patterns in T-cell responses and cytokineprofiles, in relation with clinical disease activity .
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Study design

This is an observational study in all children with juvenile dermatomyositis known in our clinic. Two groups of patients can be distinguished: newly diagnosed patients (estimated at 3-5 new patients per year) and patients that are in follow-up in our clinic (n=45).
In newly diagnosed patients a muscle biopsy is taken to confirm diagnosis. This minimally invasive procedure, during which several samples are taken through a biopsy needle, takes place under general anesthaesia, for which an intravenous access is necessary. For this study we want to use the muscle biopsies, not being used for diagnosis, and a peripheral blood sample taken during anaesthesia prior to the start of therapy. Subsequently blood sampling will take place at t=+3, t= +6, t=+12, t=+24, T= +36, t=+48, t=+ 60 months, to evaluate the immunological factors during active disease, disease in remission with and without medication. This bloodsampling will only be done in combination with routine laboratory testing. JDM patients currently known in our clinic will be followed for 5 years after diagnosis, and blood sampling will take place at the same timepoints after diagnosis as mentioned before. The control group consists of children referred to the pediatric neuromuscular

outpatient center *Spieren voor Spieren (S4S)*- for evaluation of muscle weakness, that need a muscle biopsy to establish a diagnosis. In these children muscle tissue and peripheral blood samples will only be at only one timepoint.

Study burden and risks

In most children with JDM muscle biopsies will be taken to confirm the diagnosis. Because in JDM the inflammation in the muscle tissue is scattered, routinely a minimum of three muscle needle biopsies will be taken, to ensure a biopsy with sufficient inflammation for evaluation. For our study we want to use the muscle biopsy samples, which are not used for diagnostic reasons. Blood sampling will be combined with blood sampling for regular laboratory controls. Subsequent sampling will take place in the outdoor patient visits, in combination with routine laboratory testing. The amount of extra bloodsampling (5-20 cc) will be adjusted to age and weight.

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

Diagnosis juvenile dermatomyositis criteria van Bohan and Peter,
ór referral to STC for non-inflammatory muscle weakness
age < 18 years
informed consent

Exclusion criteria

Age >18 jaar

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:	Completed
Start date (anticipated):	20-05-2011
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	12-04-2011
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	NL34124.041.10

Study results

Date completed:	19-06-2015
Actual enrolment:	25

Summary results
Trial ended prematurely