Genes involved in the induction and resolution of eczema using the Atopy Patch Test as an in vivo model for atopic dermatitis

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To investigate biomarkers that play a role in the induction and resolution of AD.Secondary objective: to develop therapeutic interventions (pharmacologically) based on the revealed biomarkers.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON44326

Source
ToetsingOnline

Brief title
APT and markers for eczema

Condition

- Epidermal and dermal conditions

Synonym
atopic dermatitis (AD), atopic eczema (AE)

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: atopic eczema, atopy patch test, induction

Outcome measures

Primary outcome

Ex vivo: mRNA expression levels of the measured markers with qPCR in snap

frozen tissue.

Secondary outcome

Ex vivo: localization of the markers with IHC on frozen slides.

Study description

Background summary

Atopic dermatitis (AD) is a chronic inflammatory skin disease, characterised by high levels of circulating IgE and skin infiltration of immune cells in both lesional and nonlesional skin. Skin T cells have been found to express a predominant Th2 type cytokine expression pattern. Nonlesional skin is suggested to be a 'pre activated' state resulting from the presence of increased numbers of inflammatory cells compared to 'healthy' skin. Immune cells from nonlesional AD skin react with a lower threshold to antigens. Reaction of immune cells with antigens results in the release of cytokines, chemokines and other inflammatory markers resulting in eczema. Little is known about the markers/intracellular pathways that play a role in the induction of AD.

The atopy patch test (APT) is a human in vivo model for AD. By application of allergens (e.g. house dust mite) to the skin for 24-48-72-96 hours an eczematous reaction that is very similar to lesional AD develops. The APT is used as a model to investigate genes involved in the induction and resolution of eczema lesions in AD patients. A biopsy at 24 hours is appropriate to study induction markers, a biopsy at 48 hours reveals which markers have an extended elevated expression but also reveals which factors decline in comparison to a 24 hrs biopsy. A biopsy at 72 and 96 hours shows which markers play a role in the resolution of the APT. We have previously shown several genes that may be involved in the induction and resolution of eczema (see attachments). However, the latter study lacked power. A sample size calculation (corrected for

multiple testing) revealed to extend the number of patients with n=10. To confirm our hypothesis that these markers are really involved in the induction and resolution of eczema (not based on 'statistical coincidence* and to correct for multiple testing), and to create a reliable selection of the genes of interest, we propose to extend the number of patients with n=10 AD patients. This additional study, will provide more insight concerning the induction and resolution of eczema, and may reveal new therapeutic targets.

Note: the 72 and 96 hours biopsies are included to study the resolution of the APT. Furthermore, the translation from genes to protein takes several hours. Therefore, a 72-96 hrs biopsy reflects the protein concentrations of 48 hours biopsies that show a high gene expression at 48 hours. The same applies to the 48 hrs biopsies compared to 24 hours biopsies in terms of protein measurments (but not gene expression)

Study objective

To investigate biomarkers that play a role in the induction and resolution of AD.

Secondary objective: to develop therapeutic interventions (pharmacologically) based on the revealed biomarkers.

Study design

- The APT is applied to the skin and biopsies are harvested after 24-48-72-96 hours after the induction of AD. Biopsies from nonlesional, lesional skin, and a control biopsy after the application of petrolatum are additionally harvested.
- from the harvested biopsies, mRNA measurments of the markers will be performed with qPCR. Localization of markers will be performed with IHC.

Study burden and risks

Participants will undergo an APT and seven skin punch biopsies (4 mm diameter) in four sessions. Performing a biopsy entails a slight risk of haemorrhage and infection. Over the past years, no SAE's were observed in patients that were included in the Biobank. A small scar at the site of biopsy will gradually fade in colour. No biopsies will be taken from the face or neck. Biopsies will only be taken from the arms and legs.
The specified number of biopsies is necessary to perform the proposed analyses. There is no direct benefit for the participants. An APT will induce erythema and pruritus with sometimes papules and vesicles. This reaction usually disappears after 72-96 hours. Erythema, pruritus, papules and vesicles normally disappear after 72-96 hours, but this process can be enhanced by application of topical steroids.

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

age 18-70 years
AE
positive APT

Exclusion criteria

Active AE on the patients back
- Not sensitized to aeroallergens, such as house dust mite (demonstrated by a positive immuno CAP test for these allergens)
- Treatment with systemic immunosuppressive medication (including corticosteroids and cyclosporin) within the 4 weeks prior to having the biopsies performed. In addition, weekly

use of equal or more than 50 grams of topical corticosteroids class IV or weekly use of equal or more than 100 grams of topical corticosteroids class III.
- Exposure of biopsy location to high levels of UV radiation (e.g. UV-therapy, use of tanning booths, sunbathing) in the 2 weeks prior to taking biopsies
- Use of antihistamines in the week or days before and during the APT (see patientinformation 'Bijlage 4: medicatielijst')

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):	16-12-2014
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	10-04-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-03-2016
Application type:	Amendment
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	NL47555.041.13