Biomarkers for Skin barrier and inflammation in Children with Atopic Dermatitis

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To determine the relationship between phenotypic, genetic and biochemical features of AD. , Relevant bimarkers of the skin barrier function including the levels of NMFs, inflammatory mediators (e.g. IL-1 cytokines), SC lipids and serine proteases...

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

Summary

ID

NL-OMON40610

Source
ToetsingOnline

Brief title
BioSCAD

Condition

- Epidermal and dermal conditions

Synonym
atopic dermatitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Stichting Steun Emma

Intervention

Keyword: Atopic Dermatitis, Childeren, Phenotype, Skin Barrier

Outcome measures

Primary outcome

Clinical and biochemical parameters in relation to the presence of AD and FLG

mutations.

Secondary outcome

Establishment of different phenotypes of AD based on the relationschip FLG

genotype and biochemical parameters

Study description

Background summary

Atopic dermatitis (AD) is the most common pediatric skin disorder in developed countries affecting 15-30% of children. Since 2006 it is known that loss-of-function mutations in the filaggrin gene (FLG) are a major predisposing factor for AD and concomitant asthma1. Up to 40% of AD patients carry at least one FLG mutation. Furthermore, infants with FLG mutations are associated with early onset and more severe disease when compared to infants without this mutation2. Approximately 10% of individuals of European ancestry are heterozygous carriers of a loss-of-function mutation in FLG resulting in a 50% reduction in expressed filaggrin protein1.
Filaggrin plays an important role in the formation of the epidermal barrier, which is profoundly impaired in AD. Filaggrin is present in the granular layer of the epidermis, where it aggregates keratin filaments, leading to the collapse of the keratinocytes into the flattened corneocytes and thus the stratum corneum (SC). Filaggrin is further metabolised into amino acids, the so-called natural moisturizing factors (NMFs), which contributes to epidermal hydration and maintaining of the acid skin mantle1. Recent studies have shown that reduced levels of NMFs are associated with impaired skin barrier and dry skin, altered composition of SC lipids, elevated pH, and enhanced levels of IL-1 cytokines likely modified through altered activity of serine proteases (KLK7 and KLK5).

Despite recent insights into AD pathogenesis many questions remain unanswered

about the mechanisms through which filaggrin deficiency and environmental factors modify the course of AD. In particular, little is understood about the role of intrinsic and environmental factors responsible for a large spectrum of disease phenotypes seen in children, such as severity and persistence the development of IgE mediated sensitization leading to clinical manifestation of allergic rhinoconjunctivitis and asthma in some, but not all children, the sensitivity of some children to develop frequent bacterial and viral superinfections, and hypersensitivity to sunlight leading to exacerbation of AD in some patients. Furthermore, some children develop an allergic contact dermatitis on top of their AD, making it difficult to determine the true course of the AD on itself. Beside these phenotypic variations in the clinical course of AD, one can also distinguish phenotypic variations in clinical manifestation of AD, such as for example AD with nummular eczema as the main presentation, AD with a prominent prurigo nodularis component, AD that is more dominant on the extensor surfaces in stead of the typical flexural locations, and a papular, mainly acral, form of AD. These phenotypic variations seem to suggest that AD is not just one disease, but a heterogeneous group of similar but separate entities. It would be useful to try to separate these entities in well defined clinical subgroups, in order to enable further prospective cohort or intervention studies tailored to these different clinical phenotypes. Next to clinical parameters, it is important to identify relevant biomarkers of skin barrier and immune profile to define these clinical subgroups that might be used in such studies

Study objective

To determine the relationship between phenotypic, genetic and biochemical features of AD. , Relevant bimarkers of the skin barrier function including the levels of NMFs, inflammatory mediators (e.g. IL-1 cytokines), SC lipids and serine proteases will be investigated in relation to the presence of disease and FLG mutations.
This may aid us in dissecting different AD subtypes, enabling individualised therapeutic approaches.

Study design

mono-centre case - control cohort study.

Study burden and risks

there are no health risks and only minor burden associated with participation in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

100 children with atopic dermatitis, male or female, aged between 0 and 12 years, will be participating in this study.;50 children without any skin disorder or atopy (such as food allergy, allergic rhinoconjunctivitis and allergic asthma), as well as no atopy in first degree relatives, male or female, aged between 0 and 12 years, will be participating as controls

Exclusion criteria

For Cases:
No clinically skin lesion to obtain tape strips from.
Use of corticosteroids or other anti-inflammatory topical treatment on the skin lesion(s) selected for tape stripping 1 week prior to the procedure.
Use of emollients, soap, and cosmetics on the skin lesion(s) selected for tape stripping 48

hours prior to and during the hospital visit day.
Use of oral antihistamin 1 week prior to the hospital visit day.
- Onset of atopic dermatitis after the age of 2
- History of remission of atopic dermatitis without treatment (except emollients) for longer than 1 year ;For controls:
history of atopy or first degree relative with atopy
Use of emollients, soap, and cosmetics on the skin lesion(s) selected for tape stripping 48 hours prior to and during the hospital visit day.

Study design

Design

Study type:	Observational non 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):	21-01-2015
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	06-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-05-2016
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	NL47401.018.13