Effects of coal tar treatment on natural moisturizing factors in atopic dermatitis patients

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To objectify skin barrier repair characteristics of coal tar in atopic dermatitis patients, by quantifying changes in NMF, lipid levels, TEWL, SCORAD-score and cytokine levels

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

Summary

ID

NL-OMON40845

Source
ToetsingOnline

Brief title
COAL

Condition

- Epidermal and dermal conditions

Synonym
dermatitis, eczema

Research involving
Human

Sponsors and support

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

Intervention

Keyword: atopic, coaltar, dermatitis, eczema

Outcome measures

Primary outcome

changes in NMF, lipid levels, TEWL, SCORAD-score and cytokine levels

Secondary outcome

Presence of filaggrine mutation

Study description

Background summary

Atopic dermatitis (AD) is a chronic and relapsing inflammatory skin disorder with a wide spectrum of clinical presentations and combinations of symptoms. It affects up to 20 percent of children and 2-10 percent of adults and often predates the development of allergic airway diseases like rhinitis and asthma

Skin barrier dysfunction, which can be inherited or acquired, is a major hallmark of AD, allowing for enhanced allergen and microbial penetration across the skin.
A defective skin barrier in AD exists even in nonlesional skin and is characterized by increased transepidermal water loss (TEWL) as well as enhanced percutaneous penetration of chemicals.3

The discovery that mutations in the gene encoding the stratum corneum (SC) structural protein filaggrin (FLG) are a remarkably strong risk factor for AD, underscores the importance of the skin barrier in AD. Among patients with moderate-to-severe AD, up to 57 percent carry 1 or more FLG-null mutations, and the population attributable risk fraction has been estimated at between 4.2 percent and 15.1 percent.4,5 Filaggrin is a major structural protein in the SC, crucial for the structural and biophysical integrity of the skin. Proteolysis of Filaggrin results in small peptides known as natural moisturizing factor (NMF). 6. These NMF keep water from evaporating from the skin and thus low levels of NMF result in a dry and easily cracked skin and unsurprisingly a filaggrin null mutation genotype is associated with a change in NMF-profile in the SC

Topical use of coal tar is believed to be the oldest known therapy for AD. Its

molecular-working mechanism however, is still under investigation. In vitro coal tar has shown to activate the aryl hydrocarbon receptor (AHR), resulting in enhanced epidermal differentiation, increasing the levels of Filaggrin and inhibiting the IL-4/STAT6 signalling pathway [5].This should, in principle, strengthen the skin barrier. In vivo this has not yet been shown.

The current standard treatment of AD is the application of topical corticosteroids and immunosuppressive ointments to counter the immunological reaction and thus control flares. However, prolonged use of immunosuppressivants treatment can induce side-effects on long-term, stressing the need to develop new treatment applications. The use of coal tar therapy has declined over the past decennia in favour of topical immunosuppressivants due the unfavourable dark colour and unpleasant odour of coaltar. Although tar is known to be carcinogenic, we know from large and long-term follow-up studies that no carcinogenic effect can be shown in the topical use of coal tar

Therapeutic intervention in AD should be aimed at both restoring skin barrier function and reducing inflammation in the entire integument in general and in AD lesions in particular, as impaired skin barrier function is present in lesion as well as clinically uninvolved skin.[7] Corticosteroids have been the mainstay of treatment for AD, in the acute as well as the chronic phase of the disease. In short-term however, corticosteroids may have a negative impact on skin barrier function leading to e.g. decreased production and secretion of epidermal lamellar bodies and decreased SC cohesion and integrity.[8] Similar observations have been encountered with the usage of calcineurin inhibitors, such as pimecrolimus and tacrolimus[9]. Therefore other substances such as coal tar should be investigated for their skin barrier restoration properties.

Study objective

To objectify skin barrier repair characteristics of coal tar in atopic dermatitis patients, by quantifying changes in NMF, lipid levels, TEWL, SCORAD-score and cytokine levels

Study design

This is a single-center, randomized, intra-individual comparison (right/left) intervention study

Study burden and risks

The risks taken with participating are low. Large and long-term follow-up studies show that no carcinogenic effect can be related to topical use of coal tar. All measurements done are non-invasive and not painfull therefore the burden of participation is low.

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

- Clinically diagnosed atopic dermatitis
- Mild to moderate atopic dermatitis, according to total SCORAD score (objective score <;25)
- Age between 18 and 70 years
- Written informed consent
- At least two symmetrical (i.e. left and right side of the body) skin sites with comparable AD severity (sign or symptoms as erythema, oedema, excoriation, lichenfication, dryness, pruritis will be scored)

Exclusion criteria

- Extensive UV exposure in the last 14 days before study and/or expected during the study.

- Other skin disease other than AD.
- Use of antibiotics prior to (4 weeks) the study and/or expected use during the study.
- Use of systemic suppressing drugs (e.g. prednisone, methothrexate) prior to (4 weeks) the study and/or expected use during the study
-Severe disorders within the last 6 months before study (e.g. cancer, acute cardiac or circularity disorders, HIV, infectious hepatitis)
-pregnancy or breastfeeding
- Investigator's uncertainty about the willingness or ability of the patient to comply with the protocol requirements.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-09-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	coaltar
Generic name:	coaltar
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	23-07-2014

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2014
Application type:	First submission
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
EudraCT	EUCTR2014-002080-15-NL
CCMO	NL48672.018.14