Mobilisation of neutrophils and premature photoaging in chronic vitiligenous skin of black skinned patients

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To further investigate the photoprotective properties of melanin and the role of skin-infiltrating neutrophils with respect to the damaging effects of solar radiation on human skin.

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

Summary

ID

NL-OMON31353

Source
ToetsingOnline

Brief title
Neutrophil mobilisation and premature photoaging in vitiligo / Vitphotoag

Condition

- Epidermal and dermal conditions

Synonym
1) elastosis solaris, sun damaged skin 2) vitiligo, white spot disease

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: black, neutrophils, photoaging, vitiligo

Outcome measures

Primary outcome

(a) Qualitative comparison of extra cellular matrix damage in longstanding sun exposed vitiligenous skin and adjacent normal skin using standard haematoxylin eosin and Elastica von Gieson staining procedures.

(b) Quantitative comparison of infiltrating neutrophils in vitiligenous and adjacent normal skin following exposure to an equal physical dose of SSR.

(c) Determining the distribution of DNA photoproducts in vitiligenous and adjacent normal skin following exposure to SSR.

(d) Determining the MED of Vitiligenous skin.

Secondary outcome

(a) Quantitative comparison of photoaging associated proteolytic and/or neutrophil associated enzymes and cytokines: MMP-1, MMP-3, MMP-8, MMP-9, Neutrophil elastase and IL-10 in irradiated vitiligenous and adjacent normal skin.

(b) Measurement of surface markers of activation on infiltrating neutrophils: CD11b, CD66b, CD63.

(c) Comparison of keratinocyte activation and keratinocyte apoptosis in vitiligenous and adjacent normal skin following exposure to SSR.

Study description

Background summary

Exposure of white skin (skin phototype I-III) to erythemogenic doses of solar simulating radiation (SSR) results in an influx of neutrophils. We have previously shown that neutrophils are a major source of enzymatically active photoaging-associated proteolytic enzymes. By this capacity they appear to be important contributors to the process of photoaging of the skin. Furthermore we have shown that neutrophils infiltrating the epidermis are a source of IL-10, a cytokine which has been associated with photo-carcinogenesis.
Black skin (skin phototype VI) is better protected against the damaging effects of solar radiation. Black skin is thus less susceptible to photocarcinogenesis and photoaging. This is most likely due to abundant melanin pigment present in the epidermis of black skin. We have shown that exposing white and black skinned persons to equal physical doses of SSR induces a strong neutrophilic infiltrate in white but not in black skin. Furthermore DNA photoproducts following exposure to SSR are limited to the suprabasal epidermis in black skin while they are distributed throughout the epidermis and upper dermis in white skin. These findings support the hypothesis that melanin plays a major role in the protection of skin against the deleterious effects of solar radiation.
Vitiligo is a skin disease in which melanocytes disappear from the skin and as a consequence the production of melanin is halted. Literature shows conflicting data on the susceptibility of vitiligenous skin to photoaging and photo-carcinogenesis.

Study objective

To further investigate the photoprotective properties of melanin and the role of skin-infiltrating neutrophils with respect to the damaging effects of solar radiation on human skin.

Study design

Volunteers will be recruited from patients with vitiligo and black skin visiting the UMC Utrecht dermatology & Allergology department and the Dutch patient*s association for vitiligo will be approached to place an advertisement on their website.
The first group of volunteers (n=6) will consist of elderly patients with longstanding vitiligo. During a single visit (~ 15 minutes) two punch biopsies (4mm diameter) will be taken from sun-exposed lesional and adjacent normal skin.
The second group of volunteers (n=6) will visit our clinic on two consecutive days (~ 50 and 15 minutes respectively). The minimal erythemal dose (MED) of lesional skin will be determined (day 1) and an area of lesional and normal skin will be exposed to 18 000 mJ per cm2 of SSR (day 1) from which two punch biopsies (4mm diameter) will be taken twenty four hours later. Two additional control biopsies will be taken from unexposed lesional and normal skin.

All procedures will be carried out by the principal investigator in the light department of our outpatient*s clinic.

Intervention

see study design.

Study burden and risks

The lesions resulting from the biopsies taken may remain visible for a prolonged period of time as hypopigmented areas. Induced redness of a small area of the skin following determination of the MED and exposure to SSR should cause no physical discomfort and may heal with some scaling within days. Serious adverse events are highly unlikely. Any effect on the disease itself is not expected. Patients will receive some financial compensation for their participation.

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

Group I and II: adult, male or female, aged 18 years or over; patients with skin phototype VI and vitiligo; the patient must be willing and able to give written informed consent.
Group I specifically: chronic vitiligo, persistant for 10 years or more, localised on sunexposed skin.
Group II specifically: it must be technically possible to determine the minimal erythemal dose.

Exclusion criteria

sunlight allergy; tendency to hypertrophic scar or keloid formation; history of alcohol or drug abuse; treatment with phototherapy or systemic (immunosuppressive) therapy such as oral steroids and cyclosporin A during the study, or within 24 weeks prior to the study; treatment with oral and local antibiotics; treatment with topical steroids or tar in the tested locations during the last 2 weeks; clinically relevant cardiovascular, gastrointestinal, liver or renal disease and/or unstable metabolic or endocrine disorders; acute or chronic local bacterial, viral or fungal diseases; women of childbearing potential not using reliable contraception; pregnancy or breast feeding; psychiatric disease or history of noncompliance which, in the investigator*s assessment would interfere with appropriate protocol treatment and monitoring.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-07-2008
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	30-10-2007
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	NL18625.041.07