Comparison of skin suction blister method with or without heat plate in a LPS challenge model in healthy volunteers

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Primary Objectives- To determine the effect of the heat plate on suction blisters in a LPS challenge modelSecondary Objectives- To evaluate the safety and tolerability of the heat plate added to the LPS challenge model;- To evaluate the correlation...

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

Summary

ID

NL-OMON51862

Source
ToetsingOnline

Brief title
Influence of heat on skin suction blisters in a LPS challenge model

Condition

- Epidermal and dermal conditions

Synonym
LPS challenge, Skin suction blister

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research

Source(s) of monetary or material Support: CHDR-funded study

Intervention

Keyword: Heat plate, LPS, Skin suction blister

Outcome measures

Primary outcome

* Clinical/biophysical measures: blister induction time, 2D and 3D images,

blister volume, erythema by clinical evaluation (erythema grading scale)

* Cellular and cytokine responses in blister exudate:

o Cytokines and chemokines

o Flow cytometry, immune cells including but not limited to:

§ Neutrophils

§ Monocytes/macrophages

§ CD4+ lymphocytes

§ CD8+ lymphocytes

§ CD56+ lymphocytes

§ CD1c dendritic cells

Secondary outcome

* NRS pain score

* Blood flow as measured with basal flow through laser speckle contrast imaging

(LSCI)

* Microcirculation as measured by side-stream darkfield microscopy (SDFM). The

following parameters will be analyzed:

o Number of vessels, vessel density, perfused number of vessels, perfused

vessel density

* Qualitative assessment of dermo-epidermal layer

* Transepidermal water loss

Study description

Background summary

Skin suction blisters (SSB) can be artificially induced to retrieve fluid and cells directly from the skin. These blisters are induced by negative pressure through a vacuum. Duration of blister formation variates, but in most cases this takes between 1-2 hours. Once the blister is formed, fluid can be harvested by fine needle aspiration or directly by using a pipet after puncturing the blister. In most cases SSB are induced on the ventral side of the forearm. The SSB model is proven to be effective in objectively evaluating human immune responses.

The suction blister device at CHDR is from Electronic Diversities (USA) and is designed with a heat plate in each suction chamber. The heat is provided by incandescent lamps which are controlled by a temperature controller. This temperature controller is set at 40 degrees Centigrade. The lamps radiate and conduct their heat to the orifice plate and provide sight on the skin area where the blister is formed.

At CHDR the suction blister device has been previously used for several studies (among which CHDR1752A, CHDR1752B and CHDR1912). In these studies, the suction blister device was used with the heat plate switched off. This was how it was tested in the USA prior to the use in our studies. Therefore, the effect of heat on endpoints like cytokine release and cellular responses is unknown. And, since previous studies reported that heat has a positive effect on blister formation and reduces blister formation time, it is interesting to determine if heat influences these endpoints.

Lipopolysaccharide (LPS) is a pro-inflammatory substance found on the outer cell membranes of Gram-negative bacteria. It protects these bacteria from phagocytosis and lysis. LPS is recognized by Toll-like receptor (TLR) 4 in a normal functioning immune system. Administration of LPS into healthy human volunteers creates a model in which immune responses can be monitored and influenced. LPS can be used for intravenous, inhaled, nasal and intradermal administration. Intradermal administration creates a rapid, limited local inflammatory reaction and allows detailed insight in the local immune response (CHDR1752A and CHDR 1752B)

The aim of this study is to determine the influence of heat on blister

formation, including cytokine release and cellular responses, in an intradermal LPS challenge model in healthy volunteers.

Study objective

Primary Objectives
- To determine the effect of the heat plate on suction blisters in a LPS challenge model

Secondary Objectives
- To evaluate the safety and tolerability of the heat plate added to the LPS challenge model;
- To evaluate the correlation between clinical measures, biophysical measures, and cellular and cytokine responses.
- To evaluate skin perfusion and local microcirculation after blister formation with laser speckle contrast imaging (LSCI) and sidestream dark field microscopy (SDFM).
- To evaluate skin morphology.
- To evaluate skin barrier function

Study design

An interventional study to determine the effect of heat on skin suction blisters after intradermal LPS injections.

Intervention

Subjects will receive in total two intradermal doses of LPS on the lower forearms on day 1. The dose per injection is 5 ng

Study burden and risks

The overall aim of this study is to determine the effect of heat on cytokine releases and cellular responses found in skin blister fluid in an LPS skin challenge model in healthy volunteers. The skin inflammation model with LPS for healthy volunteers has been proven to be safe and has been used in several studies. No medical benefit can be expected from this study for the participating subjects.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Healthy male and female subjects, 18 to 45 years of age, inclusive. Healthy status is defined by absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead ECG, hematology, blood chemistry, coagulation, blood serology and urinalysis;
2. Body mass index (BMI) between 18 and 32 kg/m2, inclusive, and with a minimum weight of 50 kg;
3. Fitzpatrick skin type I-III (Caucasian);
4. Subjects of childbearing potential must use effective contraception for the duration of the study;
5. Able and willing to give written informed consent and to comply with the study restrictions.

Exclusion criteria

Eligible subjects must meet none of the following exclusion criteria at screening:
1. Any disease associated with immune system impairment, including auto-immune

diseases, HIV and transplantation patients;
2. Any (medical) condition that would, in the opinion of the investigator, potentially compromise the safety or compliance of the patient or may preclude the patient*s successful completion of the clinical trial;
3. Any vaccination within the last month; COVID-19 vaccination is allowed up until 2 weeks before study day 1;
4. Have any current and / or recurrent pathologically, clinical significant skin condition at the treatment area (i.e. atopic dermatitis); including tattoos;
5. Hypersensitivity for dermatological marker at screening;
6. Requirement of immunosuppressive or immunomodulatory medication within 30 days prior to enrolment or planned to use during the course of the study;
7. Use of topical medication (prescription or over-the-counter [OTC]) within 30 days prior to day 1, or less than 5 half-lives (whichever is longer) on lower arms;
8. Excessive sun exposure or a tanning booth within 3 weeks of enrolment;
9. Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times a year;
10. Loss or donation of blood over 500 mL within three months prior to screening;
11. Volunteers with clinically relevant infections;
12. Current nicotine use in excess of 5 cigarettes per day or unable to abstain from smoking during the course of the study (from screening till end of study);
13. History of or current drug or substance abuse considered significant by PI (or medically qualified designee), including a positive urine drug screen;
14. Covid-19 infection (with positive test result) within the last 4 weeks.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	25-01-2022
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	17-12-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL79323.056.21