ISRCTN11296911 https://doi.org/10.1186/ISRCTN11296911

A study to investigate the effect of heat on skin suctions blisters in a model wherein inflammation of the skin is induced by lipopolysaccharide in healthy volunteers

Submission date
12/05/2022

Recruitment status
No longer recruiting

Registration date
17/06/2022

Overall study status
Completed

Last Edited
17/06/2022

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The Centre for Human Drug Research (CHDR) has conducted several studies in which blisters have been created on the skin. These blisters are raised with a device that uses a vacuum. In addition, this device contains small lamps that give off heat. In previous studies, these lights were turned off, so no heat was used to create the blisters. In this study, it will be investigated if heat influences the cellular and cytokine responses measured in the blister exudate and the formation of the blister. The CHDR has set up a model to study local inflammation of the skin. To this end, lipopolysaccharide (LPS, the major component of the outer membrane of Gram-negative bacteria) is injected in the skin where it causes a local inflammatory reaction in healthy volunteers. This inflammation model can be used to investigate the effect of (new) anti-inflammatory agents.

The aim of this study is to determine the effect of heat on blisters (the fluid in the blisters and the formation of the blisters) on skin where mild inflammation is present. A total of four blisters are made, two on both forearms.

Who can participate?
A total of 12 healthy volunteers, male and female, aged between 18 and 45 years old will participate.

What does the study involve?
First, lipopolysaccharide (LPS) is injected into the skin at two locations on the forearms. LPS is part of a bacterium. The body reacts to LPS like a bacterium with an inflammatory response. In the current study, LPS will be used to mimic inflammation in the skin in a controlled manner. No injection is given on the other two sites on the forearms. Six hours after the injections, 4 blisters will be formed on the forearms. Two blisters will be formed where the LPS was injected. The other two blisters are formed on skin on the forearms where no injection has been given (where nothing has happened). On the left arm the blisters are formed without using heat and on the

right arm the blisters are formed with heat. When the blister is fully formed, it is then punctured and the blister fluid is aspirated. After this, the roof of the blister is removed. The blister fluid and the blister roof will be analyzed for inflammatory cells and/or cytokines.

What are the possible benefits and risks of participating?
There will be no benefit from participating in this study. But participation can contribute to more knowledge about inflammation of the skin and measurements involved with this in research.

Where is the study run from?
Centre for Human Drug Research (Netherlands)

When is the study starting and how long is it expected to run for? (what are the overall start and end dates?)
December 2021 to February 2022.

Who is funding the study?
Centre for Human Drug Research (Netherlands)

Who is the main contact?
D.T. de Bruin (Project Leader), ddebruin@chdr.nl

Contact information

Type(s)
Scientific

Contact name
Dr Digna de Bruin

ORCID ID
https://orcid.org/0000-0003-2228-9127

Contact details
Zernikedreef 8
Leiden
Netherlands
2333 CL
+31 71 5246 400
ddbruin@chdr.nl

Additional identifiers

Protocol serial number
CHDR2136

Study information

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

Study objectives
The effect of heat on endpoints like cytokine release and cellular responses in blister exudate 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.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/12/2021, Stichting BEBO (Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 592-405871; info@stbebo.nl), ref: NL79323.056.21

Primary study design
Interventional

Study design
Interventional parallel open-label study.

Study type(s)
Other

Health condition(s) or problem(s) studied
Influence of heat on skin suction blisters in a lipopolysaccharide (LPS) challenge model in healthy volunteers

Interventions
All volunteers will receive two intradermal lipopolysaccharide (LPS, 5 ng) injections in both forearms. Six hours after LPS injection, blisters will be made on these sites and on two control sites (untreated skin). Volunteers will be randomized for LPS injections proximal or distal on the lower forearms. The heat plate of the suction blister device will be switched on at the right arm and switched off at the left arm. Study interventions and assessments will be performed during an ambulant visit (1 day). There is no follow-up visit.

Intervention Type
Other

Primary outcome(s)
1. Blister induction time and volume measured after formation of skin suction blisters at 6 h
2. Cellular and cytokine responses in blister exudate and epidermal sheet measured using flow cytometry and Meso Scale Discovery (MSD) at 6 h
3. Blister volume and wound healing parameters evaluated using imaging (2D and 3D) at 8 h and 3D also at 8 h 30 min
4. Redness of the skin measured using clinical erythema score at baseline and 6 h

Key secondary outcome(s)
1. Pain measured using Numeric Rating Scale (NRS) pain score at 6 h and 8 h
2. Blood flow measured with basal blow through Laser Speckle Contrast Imaging (LSCI) at 8 h 30 min
3. Microcirculation measured by sidestream darkfield microscopy (SDFM) at 8 h 30 min

4. Qualitative assessment of dermoepidermal layer by Optical Coherence Tomography (OCT) at 8 h 30 m
5. Barrier status of the skin measured using transepidermal water loss (TEWL) at 8 h 30 m

Completion date
22/02/2022

Eligibility

Key inclusion criteria
1. Healthy male and female subjects, 18 to 45 years of age, inclusive. Healthy status is defined by the 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

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
12

Key exclusion criteria
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. Or the donation of plasma within 14 days 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

Date of first enrolment
14/01/2022

Date of final enrolment
14/02/2022

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
Zernikedreef 8
Leiden
Netherlands
2333 CL

Sponsor information

Organisation
Centre for Human Drug Research

ROR
https://ror.org/044hshx49

Funder(s)

Funder type
Research organisation

Funder Name
Centre for Human Drug Research

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date