Capsaicin pain model with topical 1% ethanolic capsaicin solution

Published: 14-03-2019
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Primary objective-To determine the effect of topical capsaicin on primary hyperalgesia, as assessed by the thermal heat pain test (pain detection thresholds (PDTs))-To determine the effect of topical capsaicin on the area of secondary mechanical...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48384

Source
ToetsingOnline

Brief title
1% capsaicin solution pain model

Condition

- Other condition

Synonym
Neuropathic pain

Health condition

Pain

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Clinical Research Organization (self-funded)

Intervention

Keyword: Capsaicin, Hyperalgesia, Pain model

Outcome measures

Primary outcome

-Pain Detection Threshold (PDT) on capsaicin treated area compared with untreated area (°C), assessed with Q-Sense

-Area of secondary mechanical allodynia around the capsaicin treated area (mm2), assessed with Von Frey hair stimulation

Secondary outcome

-Pain Detection Threshold (PDT) on capsaicin treated area compared with untreated area (°C), assessed with Q-Sense

-Area of secondary mechanical allodynia around the capsaicin treated area (mm2), assessed with Von Frey hair stimulation

-Amplitude (*V) and latency (ms) of LEPs in primary, secondary, and control area (N2, P2, and N2P2)

-Electrical Burst: PDT (mA), Pain Tolerance Threshold (PTT) (mA), Area Under the VAS pain Curve (AUC) (mA*mm), and post-test VAS (mm).

-Electrical Stair (pre-cold pressor): PDT (mA), PTT (mA), Area Under the VAS pain Curve (AUC) (mA*mm), and post-test VAS (mm).

-Electrical Stair (post-cold pressor): PDT (mA), PTT (mA), AUC (mA*mm), and post-test VAS (mm).

-Conditioned Pain Modulation Response (change from electrical stair pre- and

post-cold pressor): PDT (mA), PTT (mA), AUC (mA*mm).

-Pressure Pain: PDT (kPa), PTT (kPa), AUC (kPa*mm), and post-test VAS (mm).

-Cold Pressor: PDT (s), PTT (s), AAC (s*mm), and post-test VAS (mm).

-Capsaicin pain - Numeric Rating Scale (NRS): Numeric Rating Scale (0-10 with

0=no pain & 10=worst pain imaginable)

-Subjective pain perception after LS on primary, secondary and control area

+LS-NRS: Numeric rating scale (0-10 with 0=no pain & 10=worst pain

imaginable)

+McGill Pain Questionnaire

Study description

Background summary

PainCart, a test battery of human evoked pain models, is able to provide biomarkers for nociceptive and inflammatory pain at early stages of drug development in healthy volunteers. To be able to accommodate the new analgesic drugs that are being developed and the increasing number of novel pain mechanisms involved, it is essential to continue optimizing and expanding the PainCart and the evoked pain models that it consists of. As such, CHDR is seeking to expand the PainCart with a model to robustly assess central sensitization, by utilizing the concept of inducing secondary hyperalgesia on an area surrounding injured, or sensitized skin.

A frequently used model to induce sensitization, is topical application of capsaicin, the active component of hot chili peppers. This substance selectively activates the primary nociceptive afferents of C-fibers and multimodal A*-fibers via the Transient Receptor Potential cation channel subfamily V member 1 (TRPV1) receptor. Topical application of capsaicin and its effects on sensitization have been explored in previous CHDR studies (CHDR1703, CHDR1738, CHDR1738-D). Preliminary results of CHDR1703 suggest that the current formulation (capsaicin 1% cream) does indeed induce peripheral sensitization, as observed with altered heat pain detection thresholds (PDT*s) on the primary (treated) area. However, the cream does not induce the co-expected central

sensitization, as assessed by laser evoked potentials (LEP*s) and von Frey filaments on the secondary area (site surrounding treated area). Literature suggests that a different formulation may increase the latter sensitizing effect, due to superior penetration of capsaicin through the skin. The proposed study therefore aims to validate the use of a different formulation of capsaicin for topical application (a 1% ethanolic solution), to assess allodynia and (secondary) hyperalgesia, as an extension to CHDR*s PainCart test battery.

To quantify the effects of pain in the context of this updated model, both psychophysical (using the McGill Pain Questionnaire) and physiological parameters (LEPs and heat PDT*s) will be investigated. The painful stimuli to the primary area will be induced by a laser stimulation (LS) and thermal heat pain. During LS, electroencephalography (EEG) will be used to record laser LEP*s on both the primary and secondary area. Heat PDT*s will be assessed on the primary area, to confirm peripheral sensitization. In addition, the area of primary and secondary hyperalgesia will be assessed using mechanical stimulation with von Frey filaments.

Study objective

Primary objective
-To determine the effect of topical capsaicin on primary hyperalgesia, as assessed by the thermal heat pain test (pain detection thresholds (PDTs))
-To determine the effect of topical capsaicin on the area of secondary mechanical allodynia, as assessed with Von Frey filaments (mm2)

Secondary objectives
-To determine the feasibility of measuring secondary hyperalgesia using LEPs
-To determine the intra-individual reproducibility of primary and secondary hyperalgesia/ allodynia measurements with Von Frey, LEPs and thermal heat pain.
-To assess the feasibility of incorporating the topical 1% ethanolic capsaicin pain model in the PainCart test battery
-To evaluate the effect of capsaicin application on psychophysical, electrophysiological and PainCart parameters

Exploratory objectives
-To explore the effects of capsaicin on the skin by optical coherence tomography, clinical photography, laser speckle contrast imaging, and thermal imaging

Study design

This will be an open-label single-dose proof-of-Concept study. Subjects will attend the clinic on 2 occasions that both consist of one full study day, with a wash-out period in between occasions of 7 (±2) days. Subjects will be

contacted 7±2 days after the last capsaicin administration, for a follow-up telephone call.

Intervention

50uL of 1% capsaicin in ethanolic solution applied topically on the volar forearm

Study burden and risks

The risks associated in this study can be divided into topical capsaicin and LS-related risks.

Topical capsaicin
Topical capsaicin can lead to both sensitization and defunctionalization of TRPV1 containing nerve fibres, depending on the concentration and application frequency. Sensitization could result in transient burning sensations, hyperalgesia, allodynia and erythema. Defunctionalization due to overstimulation could result in increased tactile and nociceptive thresholds, after application of highly concentrated capsaicin products (8%). Both consequences are reversible in respectively hours and weeks. In addition, as mentioned in 1.3.1 of the protocol, nerve defunctionalization is not expected in this study, given the eightfold lower dose.

LS
Repeated application of LS on the exact same location within minutes (Plaghki & Mouraux, 2003) may induce a risk of skin burning. Therefore, in this study the location of stimulation is varied within every stimulation block of multiple stimulations. In addition, the laser energy has been limited to 2 J with a diameter of 5 mm to prevent skin damage. For more information on the stimulation method, please see Section 7.1. of the protocol.

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

1. Healthy male 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. ;2. Body mass index (BMI) between 18 and 30 kg/m2, inclusive. ;3. Able to participate and willing to give written informed consent and to comply with the study restrictions.

Exclusion criteria

1. History or symptoms of any significant disease including (but not limited to), neurological, psychiatric, endocrine, cardiovascular, respiratory, gastrointestinal, hepatic, or renal disorder. ;2. Clinically significant abnormalities, as judged by the Investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects. ;3. History of alcohol or drug abuse;4. Participation in an investigational drug or device study within 3 months prior to screening. ;5. Any confirmed significant allergic reactions (urticaria or anaphylaxis) after previous exposure to capsaicin ;6. Subject indicating intolerable pain after capsaicin administration at screening;7. Any current, clinically significant, known medical condition in particular any existing conditions that would affect sensitivity to cold (such as atherosclerosis, Raynaud*s disease, urticaria, hypothyroidism) or pain (i.e., disease that causes pain, hypesthesia, hyperalgesia, allodynia, paraesthesia, neuropathy) ;8. Subjects indicating pain tests intolerable at screening or achieving tolerance at >80% of maximum input intensity for any pain test for cold, pressure and electrical tests.;9. Dark skin (Fitzpatrick skin type V - VI), wide-spread acne, tattoos or scarring on the

volar forearms.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	09-10-2019
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	14-03-2019
Application type:	First submission
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

ID: 20584
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL68698.056.19

Study results

Date completed: 06-01-2020

Results posted: 07-04-2022

First publication
04-04-2022