Capsaicin induced neurogenic inflammation of the skin: influence of migraine and estrogen level

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- Measurement of the flow response to dermal application of capsaicin in the trigeminal nerve region in women with and without migraine.- Measurement of the flow response to dermal application of capsaicin in the trigeminal nerve region at various...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Headaches
Study type	Observational invasive

Summary

ID

NL-OMON36346

Source
ToetsingOnline

Brief title
Capsaicin, estrogen and migrain

Condition

- Headaches

Synonym
headache

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: capsaicin, dermal flow, estrogen, migraine

Outcome measures

Primary outcome

Differences in capsaicin-induced vasodilatation between women with and without migraine.

Effect of estrogen en progesterone levels on the capsaicin induced vasodilatation.

Secondary outcome

not applicable

Study description

Background summary

Migraine is a chronic and debilitating neurovascular disorder. It is associated with unilateral headache attacks with dysfunction of the autonomic nervous system and is sometimes preceded by an aura. It is a condition that affects more women than men (prevalence: women 17% and men 6%). Reproductive milestones as menarche, pregnancy and menopause in women are associated with changes in attack intensity and frequency. This suggests a connection between fluctuations in estrogen levels and the occurrence of migraine attacks. Menstrual migraine, a condition in which the attacks occur primarily around the perimenstrual days, also gives strong indication for involvement of estrogen fluctuations in migraine.

The pathofysiology of migraine is still unclear. It is often assumed that vasodilatation of intra-and extracranial vessels responsible for pain during attacks. The transient receptor potential vanilloid type 1 (TRPV1) receptors on the nerve endings of the trigeminal tract appear to have a key role in the attacks. Stimulation of the TRPV1 receptor consequences in release of CGRP (calcitonin gene-related peptide). CGRP is a neuropeptide with vasodilatory effect. We think that changes in estrogen levels affect the sensitivity of the TRPV1 receptor and consequently the release of CGRP. With our research we aim to improve our understanding of this process. The TRPV1 receptors in the skin

nerves of the forehead can be stimulated by local application of capsaicin. Capsaicin is the pungent ingredient of chili peppers and is locally used as an analgesic for neuropathic pain and itching. Stimulation of the TRPV1-receptor leads via release of CGRP to cutaneous vasodilatation. Maximal TRPV1-receptor stimulation should be desired. With a laser Doppler flow scan the degree of vasodilatation can be measured. With a saliva test we measure the CGRP concentration in saliva.

Postocclusive reactive hyperaemia (PRH) is a methode used to assess microvascular function. PRH is the rapid increase in blood flow after the release of an arterial occlusion. In this study we want to assess any relation between the dermal flow response to capsaicin and the PRH.

Study objective

- Measurement of the flow response to dermal application of capsaicin in the trigeminal nerve region in women with and without migraine.
- Measurement of the flow response to dermal application of capsaicin in the trigeminal nerve region at various estrogen levels.
- Determining if the flow dermal response to capsaicin is related to the maximal dermal flow response during reactive hyperaemia.

Study design

From three hours before the test, test-subjects are not allowed to consume coffee, tea or any other caffeinated beverages. From three hours before the test, test-subjects are not allowed to eat and from two hours before the test any physically strenuous activities are prohibited.

The capsaicin test will be preformed while the test-subjects rests supine on a bed. Three small rubber electrodes containing a 0.5ml reservoir will be placed on the forehead and subsequently filled with two capsaicin solutions (0.2 mM and 20 mM) and saline. One electrode will be placed in the neck region. After a baseline measurement of the blood flow for two minutes, a small current will be run through the electrode with saline 5 times. The duration of the current will be 1 minute each time. The blood flow is then measured for an additional 30 minutes.The dermal blood flow will be measured with the PeriScan PIM 3 system.

With a saliva test we measure the CGRP concentration in saliva. Participants will have to chew on a cotton swab during 5 minutes.

A blood pressure cuff is then placed on the upper non-dominant arm to measure the Postocclusive reactive hyperaemia (PRH). For this part of the experiment the dermal flow is measured at the volar site of the forearm. The pressure in the forearm cuff is quickly increased to 200 mmHg. This pressure is maintained

for five minutes. Then the pressure in the cuff is quickly released and the PRH is continuously measured for ten minutes with the PeriScan PIM 3 system.

After the test two vials of blood will be taken for the determination of the estrogen and progesterone levels and DNA research. The total research time will be 50-70 minutes.

Study burden and risks

The amount of time consumed by this research is the only burden. There are no risks associated with this research. Capsaicin application can cause temporary redness and some irritation of the skin.

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

General Inclusion criteria:
• Women
• Age between 18 and 75 years
• Non-smoking for > 6 months
• Body mass index between 18 and 30
• Capable and willing to give informed consent
• General good health, based on medical history and physical examination;Subjects with migraine:
• Should have diagnosed migraine, fulfilling criteria 1.1. Migraine without aura of International Classification of Headache Disorders (ICHD).
• Migraine attacks should occur exclusively on day 1±2 (ie, days -2 to +3) of menstruation in at least two out of three menstrual cycles and additionally at other times of the cycle.
• Should have a natural and regular menstrual cycle
• Age between 18 and 45 years;Subjects without migraine:
• Should have a natural and regular menstrual cycle
• Age between 18 and 45 years
Postmenopausal subjects
• Should be amenorrhoeic for at least 1 year

Exclusion criteria

• Use of hormonal contraceptives or hormonal replacement therapy
• History of cardiovascular disease
• Any serious illness that can compromise study participation
• Regular use of medication outside the period of migraine attacks
• Dermal diseases at the upper frontal side of the face
• Pregnancy or breastfeeding
• History of sensitivity to the fruits of capsicum plants (eg chilli peppers)
• Alcohol or drug abuse

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2011
Enrollment:	66
Type:	Actual

Ethics review

Approved WMO Date:	15-12-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-12-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL33804.078.10