Neurogenic inflammation in diabetic polyneuropathy and Charcot neuro-osteoarthropathy: response to intracutaneous Candida albicans

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To study the inflammatory response (induration) to intracutaneous Candida albicans in healthy individuals, patients with diabetes without polyneuropathy, patients with diabetic polyneuropathy and patients with a history of Charcot neuro-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON36125

Source
ToetsingOnline

Brief title
Neurogenic inflammation in diabetes

Condition

- Diabetic complications
- Bone disorders (excl congenital and fractures)
- Peripheral neuropathies

Synonym
Charcot's disease., Diabetic polyneuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Charcot neuro-osteoarthropathy, Diabetes mellitus, Neurogenic inflammation, Polyneuropathy

Outcome measures

Primary outcome

In all groups extent of induration as a response to intracutaneous Candida

albicans extract in four concentrations (1, 1:1,7, 1:5, 1:10) after 24, 48 and

72 hours.

Secondary outcome

Temperature difference between injection site of different concentrations of

Candida albicans on the foot and arm and the same location on the contralateral

foot and arm.

In 3 participants per group (with exception of the patients with a history of

Charcot neuro-osteoarthropathy) characterization of the induration and the

difference herein between the groups by skin biopsy.

Study description

Background summary

Foot ulcers and Charcot neuro-osteoarthropathy are feared complications of diabetic polyneuropathy. Despite extensive tissue destruction (due to infection), foot ulcers are often not accompanied by systemic signs of inflammation. On the other hand, Charcot neuro-osteoarthropathy is characterized by a clinical presentation of severe inflammation (a red, warm and swollen foot). These distinct clinical presentations might be due to an

altered neurogenic regulation of the inflammatory response due to the existing polyneuropathy.
A conducted pilot study demonstrated decreased type IV hypersensitivity response to intracutaneous Candida albicans in patients with diabetic polyneuropathy in comparison to patients with diabetes without polyneuropathy and healthy controls. In one patient with a history of Charcot neuro-osteoarthropathy, the response to intracutaneous Candida albicans was exacerbated compared to patients with diabetes and healthy controls.
This leads us to hypothesize that the delayed hypersensitivity response to intracutaneous Candida albicans is decreased in patients with diabetic polyneuropathy as compared to patients with diabetes without polyneuropathy. On the other hand, we hypothesize that the delayed hypersensitivity response to intracutaneous Candida albicans is increased in patients with a history of Charcot neuro-osteoarthropathy as compared to patients with diabetes with and without polyneuropathy.

Study objective

To study the inflammatory response (induration) to intracutaneous Candida albicans in healthy individuals, patients with diabetes without polyneuropathy, patients with diabetic polyneuropathy and patients with a history of Charcot neuro-osteoarthropathy.

Study design

Observational study

Intervention

Intracutaneous injection of Candida albicans extract in four concentrations (1, 1:1,7, 1:5, 1:10)

Study burden and risks

1 venous blood sample, 1 capillary blood sample and 1 urine sample will be taken. Height, weight, pulse frequency and blood pressure will be measured. Inspection and neurological examination of the lower extremities will be performed. Conduction velocity of the n. suralis will be measured by electromyography. Pulsations of the lower extremity arteries will be palpated and the ankle-brachial index will be determined. The study requires 4 visits: the first one lasting 75 minutes, the subsequent ones lasting 30 minutes. For the patients in whom punch skin biopsies are taken the fourth visit will last 45 minutes. For the participants with polyneuropathy follow up visits after the biopsy will be planned 1, 4 and 7 days after the biopsy. For the participants without polyneuropathy follow up by telephone will be planned 4 days after the biopsy. Intracutaneous injection of Candida albicans extract is associated with

short lasting mild discomfort at the injection site. Risks for participants consist of an immediate hypersensitivity reaction to Candida albicans extract (not observed in the conducted pilot study), wound infection at the biopsy site and poor healing of the biopsy site in participants with polyneuropathy (although this is unlikely considering a previously conducted study by Krishnan et al published in Diabetes Care in 2007). There is a theoretical risk of an anaphylactoid reaction as a response to the intracutaneous injection of Candida albicans. This is however highly unlikely and has not been previously described.

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

Patients with type 2 diabetes with and without polyneuropathy aged 40-75 years. The

presence of polyneuropathy is assessed by means of the Valk score and measurement of the conduction velocity in the n. suralis.
Patients with type 2 diabetes with a history of Charcot*s disease aged 40-75 years.
Healthy controls aged 40-75 years.
Signed informed consent.

Exclusion criteria

Peripheral arterial disease.
Active Charcot's disease.
Renal insufficiency.
Systemic disease.
Malignancy.
(Diabetic) foot ulcer.
Gout.
Bacterial infection of an extremity.
Skin condition of the dorsal aspect of the foot or the medial side of the upper arm.
Bleeding disorder.
Use of medication for asthma.
Impaired immunity.
Capillary blood glucose < 3 mmol/l or > 20 mmol/l at the time of the study.
Peripheral oedema.
Vaccination in the two months prior to study inclusion.
Chemotherapy or radiation therapy in the twelve months prior to study inclusion.
Surgery in the two months prior to study inclusion.
Previous adverse reaction to Candida albicans antigen.
History of anaphylaxis.
Acute infection at the time of the study or in the month prior to study inclusion.
Transfusion in the two months prior to study inclusion.
Use of immunosuppressants in the two months prior to study inclusion.
Pregnancy or breastfeeding.

Study design

Design

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

Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-05-2012
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO

Date:	11-01-2012
Application type:	First submission
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT01370837
CCMO	NL37123.068.11