Clinical phenotyping of postherpetic neuralgia patients to optimize pain treatment.

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Objective: The primary objective is to improve defining clinical phenotypes of PHN patients using the following diagnostics; questionnaires, QST, blood and cerebrospinal fluid (CSF) assessment and skin nerve fiber density measurements. The secondary…

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

Summary

ID

NL-OMON54722

Source
ToetsingOnline

Brief title
Clinical phenotyping of postherpetic neuralgia

Condition

- Peripheral neuropathies

Synonym
pain after shingles, postherpetic neuralgia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: pain, phenotyping, postherpetic neuralgia, quantitative sensory testing

Outcome measures

Primary outcome

Main study parameters/endpoints: The main study parameters are immunological and metabolic parameters in plasma and CSF, skin nerve fiber density measurements, questionnaires, and QST. We will determine whether the addition of these main study parameters identifies other/additional clinical phenotypes than those identified with QST alone and with which minimal parameter datasets these subsets can be identified.

Secondary outcome

The secondary endpoint is effect of standard pain treatment for PHN within patient groups with the different clinical phenotypes expressed as decrease in numeric rating scale (NRS), global perceived effect (GPE), time to treatment effect, regain of function, quality of life and improvement of QST parameters assessed at one year follow up. Spinal immunological parameters and metabolites will be assessed with MRS in a subset of patients who provided additional informed consent. Individual methadone metabolism is assessed by determining CYP2B6 enzyme polymorphisms.

Study description

Background summary

Rationale: One of the four most prevalent neuropathic pain syndromes is herpes zoster induced pain, also called postherpetic neuralgia (PHN).1,2 Patients

suffering from PHN typically describe different types of pain sensations and the disease is frequently severe, debilitating and difficult to treat.3-5 Subsets of PHN patients have different underlying mechanisms responsible for the generation and maintenance of their pain.6 Recently, three different clinical phenotypes of PHN have been identified using quantitative sensory testing (QST), yet these phenotypes still overlap within 28% of patients and in 30% of patients no clinical phenotype can be assigned indicating phenotyping needs to be improved.78 There are indications that these different clinical phenotypes assessed with QST respond differently to existing treatment regimes. More research is needed to improve the accuracy of clinical phenotyping and relate differences in efficacy of existing treatment regimens to the clinical phenotypes.

Study objective

Objective: The primary objective is to improve defining clinical phenotypes of PHN patients using the following diagnostics; questionnaires, QST, blood and cerebrospinal fluid (CSF) assessment and skin nerve fiber density measurements. The secondary objective is to assess the efficacy of existing treatment regimens for the different clinical disease phenotypes of PHN at one year follow up.

Study design

Study design: Observational study

Diagnostic study procedures: Patients with pain after a herpes zoster infection referred to the pain clinic of the UMCU receive care as usual (including intake questionnaires and QST during their first visit). Patients who give informed consent will be asked to undergo one vena puncture for 20 ml blood withdrawal and two skin biopsies of 3 mm diameter each. Additional informed consent will be asked for a one time CSF withdrawal and MRS. A second QST measurement is performed at one year follow up.

Study burden and risks

Benefit: Patients will receive care as usual and have no direct benefit of participation in the study. Results will elucidate if different disease phenotypes can be distinguished and if these phenotypes predict efficacy of pain treatment for PHN patients. Potentially a better understanding of the underlying pathophysiological mechanism of PHN is obtained. Obtained knowledge of symptom- or mechanism based therapies will be applied to future patients. Burden: As part of standard care patients fill in questionnaires (Vragenlijst midden Nederland, DN4, HADS, PCS, SF12, TSK) before their first visit and six months after their first visit (BPI, DN4, GPE, HADS, NRS, PCS, SF12, TSK). A QST measurement is performed during their first visit. As part of research, a

patient will have two extra scheduled visits after giving informed consent. During the first visit one blood sample (20 ml), two skin biopsies (3 mm diameter each) and in those patients that have given informed consent for CSF withdrawal (3 ml), a spinal puncture will be performed in a day care setting. If patients have given informed consent of MRS imaging, we will aim to combine the appointments. The sample taking procedures will take maximally 30 minutes in total and MRS imaging will take 30 minutes. One year after the initial visit the patients are asked to fill in the following questionnaires (BPI, DN4, GPE, HADS, NRS, PCS, SF12, TSK) and undergo a second QST measurement. Travel expenses will be compensated for the extra two scheduled visits.
Risks: The collection of blood and the skin biopsies have negligible risks. The collection of CSF has a negligible risk of infection or post-spinal headache. Non-invasive MRS imaging has negligible risks and for patient* safety a standardized MRS checklist will be used to ensure safety.

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

- Aged 18 years or older.
- Diagnosed by a physicians with a herpes zoster skin rash.
- Pain in the dermatomes involved in the original eruption of herpes zoster.
- Able and willing to give written informed consent

Exclusion criteria

- Patients with previous neurolytic or neurosurgical treatment for PHN. (Radiofrequency treatment of the DRG is allowed).
- Patients receiving pain treatment by topical capsaicin 8% in the last 6 months
- Patients who have other types of pain, which could confound the assessment of the neuropathic pain due to PHN.
- Patients with polyneuropathy or severe other neurologic disease that might affect outcome measures.
- Patients with skin conditions in the area affected by the neuralgia that could alter sensation.
- Patients with major cognitive or psychiatric disorders.
- Problems with communication (language, deafness, aphasia etc.)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-07-2020
Enrollment:	200

Type:	Actual

Ethics review

Approved WMO Date:	19-06-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC NedMec

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	NL67311.041.19