Functioning of the HPA-axis in patients with Complex Regional Pain Syndrome

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1. To explore the complex relation between CRPS, functioning of the HPA-axis and inflammatory activation of the immune system.2. To assess associations between the HPA-axis and psychosocial determinants. 3. To explore the possible role of...

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

Summary

ID

NL-OMON52914

Source
ToetsingOnline

Brief title
CRPS HPA

Condition

- Peripheral neuropathies

Synonym
Complex regional pain syndrome, posttraumatic dystrophy

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,Stichting Erasmus Fonds Pijngeneeskunde

Intervention

Keyword: Carpal tunnel syndrome, Complex regional pain syndrome, Hypothalamic Pituitary Adrenal axis

Outcome measures

Primary outcome

The main study parameter is functioning of the HPA-axis. For optimal examination of functioning of the HPA axis various measurements of cortisol levels will be used.

- Cortisol awakening response (CAR)
- Dexamethasone suppression test (DST) with administration of 0.25 mg dexamethasone
- Hair cortisol

Secondary outcome

- General parameters for all participants:

Gender, age, medical history, medication use, weight (kg), length (cm), smoking, side of affected limb, date of diagnosis, socioeconomic status (three indices; level of education, income, occupation).

- Psychosocial determinants:

Questionnaires focusing on the severity of the pain, awareness of disease and perception, perceived health and quality of life, coping, anxiety and depression will be used.

- Cognition:

A neuropsychology test battery of ten cognitive tests will be used.

- Cortisol binding globulin (CBG)

CBG is the major transport protein for cortisol within the blood and about 75% of circulating cortisol is bound to CBG. The active fraction of plasma cortisol will thus depend on the concentration of CBG.

- Level of soluble IL2-receptor (sIL-2R) in blood;

sIL-2R levels reflect the level of T-cell activation.

- Biomarkers; sCD163 and sCD206

The soluble forms of CD206 and CD163 are suggested as biomarkers of macrophage activity and thereby inflammatory activation. Moreover, sCD163 and sCD206 serum levels are hypothesized to be indicative of in vivo corticosteroid resistance.
Both sCD163 and sCD206 will be measured in plasma using ELISA (enzyme-linked immunosorbent assay)

Additional parameters for CRPS patients:

- CRPS severity score.

- Presence of neuromodulation; if presence also specification of type of neuromodulation

Study description

Background summary

The exact pathophysiologic mechanism of Complex Regional Pain Syndrome (CRPS) is still unknown, but there is considerable evidence for the role of inflammation. Increased inflammatory activity can be related to dysfunction of the hypothalamic-pituitary-adrenal-axis (HPA axis). Dysfunction of the HPA-axis may be associated with the initiation and maintenance of inflammation in CRPS. However, the role of the HPA-axis in CRPS is still largely unexplored. To better understand and treat CRPS it is essential to understand the functioning of the HPA-axis in CRPS. Possible associations with psychosocial determinants, cognitive function and glucocorticoid sensitivity will also be investigated.

Study objective

1. To explore the complex relation between CRPS, functioning of the HPA-axis and inflammatory activation of the immune system.
2. To assess associations between the HPA-axis and psychosocial determinants.
3. To explore the possible role of glucocorticoid sensitivity in patients with CRPS.
4. To compare functioning of the HPA-axis between patients diagnosed with CRPS and patients with carpal tunnel syndrome, a different cause of neuropathic pain. Both will be compared with each other and with known normal values of healthy persons.

Study design

Observational study

Study burden and risks

The study is conducted during two visits at the outpatient clinic of the Center for Pain Medicine. Cortisol levels are measured and a dexamethasone suppression test is performed using 0.25mg dexamethasone. Multiple questionnaires will be used to obtain information about psychosocial determinants and during first visit also physical examination and cognitive tests will take place. This study carries a negligible risk related to venepuncture as well as a small risk of emotional disturbance related to the content of the questionnaires. To reduce patient burden, the questionnaires are split into two parts. The risk of the overnight dexamethasone suppression test is negligible due to using lowest possible dosage, only 0.25mg. There is no direct benefit for participants, nor does this study influence or change the treatment of a patient.

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 CRPS:
- Age >= 18 years
- Diagnosis of CRPS according to the new IASP criteria for diagnosis of CRPS
- One extremity (upper or lower) is affected
- Signed informed consent

Patients with CTS
- Age >= 18 years
- Diagnosis of CTS: clear clinical presentation where no additional investigation was necessary or confirmed with electromyography or median nerve ultrasound.

- Signed informed consent

Exclusion criteria

Patients with CRPS:
- Age < 18 years
- More than one extremity affected
- History of auto-inflammatory or autoimmune disease
- Current treatment with glucocorticoids or treatment within the last 6 months.
- Current treatment with immune-modulating medicines, like bisphosphonates, or treatment within the last 6 months.
- Suspected or confirmed pregnancy.
- Dementia
- Insufficient understanding of the Dutch language
- Allergy to dexamethasone

Patients with CTS
- Undergone CTS treatment
- (Consideration of) diagnosis of CRPS in history
- Age < 18 years
- History of auto-inflammatory or autoimmune disease
- Current treatment with glucocorticoids or treatment within the last 6 months.
- Current treatment with immune-modulating medicines, like bisphosphonates, or treatment within the last 6 months.
- Suspected or confirmed pregnancy.
- Dementia
- Insufficient understanding of the Dutch language
- Allergy to dexamethasone

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:	Recruitment stopped
Start date (anticipated):	07-05-2021
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	25-09-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-01-2023
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	NL74004.078.20