Skin biopsy as diagnostic tool in anterior cutaneous nerve entrapment syndrome (ACNES): A Pilot Study

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

Summary

ID

NL-OMON53881

Source
ToetsingOnline

Brief title
Biopsy-ACNES

Condition

- Peripheral neuropathies

Synonym
Chronic abdominal wall pain (CAWP), Neuropathic abdominal wall pain

Research involving
Human

Sponsors and support

Primary sponsor: Maxima Medisch Centrum
Source(s) of monetary or material Support: Commissie Onderzoek en Innovatie & het Wetenschapsfonds;Maxima Medisch Centrum

Intervention

Keyword: ACNES, IENFD, Skin Biopsy, Small fiber

Outcome measures

Primary outcome

The main study parameter will be IENFD (measured in IENF/mm) from both affected

and non-affected sides of the abdominal wall.

Secondary outcome

- Pain score (NRS) before treatment

- Duration of pain (months) at the time of outpatient visit

- Treatment response

Treatment response will be defined as:

1. >50% pain reduction after treatment.

2. The need for additional treatment. Treatment is unsuccessful when patients

are not satisfied with their pain relief and want additional treatment.

Study description

Background summary

The abdominal wall is an underrecognized cause of abdominal pain. Chronic abdominal pain originating in the abdominal wall is termed Chronic Abdominal Wall Pain (CAWP). A CAWP syndrome is often due to the anterior cutaneous nerve entrapment syndrome (ACNES). This is caused by unknown triggering of the anterior and lateral cutaneous branches of anterior rami of thoracic intercostal nerves 7th-12th in the rectus abdominis muscle. These nerves provide both motor innervation of the rectus abdominis muscle and sensory innervation of the abdominal wall.

The diagnosis ACNES is based on clinical findings. Comprising a combination of patient*s history, physical examination and pain relief after trigger point injection (TPI) with a local anaesthetic. Most distinctive is a continuous,

localized pain of the abdomen which can be located with a fingertip. Specific findings during physical examination are altered sensibility (hypo-, hyperesthesia or allodynia) of the skin surrounding the painful spot, altered cold perception, a disproportionate pain while pinching the skin (hyperalgesia) and a positive Carnett sign at the trigger point.

To date, no truly objective diagnostic modality is available to confirm the diagnosis. The end branches of the anterior cutaneous nerve are too small to be identified on imaging tests. Most patients had an extensive diagnostic evaluation, such as laboratory test and (multiple) abdominal imaging without abnormalities and therefore lacking an explanation for the abdominal pain.

In the ongoing search for diagnostic modalities to confirm or support the diagnosis ACNES, we looked at other neuropathic pain conditions. Patients with Small-Fibre Neuropathy (SFN) have similar sensory abnormalities (altered sensation for pain and temperature) as seen in patients with ACNES. In SFN, it is known that Aδ- and C-fibres are affected. Myelinated Aδ-fibres and unmyelinated C-fibres regulate temperature sensitivity and pain sensation of the skin. These intraepidermal nerve fibres (IENF) can be quantified by skin biopsy, defined as intraepidermal nerve fibre density (IENFD). In SFN, the intraepidermal nerve endings are degenerating, resulting in a reduced IENFD.

Although there is a resemblance in sensory symptoms, it must be realized that SFN is, in contrast to ACNES, a generalized polyneuropathy. However, skin biopsies also have been performed in single nerve entrapment neuropathies like carpal tunnel syndrome (median nerve) and meralgia paresthetica (lateral cutaneous femoral nerve). In both disorders, skin biopsies have been taken from the skin innervated by the affected nerve and compared with healthy controls or an unaffected region of the skin in the same patient. These biopsies showed a significantly reduced IENFD in the affected skin of both patient groups with carpal tunnel syndrome and meralgia paresthetica.

A reduced IENFD has also been demonstrated in different neuropathic pain conditions, but has never been examined in patients with ACNES. Therefore, we want to measure IENFD in patients with ACNES. A 3-mm punch skin biopsy will be taken from the affected skin of the abdominal wall. Skin biopsy and quantification of the IENF will be done in accordance to the guideline of the European Federation of Neurological Societies for skin biopsy in SFN. The guideline is predominantly written for skin biopsy in the diagnosis for SFN. For this indication skin biopsy is performed at the distal leg. At the distal leg, normative reference values of IENFD are known. Unfortunately, those reference values cannot be applied to IENFD for other parts of the skin, as there is a proximal to distal gradient in IENFD. The guideline recommends to take a control biopsy of the contralateral non-affected side, when measuring IENF in unilateral neuropathic pain conditions at sides other than the distal leg. Therefore, we will perform a second skin biopsy at the contralateral non-affected side of the abdominal wall.

We hypothesize that patients with ACNES will have a reduced IENFD of the affected skin compared to the contralateral non-affected skin. This will potentially demonstrate measurements of IENFD as the first objective diagnostic technique supporting the diagnosis ACNES. Moreover, it will give further insight in the pathophysiology of ACNES. This can possibly result in exploiting new, more effective, treatment options.

Study objective

Our primary objective is to determine if there is a reduced IENFD in patients with ACNES. We hypothesize there will be a reduced IENFD of the affected skin (side of the pain) in comparison to the non-affected side.

Our secondary objectives are to see if there are any correlations between reduction of IENFD and;
- Duration of pain (months)
- Average pain score on numeric pain rating scale (NRS) before start of treatment
- Treatment response

Study design

A mono-center, prospective cohort study.

Study burden and risks

Skin biopsies are a well known and often used diagnostic tool. The only reported complications are mild wound infection and bleeding. Complications are estimated at 1.9:1000 skin biopsies. Local treatment is sufficient to treat the complications.
Wound will not need sutures.
Therefore, we believe that the minimal risks of a 3-mm skin biopsy are negligible in contrast to the potential benefits (first diagnostic test in ACNES and a potential better understanding of the pathofysiology).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Unilateral ACNES
Age 21-50 years
Duration of pain >3 months

Exclusion criteria

Bilateral ACNES
Previously administered injections with corticosteroids, or PRF treatment
History of open abdominal surgery or neurectomy
Use of antiplatelet or anticoagulants
Known neuromuscular or neurodegenerative disease
Disorder known to cause a reduced IENFD

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):	24-05-2023
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	27-10-2022
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	10-05-2023
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	20-08-2024
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	NL81661.015.22