Effect of Spinal Cord Stimulation in Painful Diabetic Polyneuropathy: a multicenter Randomised Controlled Trial (PDP study)

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

Summary

ID

NL-OMON36334

Source
ToetsingOnline

Brief title
PDP study

Condition

- Diabetic complications
- Peripheral neuropathies

Synonym
Pain due to diabetic nerve damage, painful distal symmetrical diabetic polyneuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Anesthesiologie-Pijnbestrijding
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Neuromodulation, Neuropathic Pain, Painful Diabetic Polyneuropathy, Spinal Cord Stimulation

Outcome measures

Primary outcome

The main study parameter will be the mean pain intensity during daytime and/or

mean pain intensity during night time as measured on a weighted NRS and/or a

PGIC for pain and sleep measured on a 7-point Likert scale.

Secondary outcome

1) Quality of life will be measured by EQ-5D, MOS SF-36 and the modified BPI

Short Form for diabetic peripheral neuropathy;

2) Quality of sleep will be measured by the MOS sleep scale;

3) The effect of SCS on mood will be measured by the BDI;

4) The effect of SCS on blood glucose control will be investigated by measuring

HbA1c;

5) To measure the effect of SCS on large and small neurofibre functions the

modified INCAT sensory sum score (md ISS), Contact Heat Evoked Potentials

Stimulator (CHEPS), and Somato-sensory evoked potentials (SSEP) measurements

will be performed;

6) The effect of SCS on small fibre loss and possible regeneration will be

investigated by skin biopsy;

7) The effect of SCS on activities-of-daily-living will be measured with an

accelerometer (activPALTM);

8) All baseline parameters will be analyzed for their predictive value for the success or failure of SCS treatment in PDP; e.g. pain scores, NPS, EuroQol-5D, MOS SF-36, BDI, Michigan Diabetic Neuropathy Score (MDNS) , md INCAT sensory sum score, CHEPS, SSEP, HbA1c and skin biopsy;

9) Costs will be measured through the hospital registration and by means of a standardized cost-questionnaire and the EQ-5D;

10) The long term follow-up will measured for 5 years, twice each year, by using the same questionnaire and pain dairy.

Study description

Background summary

Diabetic neuropathy is one of the most common complications of Diabetes Melitus (DM). Pain is a frequent symptom of diabetic neuropathy. The prevalence of pain in diabetes patients is estimated between 11-34%. Painful diabetic polyneuropathy (PDP) is a problem with a large societal and economic impact due to the high prevalence of DM and the large impact of PDN on quality of life and daily functioning of patients. Until ths moment no effective treatment of PDP is available. A large portion of patients experience unacceptable pain despite maximal drug therapy. For this patients spinal cord stimulation (SCS) may be able to provide pain relief. SCS had been used for over 30 years now for a diversity of neuropathic pain states. Due to this large experience SCS is a safe technique. Percutaneous implantation of the lead is a minimally invasive procedure with a low risk of infection.

Study objective

The primary objective of this study is to investigate whether SCS combined with best (drug) treatment as usual (TAU) leads to clinically significant (>=50%) pain relief in patients suffering from moderate-to-severe PDP in the lower limbs after 6 months of treatment compared to best (drug) treatment as usual.

Secondary objectives to investigate after 6 months:
1) the effect of SCS on health related quality of life in PDP;

2) the effect of SCS on the quality of sleep in PDP;
3) the effect of SCS on mood in PDP;
4) the effect of SCS on blood glucose control in PDP;
5) the effect of SCS on large and small nerve fibre functions in PDP;
6) identifying predictive factors for success of SCS treatment of PDP;
7) the effect of SCS on activities-of-daily-living;
Secondary objectives to investigate after 12 months:
8) the effect of SCS on small fibre loss and regeneration in PDP (only in group 1);
9) costs, cost-utility and cost-effectiveness

Study design

The study design is a multi centre randomized controlled trial. Patients will be randomized at random into 2 groups. The first group will be treated with SCS in addition to best (drug) treatment as usual. The second group will receive best (drug) treatment as usual without SCS. Patients will be included following the in- and exclusion criteria and follow the treatment algorithm as showed below.

Group 1: the effect of SCS will be analyzed after 2 weeks of trial stimulation. Patient will receive a definitive SCS system if they meet the above mentioned criteria. The patients will be followed during 12 moths at timepoints baseline, 3, 6, 9 and 12 months.
Group 2: receives best (drug) treatment as usual (standard treatment) en will be followed during 6 months. Timepoint will be baseline, 3 and 6 months.

Intervention

The intervention is spinal cord stimulation.

Study burden and risks

Risks:
Technical adverse events:
- Lead migration (14%
- Lead breakage (7%)
- Implanted pulse generator migration (1%)
- Loss of therapeutic effect, lost or unpleasant paresthesias (12%)

Medical adverse events:
- Infection or wound breakdown (10%)
- Pain at IPG incision site (12%)
- IPG pocket fluid collection (5%)

The lead will be implanted in the operating theatre under local anesthesia

using a percutaneous technique with a Tuohy needle. The pulse generator will be implanted subcutaneously under general anesthesia.

Nature of burden cosist of:
- filling out quenstionannaires and investigations.
- group 1: total time investment 20.5 hours spread over 1 year
- group 2: total time investment 11 hours spread over 6 months
- the implantation of the lead and pulse generatir will be in total 3 hours. This only contains group 1 and is already included in the total time of 20.5 hours.

Contacts

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Selecteer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Moderate-to-severe PDP in the lower limbs
o The pain intended to treat has been present for more than 12 months
o Previous treatment has been unsuccessful (insufficient pain relief and/or unacceptable side-effects) with drugs from the following drug categories:
* Amitriptylin or an other tricyclic antidepressant and/or
* Pregabalin (Lyrica®) or Gabapentin (Neurontin®) and/or
* Duloxetine (Cymbalta®) and/or
* Tramadol or strong opioids
Patients were treated with 3 drugs from the above mentioned drug categories and followed the treatment algorithm for painful diabetic polyneuropathy according to Jensen. Starting dosage was based on individual patient characteristics. Each drug was tried for at least 3 weeks and dose was raised once, if possible. By insufficient pain relief and/or unacceptable side-effects, the drug treatment was stopped. Patients reached a steady state in medication use and it is not allowed to increase dosage during the study. Use of opioids during the study is not allowed.
• Mean pain intensity during daytime and/or night time should be 5 or higher measured on a numeric rating scale (NRS). Pain during daytime will be scored 3 times per day during for 4 days according to Jensen.
• Patient*s age is between 18 and 80 years.
• It is necessary that patients which use anti coagulation, especially coumarin derivatives, can stop for 10 days around the procedure. This will be authorized by the treating physician of the patient. There will be no bridging to heparin.

Exclusion criteria

• The patient has had neuromodulation therapy during the month before the intake
• Neuropathic pain is most prevalent in the upper limbs (NRS>3)
• Neuropathy or chronic pain of other origin than diabetes mellitus (NRS> 3)
• Use of opioids
• Addiction: drugs, alcohol (> 5E / day) and/or medication
o Drugs: cocaine, heroine, marihuana.
o Alcohol: wine, beer, liquor (max 5E / day)
o Medication: benzodiazepines.
• Insufficient cooperation from the patient (little motivation, understanding or communication)
• Blood clotting disorder
• Immune deficiency (HIV-positive, corticosteroids with a dose equivalent to > prednisolone 10 mg, immunodepressiva, etc.)
• Peripheral vascular disease without palpable peripheral pulses at both feet (inclusion is possible if pulses are absent, but ankle brachial index is between 0.7 and 1.2 in both feet)
• Active foot ulceration
• Life expectancy < 1 year

• Pacemaker
• Local infection or other skin disorders at site of incision
• Psychiatric problems potentially interfering with cooperation in the study
• Pregnancy
• Severe cardiac or pulmonary failure (> NYHA classification II)
• Unstable blood glucose control (change in HbA1c>1,0% in three months prior to inclusion)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-03-2010
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	03-03-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-06-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	23-02-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-07-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-08-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC 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
CCMO	NL30961.068.09