Feasibility, safety and efficacy of Subcutaneous Electrical Nerve Stimulation (SENS) in patients with chronic refractory angina pectoris. A pilot study.

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In preparation for a large multi-center trial on the efficacy and safety of SENS for chronic intractable angina pectoris, we want to conduct a pilot, explorative trial to assess the feasibility, safety and efficacy of SENS implantation in this...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON33732

Source
ToetsingOnline

Brief title
SENS for refractory angina pectoris.

Condition

- Cardiac disorders, signs and symptoms NEC

Synonym
angina pectoris, chest pain

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,St. Jude Medical

Intervention

Keyword: angina pectoris, neuromodulation, neurostimulation, SENS

Outcome measures

Primary outcome

Since this is an explorative study, without any explicit hypotheses beforehand,

we decided to make no formal distinction in primary and secondary endpoints.

• Feasibility of the SENS implantation procedure

- Technical: operation time, peri-operative complications, correct placement of

the electrode-leads and IPG device

- the ability to provoke paresthesias in the area of the chest pain

• Safety

All adverse events, including those expected to be unrelated to the SENS

implantation will be recorded

Related complications and anticipated and unanticipated adverse effects

reported during this study will be evaluated.

A list of expected complications is incorporated in the complication form

(appendix 1) that will be completed by the implanting neurosurgeon.

General risks associated with SENS implantation include:

• Undesirable changes in stimulation over time

• Hematoma or seroma of the wound

• Lead migration

• Infection

• Pain at sites over the implanted system components

• Mechanical failure

Treatment complications will be reported by tabulation and classification according to their level of severity (mild/moderate/severe) and in their relation to the treatment (definite/probable/possible/not related).

• Efficacy

Data will be used to provide descriptive information about the outcomes mentioned below and to generate hypotheses about the efficacy of the SENS intervention.

Efficacy evaluation will be done by measuring:

Functional capacity

Assessment is performed by making use of a standardized bicycle exercise tests (Naughton Protocol modified by Weber-Janicki). The exercise tests will be performed at baseline and at the end of the study period. The change in heart rate, rate pressure product, workload and ST-T segment and exercise capacity at

the end of exercise will be scored as a percentage of the baseline.

Frequency of anginal attacks

A diary will be used by patients to self-report the number of angina episodes, angina episode intensity and short-acting nitrates consumption (NTG). Patients will keep this diary for 7 consecutive days prior to each study-visit.
After SENS implantation, the duration and time of stimulation sessions also have to be reported in this diary.

Quality of life

The Seattle Angina Questionnaire (SAQ) is a 19-item self-administered questionnaire
measuring five dimensions of coronary artery disease: physical limitation, anginal
stability, anginal frequency, treatment satisfaction and disease perception.

Secondary outcome

Zie primary study parameters

Study description

Background summary

Angina pectoris is the main clinical symptom accompanying ischemic heart diseases.
The majority of patients suffering from ischemic heart disease can nowadays adequately be treated by either anti-ischemic medication or by revascularization procedures such as Percutaneous Coronary Interventions (PCI) or Coronary Artery Bypass Grafting (CABG).

Despite the development of these pharmacotherapeutic and surgical treatment strategies, there is a group of patients that remains severely disabled by their anginal complaints.
Since 1982 numerous studies have demonstrated that neurostimulation by means of Transcutaneous Electrical Nerve Stimulation (TENS) or Spinal Cord Stimulation (SCS) is an effective additional tool for these chronic disabled patients.
However, because of some complications (ortho-ergic skin reactions in TENS and epidural lead migration in SCS) related to these well accepted forms of neurostimulation (accepted into ACC/AHA guidelines, class 2 indication) it seems worthwhile to search for new alternatives.
Subcutaneous placement of the electrodes by using Subcutaneous Electrical Nerve Stimulation (SENS) may be a good option. SENS involves positioning electrodes just underneath the skin and can be used to target nerves and nerve endings in very specific regions, including the localized parasternal regions on the chest where patients usually experience their anginal pain.
The subcutaneous electrode placement, in contrast to the epidural placement in SCS, creates an easier accessible and less risky route. Moreover, the area for subcutaneous electrode placement in SENS is larger and small shifts of the electrode leads will not have immediate consequences for the therapy. Furthermore, there is no need for fluoroscopy to verify the position of the electrodes and SENS seems also more suitable for patients with anatomical abnormalities in the spinal area.
Given the extensive experience in our center with TENS (> 700 patients treated) and SCS for refractory angina pectoris (>130 patients treated), it seems unlikely that SENS has a higher complication rate than SCS or is less effective than SCS or TENS.
In preparation for a large multi-center trial on the efficacy and safety of SENS for chronic intractable angina pectoris, we want to conduct a pilot, explorative trial to assess the feasibility, safety and efficacy of SENS implantation in this patient group.

Study objective

In preparation for a large multi-center trial on the efficacy and safety of SENS for chronic intractable angina pectoris, we want to conduct a pilot, explorative trial to assess the feasibility, safety and efficacy of SENS implantation in this patient group.

Study design

This is a monocenter (UMCG), prospective, open label, explorative study. A limited total number of 10 patients meeting all inclusion and exclusion criteria, will be included in the study.

From previous studies with neurostimulation for angina pectoris by SCS, it is our experience that patients have a learning curve of about 6 weeks to get

entirely familiar with the use of the neurostimulation device. Study period is therefore fixed at 8 weeks.

Intervention

The SENS treatment incorporates subcutaneous implantation of 2 octopolar electrode-leads and an implantable pulse generator (IPG). Implantation will be performed under anesthesiological surveillance and local anesthesia. Proper lead placement is verified through intra-operative trial stimulation, in which paresthesias are experienced by the patient covering the field of chest pain.
A separate subcutaneous pocket for IPG placement will be made at the left sub-clavicular site.
The two electrode-leads will subcutaneously be tunneled to this pocket site and connected to the IPG
At the end of the operative procedure the IPG settings (pulse width, frequency and intensity of the electrical pulses) will be programmed.
The patient is regarded to stimulate three times one hour every day, with regular periods in between. In addition, if a patient is experiencing an anginal attack, he/she is advised to rest, to activate the stimulator and proceed stimulating for 10 minutes. The patient is allowed to stimulate before the onset of an anginal attack and at circumstances (exercise) at which he knows anginal attacks are provoked.

Study burden and risks

A study-visit is planned at baseline and at 8 weeks after SENS implantation. Patients are in any case candidates for neurostimulation treatment, and usual care includes a visit prior to implantation and a viste at 6-8 weeks post-implantation. Extra burden associated with study participation includes administration of a questionnaire (2x), a patientdiary (2x) and performing a bicycle-exercisetest (2x).

The risks of implantatie are considered equal to those associated with the customary SCS implantationprocedure.
Except the risks for operations in general (as infection or bleeding) there are risks associated with the implanted system, such as:
- repulsion of the implantated devices
- undesirable changes in stimulation through:
o changes in electrode position
o changes in the tissue around the electrodes
o lead defects

These evens may require adjustment of the stimulationparameters or re-operation.

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

- stable angina pectoris, Canadian Cardiovascular Society (CCS) scale, class III-IV, therapeutic refractory for at least 3 months
- anginal pain in the retrosternal and precordial area
- angiographically documented coronary artery disease
- demonstrated ischemia (by exercise test, 48h ECG registration, nuclide scan or PET)
- optimal anti-anginal medication for >= 1 month
- age >= 18 years

Exclusion criteria

- Short life expectancy (i.e. < 1 year)

- Cardiac syndrome X (i.e. small vessel disease or microvascular angina pectoris)
- Vaso-spastic angina pectoris
- Myocardial infarction < 3 months.
- Severe heart failure NYHA class III-IV
- Significant valve insufficiency (grade IV/IV) or valve stenosis
- Treatment with TENS in the 2 weeks prior to start of the study (i.e.SENS implantation)
- Skin-sensibility disorders in anginal area
- Child bearing potential
- Inability to perform exercise tests
- Pacemaker dependency.
- Inadequately regulated hypertension
- Inadequately regulated diabetes mellitus
- Psychological inability which can cause significant instruction or compliance-problems
- Inappropriate use of drugs (opiates, cocaine etc) or alcohol by the patient.
- The presence of other neurostimulation device(s)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2009
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Generic name:	Neurostimulation device
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL25804.042.08