The DRG-STIM Study: Spasticity and Postural Stability after Long-Term Dorsal Root Ganglion (DRG)-Stimulation: A One-Year Safety and Preliminary Efficacy Study in 10 Patients with Spinal Cord Injury (SCI)

Published: 26-08-2020
Last updated: 08-04-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Spinal cord and nerve root disorders
Study type	Interventional

Summary

ID

NL-OMON50137

Source
ToetsingOnline

Brief title
DRG-STIM STUDY

Condition

- Spinal cord and nerve root disorders

Synonym
paraplegia, Spinal Cord Injury (SCI)

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

Intervention

Keyword: Dorsal Root Ganglion, Neuromodulation, Spasticity, Spinal Cord Injury

Outcome measures

Primary outcome

The main study parameter is (a change in) spasticity (frequency and/or intensity) in patients with motor complete and incomplete SCI who have been implanted with a permanent DRG stimulator for one year. At ten points over this year, clinical changes will be recorded and analyzed.

Secondary outcome

The secondary study parameters include (any changes in) postural stability as well as patient-reported differences in secondary health outcomes (functional independence, pain, bladder and bowel function, sexual function, and quality of life). The safety of chronic DRG stimulation will be monitored throughout the study.

Study description

Background summary

Dorsal Root Ganglion (DRG) stimulation is a currently available treatment modality proven to be effective in its application for chronic pain. In a previous pilot study (MEC2017-107) performed by our research group, we demonstrated that DRG stimulation is also able to evoke both isotonic and isokinetic motor responses in patients with Spinal Cord Injury (SCI).

Additionally, we observed beneficial stimulation-induced secondary health effects. This included a decrease in severity and frequency of spasticity, and an improvement of postural stability as reported by a number of patients. Both secondary effects are considered to have a larger impact on a patient*s quality of life (QoL) as compared to treatments involving regain of locomotion. Based on these findings, we intend to further assess the particular efficacy as well as the safety of long-term DRG stimulation in patients with chronic SCI for these secondary health effects.

Study objective

The primary aim of this case series is to investigate the safety and efficacy of long-term DRG stimulation in reducing spasticity in patients with motor complete and incomplete SCI. The secondary aim concerns improving postural stability through stimulation as well as positively affecting a number of other secondary health outcomes, namely, functional independence, pain, bladder and bowel function, sexual function, and quality of life.

Study design

Prospective case series

Intervention

The invasive interventions in the study consist of:
1) Surgical placement of max. 8 DRG-leads (under local anesthesia) for a trial phase (2 weeks)
2) After 2 weeks of trial phase: surgical removal of surplus DRG-leads (under local anesthesia). Max. 4 of the most effective DRG-leads will be left in situ and connected to a subcutaneously placed IPG (battery).

Prior to inclusion in the study period, the patients will be subjected to a screening consisting of medical history, neurological and neurophysiological tests (e.g. H-reflex) and a MRI. The MRI will contribute to determining a priority list of reachable and stimulateable DRGs associated with the spasticity-related myotomes and/or dermatomes. If <2 levels are expected to be implantable based on the MRI, the patient will have to be excluded.

After inclusion in the study period the patient will be subjected to the following contact- and measurement points:
After inclusion of the patients an initial baseline measurement (B0) will be conducted to assess current spasticity, postural stability and secondary health factors. Then, the patient will undergo the first surgical procedure where a maximum of eight temporary DRG leads will then be surgically placed on the DRG-levels expected to be most successful. On the same day of surgery (in the afternoon), the patient will be subjected to EMG-measurements under supra-motor

threshold stimulation on different (combinations of) DRG-leads with the purpose of determining the dermatome coverage of every lead (C1).

The patient then starts the two-week trial phase, during which a maximum of four leads deemed most effective are identified and stimulated with an external pulse generator (EPG). If deemed necessary, there are two moments for the stimulated leads or stimulation parameters to be optimized during this phase (O1 and O2). After these two weeks, should the patient show a minimally clinically important difference in spasticity, the internal phase will commence with surgical removal of all surplus leads and connection of a maximum of four most optimal leads to a subcutaneous battery (IPG) placed permanently. A second baseline measurement (B1) will follow the second surgery to objectify any changes to spasticity, postural stability, and secondary health outcomes and will serve as a comparative baseline for both short and long term changes to these objectives. After one month, another measurement (T1), with the same measurements as in B1, will take place. This is followed by a stim-off period in which the DRG stimulator will be switched off for two weeks as an internal control and evaluation of the carry on effects of the stimulation. The stimulator will then be turned back on to previously defined parameters and over the next 10 months, three more in-house measurements (T2-T4) and two home visits (H1-2) will be performed. After 12 months (last study follow up visit) patients are asked whether they prefer to continue using DRG stimulation treatment or have the system removed. All patients will then be followed in accordance with standard medical care. This entails regular check-up appointments at the department of Pain Medicine (outpatient clinic), in parallel to the standard clinical protocol for DRG-devices implanted for chronic pain. If necessary, a member of the research team can join these appointments to advice on e.g. stimulation parameters adjustments for treatment optimization.

This study also aims to investigate the safety of long-term DRG-stimulation through the monitoring of (S)AEs. These will be assessed for each patient starting from their first study treatment (implantation) to two weeks after study completion (T4).

Study burden and risks

The Center for Pain Medicine of the Erasmus MC performs more than 30 DRG placements annually, with low complication rates. The patients in this long-term efficacy study will undergo two surgical procedures under local anesthesia and will eventually keep a maximum of four permanent DRG leads, which are subcutaneously connected to an implanted pulse generator. Risks that may occur for patients who are implanted with a DRG device include possible infection, bleeding, cerebrospinal fluid (CSF) leakage, numbness, and pain below the level of the implant. During the implantation, X-rays are used to guide the process of lead-placement. The radiation exposure of this procedure (3 mSv) confounds to ICRP62 guidelines. These risks are considered to be

relatively low when performing the procedure in patients for the indication of neuropathic pain. We expect the same for patients with SCI.

As part of the screening for inclusion, a lumbar MRI will be made. The exclusion of patients with non-MRI compatible devices, as well as the relative short imaging duration, will limit the risk and discomfort of patients during this period. There are no risks associated with EMG measurements using surface electrodes. None of the other clinical outcome measures are expected to pose a risk and the frequency and duration of the questionnaires are considered to be of moderate experimental burden to the included patients.

We conclude there are moderate risks associated with participation and the burden can be considered moderate. However, the potential clinical implications and symptom relief which could potentially be achieved in this patient, in our eyes justifies the burden.*

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

- Paraplegia caused by trauma, post-surgical neurological deficits or pathological spinal compression > than one year prior to inclusion
- Grade A-D neurological deficit on the American Spinal Injury Association Impairment Scale (AIS) (see research protocol chapter 4)
- Age >=18 years
- Patient-reported and clinically confirmed refractory spasticity

Exclusion criteria

- Level >=3 on the American Society of Anesthesiologists (ASA) Classification
- Implantation with non-MRI compatible devices/materials
- Polyneuropathy (PNP) or peripheral motor neuron disease as assessed during screening measurement
- Complete absence of H-reflexes as assessed during screening measurement
- Lumbar MRI shows <2 possible implantable DRG-levels as judged by surgeon
- Severe psychopathology
- Active malignancy
- Vestibular system impairments
- Intrathecal Baclofen Pump Placement
- Pregnancy
- The intention of moving abroad within the next year after inclusion

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending

Start date (anticipated):	01-07-2020
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO Date:	26-08-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-10-2020
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	NL68741.078.20