A multi- center, randomized, cross-over study to demonstrate the efficacy of pudendal neuromodulation for the treatment of neurogenic overactive bladder

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

Summary

ID

NL-OMON34854

Source
ToetsingOnline

Brief title
Acceptance

Condition

- Spinal cord and nerve root disorders
- Bladder and bladder neck disorders (excl calculi)

Synonym
neurogenic overactive bladder, urinary incontinence

Research involving
Human

Sponsors and support

Primary sponsor: Medtronic International Trading Sarl
Source(s) of monetary or material Support: Medtronic International Trading Sarl

Intervention

Keyword: InterStim® therapy, Neurogenic Overactive bladder, Pudendal neuromodulation, Urinary incontinence

Outcome measures

Primary outcome

The mean difference in functional bladder capacity, as measured by the average voiding volume per episode, between stimulation ON for 4 weeks and OFF for 4 weeks.

Secondary outcome

The effect of pudendal neuromodulation (PNM) stimulation ON or OFF on:

• Urgency urinary incontinence as measured by the average number of incontinence episodes per day.

• The maximum voided volume per episode

• Average number of voiding episodes per day

• Average number of urgency episodes per day

Assess therapy effects after 6 and 12 months of treatment:

• On functional bladder capacity as assessed by the average voiding volume per episode

• On urgency urinary urine incontinence measured by the average number of incontinence episodes per day.

• On the maximum voided volume per episode.

• On the average number of voiding episodes per day

• On the average number of urgency episodes per day

• On patient*s quality of life (Qualiveen)

• On bladder capacity as measured by urodynamics

• Collection of safety data

Explorative outcome measures:

• To assess the effect of therapy on patient*s general health using the EQ-5D

questionnaire

• To assess the effect of PNM on fecal constipation and fecal incontinence

• To assess the effect of PNM on sexual function

• To collect information on the direct medical resource use and cost impact of

the therapy on patients.

Study description

Background summary

Pelvic floor dysfunctions such as overactive bladder, urinary retention and fecal incontinence affect millions of people worldwide. These conditions seriously impair their quality of life and well-being. Neurogenic overactive bladder with incontinence is secondary to confirmed pathology of the nervous system. This is very difficult to treat and conservative methods often fail.
The InterStim device delivers stimulation therapy for the treatment of chronic, intractable (functional) disorders of the pelvis and lower urinary or intestinal tract through the sacral nerve or the pudendal nerve systems.
Treatment of neurogenic overactive bladder by stimulation of the sacral nerve is tested in small scale studies and reported with inconsistent degrees of success.
The pudendal nerve is closer to the bladder, but has historically been difficult to access, so limited clinical data is available. But with new developments, the nerve is now accessible and treatment is minimally invasive. Clinical data is promising, but is limited to a very small number of centers and to case series.

Study objective

The purpose of this trial is to demonstrate the superior efficacy of pudendal neuromodulation in treating patients with neurogenic overactive bladder, who have failed conservative treatment, in a randomized cross-over trial. Symptoms of urinary incontinence are compared per patient when stimulation is switched on for 4 weeks to stimulation switched off for 4 weeks.

Study design

This is a prospective, interventional, randomized, crossover, post market approval, multi-center study. The study will be conducted in 4 to 10 medical centers in Europe. A minimum of 4 and a maximum of 12 patients will receive a permanent implant at each site.
Up to 72 patients suffering from neurogenic overactive bladder, who have failed conservative pharmacotherapy, will be screened and checked eligibility during visit 1 and 2. Selected patients will will have implanted a tined lead at visit 3 and undergo test stimulation period.
Patient who have successfully undergone test stimulation will receive an implant at visit 5 and randomized in a 1:1 ratio to one of the two groups:
• Group ON/OFF: stimulation ON for 4 weeks, followed by stimulation OFF for 4 weeks;
• Group OFF/ON: stimulation OFF for 4 weeks, followed by stimulation ON for 4 weeks.
Patient will be recruited until a total of 36 patients have received the implantable neurostimulator.
After this cross-over period, in which patients have to visit the hospital twice, patients will have stimulation ON for the remainder of the study to 12 months post implant. During this period patients will be asked to visit the hospital for 2 follow up visits. After the month 12 follow up visit, patients will return to standard medical care.
Patient with unsuccessful test stimulation may undergo a second test stimulation. All patients who do not have successful test stimulation will be exited from the study and return to standard medical care. If the investigator decides to continue with the neurostimulator implant, the patient will be exited from the study without explanting the lead

Intervention

Patients who are, after screening, eligible for participation in the trial will receive a lead implant at visit 3 to assess patient*s initial response to pudendal neuromodulation. The position of the lead will be tested during acute stimulation. Hereafter, a sub-chronic stimulation period (approximately 2 to 3 weeks) with home evaluation using a test stimulation will follow. The patient has to complete a 5-day voiding diary.
Patients with successful test stimulation (defined as a minimum of 100 mL increase from baseline in the functional bladder capacity calculated from the voiding diary) will be implanted with the neurostimulator and randomized.

Study burden and risks

The burden for the patient consist of being implanted with a neurostimulator during two surgeries. The main risks associated with these surgeries are standard risks for surgical intervention (like wound infection and use of local or general anesthesia).
There are also specific risks associated with the InterStim therapy on pudendal neuromodulation. Possible risks are allergic reactions on the implanted materials and incorrect functioning of the system after implantation. This might affect the urinary, fecal or sexual function.
The InterStim therapy is CE marked which certifies that the therapy fulfills all preclinical testing and safety requirements , and is justified for use in human subjects.
Most important risks of the treatment are mentioned in the Information for Prescribers InterStim Therapy manual and the Patient manual.
Additional burden for the patients are frequent study visits (maximum of 9 visits), including blood sampling, physical examination, collections of urine during 5-days period, kidney ultrasounds and completion of patient*s questionnaires

Contacts

Public
Medtronic International Trading Sarl

Route du Molliau, Case Postale
CH-1131,Tolochenaz
Zwitserland
Scientific
Medtronic International Trading Sarl

Route du Molliau, Case Postale
CH-1131,Tolochenaz
Zwitserland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Eighteen years of age or older;
• Incomplete upper motor neuron lesion due to trauma or disease of the spinal cord (1 year post-lesion);
• Urodynamically proven overactive detrusor function;
• Minimum of 2 leaks or 2 notices of leaks per day (demonstrated on a 5-day voiding diary);
• Mean functional bladder capacity (volume voided per episode) of > 100mL;
• Normal upper urinary tract function as assessed by ultrasound imaging;
• Failed, intolerance or incomplete response to conservative pharmacotherapy;
• Failed or insufficient improvement of symptoms with conservative non pharmacotherapy treatment.

Exclusion criteria

• Complete spinal lesion or complete bilateral lesion of sacral/pudendal nerves;
• Primary stress incontinence or mixed incontinence where stress component overrides the urge component;
• Degenerative disease of the central nervous system;
• Urinary tract mechanical obstruction such as benign prostatic hyperthropy, cancer or urethral stricture.
• Symptomatic urinary tract infection
• Morphological abnormalities of the bladder

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-01-2011
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	InterStim therapy
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	12-05-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-01-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-04-2011
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	NL30701.068.09
Other	NTC01023269