A randomized, multicentre, double-blind, parallel, sham-controlled study of the gammaCore®, a non-invasive neurostimulator device for the acute relief of episodic and chronic cluster headache.

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Primary Objective:The primary objective is to compare the pain free rates at 15 minutes following the use of GammaCore® with that of a sham device, for acute treatment of cluster headache attacks.Secondary Objectives:The secondary objectives will...

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

Summary

ID

NL-OMON40599

Source
ToetsingOnline

Brief title
GC-003

Condition

- Headaches

Synonym
cluster headaches

Research involving

Human

Sponsors and support

Primary sponsor: electroCore LLC
Source(s) of monetary or material Support: industrie

Intervention

Keyword: cluster headache, gammaCore®, neurostimulator, non-invasive

Outcome measures

Primary outcome

Primary endpoint:

The primary endpoint is pain free rates at 15 minutes comparing active and sham.

Secondary outcome

Secondary endpoints:

- Change in mean attack duration for each treatment group from the run-in period (baseline) to visit 3 (randomized period)

- The reduction in mean disability, will compare the run-in period (baseline) to visit 3 (randomized period) of the two treatment groups

- Reduction in mean attack severity from the run-in period (baseline) to visit 3 (randomized period)

- Pain free rates at 30 minutes

- Outcome for QOL questionnaires at V3 and at V4 compared with V2

- Dayslost from work at V3 and at V4 compared with V2

- Acute rescue treatments or medications at 15 minutes from start of use of the study device between active and sham group.

- Subject satisfaction between active and sham group

- Number of adverse events between active and sham group

Study description

Background summary

Cluster headache is a seriously debilitating disorder estimated to affect about 0,1 % of the Western European and North American populations. Characterized by excruciating unilateral pain in rapid and frequent succession, cluster headaches present such severe symptoms among those afflicted that patients routinely report they have not has a more painful experience. Sufferers typically experience between 1 and 3 hours lasting from 15 minutes and up to 3 hours and are classified separately to migraine in the International Classification of Headache Disorders-second edition. In contrast to migraine, cluster headache is about 3 times more common in males. Currently, the underlying cause of cluster headache is not fully understood, but it is thought that abnormalities of the hypothalamic region are crucial1. Standard of care treatment include both abortive and prophylactic medications; both with limited efficacy4. During the onset of headache, many people respond to inhalation of 100% oxygen7.Triptans, nasally as well as subcutaneously, have both been shown to be effective on acute cluster headache attacks, although there remains an important and pressing need for new treatments of the acute attack of cluster headache.
The social and economic burden of cluster headache is significant. Patients with chronic and active episodic cluster headaches are severely impaired in non-economic and economic domains such as disability, working life and psychiatric complaints. Symptoms suggestive of psychiatric co-morbidity: depressive symptoms (56%), signs of agoraphobia (33%) and suicidal tendencies (25%) are frequently reported. A study by D*Amico et. al. found that 36% of cluster headache patients have lost their job and half of the patients had reduced work time by at least 50%.
Considering the inadequacy of current pharmacologic therapy and considerable economic and social burden of this debilitating disorder, further research is warranted on alternative prophylactic and acute treatment options.
The vagus nerve serves an important function in mediating pain signals to the sensory cortex. Vagus nerve stimulation (VNS) is a procedure that has been used for the treatment of epilepsy and medication resistant depression and recently has shown a decreased incidence and severity of cluster headache symptoms. There is a considerable unmet need for a novel, patient controlled, and non-invasive way to prevent /treat cluster headache symptoms. Such a treatment has the potential to not only improve patient quality of life, but also to reduce lost workdays and reduce healthcare expenditure for the large number of

people who suffer from cluster headache.

Study objective

Primary Objective:
The primary objective is to compare the pain free rates at 15 minutes following the use of GammaCore® with that of a sham device, for acute treatment of cluster headache attacks.

Secondary Objectives:
The secondary objectives will compare each treatment group and are:
1. Reduction of disability: 5 step disability scale (1=minor, 2=minor/moderate, 3=moderate,4=moderate/severe and 5=severe)
2. Reduction of mean attack severity
3. Quality of Life: EQ-5D-3L
4. Quality of Life: Headache Impact Test (HIT-6)
5. Need for rescue therapy in addition to study treatment
6. Onset, severity, duration and frequency of adverse events (anticipated and unanticipated), including determination of device-relatedness
7. Number of SoC rescue treatments or medications needed at 15 and 30 minutes post stimulation
8. Pain free rates at 30 minutes

Study design

The study is a prospective double blind, randomized, sham-controlled, multi-center investigation designed for comparison of two parallel groups, GammaCore® (active treatment) and a sham, (inactive) treatment. The study period will begin with a one-week run-in period, followed by a two week comparative period when the subjects will be randomized (1:1) to either active treatment or sham (inactive) treatment. The comparative period will be followed by an open label two week period, where the subjects in the sham treatment group will switch in treatment assignment and receive an active treatment and the active group will continue to receive an active treatment.

Intervention

Once subjects have completed the run-in period, they are randomized to continue in a two-week comparative period. During this period, the control group will treat with the sham (inactive) device and the active group will be provided with a GammaCore® device for acute treatment of their attacks. Subjects will self-administer treatment, ipsilateral to the attacks, by three 90-120-second stimulations consecutively administered at the onset of pain or symptoms.

Study burden and risks

There are no significant risks identified with the participation in this study however study subjects can experience transient symptoms such as:
- Shortness of breath (dyspnea), hoarseness or change in voice during treatment.
- Light-headedness, dizziness, chest pain, fainting (possibly associated with transient hypotension, bradycardia or decreased MAP)
- Transient pain and muscle twisting during treatment
- Tingling, pricking or a feeling of *pins and needles* on the skin where the device is applied (paraesthesia or dysaesthesia) lasting beyond the treatment period
- Minor skin irritation from conductive gel
- Fainting (Syncope) during treatment
- Continued or increased progression of cluster headache symptoms
- Bradycardia
- Tachycardia
- Change in mean arterial pressure (MAP)

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

Inclusion Criteria
1. Is 18 years or older
2. Has been diagnosed with episodic or chronic cluster headache in accordance with the ICHD-2 Classification criteria (2ndEd)
3. Is capable of completing the 5-point pain scale, disability scale and other self-assessment questionnaires.
4. Agrees to refrain from starting new medication aimed to control the cluster headache for the duration of the run-in and randomized phase
5. Is able to provide written Informed Consent

Exclusion criteria

Exclusion Criteria
Subjects meeting any of the following criteria can not be included in this research study
1. Episodic cluster headache sufferers who are not in a cluster headache bout at the time of screening and enrollment
2. Need to commence treatment with oral or injectable steroids for eventual concomitant medical conditions
3. Has a lesion (including lymphadenopathy), dysaesthesia, previous surgery or abnormal anatomy at the gammaCore® treatment site
4. Is currently taking medication for indications other than cluster headache that in the opinion of the clinician may interfere with the study
5. Has a history of any cranial aneurysm, intracranial haemorrhage, brain tumours or significant head trauma
6. Diagnosed or suspected secondary headache
7. Has other significant pain problem that might confound the study assessments in the opinion of the investigator
8. Has known or suspected severe atherosclerotic cardiovascular disease, severe carotid artery disease (e.g. bruits or history of transient ischemic attack (TIA) or cerebral vascular accident CVA), congestive heart failure (CHF), known severe coronary artery disease or recent (5 years) myocardial infarction
9. Has an abnormal baseline ECG (e.g. second and third degree heart block, atrial fibrillation, atrial flutter, recent history of ventricular tachycardia or ventricular fibrillation, or clinically significant premature ventricular contraction)
10. Has had a cervical vagotomy
11. Has uncontrolled high blood pressure
12. Is currently implanted with an electrical and/or neurostimulator device, including but not limited to cardiac pacemaker or defibrillator, vagal neurostimulator, deep brain stimulator, spinal stimulator, bone growth stimulator, or cochlear implant
13. Has a history of carotid endarterectomy or vascular neck surgery

14. Has been implanted with metal cervical spine hardware or has a metallic implant near the gammaCore stimulation site
15. Has a recent (12 months) or repeated history of syncope
16. Has a recent (12 months) or repeated history of seizures
17. Has a known or suspected history of substance abuse or addiction, or overuse of acute headache medication
18. Has psychiatric or cognitive disorder and/or behavioural problems which in the opinion of the clinician may interfere with the study
19. Is pregnant, nursing, thinking of becoming pregnant during the study period
20. Is participating in any other therapeutic clinical investigation or has participated in a clinical trial within a 30 days period prior to this study
21. Is a relative of or an employee of the investigator or the clinical study site

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-03-2014
Enrollment:	35
Type:	Actual

Medical products/devices used

Generic name:	gammaCore®
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	12-03-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	04-06-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	29-07-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	01-12-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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
ClinicalTrials.gov	NCT01958125
CCMO	NL45248.058.13

Study results

Date completed:	07-10-2014
Actual enrolment:	35

Summary results
Trial is onging in other countries