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Tined lead test stimulation to predict long-term benefit from sacral nerve stimulation in patients with chronic constipation (TiLTS-cc)

Submission date
30/08/2012

Recruitment status
No longer recruiting

Registration date
10/10/2012

Overall study status
Completed

Last Edited
15/10/2020

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Constipation is common, but in some people laxatives and standard treatments fail to work, causing distressing symptoms and severely affecting quality of life. This is known as refractory chronic constipation. When the cause of the chronic constipation is unknown this is termed idiopathic.
To help the bowel to work, these patients may be offered a treatment known as sacral nerve stimulation (SNS). This assessment has the potential to tell us who will benefit long-term from SNS. All patients who report improvements will be offered permanent SNS, so that no patients are disadvantaged by the study. Better targeting of this treatment will prevent disappointment for patients and waste of resources for the NHS.

Who can participate?
Patients with chronic constipation

What does the study involve?
The study involves an initial period of assessment with questionnaires and an X-ray examination to measure the speed of passage through the digestive system. Patients then have a small operation to site the tined lead into their back at the sacral nerve and a connecting lead exits through the skin. This is attached to a temporary stimulation box and patients have 6 weeks of testing, which is blinded (they do not know if the stimulation is active or sham), and randomized (they do not know the order of active or sham stimulation). Further assessments are conducted during this time to decide if a patient has become a responder to treatment. All patients who are responders are then implanted with the permanent SNS device called an implantable pulse generator (IPG) which is assessed over the next six months to determine whether the testing technique can predict who will respond to treatment long term.

What are the possible benefits and risks of participating?
Patients who participate in clinical trials are known to benefit more from treatment just through the process of close monitoring and observation that occurs during a trial. Patients in this study also have an extended period of temporary testing and so have a higher than normal chance of

responding to treatment and therefore being offered the permanent IPG, which is currently not NICE approved. As the extended testing phase involves a wire exiting the skin there is also a theoretical chance of a higher infection rate from participation in this trial, although to date this is not seen in practice or in pilot studies.

Where is the study run from?
1. University Hospital of North Durham (UK)
2. Castle Hill Hospital, Hull (UK)
3. The Royal London Hospital, London (UK)
4. Queen Elizabeth Hospital, Gateshead (UK)

When is the study starting and how long is it expected to run for?
October 2012 to October 2015

Who is funding the study?
National Institute for Health Research (NIHR) - Research for Patient Benefit Programme grant (UK)

Who is the main contact?
Professor Yan Yiannakou

Contact information

Type(s)
Scientific

Contact name
Prof Yan Yiannakou

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Additional identifiers

Protocol serial number
TiLTS-cc Version 11, Date 08/08/2012

Study information

Scientific Title
Tined lead test stimulation to predict long-term benefit from sacral nerve stimulation in patients with chronic constipation (TiLTS-cc)

Acronym
TiLTS-cc

Study objectives
The tined lead test stimulation (TiLTS- using randomised and double-blinded active and sham subsensory sacral nerve stimulation) can predict long term response (at 6 months) to sacral nerve stimulation in patients with idiopathic constipation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East - Northern & Yorkshire, UK, 24/08/2012, ref: 12/NE/0228

Primary study design
Interventional

Study design
Multi-centre prospective interventional randomized double-blinded placebo controlled linear cross-over study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic (Idiopathic) constipation

Interventions
Sacral nerve stimulation using a tined lead as an extended testing phase to evaluate the predictive value of this form of testing by comparing the long-term (6 months) response to permanent sacral nerve stimulation in the groups classified by the test.. The tined lead test stimulation (TiLTS) is of 6 weeks duration and involves an "active" period of 2 weeks of active subsensory sacral nerve stimulation, and a placebo or "sham" period of 2 weeks of pretend subsensory sacral nerve stimulation. These periods are around a central 2 weeks of "no" testing (a washout period) giving a total of 6 weeks in this testing phase. Study participants are randomised into either group A or B who receive the active and sham testing in reversed orders, and so blinding both the assessment researchers and participants to the order of active and sham testing. Participants will identify on a visual analogue scale of 0-100 on how much they feel each 2 week period has improved their symptoms compared to baseline. responders of a 2 week testing period are classified by indicating 24 or greater on the VAS. After study termination this data is used to classify participants into either discriminate or indiscriminate responders as identified by the testing phase. The responders are implanted with a permanent sacral nerve stimulator Implantable Pulse Generator (IPG) and follow up commences for 6 months (this is the usual sensory SNS). Full assessments are completed at 3 and 6 months and long term responders identified at 6 months by the PAC-SYM measure. Total duration of participant involvement is 32 weeks.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Using the Patient Assessment of Constipation-Symptoms (PAC-SYM), long-term (6-month) responders are classified as those who have a 0.5 reduction in PAC-SYM scores from baseline. The primary outcome measure is therefore the response rate at 6 months comparing

discriminate (those who respond to active testing only) versus indiscriminate (those who respond to placebo testing or both placebo and active testing). The analysis will be performed using Fisher's exact test in SPSS.

Key secondary outcome(s)
Secondary outcome measures are 3 and 6 month assessments comparing discriminate with indiscriminate groups against baseline data of global assessment of symptoms:
1. PAC-SYM
2. Patient Assessment of Constipation-Quality of Life (PAC-QOL)
3. Euro-QOL & EQ-5D to calculate cost-effectiveness and QALYS.

Daily diary exercise scores are calculated for symptoms on a scale that is recorded on a daily basis. This includes:
1. Pain (Abdominal pain score) 0= No pain, 1= Not very severe, 2= Quite severe, 3= Severe, 4= Very severe.
2. Spontaneous complete bowel movements (The number of times you opened your bowels spontaneously and felt empty afterwards)
3. Bloating (Bloated, distended, tight tummy)- 0= No bloating, 1= Not very much bloating, 2= Quite a lot of bloating, 3= Severe bloating, 4=Very severe bloating.
4. Strain (Need to strain to pass stool) - 0= No strain, 1= Mild strain, 2= Moderate strain, 3=Severe strain, 9= Did not open bowels today (answer of 9 is omitted from total score calculation)
5. Laxative Score (Compared with your usual laxatives the amount you took today was +1= more, 0= same, -1= less)
6. Laxatives (have you taken any laxative medication today) 0=no, 1= yes.
These separate items are totalled for one week at a time. These totals are calculated at baseline for 2 weeks, throughout the 6 weeks of TiLTS testing and for 2 further weeks at month 3 and 6 of follow-up.

Completion date
01/10/2015

Eligibility

Key inclusion criteria
1. Males and females age 18 years or older
2. Constipation according to the ROME III* criteria for functional constipation
3. Constipation predominant irritable bowel syndrome (IBS-C)
4. Unknown (idiopathic) aetiology of constipation, as determined by the clinician
5. Symptoms not adequately relieved by the standard treatments of lifestyle modification, laxatives, suppository, and enema
6. Symptoms not adequately relieved after a trial of Prucalopride 2mg once daily, given according to licence
7. The recruiting clinician must be confident that the patient understands and that the consent process is adequate. Translation services will be provided for non-English speaking patients

*For research purposes the Rome III Criteria for functional constipation are accepted and will be used in the study (Drossman, 2006).

Using the Rome III criteria the diagnosis of constipation requires at least 2 of the following:
1. Straining during at least 25% of defecations

2. Lumpy or hard stools in at least 25% of defecations
3. Sensation of incomplete evacuation for at least 25% of defecations
4. Sensation of anorectal obstruction/blockage for at least 25% of defecations
5. Manual manoeuvres to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)
6. Fewer than 3 defecations per week

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Age of less than 18 years
2. Patients who are not fit enough to undergo the procedure (as per clinical judgement of PI)
3. Severe psychiatric disease at study recruitment
4. Persistent diarrhoea (except when due to laxative use)
5. Uncontrolled or decompensated cardiac, respiratory, endocrine, renal, or hepatic disease; as the clinical judgement of the site PI
6. The presence of any progressive neurological disease, or any neurological disease restricting the patients mobility and independence. Patients who have a mild non-progressive neurological disease not restricting their ambulation or independence, and not causing or contributing to their constipation will not be excluded
7. Secondary causes of constipation
8. Active systemic infection, as the clinical judgement of the site PI
9. Known pregnancy, suspected pregnancy or patients wishing to conceive
10. Subjects currently participating in or within 30 days of any interventional treatment study
11. Severe incapacity of higher mental function such that informed consent cannot be achieved. This will be determined by clinical judgement
12. Severe incapacity of higher mental function or physical abilities such that questionnaires cannot accurately be completed
13. Any patients on variable or unstable doses of anti-cholinergic drug, iron supplements, antidepressant, or opioid medications are excluded

*It is the clinical decision of the investigators as to the cause of secondary constipation, reiterating that this study is to investigate 'idiopathic' constipation. The assessing clinician must decide that constipation is idiopathic and that it is not secondary to chronic drug (e.g. opioid) use. Secondary causes can also include aetiologies such as congenital, metabolic, traumatic, inflammatory, ischaemic, and neoplastic in origin. Patients on stable doses (3 months of unaltered doses) of known constipating medications are considered suitable if these medications are deemed not causative (i.e. secondary) of their constipation.

**In ladies of child bearing age a pregnancy test must be performed before transit studies at baseline, and participants must agree to use adequate contraception for the duration of the study.

Date of first enrolment
01/10/2012

Date of final enrolment
01/10/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospital of North Durham
Durham
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DH1 5TW

Study participating centre
Castle Hill Hospital
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Study participating centre
The Royal London Hospital
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Study participating centre
Queen Elizabeth Hospital
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NE9 6SX

Sponsor information

Organisation
County Durham and Darlington NHS Foundation Trust (UK)

ROR
https://ror.org/03vamsh08

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research [NIHR] - Research for Patient Benefit Programme (UK) ref: PB-PG-1010-23212

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration