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Diaphragm Pacing in motor neurone disease/ Amyotrophic Lateral Sclerosis

Submission date
11/05/2011

Recruitment status
No longer recruiting

Registration date
31/05/2011

Overall study status
Completed

Last Edited
01/07/2016

Condition category
Nervous System Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease (after a famous baseball player who suffered from it), is a serious condition which affects the nervous system. When a person is suffering from ALS, the nerve cells in the brain and spinal cord which control the movement of muscles (motor neurons) are gradually lost (neurodegeneration). The disease often begins with muscle twitching and weakness in the arms or legs, eventually leading to paralysis. ALS is ultimately fatal, as it affects the muscles involved with breathing. The diaphragm is a large dome-shaped muscle which separates the lungs from the digestive organs in the abdomen. It is one of the most important muscles involved in ventilation (breathing in and out), helping to inflate and deflate the lungs by moving down and up. When the diaphragm is weakened, a person is not able to get enough oxygen into their lungs (respiratory failure), which eventually leads to death. Non-invasive ventilation therapy (NIV) is the standard treatment given to respiratory failure patients with ALS. In this type of treatment, patients wear a mask over their nose and mouth which "pushes" air into their lungs, allowing them to get enough oxygen. Eventually however, this treatment stops being effective, as the ALS causes the diaphragm to become more and more weak. Diaphragm pacing (DP) is where a device (diaphragm pacemaker) is implanted into the diaphragm muscle to help support breathing. The diaphragm pacemaker sends pulses of electricity to the muscle, helping it to contract (causing air to be sucked into the lungs) and relax (pushing air out of the lungs). The pacemaker is attached to a small box which is easy to carry around, allowing patients more independence than when having NIV. The aim of this study is to find out whether giving DP and NIV together can help to improve quality of life for ALS patients with respiratory failure, compared to NIV alone.

Who can participate?
Adults suffering from familial or sporadic amyotrophic lateral sclerosis (ALS).

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group (control group) continue with standard care, which involves them attending hospital in order to receive regular NIV. Those in the second group (intervention group) have an operation so that the diaphragm pacemaker can be placed in the diaphragm muscle. These participants are also given the standard treatment of NIV when needed. At 2, 3, 6, 9 and 12 months, participants in both

groups complete a number of questionnaires to assess their quality of life. Participants in the intervention group also attend an additional follow-up appointment one week after their operation. A small group of participants from this group are also interviewed so that more information about how the DP has affected their lives.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Seven specialist ALS and respiratory centres in the UK

When is the study starting and how long is it expected to run for?
March 2007 to September 2010

Who is funding the study?
National Institute of Health Research (UK)

Who is the main contact?
Dr Christopher McDermott

Contact information

Type(s)
Scientific

Contact name
Dr Christopher McDermott

Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 09/55/33, DiPALS , Protocol v1

Study information

Scientific Title

A randomised controlled trial evaluating NeuRx/4 Diaphragm Pacing (DP) in patients with muscle weakness due to motor neurone disease/Amyotrophic Lateral Sclerosis

Acronym
DiPALS

Study objectives
The proposed study will assess if treatment with DP prolongs life and maintains quality of life when given in addition to current standard care with Non Invasive Ventilation (NIV).

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East of England - Cambridge Central, 11/EE/0226 - approval pending as of 13 /05/2011

Study design
Multicentre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please contact C.Maguire@sheffield.ac.uk for a patient information sheet

Health condition(s) or problem(s) studied
Motor neurone disease

Interventions
54 participants to be recruited to each of the 2 arms.

Arm 1 = Standard care alone (NIV), Arm 2 = Standard care (NIV) plus DP

NIV arm patients will attend clinic for initiation of NIV with a possible overnight stay. Baseline NIV settings, NIV prescription given, type of interface, humidification and type of machine will be recorded. The patient will take home a Patient Diary and be asked to record the amount of NIV used.

In the DP arm participants will be admitted to hospital for insertion of the DP device. A pre-operative safety check will occur either during the admission or in the week leading up to

surgery. During the implantation procedure, incisions of 0.5 to 1 inch long will be made in the abdomen. More than one incision will be made so instruments can be passed through the abdominal wall as per standard laparoscopic procedure. The surgeon will identify the best location to place the electrodes within the diaphragm. A probe will be used to temporarily place an electrode on the surface of the diaphragm and to stimulate the diaphragm muscle at several locations to find the best location. Two electrodes will then be placed in each side of the diaphragm muscle. The lead wires from these electrodes will travel under the skin to the abdominal wall. The wires will be trimmed so that the ends sticking out of the skin are only 2 - 6 inches in length. An X-ray will be taken following the surgery to check the position of the wires and to make sure no air has travelled above the diaphragm and into the chest. If the damage to the nerve supply to the diaphragm is too great it is possible that the diaphragm will not be able to be stimulated with the electrodes and diaphragm pacing system. The scan/x-ray of the diaphragm performed during screening are an attempt to assess whether the diaphragm is stimulatable. However it is only possible to know for sure during the operation. If during the operation it is clear that the diaphragm is not stimulatable then the operation will be stopped and the device will not be inserted.

Evaluation of the electrodes and system will be performed prior to discharge from hospital. A system check of the wires will be completed. Electrode evaluation will be performed by adjusting individual stimulus parameters (pulse amplitude, width, and frequency) using the clinical station so that a comfortable level of stimulation can be identified for the diaphragm conditioning sessions. The patient will be given a daily target for the number and length of diaphragm pacing sessions. This will be recorded by the study team member in the patient diary.

Training of the participant and their caregiver will take place prior to discharge. This will include instruction in the care and use of the stimulator and data collection in the patient diary. Verbal and written instruction will be provided in a patient/caregiver instruction manual. Following surgery a one week follow up appointment will be booked for participants in the treatment arm before they leave the hospital.

Participants (in both arms) will return at 2, 3, 6, 9 and 12 months post randomisation for data collection which includes quality of life outcome measures. An option of home visits or collecting data over the phone will also be available should the participant wish. Survival data will be collected until the completion of the study. A final survival check will be performed on all participants following the last follow up visit for the last participant recruited.

A sub sample of 12 participants from the DP group will be selected for the qualitative interviews. These will take place 1 and 6 months post implantation and participants will be given the choice of coming into clinic or a home visit for the interview. All interviews will be transcribed and analysed by the qualitative researcher. All other data will be stored in a central database and will be accessed by trial research staff through username and password. Health economics model will be drawn up and used to analyse quality of life and cost data by an experienced health economist.

Intervention Type
Device

Primary outcome measure
The primary objective of this trial will be to evaluate the effect of Diaphragm Pacing (DP) on survival over the study duration in patients with MND/ amyotrophic lateral sclerosis (ALS) with respiratory muscle weakness.

Secondary outcome measures
To evaluate the effect of DP on:

Efficacy endpoints
1. Quality adjusted life years (QALYs) as calculated by combining EQ-5D and mortality data
2. Quality of life: sleep apnoea quality of life index (SAQLI), and SF-36
3. Quality of life of the main carer of the patient (Caregiver Burden Inventory)

For each efficacy endpoint, the treatment effect will be assessed by analysing the difference between groups over the 12-month follow-up period, and the difference at 12 months.

Safety endpoints
Safety (adverse events) and tolerability (patient withdrawal from treatment)

Overall study start date
04/07/2011

Completion date
02/02/2015

Eligibility

Key inclusion criteria
1. Age 18 or older
2. Familial or sporadic MND/ALS diagnosed as laboratory-supported probable, probable, or definite according to the World Federation of Neurology El Escorial criteria
3. Stabilised on Riluzole therapy
4. Respiratory insufficiency as determined by one or more of:
4.1. Forced Vital Capacity (FVC) less than 75% predicted/Sniff Nasal Inspiratory Pressure (SNIP) less than 40 cmH2O
4.2. Supine vital capacity (VC) less than 75% of sitting or standing VC
4.3. Partial pressure of carbon dioxide in the blood (PaCO2) > 6kPa (daytime)
4.4. Significant overnight oxygen (O2) desaturation (>5% of night with Sp02 <90% during overnight oximetery)
5. Bilateral phrenic nerve function clinically acceptable as demonstrated by bilateral diaphragm movement with diaphragm ultrasound or X-ray fluoroscopy
6. Forced Vital Capacity (FVC) > 50% predicted or sniff nasal inspiratory pressure (SNIP) > 30 cmH2O in patients unable to perform FVC (bulbar patients)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
108

Key exclusion criteria
1. Prior NIV prescription
2. Pre-existing implanted electrical device such as pacemaker or cardiac defibrillator
3. Underlying cardiac, pulmonary diseases or other disorders that would affect pulmonary tests independently of MND/ALS or would increase the risk of general anaesthesia
4. Current pregnancy or breastfeeding
5. Significant decision making incapacity preventing informed consent by the subject due to a major mental disorder such as major depression or schizophrenia or dementia
6. Marked obesity affecting surgical access to diaphragm or significant scoliosis/ chest wall deformity
7. The involvement in any respiratory trial that can influence the safety or outcome measures of this study within three months of the planned implantation of the device or during the year of follow up
8. Pre-existing diaphragm abnormality such as a hiatus hernia or paraoesophageal hernia of abdominal contents ascending into the thoracic cavity

Date of first enrolment
04/07/2011

Date of final enrolment
02/02/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Sheffield
Sheffield
United Kingdom
S10 2HQ

Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust (UK)

Sponsor details

STH Research Department
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11 Broomfield Rd
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S10 2SE

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Motor Neurone Disease Association (MNDA) (UK)

Alternative Name(s)
MND Association, MNDA

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	16/08/2012		Yes	No
Results article	results	01/09/2015		Yes	No
Results article	results	01/06/2016		Yes	No