ISRCTN99704819 https://doi.org/10.1186/ISRCTN99704819

Sleep-disordered breathing in patients with implanted cardiac devices: assessment of the change in sensitivity to carbon dioxide with cardiac resynchronisation therapy

Submission date 16/04/2014	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 25/06/2014	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 04/11/2020	**Condition category** Circulatory System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

Central sleep apnoea (CSA) is a sleep disorder where the patient stops breathing for typically 10-30 seconds at a time, leading to a decrease in the amount of oxygen in the blood (blood oxygen saturation level). It affects up to half of patients with severe heart failure and is associated with a poor prognosis. It occurs when the brains respiratory control centres becomes imbalanced during sleep and is caused largely by an exaggerated response to rising carbon dioxide levels in the blood, which normally drives how hard we breath. Sufferers have episodes of not breathing, or very shallow breathing, followed by a period of deep, or sometimes rapid, breathing. Cardiac Resynchronization therapy (CRT), in which a pacemaker is implanted to improve co-ordinated contraction of the heart, has been shown to reduce the severity of CSA in some patients. The aim of this study is to find out whether this improvement is due to normalization of the body's response to carbon dioxide in the blood. It is thought that CRT improves CSA by normalizing the brain's response to carbon dioxide.

Who can participate?

Patients undergoing implantation of a biventricular pacemaker, with heart failure and an ejection fraction (volume of blood pumped from the heart when it beats) of less than 40%

What does the study involve?

The study involves each participant taking part in a home sleep study assessment using a Embletta, (which monitors breathing pattern, airflow, the rise and fall of the chest and stomach, snoring, body position and oxygen levels when the person is asleep) before having their pacemaker is implanted. If the patient is found to have at least moderate CSA (experimental group), or if they have no significant CSA (control group), they will then be invited to have a carbon dioxide sensitivity test (Read-Rebreathe method). This involves breathing in and out of a bag for around 5 minutes. The depth and frequency of breathing is measured against the rising level of carbon dioxide in the air. This test is repeated 6 weeks and 6 months after the pacemaker is implanted.

What are the possible benefits and risks of participating?
This study allows physicians to assess the patient's nocturnal breathing patterns and may lead to treatment for previously undiagnosed problems. The study is very safe with no appreciable risk.

Where is the study run from?
Royal Brompton and Harefield NHS Trust (UK)

When is the study starting and how long is it expected to run for?
April 2014 to October 2015

Who is funding the study?
Boston Scientific (USA)

Who is the main contact?
Dr Simon Pearse

Contact information

Type(s)
Scientific

Contact name
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Royal Brompton Hospital
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Additional identifiers

Protocol serial number
16260

Study information

Scientific Title
Sleep-disordered breathing in patients with implanted cardiac devices: assessment of the change in sensitivity to carbon dioxide with cardiac resynchronisation therapy - an observational case-controlled study

Study objectives
Heart failure, where the output of blood from the heart is inadequate for the body's requirements, is a common clinical problem with a poor prognosis despite advances in pharmacological, surgical and pacing therapy. Around half of patients with heart failure suffer from sleep-disordered breathing (SDB). This may be obstructive sleep opnoea (OSA - due to decreased muscle tone in the throat and associated with obesity, predisposing to hypertension,

stroke and heart disease) or central sleep apnoea (CSA). CSA is a type of SDB in which breathing may be excessively deep for a time and then very shallow or even cease for short periods. This pattern of breathing is associated with more severe heart failure and a poor prognosis. A novel algorithm (ApneaScan, Boston Scientific plc) has been developed on certain pacemakers to detect SDB. We are validating this algorithm in a parallel study.

The depth and frequency of breathing is predominantly influenced by the level of carbon dioxide in the blood. Rising levels of carbon dioxide stimulate the brain to make us breath harder, thereby restoring carbon dioxide levels back to baseline. One of the major causes of CSA is an exaggerated response to carbon dioxide, which is found in patients with heart failure. This sets in place a cycle of over-breathing followed by cessation of breathing. The aim of this study is to evaluate whether Cardiac Resynchronisation Therapy (CRT) via a biventricular pacemaker, which increases the efficiency of the heart and can improve heart failure symptoms and prognosis, has an effect on the brain's response to carbon dioxide and whether this depends on the presence or absence of CSA.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Bromley Research Ethics Committee, 26/02/2014, ref: 14/LO/0078

Study design
Non-randomised; Observational; Design type: Case-controlled study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Cardiovascular disease; Subtopic: Cardiovascular (all Subtopics); Disease: Cardiovascular

Interventions
This trial tests how the depth and frequency of breathing changes with rising inspired carbon dioxide levels. This relationship is tested before and after implantation of a biventricular pacemaker for the treatment of heart failure. This involves breathing in and out of a 5-litre bag using a mouthpiece similar to that found on a snorkel. As the patient breathes, the amount of carbon dioxide in the gas mixture rises, which stimulates faster and deeper breathing. We measure the carbon dioxide concentration against the depth and frequency of breathing (measured by a tachometer). The whole test takes around 20 minutes and the measurement period (whilst breathing in to the bag) around 5 minutes. Patients will be tested before the pacemaker is implanted, 6 weeks later and 6 months later. In addition, the patient's notes will be reviewed after 2 years to document adverse heart failure events.

Intervention Type
Device

Phase
Not Applicable

Primary outcome(s)
Hypercapnic Ventilatory Response; Timepoint(s): Change in Minute Ventilation per unit rise in end tidal CO2

Key secondary outcome(s))
Apnoeic-Hypopnoeic Index; Timepoint(s): Measured at 6 weeks and 6 months post-implantation of pacemaker

Completion date
01/10/2015

Eligibility

Key inclusion criteria
1. Heart failure (of any aetiology) and a reduced ejection fraction (<40%) due to undergo implantation of a Boston Scientific biventricular pacemaker or defibrillator with the ApneaScan function
2. They must meet UK guidelines for biventricular pacemaker implantation
3. They should be on optimal medical therapy for heart failure
4. They must be aged 18 or over and be able to give valid written consent for this study
5. They must be ambulatory
Target Gender: Male & Female; Upper Age Limit 100 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Patients receiving pacemakers without the ApneaScan function
2. Patients unable or unwilling to attend follow-up testing
3. Patients receiving devices for indications other than heart failure with reduced ejection fraction
4. Patients with obstructive sleep apnea already on continuous positive airway pressure (CPAP) therapy
5. Patients unable to walk

Date of first enrolment
09/04/2014

Date of final enrolment
01/10/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Brompton Hospital
London
United Kingdom
SW3 6NP

Sponsor information

Organisation
Royal Brompton & Harefield NHS Trust (UK)

ROR
https://ror.org/02218z997

Funder(s)

Funder type
Industry

Funder Name
Boston Scientific Corporation

Alternative Name(s)
Boston Scientific, Boston Scientific Corp., BSC

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location

United States of America

Results and Publications

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?
HRA research summary			28/06/2023	No	No