ISRCTN62199741 https://doi.org/10.1186/ISRCTN62199741

Adenosine testing to determine the need for pacing therapy in unexplained syncope

Submission date
11/11/2011

Recruitment status
No longer recruiting

Registration date
13/12/2011

Overall study status
Completed

Last Edited
17/06/2019

Condition category
Circulatory 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
Diagnosing the causes of blackouts can take many months, using tests that can be lengthy and uncomfortable. A new test, lasting a few minutes, using a drug called adenosine has been used in a number of hospitals across the world to help uncover the cause of blackouts. In this study we hope to find out whether or not the adenosine test can identify those with blackouts who could be treated with the implantation of a pacemaker.

Who can participate?
It is planned that a total of 180 patients will participate in the study, 90 who will receive a pacemaker and a further 90 who will receive an implantable loop recorder (a device implanted under the skin that records heart rate and ECG for up to 3 years).

What does the study involve?
We are asking patients who present to the Accident and Emergency Department or Medical Assessment Suite at the Royal Victoria Infirmary, Newcastle upon Tyne (UK) with a blackout and in whom the reason for the blackout is not clear following a description of the event, a physical examination, blood pressure measurements lying down and standing up and an electrocardiogram (ECG; recording of the heart rate and rhythm) to participate. If they agree to participate after a minimum of 24 hours to think things over arrangements will be made to bring them to the Falls and Syncope Service at the Royal Victoria Infirmary, Newcastle upon Tyne at no cost to themselves. They will be given a dose of 20 mg adenosine directly into a vein in the arm whilst attached to a cardiac monitor. Should there be temporary block of the electrical connection between the top and bottom chambers of the heart for more than 10 seconds or temporary halting of the heart's own pacemaker activity for greater than 6 seconds then the adenosine test is deemed to be positive. Should neither of these things happen, the test is deemed negative. Those who have a positive test will be asked to consent to the implantation of a permanent pacemaker which will be done in Cardiac Catheter Laboratory at the Freeman Hospital, Newcastle upon Tyne. The pacemaker is a device which sits under the skin under the left collar-bone in the hollow of the shoulder and connects to the heart through two leads which travel in the vein that leads back to the heart from the arm. It is designed to detect slow heart rates/rhythms and treat them by stimulating the heart to beat. After implantation, the pacemaker will either be turned on (capable of treating slow heart rates) or turned off (capable

only of monitoring slow heart rates). Neither the patient or the researcher will know whether or not your pacemaker is turned on or off. After six months, those who have had the pacemaker turned off will have it turned on and vice versa. Again, neither you nor the researcher will know in which mode the pacemaker is working. This is important to ensure that nobody can accidentally influence whether pacing affects you having further blackouts. Those who have a negative adenosine test will be asked to consent to the implantation of a loop recorder. This is a small device that sits under the skin below the left collar-bone like a pacemaker but does not have the leads that travel to the heart. It continuously monitors the heart rate/rhythm but cannot treat any slow heart rates. Both those who receive a pacemaker and those who receive a loop recorder will be asked to report any blackouts that happen over the course of the year by completing a diary that is sent by post every week (a pre-paid envelope will accompany the diary so that it cab be returned by post without any cost). Should a blackout happen we will arrange for you to come to the Freeman Hospital so that we can check the heart rate/rhythm recorded by the pacemaker or loop recorder.

What are the possible benefits and risks of participating?
Firstly, the administration of adenosine can have side effects which include flushing, light-headedness, a sensation of difficulty in breathing, nausea and chest pressure but these last for a very short period of time (a few seconds up to a minute at most). Less commonly people can have sweating, nervousness, blurred vision, a metallic taste or a burning sensation and a fast heart rate for a few minutes. On very rare occasions people may blackout for a very short time during the test. These side effects are only found at the time of injection. The implantation of a permanent pacemaker is a well-tolerated and generally safe procedure but there are risks attached. The most serious potential risk is a puncture of the lung (pneumothorax) that occurs in 2% of cases but is readily treatable. The most common risk is displacement of one of the leads within the heart requiring another procedure to reposition it that occurs in 5% of cases. Other important risks are those of infection and haematoma (collection of blood) formation around the pacemaker requiring a further procedure that occurs in 1% of cases. A general anaesthetic is not required for the procedure. The implantation of a loop recorder is more straightforward than a pacemaker and is very safe with less than 1% chance of bleeding/infection. There is no risk of a pneumothorax or lead displacement.

Where is the study run from?
Royal Victoria Infirmary and Freeman Hospital in Newcastle upon Tyne (UK)

When is the study starting and how long is it expected to run for?
December 2011 to December 2015

Who is funding the study?
The research is funded by the British Heart Foundation and by Medtronic Inc, a pacemaker company who supplies some of the devices.

Who is the main contact?
1. Dr Iain Matthews (Research Doctor), iain.matthews@nuth.nhs.uk
2. Dr Steve W Parry (Chief Investigator), steve.parry@nuth.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Steve Parry

Contact details
Falls and Syncope Service and Institute for Ageing and Health
Royal Victoria Infirmary
Newcastle upon Tyne
United Kingdom
NE1 4 LP
+44 (0)191 282 5893
steve.parry@nuth.nhs.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01481168

Secondary identifying numbers
5883

Study information

Scientific Title
Adenosine testing to DEtermine the need for Pacing Therapy with the additional use of an Implantable Loop Recorder (ADEPT-ILR study) - the efficacy of permanent pacing in patients presenting to emergency medical services with syncope and a positive intravenous adenosine: a randomised, double-blind, placebo-controlled, cross-over trial

Acronym
ADEPT-ILR

Study objectives
A permanent pacemaker implant in those with a positive intravenous adenosine test will prevent further syncopal episodes (which are secondary to bradycardia).

The intravenous adenosine test has been shown in small studies to identify bradycardia pacing indications. Permanent pacemaker implantation is the definitive treatment for bradycardia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East - Newcastle and North Tyneside 2, 06/02/2012, ref: 11/NE/0373

Study design
Randomised double-blind placebo-controlled cross-over trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Syncope

Interventions
1. Administration of 20mg intravenous adenosine
2. Dual chamber permanent pacemaker implantation and subsequent randomisation to ODO or DDD+/-R pacing
3. Implantable loop recorder insertion

Intervention Type
Device

Primary outcome measure
Syncope burden as measured by number of syncopal episodes and recorded by weekly postal patient diaries with telephone reminders to ensure adequate return

Secondary outcome measures
1. Time to first syncope
2. Number of patients with recurrent syncope
3. Quality of life as measured via the condition-specific instrument the Impact of Syncope on Quality of Life questionnaire with general health-related quality of life measured via the WHOQoL-Brief and WHOQoL-Old instruments
4. Health economic analysis: Costs and benefits of the intervention to health and social services.
4.1. Use of EQ-5D questionnaire to establish the cost per Quality Adujusted Life Year (QALY)
4.2. The analysis will include the patients described above as well as a historical comparator group of consecutive patients derived from the database held by the Falls and Syncsope Service who have not undergone adenosine testing. This group is particularly important to establish the utility of adenosine testing in the diagnosis of unexplained syncope.
5. ECG diagnosis on ILR following syncopal episode in adenosine negative group

Overall study start date
01/12/2011

Completion date

01/12/2015

Eligibility

Key inclusion criteria
1. Patient has provided written informed consent for participation in the study prior to any study specific procedures
2. Male or female
3. Age 40 years or above
4. No cause of syncope clearly identified on clinical examination, lying and standing blood pressure measurements and standard 12 lead electrocardiogram (ECG)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
180

Key exclusion criteria
1. Asthma or chronic obstructive pulmonary disease
2. Severe coronary disease:
2.1. Myocardial infarction within 3 months
2.2. Known coronary stenosis >70%
2.3. NYHA heart failure or angina symptoms Class III or IV)
3. Known severe cerebrovascular disease or known significant internal carotid artery stenosis (>70%)
4. Prolonged corrected QT interval
5. Unablated accessory pathway
6. Pregnancy or lactation
7. Use of dipyridamole or any rate-limiting medication that cannot be safely discontinued
8. Hypertrophic cardiomyopathy
9. Cardiac transplantation
10. Concurrent participation in another investigational study or trial
11. Inability to give informed consent; carer/proxy assent will be allowed in this study
12. Cause of syncope established from initial clinical history and examination, lying and standing blood pressure and ECG

Date of first enrolment
01/12/2011

Date of final enrolment
01/12/2015

Locations

Countries of recruitment
United Kingdom

Study participating centre
Royal Victoria Infirmary
Newcastle upon Tyne
United Kingdom
NE1 4 LP

Sponsor information

Organisation
Newcastle upon Tyne NHS Foundation Trust (UK)

Sponsor details
c/o Ms Amanda Tortice
Joint Research Office
Royal Victoria Infirmary
Newcastle upon Tyne
England
United Kingdom
NE1 4LP
+44 (0)191 282 5959
amanda.tortice@ncl.ac.uk

Sponsor type
Hospital/treatment centre

Website
http://www.newcastle-hospitals.org.uk/

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation Clinical Research Training Fellowship (UK) ref: FS/11/13/28690

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Medtronic Inc (USA) are providing 25 permanent pacemakers and 25 implantable loop recorders free of charge for the duration of the treatment phase of the study

Results and Publications

Publication and dissemination plan
The results of the trial will form part of an MD thesis and are also part of a paper intended for submission to a Cardiology journal.

Intention to publish date
01/08/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Stored in repository