ISRCTN52505169 https://doi.org/10.1186/ISRCTN52505169

Thyroxine in acute myocardial infarction

Submission date
08/01/2015

Recruitment status
No longer recruiting

Registration date
09/01/2015

Overall study status
Completed

Last Edited
22/07/2020

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This study will look at whether people who have recently had a heart attack and have a borderline underactive thyroid would benefit from being treated with levothyroxine for a year. It is not known whether taking levothyroxine may benefit heart function, make blood clots smaller and improve blood circulation or not.

Who can participate?
Adults aged between 18-75 years that have recently had a heart attack and have a borderline underactive thyroid.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given levothyroxine. Those in group 2 are given a dummy medication (placebo). There are 11 visits over a year. These include a screening visit where questions are asked about the participants medical history, measure height, weight, blood pressure and pulse. Samples of blood are taken to look at thyroid function, cholesterol levels and circulation health. Subsequent visits involve Magnetic Resonance Imaging (MRI) cans of the heart, measuring stiffness of the blood vessels, clotting tests and further thyroid function tests. Each participant is asked about their general health and heart at the end of the study also asked to complete three questionnaires about their general health and heart. Their weight, blood pressure and pulse are taken once more and blood samples are taken to look at thyroid function, cholesterol levels and circulation health.

What are the possible benefits and risks of participating?
Any test may detect abnormalities that may be unrelated to the thyroid or heart condition – termed as incidental findings. In these cases, the participants GP will be informed. It is hoped that this study will provide valuable information about whether people with a borderline underactive thyroid who have recently had a heart attack would benefit from taking the correct dose of levothyroxine. The study may not directly benefit participants but they may benefit from a better understanding of borderline underactive thyroid gland and heart disease. The disadvantages for participants are that they will have blood samples taken more frequently than usual. They may get a small bruise, have discomfort or very rarely get an infection at the needle site. In addition the MRI scan can be noisy. Headphones are provided so that the participant can listen to music during the procedure. Some people may find the MRI scanner to be claustrophobic. Relaxation techniques can be advised if this happens. When participants attend

for the clotting chamber test at the RVI they will need to have an overnight fast for 8 hours although water can be taken. If participants are taking painkillers called NSAIDs (such as ibuprofen and diclofenac) they will be asked to stop taking them at least 3 days before these visits.

Where is the study run from?
The Newcastle MR Centre at the Campus for Ageing and Vitality at Newcastle General Hospital or the Clinical Research Facility at the Royal Victoria Infirmary in Newcastle (UK).

When is the study starting and how long is it expected to run for?
December 2014 to April 2018

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

Who is the main contact?
Miss Lorna Ingoe

Contact information

Type(s)
Scientific

Contact name
Miss Lorna Ingoe

Contact details
Department of Diabetes and Endocrinology
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
United Kingdom
NE9 6SX

Additional identifiers

EudraCT/CTIS number
2014-001369-28

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
17699

Study information

Scientific Title

ThyrAMI: Multi-centre double-blinded placebo-controlled RCT (cTIMP) of sub-clinical hypothyroid individuals post acute myocardial infarction

Acronym
ThyrAMI

Study objectives
To determine whether treatment of sub clinical hypothyroidism with levothyroxine following acute myocardial infarction improves left ventricular function, thrombus area, endothelial function, health status, quality of life and is safe.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Sunderland Research Ethics Service, 28/05/2014, ref: 14/NE/0151

Study design
Randomised; Interventional; Multicentre

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 use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Metabolic and endocrine disorders; Subtopic: Metabolic and Endocrine (all Subtopics); Disease: Metabolic & Endocrine (not diabetes)

Interventions
There are two arms on the study. One arm is the active study drug Levothyroxine and the second arm is the placebo control. Randomisation is 1:1.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Levothyroxine

Primary outcome measure
The primary outcome measure will be change in left ventricular ejection fraction as assessed by magnetic resonance imaging. Cardiac magnetic resonance (MR) is considered the gold standard for evaluating cardiac volumes and function. Gradient echo sequences provide a naturally high level of contrast between intra-cavitary blood and myocardium, thus allowing an accurate and reproducible determination of LV volumes, mass and calculation of stroke volume and ejection fraction. In this context, additional information can also be drawn from application of the more recent cardiac MR tagging analysis, which represents a non-invasive highly accurate method for direct quantification of regional systolic function. Cardiac MR imaging will be performed at the dedicated 3T MRI centre in Newcastle University.

Secondary outcome measures
1. Left ventricular systolic and end diastolic volumes and myocardial viability: Cardiac MR parameters of both global and segmental LV function measurements will be obtained as per standardised protocols already in place in the Newcastle MR centre using a steady state free precession or fast gradient echo technique. In addition, further scans will be obtained 15-20 minutes after intra-venous gadolinium-chelate administration (delayed enhancement MRI). Regions of non-viable myocardial tissue will be identified as areas of increased enhancement (hyper enhancement) whereas viable tissue will have null (black) on the acquired images.
2. Thrombus burden: The Badimon chamber is a highly reproducible clinical ex vivo model of thrombosis that mimics flow conditions within the coronary circulation of man. The device incorporates two chambers with internal flow channels of different diameters, one simulating high-shear flow of 1690 ml/s and the other simulating low-shear flow. The internal flow channels are lined with porcine aortic tunica media - the thrombogenic substrate. After perfusion with venous blood from the patient, flowing at 10 mL min -1 for 5 min, aortic segments are fixed in 10% formalin for 72 h. Total thrombus burden is measured using a validated computer-assisted planimetry using IMAGE-PRO PLUS software (Media Cybernetics, Inc., Bethesda, MD, USA). The results are the mean of the analyzed sections (μm2 .mm-1). The measurements will be performed at the Clinical Research Facility (CRF), where they have considerable experience of using this technique in other high vascular risk groups.
3. Thromboelastography (TEG®): This is a non-invasive measure of evaluating efficiency and quality of ex vivo thrombus formation. Quantitative measures include clotting time parameters, clot strength and clot lysis. These parameters have been validated as highly correlated with longer term cardiac outcomes in several conditions of risk. TEG® will be measured at the CRF, RVI, Newcastle.
4. Endothelial function: Endothelial dysfunction is the earliest stage in the atherosclerosis disease process. In this study, endothelial function will be assessed by measuring peripheral arterial tone using a validated tool, EndoPAT®. Endothelial function assessment using EndoPAT® has been shown to have a high degree of correlation with coronary artery endothelial function (24), severity and extent of coronary artery disease, traditional cardiovascular risk factors and in predicting future cardiovascular events. EndoPAT® assessments will be performed at the Clinical Research Facility, RVI, Newcastle at baseline and at end of study.
5. Platelet reactivity: The reactivity (inhibition) of platelets to anti-platelet agents such as aspirin, clopidogrel, prasugrel and ticagrelor will be quantified by the point of care monitor VerifyNow® (Accumetrics, CA, USA). Arachidonic acid reactive units and P2Y12 reactive units will be recorded at baseline and at the end of the study. This test will not be carried out in individuals on anticoagulants such as warfarin.

6. Safety assessments: Safety of levothyroxine therapy in post AMI patients will be assessed at each study visit by enquiry of symptoms by New York Heart Assessment (NYHA) category classification, ECG recording for rhythm disturbance and peripheral oxygen levels by pulse oximetry (at rest).
7. QoL and depression: This will be assessed by validated tool of measuring health status, the Short Form 12 four week recall (SF-12®), a disease specific questionnaire for heart failure, the Minnesota Living With Heart Failure Questionnaire®, and the Centre for Epidemiologic Studies Depression Scale (CES-D), at baseline and at end of the study.

Overall study start date
15/12/2014

Completion date
30/04/2018

Eligibility

Key inclusion criteria
1. Males and females aged between 18-75 yrs
2. Serum TSH between 4.01 -10.00 mU/L with normal free thyroxine levels (9 – 25 pmol/L) on two occasions (on day of admission for AMI and 7-10 days after AMI)
3. Acute myocardial infarction diagnosed on admission to hospital (chest pain with dynamic ECG changes or increase troponin enzymes (at least a fourfold increase above normal range)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
Planned Sample Size: 100; UK Sample Size: 100

Total final enrolment
95

Key exclusion criteria
1. Patients on medications affecting thyroid function (levothyroxine, carbimazole, propylthiouracil, amiodarone, lithium)
2. Patients who are unable to provide written informed consent
3. Patients with advanced malignancy (who, in the opinion of the investigator, is unlikely to

survive for more than 6 months)
4. Patients with sustained ventricular tachycardia requiring treatment which occurs >24hrs after myocardial re-perfusion/revascularisation
5. Patients who have contra-indications to MR scanning (cardiac pacemaker, metallic heart valves, cochlear implants, coronary artery stents incompatible with MR scanning, etc.)
6. Patients who are unlikely or unwilling, in the opinion of the investigator, to attend for study specific visits
7. Participants whose serum TSH is >10.0 or <4.0 on either occasion
8. Patients who are already participating in another interventional study

Date of first enrolment
08/12/2014

Date of final enrolment
30/04/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Gateshead Health NHS Foundation Trust
Department of Endocrinology
Gateshead
United Kingdom
NE9 6SX

Sponsor information

Organisation
Gateshead Health NHS Foundation Trust

Sponsor details
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
England
United Kingdom
NE9 6SX

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01aye5y64

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

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	25/03/2015		Yes	No
Abstract results	results presented at Society for Endocrinology BES :	20/10/2017		No	No
	results		22/07		

Results article	21/07/2020 /2020	Yes	No
HRA research summary	28/06 /2023	No	No