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Investigating the risk of heart and blood vessel problems in mild overactive thyroid disorder

Submission date
02/03/2020

Recruitment status
No longer recruiting

Registration date
03/03/2020

Overall study status
Completed

Last Edited
03/12/2021

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
An overactive thyroid, also known as hyperthyroidism or thyrotoxicosis, is where the thyroid gland produces too much of the thyroid hormones. Subjects with mild form of overactive thyroid gland (subclinical hyperthyroidism) have an increased risk of developing diseases affecting blood vessels and heart such as fast and irregular heart rhythms, heart failure and possibly death due to vascular conditions. The exact reason for this risk is not known. Traditional risk factors such as high blood pressure and abnormal lipid levels are usually not affected in this condition. Hence, we wished to study newer cardiovascular risk markers such as endothelial progenitor cells (EPC, one type of stem cells), circulating endothelial cells (CEC, which are shredded cells lining the blood vessels), C reactive protein (CRP, known vascular risk factor), in patients with mild form of overactive thyroid.

Who can participate?
Adults aged 21 - 85 years, with diagnosis of subclinical hyperthyroidism confirmed at least on two occasions (low serum TSH with normal FT4).

What does the study involve?
Participants will be randomly allocated to receive either thyroid drug carbimazole (drug used to treat overactive thyroid condition) or placebo pill for 6 months.

What are the possible benefits and risks of participating?
Benefits: There is no direct benefit for the participants taking part in this study. The researchers hope that the research outcomes may help to treat this condition in future.
Risks and Side Effects: Side effects related to the use of Carbimazole (if taking carbimazole tablet) include agranulocytosis (agranulocytosis means a failure of the bone marrow to make enough white blood cells, neutrophils and bone marrow is the soft tissue inside bones that helps form blood cells), liver function abnormalities such as cholestatic hepatitis and allergic reactions. They are quite rare in clinical practice (less than 0.5%), but this can not be prevented.

Where is the study run from?
Tan Tock Seng Hospital (Singapore)

When is the study starting and how long is it expected to run for?
December 2012 to January 2018

Who is funding the study?
National Healthcare Group - Small Innovative Grant, SIG/12011 (Singapore)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Singapore health sciences authority (HSA) clinical trials ref; CTC 1200221

Study information

Scientific Title
The role of endothelial progenitor and circulating endothelial cells in cardiovascular risk of patients with sub clinical hyperthyroidism

Acronym

EPISH

Study objectives
Increased cardiovascular risk in subclinical hyperthyroidism (SH) is contributed to by reduction in CEPC and increased circulating endothelial cells.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/04/2012, NHG Domain Specific Review Board (DSRB) Singapore (6 Commonwealth Lane, Level 6 GMTI building, Singapore, 149547, Singapore; +65 64968900; no email provided), ref: 2011/02144

Study design
Interventional single centre randomized 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 use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Sub clinical hyperthyroidism

Interventions
Treatment with carbimazole or placebo for 6 months.

Randomisation process will be done electronically using randomization codes with the help of medical statistician at the CRU (TTSH) in blocks of 4 (for carbimazole or placebo pill). Randomization will be done online (intranet access) in which only coordinators (unblinded) will be given access to the system.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)

Carbimazole

Primary outcome measure
Levels of circulating endothelial progenitor cells (EPC), circulating endothelial cells (CEC), Hs CRP, ADMA, lipoprotein-associated phospholipase A2 (Lp-PLA2) activity, Neutrophil lymphocyte ratio and monocyte lymphocyte ration in peripheral blood measured using an assay of blood sample at baseline and 6-months

Secondary outcome measures
At baseline and 6-months:
1. Anthropometry
1.1. Blood pressure (mmHg)
1.2. Weight (kg)
1.3. BMI (kg/m²)
2. Thyroid hormones, and endothelial markers such as EPC, CEC, ADMA measured by blood test
3. Cognitive assessments:
3.1. Mini mental state examination (MMSE)
3.2. Montreal cognitive assessment (MoCA)

Overall study start date
19/12/2012

Completion date
31/01/2018

Eligibility

Key inclusion criteria
1. Diagnosis of subclinical hyperthyroidism confirmed at least on two occasions (low serum TSH with normal FT4) and one normal FT3 levels within three months prior to the recruitment
2. Aged 21-85 years
3. Written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
40

Total final enrolment
40

Key exclusion criteria

1. Sick euthyroid syndrome
2. Recent radioiodine therapy (within 1 year of screening visit)
3. Pregnant or breastfeeding patients
4. Acute medical illnesses such as infections and active cancer

Date of first enrolment
19/12/2012

Date of final enrolment
31/01/2018

Locations

Countries of recruitment
Singapore

Study participating centre
Tan Tock Seng Hospital
11 Jalan Tan Tock Seng
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Sponsor information

Organisation
Tan Tock Seng Hospital

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Sponsor type
Hospital/treatment centre

Website
https://www.ttsh.com.sg/

ROR
https://ror.org/032d59j24

Funder(s)

Funder type
Government

Funder Name
National Healthcare Group-Small Innovative Grant, SIG/12011

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/04/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request available for up to 6 years after completion of the study.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v12	05/12/2019	06/03/2020	No	No
Results article		26/11/2021	03/12/2021	Yes	No