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Is metomidate PET-CT superior to adrenal venous sampling in predicting outcome from adrenalectomy in patients with primary hyperaldosteronism?

Submission date
13/12/2016

Recruitment status
No longer recruiting

Registration date
12/01/2017

Overall study status
Completed

Last Edited
13/02/2024

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Hypertension (high blood pressure) is a major risk factor for stroke, heart attack, and kidney disease.
Approximately 16 million people in the UK have hypertension and over 60,000 preventable deaths per
year from stroke and heart attack are down to inadequate blood pressure control. Most cases of hypertension have no identifiable cause, but in some patients an underlying condition can be found. One possible cause of hypertension is Conn's syndrome in which the adrenal glands (glands located on top of the kidneys) produce too much of a hormone called aldosterone. This hormone causes the body to retain salt, leading to the development of hypertension. Conn's syndrome carries an even higher risk of stroke or heart attack than other forms of hypertension. It is usually diagnosed by measuring aldosterone levels in a blood sample. In at least half of patients with Conn's syndrome, the condition is due to a benign (non-cancerous) nodule (lump) in one of the adrenal glands. The discovery and removal of these nodules often allows the hypertension to be cured, avoiding the life-long need to take drugs. The current diagnostic test these nodules involves taking blood from both adrenal glands, which can be a difficult and demanding procedure. This study is looking at a newly developed, special type of CT scan, which makes nodules light up on the scan if visible. The aim of this study is to find out whether this new adrenal scan (which is quick and painless) is more accurate than the existing test for diagnosing adrenal nodules.

Who can participate?
Adult patients with high aldosterone levels

What does the study involve?
All participants have the two investigations performed in a random order. The first investigation involves having a small tube (cannula) inserted into the veins supplying the adrenal glands to take samples of blood. These samples are then tested in the laboratory. The second

investigation involves having a body scan to look for nodules. The scan lasts for approximately an hour and for the three days before having the scan patients take a type of steroid medication called dexamethasone.

What are the possible benefits and risks of participating?
Participants benefit from undergoing extensive examinations as well as having follow- up care with a specialised research team. If the investigations locate the aldosterone producing adenoma, once removed it is anticipated that high blood pressure will either be cured or require less medication. The main disadvantage is that patients will be asked to attend on two days (once for PET CT scan and again for adrenal vein sampling) rather than just for AVS which is the usual diagnostic test offered. The radiation exposure from the 11C metomidate PET CT scan is 8 millisieverts (mSv) and is similar to the dose from a whole-body computed tomography (CT) scan, or to about 3 years' exposure to background radiation in the UK. This is equal to approximately a 1 in 3000 risk of developing cancer and to put this into context, the natural life time incidence of developing cancer is estimated to be about 1 in 3.

Where is the study run from?
Queen Mary University of London (UK)

When is the study starting and how long is it expected to run for?
September 2015 to November 2022

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

Who is the main contact?
Mrs Jackie Salsbury
jackie.salsbury@qmul.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mrs Jackie Salsbury

Contact details
The Barts Heart Centre
William Harvey Research Institute
Queen Mary University of London
Charterhouse Square
London
United Kingdom
EC1M 6B

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT02945904

Secondary identifying numbers
011149; EME 14/145/09

Study information

Scientific Title
Is metomidate PET-CT superior to adrenal venous sampling in predicting outcome from adrenalectomy in patients with primary hyperaldosteronism? (MATCH): a multi-centre, randomised, within-patient comparison of diagnostic techniques

Acronym
MATCH

Study objectives
The purpose of this clinical trial is to improve prediction of outcomes from surgical intervention in patients with primary aldosteronism, and evaluate the merits of noninvasive metomidate PET CT versus adrenal vein sampling in the diagnosis of surgically correctable aldosteronism.

More details can be found at: https://www.journalslibrary.nihr.ac.uk/programmes/eme/1414509/#/

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – Dulwich Research Ethics Committee, 05/08/2016, ref: 16/LO/1242

Study design
Observational multi-centre cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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

Health condition(s) or problem(s) studied
Primary aldosteronism

Interventions
This is an observational cohort study which takes place within existing secondary and tertiary care practice of the NHS. It is a multi-centre study in which all participants to have the same two investigations performed in random order. These are as follows:

11C-metomidate PET CT
This is a one-hour non-invasive study, prior to which participants are treated with dexamethasone for 3 days.

Adrenal vein sampling
This is an invasive investigation in which both adrenal veins are cannulated and blood collected for measurement of adrenal steroid hormones. Adrenocorticotrophic hormone (ACTH) is administered prior to AVS in order to ensure steroid hormone secretion during the procedure.

The investigators will standardise the start-time of treatment with spironolactone, which is first-choice treatment for participants with primary aldosteronism, in order that the pre-spironolactone blood pressure and biochemistry can be compared with subsequent measurements post-surgery, and the changes during the first month of spironolactone treatment can be used to assess their value in predicting response to surgery.

Sub-study of repeat metomidate PET CT before and after spironolactone therapy
In order to determine whether it will be necessary for the start of spironolactone treatment to be delayed in all participants until after both investigations are completed, the investigators will perform a sub-study, early in MATCH, in which 6 patients have their PET CT repeated after at least 6 weeks treatment with spironolactone. (This is the conventional period of time for which spironolactone is withdrawn prior to AVS)

Intervention Type
Other

Primary outcome measure
1. Aldosterone renin ratio in patients with primary aldosteronism (Conn's adenoma) is measured using serum aldosterone and renin ratio at baseline and 6 months after treatment
2. Home systolic blood pressure is measured using an automatic brachial blood pressure monitor at baseline and 6 months after treatment

Secondary outcome measures
1. Number of patients achieving home systolic blood pressure <140mmHg on no treatment is measured by an automatic brachial blood pressure monitor at baseline and 6 months after treatment
2. Number of participants requiring less antihypertensive medication following treatment is measured using class and dosage of antihypertensive medications at baseline and 6 months after treatment
3. SUV max ratios between adenoma and normal adrenal are measured using 11-C Metomidate PET CT scan at baseline and 6 months after treatment
4. Reduction in home systolic blood pressure mmHg on 4-week spironolactone therapy is measured using an automatic brachial blood pressure monitor at baseline and 4 weeks
5. High sensitivity troponin serum level is measured using serum troponin levels at baseline and

6 months after treatment
6. Serum brain natriuretic peptide level is measured using serum brain natriuretic levels at baseline and 6 months after treatment

Overall study start date
10/09/2015

Completion date
30/11/2022

Eligibility

Key inclusion criteria
1. Male or female age >18 years
2. Diagnosis of PHA based on published Endocrine Society consensus guidelines
3. Patients will be enrolled/consented when they have had each of the following:
3.1. At least one paired measurement of plasma renin and aldosterone, measured off spironolactone, showing an elevated ARR
3.2. Either a plasma aldosterone >190 pmol/L after saline infusion or 'spontaneous hypokalemia + plasma renin below detection levels + plasma aldosterone > 550 pmol/L)' (as per Endocrine Society guidance)
3.3. A CT or MRI scan of the adrenals with probable or definite adenoma(s)
4. Patients with elevated ARR can be put forward for consideration by the MDT as exceptional cases in whom spironolactone is not (fully) withdrawn, and/or saline suppression is not performed, IF:
4.1. Plasma Aldosterone > 450 pmol/L AND plasma renin <0.5 pmol/ml/hr (<9 mU/L) if measured on treatment with ACEI (Lisinopril >=20 mg or equivalent) or ARB (Losartan 100 mg or equivalent); OR
4.2. Age <40 AND definite adrenal adenoma on CT or MRI Patients whose CT/MRI does not show probable or definite adenoma must also be reviewed by MDT before enrolment/consent
5. All patients will have a positive Aldosterone renin ratio (ARR) serum measurement with another local diagnostic confirmatory test as specified from local specialised APA Guidelines. This is often standard cross-sectional imaging by CT or MR scanning. Any exception to recommended diagnostic criteria will be subject to approval by monthly MDT

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
140

Total final enrolment
143

Key exclusion criteria
1. Those patients who indicate that they are unlikely to proceed with surgery will not be recruited, because there will be no outcome change in blood pressure, restoration of normal renin/angiotensin physiology) against which to compare the accuracy of the two Investigations
2. Patients contraindicated for spironolactone therapy
3. Any patients continuing on beta-blockers or direct renin blockers
4. Pregnant/breastfeeding females or women unable/unwilling to take secure contraceptive precautions whilst undergoing investigations
5. Patients unwilling/unable to take the dexamethasone required to prepare for a metomidate PET-CT scan
6. Any illness, condition or drug regimen that is considered a contraindication by the PI

Date of first enrolment
01/12/2016

Date of final enrolment
01/10/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Mary University of London
The Barts Heart Centre
William Harvey Research Institute
Charterhouse Square
London
United Kingdom
EC1M 6BQ

Sponsor information

Organisation
Queen Mary University of London

Sponsor details
Joint Research Management Office
Queen Mary Innovation Centre

5 Walden Street
London
England
United Kingdom
E1 2EF

Sponsor type
University/education

ROR
https://ror.org/026zzn846

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
01/12/2021

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol (other)		16/01/2023	13/02/2024	No	No
Results article		16/01/2023	13/02/2024	Yes	No
Statistical Analysis Plan		16/01/2023	13/02/2024	No	No