ISRCTN98001632 https://doi.org/10.1186/ISRCTN98001632

MRI assessment for beta-blockers in portal hypertension

Submission date
17/05/2017

Recruitment status
No longer recruiting

Registration date
19/05/2017

Overall study status
Completed

Last Edited
18/07/2017

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Portal hypertension (PHT) is where the blood pressure in the main vein of the liver (the portal vein) becomes too high. If a person has cirrhosis (irreversible scarring of the liver caused by liver disease), blood flow through the portal vein is disrupted, leading to an increase in blood pressure. This can lead to the smaller veins that supply the portal vein bursting, causing bleeds inside the gullet (varices). Non-selective beta-blockers (NSBB) are a type of medication used to treat various conditions including angina (chest pain) and high blood pressure. Long-term treatment with beta-blockers can help to reduce the risk of varicies, but less than one third of patients respond to these drugs and a fifth stop treatment due to side effects. New drugs are emerging that may be more effective and better tolerated. The aim of this study is to find out whether it is possible to develop an effective noninvasive test to monitor the effect of drugs on portal hypertension.

Who can participate?
Adults with liver cirrhosis, who need NSBB treatment for portal hypertension as part of their standard NHS care

What does the study involve?
Participants due to receive NSBB treatment as part of their normal care are randomly allocated to receive treatment with one of two NSBBs. Those in the first group are treated with propranolol and those in the second group are treated with carvedilol (a newer NSBB that is thought to work in a different way). Before starting their treatment and then four weeks later, participants in both groups undergo an MRI scan (a type of body scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body) to assess the severity of their liver diseases. In addition, participants also undergo routine laboratory investigations to assess blood flow and general health.

What are the possible benefits and risks of participating?
There are no direct benefits or risks involved with participating.

Where is the study run from?
Royal Infirmary of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
December 2014 to March 2016

Who is funding the study?
Chief Scientist Office (UK)

Who is the main contact?
Dr Jonathan Fallowfield
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
1.2

Study information

Scientific Title
Non-invasive assessment of haemodynamic response to beta-blockers using magnetic resonance imaging in patients with portal hypertension

Study objectives
The aim of this study is to find out whether it is possible to develop an effective noninvasive test to monitor the effect of drugs on portal hypertension (the major cause of complications and death in liver cirrhosis).

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Scotland 02 REC, 29/09/2014, ref: 14/SS/1050

Study design
Single-centre open-label randomised parallel trial

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Portal hypertension

Interventions
Patients with liver cirrhosis who were about to commence non-selective beta-blocker (NSBB) therapy as part of clinical management of portal hypertension (PHT) are enrolled into the study.

Upon enrolment, information on liver disease aetiology, past medical history, medication and alcohol history, and results of the most recent upper gastrointestinal endoscopy are recorded. Prior to starting NSBB therapy, patients undergo a physical examination and routine laboratory investigations (full blood count, coagulation screen, liver and renal function tests), followed by a baseline research MRI scan (phase-contrast MR angiography, liver and spleen T1 mapping). Liver disease severity is also assessed at baseline according to Model for End Stage Liver Disease (MELD) and Child-Pugh score.

Patients are randomised in a 1:1 ratio to once-daily treatment with carvedilol or modified-release propranolol at an initial dose of 6.25mg or 80mg respectively. Patients' compliance with medication and adverse event monitoring are assessed at an initial follow-up visit after 1 week of NSBB therapy. Provided that NSBB are tolerated clinically and haemodynamically (resting heart rate (HR) ≥50 beats per minute (b.p.m), systolic blood pressure ≥95 mmHg), the dose is escalated to the clinical target dose of 12.5mg of carvedilol or 160mg of propranolol.

Further treatment compliance and adverse event monitoring takes place by weekly telephone consultations. After 4 weeks, when established on NSBB, the second research MRI scan is performed. An interval of 4 weeks has been chosen as haemodynamic responses to NSBB after chronic use exceed the acute response rate. Consistent with a previous landmark NSBB trial in PHT, treatment is targeted at a resting HR reduction of more than 25% from baseline; this was defined as a clinical haemodynamic response to NSBB (HR responders). Following the study, participants continue taking NSBB and are managed by their existing NHS consultant.

Intervention Type
Device

Primary outcome(s)
Volumetric blood flow [L/min] in selected blood vessels (proper hepatic artery, portal vein, superior mesenteric artery, superior aorta, inferior aorta, renal arteries and azygous vein) measured by phase-contrast MR angiography at baseline and 4 weeks.

Key secondary outcome(s))

Correlation between MRI blood flow measurements and liver disease severity (using MELD and Child-Pugh scores) assessed at baseline and at 4 weeks.

Completion date
31/03/2016

Eligibility

Key inclusion criteria
1. Male or female patients aged 18-80 with liver cirrhosis
2. Portal hypertension in whom commencement of beta-blockers is clinically indicated

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Contraindication to Beta-Blocker therapy (such as moderate to severe asthma)
2. Contraindication to MRI scan
3. Contraindication to administration of gadolinium-based MRI contrast (including eGFR <30mL /min)
4. Concomitant use of other vasoactive drugs (e.g. nitrates, phosphodiesterase inhibitors)
5. Previous TIPSS insertion
6. Portal vein thrombosis
7. Hepatocellular carcinoma
8. Pregnancy or breastfeeding
9. Inability to obtain informed consent (e.g. refusal/overt hepatic encephalopathy)

Date of first enrolment
01/01/2015

Date of final enrolment
01/03/2016

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Drive
Edinburgh
United Kingdom
EH16 4SA

Sponsor information

Organisation
University of Edinburgh/ACCORD

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Government

Funder Name
Chief Scientist Office

Alternative Name(s)
CSO

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Data from this clinical research study is held by the University of Edinburgh and is available on request by contacting Sheila.Marshall@ed.ac.uk.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2017		Yes	No
HRA research summary			28/06/2023	No	No