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Intracerebral haemorrhage: Imaging microglial activation and blood-brain barrier leakage (IMAGE-ICH)

Submission date
16/09/2015

Recruitment status
No longer recruiting

Registration date
22/10/2015

Overall study status
Completed

Last Edited
24/07/2020

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
The researchers are interested in developing a new treatment for patients with a stroke caused by bleeding into the brain (intracerebral haemorrhage). In the hours to days after bleeding occurs, we know that inflammation occurs in the brain around the blood clot. Although inflammation is the body's natural response to injury, when it continues unchecked it can worsen damage. It is known that it does worsen damage after an intracerebral haemorrhage and we want to investigate whether blocking inflammation can improve outcomes. Between the blood and brain, there is a blood-brain barrier. How much of a drug can get to where it needs to act in the brain is largely governed by how well it can cross the blood-brain barrier. This makes the blood-brain barrier very important in drug development, as drugs to block brain inflammation have to cross it to get to where they need to go. However, when the brain is damaged, the blood--brain barrier can become leaky. We know very little about this after intracerebral haemorrhage. This study will determine how leaky the blood--brain barrier is in the first three days after intracerebral haemorrhage.

Who can participate?
Adult intracerebral haemorrhage patients

What does the study involve?
Participants undergo an MRI scan to measure leakiness in the first 3 days after their stroke. Twenty of these patients will go on to have a PET scan to show brain inflammation 2- 7 days after their stroke. By putting the two scans together, the researchers will be able to estimate how much of an anti-inflammatory drug will get to inflamed areas in the brain. This will indicate how much of the drug to give and when to give it in subsequent studies.

What are the possible benefits and risks of participating?
There are no benefits to participation in the study but this will be made clear to participants at first approach. Participants will be exposed to ionising radiation during the PET scan. The

maximum dose that is received as part of the scan is equivalent to 1.4 years of background radiation in the UK. There may also be discomfort associated with the blood sampling and MRI /PET scan.

Where is the study run from?
Salford Royal NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
October 2015 to June 2018

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

Who is the main contact?
Sharon Hulme

Contact information

Type(s)
Scientific

Contact name
Mrs Sharon Hulme

Contact details
Clinical Sciences Building
Salford Royal NHS Foundation Trust
Stott Lane
Salford
United Kingdom
M6 8HD

Type(s)
Scientific

Contact name
Dr Adrian Parry-Jones

ORCID ID
https://orcid.org/0000-0002-4462-3846

Contact details
Clinical Sciences Building
Salford Royal NHS Foundation Trust
Stott Lane
Salford
United Kingdom
M6 8HD

Additional identifiers

Protocol serial number
19650

Study information

Scientific Title
IntraCerebral Haemorrhage: Imaging Microglial Activation and blood-brain barrier leakaGE (IMAGE-ICH) - an observational cohort study

Acronym
IMAGE-ICH

Study objectives
Observational study to determine the extent to which blood-brain barrier breakdown during acute ICH co-localises with activated microglia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Northwest-Haydock committee, 20/10/2015, ref: 15/NW/0677

Study design
Non-randomised; Observational; Design type: Cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Stroke; Subtopic: Acute Care; Disease: In hospital study, Community study

Interventions
This is an observational study, thus no intervention is being tested. Baseline assessment will include demographics, premorbid health and medications, details of presenting signs and symptoms, clinical observations, National Institutes of Health Stroke Scale (NIHSS), and details of clinical management. A research MR scan will be performed within 3 days of onset, at SRFT. If additional inclusion criteria are met, participants will undergo a [11C](R)-PK11195 PET scan at 2-7 days after symptom onset. Blood samples will be collected for CRP, IL-6, ESR and FBC at each scanning session. A 90-day assessment will measure clinical outcomes and complete participation.

Intervention Type
Other

Primary outcome(s)
To determine the extent to which blood-brain barrier breakdown during acute ICH co-localises with activated microglia

Key secondary outcome(s))
1. To determine whether the magnitude and extent of blood-brain barrier breakdown is associated with haematoma size and location after ICH
2. Perform exploratory analyses testing for associations between blood-brain barrier permeability and brain inflammation with peripheral inflammatory markers and clinical outcomes

Completion date
28/02/2021

Eligibility

Key inclusion criteria
1. Age 18 or over
2. Acute, spontaneous, supratentorial ICH within 24 h of symptom onset
3. Glasgow coma scale (GCS) score = 9
4. Research MR scan can be performed within 3 days of symptom onset

Additional inclusion criteria for PET imaging (d 2-7):
5. GCS = 14
6. Able to transfer from chair to bed with assistance of two people
7. Deemed medically stable by medically- qualified researcher for transfer to Wolfson Molecular Imaging Centre (WMIC) on day of PET scan

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Contraindication to magnetic resonance (MR) scanning
2. Pre-existing -brain lesion (e.g. tumour, previous stroke) that is likely to interfere with the planned analysis
3. ICH known or strongly suspected of being secondary to a structural vascular malformation (e.g. cerebral aneurysm, arteriovenous malformation, cavernoma, dural arteriovenous fistula), tumour, haemorrhagic transformation of an ischaemic stroke, or venous sinus thrombosis
4. Clear history of recent (<7 days prior to onset) head trauma, thought to be the cause of intracerebral haemorrhage
5. Any known inflammatory disease which in the opinion of the PI may interfere with interpretation of the study results
6. Known, uncorrected bleeding disorder

7. Female patient who may be pregnant or who is breastfeeding
8. Significant renal impairment (estimated glomerular filtration rate < 30)
9. Any other significant disease or disorder which, in the opinion of the PI or his delegatee, may put the participant at risk
because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study
10. Neurosurgical procedure performed since admission or booked for surgery
11. Treatment with drugs known to or likely to interfere with PK11195 binding (including benzodiazepines, steroids, minocycline) that cannot be stopped in sufficient time to prevent interference with PET scanning

Date of first enrolment
15/10/2015

Date of final enrolment
30/09/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Salford Royal NHS Foundation Trust
Salford
United Kingdom
M6 8HD

Sponsor information

Organisation
University of Manchester (UK)

ROR
https://ror.org/027m9bs27

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

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the CI, Dr Parry-Jones. At the end of the programme of study, the anonymised data will be securely transfer onto the University of Manchester Research Data Management Service (RDMS) for managed, secure and replicated storage. The RDMS allows researchers to curate and preserve their data after project completion as well as facilitating publishing and sharing of primary research data along with appropriate metadata. Consent was obtained from participants included in the study and all gave their permission for long-term retention and sharing of their anonymised data.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes