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Desmopressin for treatment of stroke patients on antiplatelet therapy

Submission date
08/10/2018

Recruitment status
No longer recruiting

Registration date
22/10/2018

Overall study status
Completed

Last Edited
22/06/2023

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Haemorrhagic stroke, an emergency caused by bleeding in the brain, often leads to death or long-term disability. A quarter of these patients are taking blood-thinning drugs (antiplatelet drugs, such as aspirin) because they are at risk of a heart attack or ischaemic stroke. Patients taking these drugs are more likely to die or be disabled if they have a haemorrhagic stroke. At present, there is no effective treatment for reversing their effects. Desmopressin is a drug which may reverse the effects of antiplatelet drugs and stop bleeding. The aim of this study is to assess whether it is feasible to run a large trial to see if desmopressin can reduce the number of people who die or are disabled after haemorrhagic stroke.

Who can participate?
Patients aged over 18 with an intracerebral haemorrhage who are taking a daily oral antiplatelet drug

What does the study involve?
Participants are randomly allocated to be treated with either desmopressin or a dummy drug given as a drip via a cannula (needle inserted into a vein, usually into the back of the hand) over about 20 minutes. The treatment is given once, then the treatment stops. Three blood samples are taken from a vein in the arm: one before the treatment to assess blood clotting, one immediately after and another 24 hours after treatment to check salt levels in the blood stream. Wherever possible these are taken with routine blood samples. During the next 7 days, a nurse checks the participant looking in particular for signs of side effects of the treatment. A brain scan is also repeated the day after the treatment to assess the effects of the treatment. The researchers contact the participant's GP or check with the NHS Information Centre to check on their condition three months after their stroke and to confirm their contact details. Participants are then contacted for a telephone consultation with a member of the research team to check their condition at that time. It involves asking how they are able to move around, about how they feel their life has been affected by the stroke and some brief memory tests. Other than described here, treatment is exactly the same as for all stroke patients.

What are the possible benefits and risks of participating?
Participation in this study may reduce the symptoms of haemorrhagic stroke or improve long-

term recovery. However, this cannot be promised, and participation is voluntary. The information obtained may benefit other people who have a stroke in the future. Treatment with any drugs can result in possible side effects and the side effects from desmopressin are generally mild. They can include headache, abdominal pain, low blood pressure and dizziness. The drug can increase the risk of seizures but this is very rare. However, because the treatment works by stopping bleeding there is a chance it can cause an increase in blood clot formation. This can occur in the legs (deep vein thrombosis, DVT) or the lungs (pulmonary embolism, PE) and is potentially very serious and maybe even life threatening. Participants who have previously suffered from blood clots in the legs or lungs may not be able to participate in this study. In 65 previous studies where desmopressin has been used to reduce bleeding during operations, desmopressin was safe. There was no increase in serious side effects, such as blood clots, in the patients who were treated with desmopressin. Because desmopressin is already routinely used in a number of bleeding conditions, the potential benefit of the drug (stopping bleeding in to the brain) is expected to outweigh the low risk of serious side effects (such as blood clots). However, this is not known for certain and all participants will be monitored closely for side effects. Participants must inform their doctor or member of the research team if they feel they have had a reaction to the medication. The blood samples can cause mild discomfort/pain and slight bruising. The extra CT brain scan performed as part of this trial takes less than 5 minutes and does not involve any injections. The scan uses x-rays, which in large amounts can be harmful, but for this extra CT head scan the additional risk from the scan has been judged to be extremely small and is comparable with the annual risk of dying from an accident in the home.

Where is the study run from?
University of Nottingham (UK)

When is the study starting and how long is it expected to run for?
October 2018 to June 2022

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

Who is the main contact?
Diane Havard
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-001904-12

Integrated Research Application System (IRAS)
233744

ClinicalTrials.gov (NCT)
NCT03696121

Protocol serial number
CPMS 38963, IRAS 233744

Study information

Scientific Title
Desmopressin for reversal of Antiplatelet drugs in Stroke due to Haemorrhage (DASH)

Acronym
DASH

Study objectives
Current study hypothesis as of 12/02/2020:
To assess the feasibility of screening, checking the eligibility, approaching, randomizing, administering the intervention and completing follow up for patients treated with desmopressin or placebo to inform a definitive trial

Previous study hypothesis:
To assess the feasibility of a large randomised trial to see if Desmopressin can reduce the number of people who die or are disabled after haemorrhagic stroke.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Nottingham 2 Research Ethics Committee, 22/08/2018, ref: 18/EM/0184

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Haemorrhagic stroke

Interventions
Patients will be randomly allocated to receive either:
Intravenous desmopressin: 20 µg in 50 ml Sodium Chloride 0.9% infused over 20 min
Comparator: placebo (Sodium Chloride 0.9% intravenous infusion) administered by identical regimen

The participant's involvement in the trial will last for 90 days, from randomisation (day 1) until final follow-up at 90 days.

Baseline (Day 1): CT scan to confirm the diagnosis of haemorrhagic stroke, clinical assessment, blood sample to assess baseline clotting function (P-selectin), blood sample to look for changes in clotting function one hour after administration of desmopressin, blood pressure measurement after treatment is complete.

End of treatment (24 hours after treatment - day 2):Clinical assessment, blood sample to assess serum sodium, CT brain scan to assess bleeding and to look for any increased bleeding.

Day of discharge/death: document discharge destination(e.g. home/hospital/rehabilitation unit) and length of hospital stay.

Day 90 – telephone interview: completion of questionnaires - Disability (Barthel index, Quality of life (EuroQol) and Cognition (telephone MMSE)

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
The feasibility of randomising, administering the intervention, and completing follow-up for patients treated with desmopressin or placebo to inform a definitive trial; Timepoint(s): End of the study; assessed using:
1. Number of eligible patients who receive allocated treatment
2. Rate of eligible patients randomised
3. Proportion of eligible patients approached
4. Proportion of eligible patients randomised and reasons for non-randomisation
5. Adherence to intervention
6. Proportion of participants followed up to 90 days and reasons for loss to follow up
7. Proportion of randomised participants with full outcome data available, and reasons for non-availability

Key secondary outcome(s))
1. Hyponatraemia, measured using U&E blood test (Sodium Na level) at 24 hours
2. Early case fatality <28 days, measured using SAE recording/death/discharge CRF
3. Case fatality at day 90, measured using alive and well check GP
4. Serious adverse events (including thromboembolic events) up to day 90, measured using SAE reporting CRF
5. Change in intracerebral haemorrhage volume at 24 hours, measured using CT/MRI scan volume measurement
6. Discharge destination, measured using discharge CRF at discharge
7. Disability, measured using the Barthel index at day 90
8. Quality of life, measured using EuroQol at day 90
9. Cognition, measured using telephone MMSE at day 90
10. Length of hospital stay, measured using hospital admission record at discharge
11. Health economic assessment using EQ-5D at day 90 follow up
12. Assessment of baseline platelet dysfunction (P-selectin) and correlation with response to desmopressin, measured using P-selectin blood test at enrollment after consent pre-treatment
13. Change in factor VIII, VWF antigen and VWF activity at one hour after administration of desmopressin, measured using factor VIII, VWF antigen and VWF assays done on blood tests taken before and after treatment

Completion date
30/06/2022

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 12/02/2020:
1. Aged >18 years
2. Confirmed intracerebral hemorrhage on imaging
3. Less than 24 hours from onset of symptoms (or from when last seen healthy)
4. Prescribed and thought to be taking a daily oral antiplatelet drug in the preceding seven days (cyclooxygenase inhibitors, phosphodiesterase inhibitors or P2Y12 inhibitors)
5. Signed consent (patient/personal/professional representative)

Previous participant inclusion criteria:
1. Adults (>17 years)
2. Confirmed intracerebral haemorrhage on imaging
3. Less than 12 hours from onset of symptoms [or from when last seen healthy]
4. Prescribed and thought to be taking a daily oral antiplatelet drug in the preceding seven days (cyclooxygenase inhibitors, phosphodiesterase inhibitors or P2Y12 inhibitors)
5. Signed consent (patient/personal/professional representative)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
54

Key exclusion criteria
1. Aneurysmal subarachnoid haemorrhage known at time of enrolment
2. Haemorrhage known to be due to transformation of infarction
3. Haemorrhage known to be due to thrombolytic drug
4. Haemorrhage known to be due to venous thrombosis
5. Risk/s of fluid retention associated with desmopressin judged clinically significant by the attending physician (for example patients with pulmonary oedema and/or cardiac failure)
6. Significant hypotension (systolic blood pressure < 90mmHg)
7. Known drug-eluting coronary artery stent in previous three months
8. Allergy to desmopressin
9. Pregnant or breastfeeding
10. Life expectancy less than four hours, or planned for palliative care only
11. Glasgow coma scale less than 5
12. mRS > 4
13. Participation in another concurrent drug trial

Date of first enrolment
01/11/2018

Date of final enrolment
31/03/2022

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
NHS Grampian
Summerfield House
2 Day Road
Aberdeen
United Kingdom
AB15 6RE

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
Royal Devon & Exeter NHS Foundation Trust
Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
University Hospitals of North Midlands NHS Trust
Newcastle Road
Stoke on Trent
United Kingdom
ST4 6QG

Study participating centre
Derby Teaching Hospitals NHS Foundation Trust
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
St Georges University Hospitals NHS Foundation Trust
St Georges Hospital
Blackshaw Road
Tooting
London
United Kingdom
SW17 0QT

Sponsor information

Organisation
University of Nottingham

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: PB-PG-0816-20011

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Professor Nikola Sprigg (nikola.sprigg@nottingham.ac.uk).

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?
Results article		01/07/2023	22/06/2023	Yes	No
Protocol article	Peer reviewed protocol article	10/11/2020	11/08/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes