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Improving recovery in patients with stroke following brain hemorrhage (bleeding) using a blood pressure measuring machine

Submission date
22/12/2019

Recruitment status
No longer recruiting

Registration date
04/01/2020

Overall study status
Completed

Last Edited
12/03/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Brain haemorrhage or bleeding in the brain is a devastating type of stroke. It has long term consequences resulting in either weakness or vision loss or speech problems or more. The blood in the brain is irritant to the brain cells which leads to swelling of the brain. The brain swelling due to brain haemorrhage reaches its maximum in the first seven days after stroke. This brain swelling also causes additional damage to the brain cells. This further decreases the chances of recovery in a patient with brain haemorrhage. Currently, there are no strategies to decrease brain swelling apart from early blood pressure control and stroke unit care (care in specialised area of hospital with specially trained doctors, nurses, speech therapist, physical therapist and occupational therapist).

Remote ischemic conditioning is a novel therapy that involves inducing ischemia (a state of low blood flow to parts of the body) like conditions in the arm muscles for a few minutes with the help of a blood pressure machine followed by a period of relaxation. This is very much like the pressure you may have noticed while getting your BP checked, except this feeling of pressure would persist for five minutes. This intervention is not only cheap but also can be tolerated by the patient easily as has been shown in many research studies. The intervention can be done repeatedly, four times in one session and can be done multiple times over a few days. This may lead to release of positive signals from the arm muscles that can reduce swelling in the brain by reducing brain inflammation.

We hope to deliver this therapy within the first few hours after the occurrence of brain haemorrhage and continue for 7 days. We hope this may reduce the brain swelling and thus improve recovery in patients with a brain haemorrhage. We will include a total of 60 patients in our study, 30 patients will receive the new therapy in addition to the current best management available and 30 patients will get the current best management only. The new therapy will be delivered by trained person involved in the study while the patient stays admitted in the hospital. If the patient is discharged early the new therapy will be stopped without affecting the study. The current best management involves lowering of blood pressure and care in specialised area of hospital called stroke unit. We will take pictures of the brain with help of the CAT

scanner and measure the brain swelling. A person who does not know about the patients will independently measure the swelling in the brain. We will then perform an analysis of this type of intervention is useful or not.

Who can participate?
We will include a total of 60 patients in our study. These patients must be adults, diagnosed with an acute stroke, within 6 hours of onset, with intracerebral haemorrhage seen on CT and for this to be their first stroke.

What does the study involve?
All patients will receive standard of care management for brain hemorrhage.

Half of the patients will be randomly allocated to receive additional remote ischemic conditioning where we will apply pressure on the arm with help of a manual blood pressure machine. We will keep the pressure for few minutes and release. We will deliver this therapy two times a day for seven days. Medical and nursing information during your stay in the hospital will be used in the study.

Brain scan with CT will be done at admission, 24 hrs and at day 7 as part of routine care.We will take the images of the serial brain scan done to assess the brain swelling. We will also collect information about the blood pressure readings over the period of seven days. After 90 days we will contact patients and/or their families either in hospital or by telephone to ask about recovery following stroke.

What are the possible benefits and risks of participating?
Remote ischemic conditioning in healthy people have no side effects or adverse effects. However in patients with low platelet count they may have brief periods of red rash on the arm. These are only temporary. All our patients will be closely monitored for any new side effects.

Where is the study run from?
The study will be done at the Stroke Unit, Department of Neurology, Christian Medical College and Hospital, Ludhiana.

When is the study starting and how long is it expected to run for?
Patient recruitment for the study began 05/09/2018 and the study will run until 20/12/2019.

Who is funding the study?
The study is funded by the Department of Neurology, Christian Medical College, Ludhiana.

Who is the main contact?
The main contact is Dr Mahesh Kate, mahesh@ualberta.ca

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
Nil known

Study information

Scientific Title
Remote Ischemic COnditioning to reduCe periHematoma Edema in inTracerebral hemorrhage patients (RICOCHET)

Acronym
RICOCHET

Study objectives
Remote ischemic conditioning reduces the edema extension distance at 7 days in patients with acute intracerebral hemorrhage (ICH) compared to standard of care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Ethics Committee, Christian Medical College and Hospital, Ludhiana, Punjab, India, 141008, 14/08/2018, ref: 201809408/IECCMCL/DM Thesis-Neurol

Study design
Randomized controlled single-center, interventional trial with a blinded end-point with 1:1 allocation of intervention or standard of care.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Intracerebral hemorrhage (stroke)

Interventions
Patients with acute stroke syndrome presentation within the first 6 hours of symptom onset undergo a CT scan of the head. They are screened for the presence of intracerebral hemorrhage by the Emergency Physician or Neurologist on call. Patients with intracerebral hemorrhage and surrogate decision-makers are approached by the study investigator either in the emergency department or after the admission to stroke unit with an information sheet of the consent form. The study investigator explains all the study procedures and answers the questions. If the patient or surrogate agrees to participate in the study they sign the consent form. The study investigator then calls the blinded study investigator to assign the study group. The blinded investigator then assigns the study group. The blinded study investigator with the help of an online randomizer, random.org, has created a sheet with block randomization with a set of 5 before the study began. The study investigators are unaware of the randomization process. The patients were planned to be randomized at a ratio of 1:1. Patients were randomized to either remote ischemic conditioning (RIC) or control groups.

Intervention group:
RIC was delivered in two sessions a day in both the arms for 7 days or up to the time of discharge whichever was earlier. The study investigator delivered the first session of remote ischemic conditioning as early as possible usually within one hour. The subsequent sessions are timed so that they are 12 hours apart. Each cycle consists of 5 minutes of pressure (ischemic) and 5 minutes of relaxation (reperfusion). The pressure was increased 30 mmHg above the systolic pressure in the upper arm or to a maximum of 200 mmHg. The patients received 4 cycles per session, so a typical intervention session would last for 35 minutes. The intervention was delivered with the help of a manual aneroid blood pressure machine and a standard brachial blood pressure cuff. The intervention was delivered by the study personnel.

Control group:
All patients in the control group received standard care of care with blood pressure management and stroke unit care.

All patients underwent a CT scan of the head on day 7 or at the time of discharge to assess for perihematomal edema. To assess for clinical outcomes we followed the patient physically or by telephone at 90 days after symptom onset.

Intervention Type
Device

Phase
Phase II

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome measure
Edema extension distance (EED) assessed on computed tomography of the head, on day 7 or day of discharge whichever is earlier. This was assessed with the help of a software ANALYZE PRO ver 1 (Biomedical Imaging Resource). The software allows measuring of the hypodense area surrounding the hematoma in threshold-based (5-23 Hounsfield units) manner with semiautomatic tools. The measured perihematomal edema volume (ml) is then run through an equation proposed by Parry-Jones et al to obtain edema extension distance (cm). EED is a surrogate measure of perihematomal edema and is independent of intraparenchymal hematoma volume.

Secondary outcome measures
1. Hematoma growth volume at 24 hours and 7 days. Measured by computed tomography of the head and assessed with help of ANALYZE PRO ver 1 (Biomedical Imaging Resource) with threshold-based semiautomatic tools. The hematoma growth was calculated by subtracting the final hematoma volume from the baseline hematoma volume. According to previous studies, hematoma expansion or hematoma growth volume was defined as an absolute increase in the hematoma volume of more than 3 ml.
2. Absolute perihematoma edema (PHE) volume at 24 hours and 7 days measured by computed tomography of the head.
3. Relative PHE volume at 24 hours and 7 days measured by computed tomography of the head.
4. Degree of disability/dependence following stroke measured by Modified Rankin scale (mRS) at day 90, either through individual assessments on follow up or through telephone interviews.

Overall study start date
14/04/2018

Completion date
20/12/2019

Eligibility

Key inclusion criteria
1. Adult patients presenting with clinical syndrome of acute stroke
2. First-ever stroke
3. ICH confirmed on CT of the brain
4. Symptom onset within 6 hours (prior to randomization)

Participant type(s)
Patient

Age group

Adult

Sex
Both

Target number of participants
60

Key exclusion criteria
1. Parenchymal hematoma volume >60 ml on baseline CT head
2. Patients with a deranged bleeding profile or platelet count less than 200,000/mm3
3. Injury or easy bruising of the upper arm skin due to underlying skin condition
4. Pain or tenderness in the upper arm muscles
5. Fever on admission
6. Secondary ICH (cerebral venous thrombosis, aneurysmal hemorrhage, traumatic and hemorrhagic transformation of ischemic stroke)
7. Patient on sulfonylurea medication for diabetes control
8. Patients with known upper arm peripheral arterial disease

Date of first enrolment
05/09/2018

Date of final enrolment
16/09/2019

Locations

Countries of recruitment
India

Study participating centre
Christian Medical College, Ludhiana
Neurology Office
Christian Medical College and Hospital
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Sponsor information

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Sponsor type
University/education

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Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Department of Neurology, Christian Medical College, Ludhiana

Results and Publications

Publication and dissemination plan
We hope to present the study in the ESO-WSO 2020 conference and publish it in Stroke Journal at the same time. We will hold a dissemination conference with the media after the publication of the results.

Intention to publish date
12/05/2020

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

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?
Participant information sheet		02/01/2020	10/01/2020	No	Yes
Abstract results	Abstract presented at ESO-WSO 2020 Joint Meeting	07/11/2020	07/01/2022	No	No

Results article	03/05/2024	12/03/2025	Yes	No