

Prevention Of Hypertensive Injury to the Brain by Intensive Treatment after Intracerebral Haemorrhage: A Pilot Study (PROHIBIT-ICH)

PATIENT INFORMATION SHEET

We'd like to invite you to take part in our research study. The aim of the study is to compare blood pressure (BP) treatment (to a target of 120/80mm Hg, guided by a special BP monitor linked to our research team by Bluetooth technology), versus standard care. The more intensive BP lowering treatment is promising, but is not yet proven. Our study will therefore assess the feasibility, safety and effectiveness of this intensive BP treatment strategy. Before you decide to take part, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information, and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask us.

What is the purpose of this study?

About 1 in 10 strokes are due to a bleed into the brain from a ruptured (burst) artery, called intracerebral haemorrhage (ICH). The symptoms of ICH are due to nerve cell damage or swelling, and depend on where in the brain the bleeding has occurred; they can include drowsiness, nausea and vomiting, headaches, weakness of one or more limbs, loss of vision or speech, or seizures. In some cases, ICH is caused by injury or surgery, in others it happens suddenly without warning (“spontaneous”).

Spontaneous ICH is sometimes the result of high BP which, over time, causes damage to the small blood vessels supplying the brain, making them more likely to rupture. The main cause of spontaneous ICH is called “small vessel disease” (SVD), this may be because of poor BP control. Magnetic Resonance Imaging (MRI) has improved our ability to see the effects of SVD on scans of the brain after ICH.

The aim of this research study is to determine whether frequent measurements of BP using a monitor that securely sends readings automatically to our research team by Bluetooth

technology (called “telemetric” monitoring) can be used to safely guide medication changes to “intensively” lower BP (to a target of 120/80mmg Hg) to reduce damage to the small blood vessels in the brain after spontaneous ICH. At multiple sites in the UK, participants will be randomly allocated to either intensive BP treatment guided by telemetric home monitoring or standard care in adult ICH survivors. We will follow-up these two groups of participants to assess whether BP lowering using this home monitoring is feasible, safe and effective in reducing brain injury. We will measure BP control at 3 months. To measure its effectiveness in reducing brain injury, MRI scans will be taken before starting monitoring and after a year. A sample of blood will also be collected to find out if there are any genetic variations associated with ICH or SVD.

Why have I been invited to take part in this study?

You have been invited to take part because you are over the age of 40 and have had a spontaneous ICH, most likely due to SVD, confirmed on a brain scan.

Do I have to take part?

No. Participation in this study is entirely voluntary. It is entirely up to you to decide if you would like to participate or not. If you agree to participate, you will be asked to read and sign a consent form. You are free to withdraw from the study at any time, without giving a reason. This will have no impact on your clinical care.

What will happen to me if I decide to take part?

You will meet a member of the research team at your hospital, who will be able to answer any questions you may have. If you are eligible and willing to participate in the study, we will collect information regarding your health status, memory and thinking (cognition), and quality of life. We will take a small blood sample (equivalent to one teaspoonful or 5-10 millilitres of blood), and you will have an MRI scan of the brain. Your local team will send all of this information, and your blood sample, to our PROHIBIT-ICH study co-ordinator at UCL.

You will be invited back for follow up after 3 months and 1 year, where you will be asked about any medical problems or admissions to hospital since you joined the study and how you are recovering. You will also be asked to do some memory tests and be fitted for 24

hours with a BP monitor that records BP every 30 minutes during the day and hourly at night. You will have another MRI of the brain at the 1 year follow up.

Half of the participants recruited to the PROHIBIT-ICH study will be randomly (by chance) allocated to monitor their BP at home using a telemetric monitor, this is called randomisation. Randomisation will be carried out by using a computer, it will allocate at random half of the group to use the BP monitors and the other half without it. BP data will be automatically sent to our Oxford study centre to monitor and change medicine dose to reach an BP target of 120/80mm Hg. The other half of participants will receive usual clinical care including BP control monitored by their hospital stroke team and their General Practitioner.

If you are selected to monitor your blood pressure at home, you will be shown how to use the monitor and will be asked to measure your blood pressure in a seated position three times over ten minutes (in your non-dominant arm (the one that you don't usually use for things like writing) unless you have been told otherwise), when waking in the morning, in the early afternoon, and before going to bed. This will need to be done for at least one month, and possibly up to three months, depending on how quickly your blood pressure reaches the intensive target. These BP measurements will be transmitted to a co-ordinating centre in Oxford via Bluetooth technology and assessed daily by a dedicated research team of nurses and doctors who will contact you by phone if a change in medication is indicated. The GP will also be notified by the co-ordinating centre. After three months, you will be asked to take readings three times over ten minutes, once a week until you are seen again at one year.

What are the possible benefits of taking part?

Participation in the study will allow you access to a team with expertise in ICH, providing you with more information regarding your disease, as well as its prognosis. If randomly selected to intensive treatment, monitoring your BP at home should allow you to understand and manage your own BP better. All participants in the study, regardless of whether they have home monitoring, will receive a research quality brain scan, careful follow-up of their progress after their ICH, and the opportunity to benefit from up to date information from a specialist stroke research team. Our study will increase understanding about whether more intensive lowering of BP in survivors of ICH is feasible, safe and effective in reducing brain

injury on MRI scans. If successful, we hope that this trial will lead to a larger trial. Our research will benefit the ICH research community and ultimately improve care for ICH survivors.

Are there any possible disadvantages or risks from taking part?

The collection of a blood sample from your arm is a standard procedure that is usually very safe, though can cause slight discomfort. Very rarely, a blood test can cause bruising, fainting or light-headedness, but the risks will be minimised because the collection of blood is done only by experienced and trained practitioners.

The MRI scan is noisy and, rarely, may provoke claustrophobia. Noise is minimised using earplugs and anxiety and claustrophobia are reduced by continuous communication during the scan via intercom. The scanning team will be able to remove you from the scanner at any time at your request.

Taking blood pressure readings may be uncomfortable due to a squeezing sensation, but this will only last a few seconds. These readings will be performed by an experienced professional whilst you are in hospital and by you or your carer when you have been discharged from hospital.

All staff on the study will be fully trained in good clinical practice, and will always consider your well-being as their primary concern. You can withdraw from the study at any time without affecting your clinical care.

Will my General Practitioner/family doctor (GP) be informed of my participation?

Yes, they will be aware of your participation in the study. Should you be randomly selected to home BP monitoring, any advised adjustment of BP medications will also be communicated to your GP.

What will happen to the results of this study?

The information from all participants taking part in this study will be collected and stored at UCL and Oxford. After analysing the data, the results will be reported to the funder of the study and published in scientific journals. Following completion and publication, these results will be posted on a study website for participants to view.

What if something goes wrong?

The UCL Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment which is provided.

What will happen if I don't want to carry on with the study?

Participation is entirely voluntary and you may withdraw at any time, without providing a reason.

Will my taking part in this study be kept confidential?

All information relating to your blood tests, MRI scans and any of your medical records will be kept strictly confidential and will only be used for medical research. Patient identifiable information will be anonymised in any reports. The research teams will ensure that patient identities are protected from any unauthorized parties. The clinical data records will be kept securely at the Stroke Research Centre, UCL. Prof David Werring, the Chief Investigator, will be responsible for the security and access to the information. The blood pressure data will be kept securely at the Centre for Prevention of Stroke and Dementia at the University of Oxford. Prof Peter Rothwell will be responsible for the security and access to the information. Data from the PROHIBIT-ICH study may be used for future research on stroke by UCL, and other research institutions in the UK or worldwide, but your confidentiality will be maintained. Your medical records may be inspected by competent authorities and properly authorized persons, but if any information is released outside the trial office it will be transferred in a secure manner. The results of the study will be published in medical journals or other public sites. We keep research results strictly confidential.

Who is organising and funding the study?

The research is being organised Professor David Werring, Professor of Clinical Neurology, Stroke Research Centre, UCL Institute of Neurology, and Prof Peter Rothwell, Action Research Professor of Neurology and Director of the stroke prevention research unit, Centre for Prevention of Stroke and Dementia, University of Oxford.

The Stroke Association has funded this study.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by **XXXXXXXXXXXXXXXXXXXXXXX** Research Ethics Committee.

In summary, if you take part, you will have:

- A short initial assessment to determine eligibility
- Questionnaires (clinical, cognitive, quality of life) at the beginning of the study, at 3 months and 1 year
- A blood sample collected upon entering the study
- An MRI scan upon entering the study and at 1 year follow up
- Either be assigned to usual care or receive a telemetric blood pressure monitor to measure BP 3 times daily (early morning, early afternoon and evening), with each time taking 3 readings over 10 minutes, and accordingly, receive adjusted BP treatment
- A 24 hour blood pressure monitor at follow up at the beginning, 3 months and 1 year.

Thank you for reading this information sheet and taking the time to consider participating in this study. If you agree to take part, you will be given a copy of this information sheet and a copy of the signed consent form.

Further information can be obtained from:

University College London (UCL)	
Professor David Werring Professor of Clinical Neurology Stroke Research Centre UCL institute of Neurology Russell Square House 10-12 Russell Square London WC1B 5EH d.werring@ucl.ac.uk Tel: 020 3108 7493	Shahena Butt PROHIBIT-ICH Study Co-ordinator Stroke Research Centre UCL Institute of Neurology Russell Square House 10-12 Russell Square London WC1B 5EH shahena.butt@ucl.ac.uk Tel: 0203 108 6181
University of Oxford	
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