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Remote ischaemic Conditioning After Stroke Trial (ReCAST)

Submission date	Recruitment status	[X] Prospectively registered
28/11/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/11/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
28/08/2019	Circulatory System	

Plain English summary of protocol

Background and study aims
Stroke is the third leading cause of death worldwide and is devastating to both patients and carers. In the United Kingdom there are 110,000 first strokes and 30,000 recurrent strokes each year, which consumes up to 6% of NHS resources. There are only a few effective treatments for stroke and recent research has failed to demonstrate effectiveness of novel drug treatments, therefore, new approaches to reduce the burden of stroke on society are required. The concept of ischaemic conditioning (IC) is an approach used to protect organs/tissue from something called ischaemia/reperfusion injury (the injury a tissue sustains as a result of reestablishing its blood flow after it has been blocked). Remote ischaemic conditioning (RIC) means briefly interrupting the blood supply to an area (i.e. the arm) distant from an organ you are trying to protect (i.e. the brain). Experiments in animals have shown RIC to protect the brain from injury caused by a stroke when RIC is applied soon after the stroke has occurred. In people, RIC can be achieved by inflating a blood pressure (BP) cuff on the arm several times very soon after a stroke. RIC is already used during cardiac surgery and it may help protect the heart after a heart attack. In a recent study of 333 patients with a heart attack, RIC applied by paramedics, whilst the patient was still in the ambulance, helped to decrease the amount of damage to the heart and had a favourable safety profile. RIC is an attractive prospect in the clinical setting since it bears little cost and would be simple to administer by medics and allied health professionals (nurses, paramedics) and could be applied very quickly. A typical protocol would involve inflating a blood pressure cuff, applied to a patients upper arm, to a level exceeding their current blood pressure, for a period of 5 minutes. This would then be repeated 4 times. We therefore plan to commence an initial small study evaluating the tolerability, feasibility and safety of RIC in patients with very early stroke.

Who can participate?
We will recruit 30 patients from the Royal Derby Hospital Stroke Unit over 15 months (2 per month).

What does the study involve?
Patients will be randomly allocated to the intervention or sham procedure. The intervention will be 4 cycles RIC (alternating 5 minutes inflation, 5 minutes deflation of a standard upper arm BP cuff), applied within 12 hours of stroke onset. Patients randomised to the sham procedure will

receive 4 cycles of BP cuff inflation (up to 30mmHg a very low level that will not obstruct the blood supply to the limb) and deflation.

What are the possible benefits and risks of participating?
The results will inform the design of future trials of a potential intervention that is practical, noninvasive and simple to administer. Risks: discomfort or pins and needles when the blood pressure cuff is inflated.

Where is the study run from?
Royal Derby Hospital Stroke Unit (UK)

When is the study starting and how long is it expected to run for?
The study will commence in March 2013 and will run for 2 years

Who is funding the study?
British Medical Association (UK)

Who is the main contact?
Dr T. England
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02779712

Protocol serial number
13466

Study information

Scientific Title
Remote ischaemic Conditioning After Stroke Trial (ReCAST): a randomised controlled trial

Acronym
ReCAST

Study objectives
Stroke has an enormous impact on both individual and society. Novel treatments are required to relieve this burden and remote ischaemic conditioning (RIC) is one such approach. RIC means briefly interrupting the blood supply to an area (i.e. the arm) distant from an organ you are trying to protect (i.e. the brain). Experiments in animals have shown RIC to protect the brain from injury caused by stroke. In humans, RIC could be achieved by inflating a blood pressure cuff on the arm several times very soon after a stroke. The mechanisms of protection are unclear but may be due enhancing the bodys ability to protect itself by altering the blood flow to the brain or by reducing the harmful effects of inflammation. RIC is already used during cardiac surgery and it may help protect the heart after a heart attack. We plan to conduct a pilot clinical trial assessing the tolerability and feasibility of RIC patients after stroke, whilst investigating how it might work. The results will inform the design of future trials of a potential intervention is that is pragmatic, noninvasive and simple to administer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee West Midlands Staffordshire, 19/12/2012, ref:12/WM/0339

Primary study design
Interventional

Study design
Randomised interventional trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Stroke Research Network; Subtopic: Acute Care; Disease: Device used

Interventions
30 patients will be randomised on a 1:1 basis to receive either:
Remote ischaemic conditioning (RIC group): 4 cycles of intermittent limb ischaemia - alternating 5 minutes inflation (up to 20mmHg above systolic BP) followed by 5 minutes deflation of a standard upper arm blood pressure cuff in the non-paretic arm; or
Control group: 4 cycles of inflation and deflation up to 30mmHg in the non-paretic arm
Follow up on Day 4 and Day 90.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Tolerability (duration cuff tolerated, number of cycles, drop out rate) and feasibility (accrual rate, proportion of patients knowing if they received RIC or sham) of RIC after hyperacute ischaemic stroke

Key secondary outcome(s)
Clinical safety (day 4±1, day 90±7):
Serious adverse events (SAE); death (cause); recurrence/progression; neurological deterioration (increase in NIHSS >4 points); vascular events (including limb ischaemia, venous thrombo-embolism); neurovascular limb damage and tissue injury.

Laboratory measures: (Day 0, day 4±1, day 90±7)
Surrogate markers of efficacy, plasma S100B and MMP-9 levels by multiplex analysis; markers of inflammation and vascular function including but not limited to plasma CRP, e-selectin and vCAM by multiplex analysis; circulating endocannabinoids levels; plasma SOD activity by bioassay.

Haemodynamic parameters:
Transcranial Doppler (TCD), continuous recording during RIC, measures middle cerebral artery blood flow velocity/pulsatility index (a surrogate for cerebral blood flow (CBF)). Day 0 pre and post RIC, day 4±1 and day 90±7: central BP, pulse pressure, heart rate, rate-pressure product; aortic compliance and pulse wave velocity.

Clinical efficacy: (Day 4±1, day 90±7)
Impairment (NIHSS, motoricity index); dependency (modified Rankin Scale (mRS)); disability (Barthel Index(BI)<60)); functional independence (extended activities of daily living (EADL)); Zung depression scale; cognition (MMSE). At discharge/death: Length of stay in hospital; discharge disposition.

Completion date
03/12/2015

Eligibility

Key inclusion criteria
1. Age > 18 years
2. Clinical stroke (lacunar or cortical) of ischaemic subtype
3. Within 12 hours of stroke onset
4. Arm and/or leg weakness at the time of randomisation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Premorbid dependency, modified Rankin scale (mRS) >3
2. Known subclavian or brachial artery stenosis
3. Dementia
4. Coma [Glasgow Coma Scale (GCS< 8)]
5. Malignancy or significant comorbidity
6. Participation in other drug trials
7. Pregnancy

Date of first enrolment
04/03/2013

Date of final enrolment
03/12/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The University of Nottingham
Nottingham
United Kingdom
NG5 1PB

Sponsor information

Organisation
University of Nottingham (UK)

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type

Other

Funder Name
British Medical Association (BMA) (UK)

Alternative Name(s)
The BMA, The British Medical Association (BMA), BMA

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2017		Yes	No
HRA research summary			28/06/2023	No	No