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Predicting Outcome and Measuring Benefit from botulinum therapy in Stroke

Submission date
12/05/2010

Recruitment status
No longer recruiting

Registration date
12/05/2010

Overall study status
Completed

Last Edited
23/04/2021

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
People with stroke often say they cannot use their affected arm and hand. There are many potential causes, but one problem likely to contribute is a type of muscle stiffness (spasticity). People with spasticity experience unwanted muscle activity, spasms and tightness or stiffness, making movement of the hand extremely difficult. Botulinum toxin is a purified protein derived from the bacteria Clostridium botulinum and is licensed in the UK for treating muscle spasticity after stroke. It works by blocking the signal from the brain to the muscle nerve endings in the area close to the injection site. The overactive muscle is temporarily paralysed (the effects wear off after about three months), providing a window of opportunity where physiotherapy may be more effective. We aim to investigate whether Botulinum toxin injections can help in less severe spasticity so that active functional use of the arm and hand can be improved. While there have been some reports of success from doctors and patients, there is no current definite proof that it works, so this expensive drug is not routinely offered. In total, we will be investigating 30 similar people with stroke.

Who can participate?
You may be able to participate if:
- You have had a stroke and have difficulty using your arm and hand.
- You are able to pick up, move, set down and let go of a cup (it doesn't matter if letting go is very slow or difficult).
- You are aged 18 years or older.
To enroll you will need to give your informed consent.

What does the study involve?
To find out whether the botulinum toxin injections help, we will compare a group of people who are injected with botulinum toxin with another group who are injected with a water solution. The water solution looks like the genuine medicine, but has no active ingredient and so is called a placebo.
You will be randomly allocated to a botulinum toxin group or a placebo group and you have a 50% chance of being in either group. Neither you nor your doctor or physiotherapist will know which group you are in.
You will attend the National Hospital for Neurology and Neurosurgery for assessment and

treatment over a period of four months.
On your first visit you will be assessed by a group of doctors and physiotherapists for suitability for the study. If you are suitable and decide to take part, you will be asked to sign a consent form and complete some baseline tests and questionnaires, before being given the injections into the muscles in your hand and arm.
You will then come for 10 physiotherapy sessions, spread over 4 weeks and each lasting around an hour. You will work on strengthening exercises for specific muscles and practice skilled hand tasks. You will also be expected to do some practice at home and to record this in a diary. After this, you will come a further three times for follow up assessments. Lastly, we will contact you three months after your last assessment visit to repeat the questionnaires by telephone or by post.
During the study you will not be able to take any new drugs for spasticity or increase the dose of any drugs you are already taking for spasticity.
You are free to refuse to take part or to withdraw from the study at any time without having to give a reason.

What are the possible benefits and risks of participating?
Possible disadvantages and risks of taking part: You may have some mild muscle soreness from the strength tests. This should not last longer than 48 hours. You may also experience some very mild skin redness or irritation from the tape used to attach the electrodes and skin markers to your arm. This should not last longer than a few hours.
Side effects of any treatment received when taking part: Botulinum toxin A is already used regularly in people who have had a stroke with few side effects. One in six people in clinical trials for spasticity of the upper limb experienced side effects. In general, side effects occurred within the first few days following injection and were short lasting. In rare cases, they lasted several months or longer. The most commonly reported side effects are local muscle weakness, which is the expected action of the drug and, as with any injection, localised bleeding, pain, tenderness and/or bruising. Fever and flu have also been reported after injections of botulinum toxin. The potential risk in pregnancy for the unborn child or in breast feeding infants is unknown. Botulinum toxin should not be used during pregnancy or breast feeding.
Possible benefits of taking part: You will see a specialist team with expertise in treating your condition, and will have the opportunity to ask any questions or raise any concerns you may have. We cannot promise that the study will help you as an individual and there is a 50% chance that you will receive the placebo injections. Every participant will take part in an intensive physiotherapy programme. You may see some improvement with this. We expect the information we collect from the study to help improve the future treatment of people with stroke.

Where is the study run from?
National Hospital for Neurology and Neurosurgery, London.

When is the study starting and how long is it expected to run for?
The study started in 2009 and is expected to last until the end of 2012.

Who is funding the study?
This study has been funded by a research grant from the UK Stroke Association.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2009-009357-22

Protocol serial number
5644

Study information

Scientific Title
A single centre randomised interventional treatment trial of botulinum toxin-A versus placebo in the improvement of active function in upper limb disability of stroke survivors

Acronym
PrOMBiS

Study objectives
Upper limb disability is a major problem for many stroke survivors; clinical and experimental observation suggests that disordered grasp release is a significant contributory factor. This study will investigate whether botulinum toxin-A improves active function in the impaired limb. Previous studies have shown passive improvement in tone, but functional benefit has not been convincingly or consistently demonstrated. This may be due to limitations in functional outcome measures and inaccurate selection of participants. We will use novel and unique outcome measures that will 1) objectively measure a functionally relevant grasp release task, and 2) use a gold standard measure of spasticity (our customised servomotor) to accurately predict who will benefit from treatment (and compare this to conventional portable EMG studies).

We will carry out a double-blind RCT with subjects (n=30) more than 3 months post-stroke, randomised to treatment or placebo group. Participants will be given injections (toxin or placebo) followed by standardised, effective upper-limb physiotherapy. The study is powered to detect between-group differences in grasp release.

This study will indicate whether active functional benefit results from treatment with botulinum toxin and physiotherapy, and will guide the accurate selection of participants likely to benefit both in clinical practice and future intervention trials.

Please note that as of 25/08/2011, the end date for this trial has been extended from 29/01 /2011 to 31/12/2012.

Please note that as of 20/03/2013, the anticipated end date for this trial was updated from 31/12 /2012 to 31/12/2013

Ethics approval required
Old ethics approval format

Ethics approval(s)
UCLH Research Ethics Committee A approved on the 7th April 2009 (ref: 09/H0714/5)

Study design
Single centre randomised interventional treatment trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Stroke Research Network; Subtopic: Rehabilitation; Disease: Drug type, Therapy type, In hospital study

Interventions
Injections of investigative medical product (IMP) or placebo followed by 10 sessions of standardised physiotherapy.

Follow up length: 6 months
Study entry: single randomisation only

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Botulinum toxin A (onabotulinumtoxinA)

Primary outcome(s)
The functional grasp release task at baseline, 1 month and 3 months

Key secondary outcome(s))
1. 9-Hole peg test
2. Action Research Arm Test

3. Arm Activity Measure
4. EQ-5D
5. Goal Attainment Score
6. Measure of Muscle Stiffness and Spasticity
7. Muscle strength

Measured at baseline, immediately after treatment, at one month and at 3 months plus a further 6 month follow up just with the questionnaires by post.

Completion date
31/12/2013

Eligibility

Key inclusion criteria
1. Clinically confirmed diagnosis of stroke
2. More than 1 month post-stroke
3. An Ashworth score of 2 or more
4. The ability to pick up a mug and move it to another position (so that participants are able to use any improvement in hand control in functional reach and grasp tasks)
5. Aged 18 years and over (no max), both male and female participants

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Not Specified

Lower age limit
18 years

Sex
All

Total final enrolment
28

Key exclusion criteria
1. Orthopaedic impairments affecting the hemiplegic upper limb or spine
2. Additional neurological impairment not related to stroke
3. Shoulder or wrist pain (greater than 3 on a 0 - 10 visual analogue scale) whilst performing the experimental tasks
4. Severe cognitive impairment preventing informed consent and/or the ability to follow task instructions
5. Anti-coagulation with an international normalised ratio (INR) of greater than 2

Date of first enrolment

03/07/2009

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Institute of Neurology
London
United Kingdom
WC1N 3BG

Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research organisation

Funder Name
The Stroke Association (UK)

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				Yes	No
Results article		01/01/2020	23/04/2021	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes