ISRCTN13020412 https://doi.org/10.1186/ISRCTN13020412

Establishing the effect(s) and safety of Fluoxetine initiated in the acute phase of stroke

Submission date
28/11/2014

Recruitment status
No longer recruiting

Registration date
19/12/2014

Overall study status
Completed

Last Edited
27/07/2020

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Stroke is a serious, life-threatening medical condition that happens when the blood supply to a part of the brain is cut off, usually due to a blood clot (ischemic) or haemorrhage. Symptoms vary according to how much of the brain is affected and where in the brain the stroke occurs but includes paralysis, muscle weakness and speech problems. A stroke can also have an impact on the sufferers emotions and can lead to anxiety, depression and personality changes. Fluoxetine (otherwise known as Prozac) has been used for many years to treat depression. However, there is evidence to suggest that it may also have other effects of the brain and enhance brain plasticity (the reorganisation of neural pathways in the brain) in a number of different ways. One small study, for example, has shown that, if taken soon after a stroke, fluoxetine might improve the recovery of arm strength and lead to greater restoration of movement of the limbs. We want to see whether fluoxetine, taken for 6 months, improves patient recovery after a stroke if taken within 2-15 days of the stroke occurring.

Who can participate?
Adult patients (at least 18 years old) who have had a stroke (either ischemic or haemorrhagic) within the last 2-15 days and still have some residual problems caused by the stroke e.g. weakness, or problems with their speech (speech impairment).

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given fluoxetine caplets for 6 months. Those in group 2 are given a placebo (or dummy pill) for 6 months. The patients are contacted after one week of starting their treatment, and then again after one month, to check on their well-being and that they are still taking their allocated caplets. Each participant is asked about any bad side effects and how much training they have had with e.g. a physiotherapist, occupational- or speech-therapist. The stroke research team contacts each participant at 3 months to check whether they are still taking the capsules, and ask about bad side effects, and about how they are feeling (mood). If all is well, the participant is given enough medication to cover the rest of the study period. The participant is asked to stop the study medication is stopped after 6 months and repeat assessments that they did before they started the study at the local hospital. They are also asked to fill in questionnaires together with their next of kin or carer. These questionnaires are sent to the trial main centre. If needed,

they can also be filled in with the help of a trial nurse over the telephone. The participants are contacted again one month after they have stopped the medication to see how they have progressed. At 12 months after recruitment, participants are asked to complete the same questionnaires again about how well they have recovered from their stroke and what problems they now have after the stroke e.g. weakness in limbs, memory problems, problems with speech, low mood. These questionnaires can again be completed on paper or by telephone. The researchers then collect data on long-term recovery through national statistics.

What are the possible benefits and risks of participating?
Taking fluoxetine may improves recovery from stroke in hose patients that have taken it. However, this is not guaranteed and there may be side effects from taking the medication.

Where is the study run from?
1. Karolinska Institute (Sweden)
2. Karolinska University Hospital (Sweden)

When is the study starting and how long is it expected to run for?
October 2014 to October 2018

Who is funding the study?
1. The Swedish Heart Lung Fund (Sweden)
2. King Gustaf V's and Queen Victoria's Freemason Foundation (Sweden)
3. The Swedish Stroke Association (Sweden)
4. Swedish Research Council (Sweden)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-006130-16

ClinicalTrials.gov (NCT)
NCT02683213

Protocol serial number
EFFECTS2012

Study information

Scientific Title
Efficacy oF Fluoxetine – a randomisEd Controlled Trial in Stroke

Acronym
EFFECTS

Study objectives
Routine administration of fluoxetine 20mg once daily in the 6 months initiated during the acute stroke improves the patient's functional outcome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The regional ethics committee at Karolinska Institute (Karolinska Institutet), 30/08/2013, ref: 2013/1265-31/2

Study design
Multicentre parallel-group double-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Ischaemic or haemorrhagic stroke

Interventions
Fluoxetine 20mg once daily or matching placebo capsules for 6 months

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)

Fluoxetine

Primary outcome measure
Modified Rankin scale at 6 months

Secondary outcome measures
1. Deaths from all causes by 6 and 12 months. Death from all causes until the end of the trial ascertained via the medical record system at the local centres which is linked to National Registry (Folkbokföringsregistret) (local follow up)
2. The EuroQoL (EQ5D-5L) to provide an overall measure of health related quality of life (HRQOL) and to allow a health economic analysis based on quality adjusted life years
3. The mental health inventory 5 (MHI 5) will provide a measure of depression and anxiety. This brief measure performs well, compared with longer questionnaires (e.g. MHI-18, GHQ-12, GHQ-30, in the detection of depression and anxiety
4. The vitality subscale of the Health Questionnaire, equivalent to SF 36, will be used to assess patients level of fatigue
5. The Stroke Impact Scale (SIS) will provide an overall assessment of patient outcome as well as allowing us to assess the effect of treatment on specific outcomes of importance to the patients. The SIS is a stroke-specific, comprehensive, health status measure. The scale was developed with input from both patients and caregivers and includes 8 domains (strength, hand function, ADL/IADL, mobility, communication, emotion, memory and thinking, participation) from across the full impairment-participation continuum (Duncan 1999; 2003). It also provided an overall assessment of recovery. The scale has been evaluated successfully for use by proxy respondents and has been delivered as both telephone and postal questionnaires
6. New diagnosis of depression since randomization. We will record whether a depression has been treated by the PI; or resulted in a referral for specialist assessment and whether the diagnosis was confirmed by a psychiatrist and whether antidepressant medication was initiated; whether there was any attempt at suicide or self-harm. We will also, prior to dispensation of the study-medication for the second three-months' period undertake an investigator-lead 10-item MADRS, and a DSM-IV diagnosis to identify or rule out a depression. Records will be made as to action/s taken in relation to the study-medication. (as reported by the local centres)
7. Other adverse events to be recorded include: further strokes, acute coronary events, upper gastrointestinal hemorrhage, falls resulting in injury, new fractures, epileptic seizures, symptomatic hypoglycemia (<3 mmol/l), hyperglycemia (>22mmol/l) hyponatremia (<125mmmol/l) (as reported by the local center)
8. Health and social care resources used during follow up including: days in hospital and days in care home since enrolment; and intensity of training formal carers at home – total number of visits per week at the time of follow up, as reported by the local centre
9. Adherence to EFFECTS trial medication
10. By investigation face-to-face (at baseline and at 6 months at local centre):
10.1. National Institute of Health Strokes Scale (NIHSS) to assess motor function and for randomization also aphasia
10.2. Norsk Grunntest for Afasi, one part to assess the patient's yes and no-communication-capability and comprehension;
10.3. MADRS + DSM-IV/DSM-V to identify depression, minor and major;
Montreal Cognitive Assessment (MoCA) to asses the patients' cognitive function.
11. Patients' report - the patient will receive a diary which contains contact details for the local trial centre, prompts the recording and reporting of adverse event and gives the means to recording the form and extent of training

Completion date

31/10/2018

Eligibility

Key inclusion criteria
1. Age ≥ 18
2. Informed consent can only be obtained from a patient who according to the trial investigator is mentally capable of decision-making and who, after having received information and got answers to their questions, wants to participate in the trial
3. Brain imaging is compatible with intra cerebral hemorrhage or ischaemic stroke
4. Randomization can be performed between 2 and 15 days after stroke onset and by the research group at the patient's local/emergency hospital
5. Persisting focal neurological deficit is present at the time of randomization severe enough to warrant treatment from the physicians and the patient's and relative's perspective

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
1500

Key exclusion criteria
1. Subarachnoidal hemorrhage (except where secondary to a primary intracerebral hemorrhage)
2. Unlikely to be available for follow up for the next 12 months e.g. no fixed home address
3. Unable to speak Swedish and no close family member available to help with follow up forms
4. Other life threatening illness (e.g. advanced cancer) that will make 12-month survival unlikely
5. History of epileptic seizures
6. History of allergy or contraindications to fluoxetine including:
6.1. Hepatic impairment (S-ASAT/ALAT > 3 upper normal limit)
6.2. Renal impairment (S-Creatinine levels > 180 micromol/L)
7. Pregnant or breastfeeding, women of childbearing age not taking contraception. Minimum contraception is an oral contraceptive. An HCG-test is to be made prior randomization and after the end of trial medication
8. Previous drug overdose or attempted suicide
9. Already enrolled into a CTIMP
10. Current or recent (within the last month) depression requiring treatment with an SSRI

antidepressant
11. Current use of medications which have serious interactions with fluoxetine
11.1. Use of any mono-amino-oxidase inhibitor (MAOI) during the last 5 weeks

Date of first enrolment
20/10/2014

Date of final enrolment
31/10/2017

Locations

Countries of recruitment
Sweden

Study participating centre
Danderyd Hospital
Danderyd Hospital
Department of Medicine
Stockholm
Sweden
SE-182 88

Study participating centre
Karolinska University Hospital
Department of Neurology
Stockholm
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Sponsor information

Organisation
Karolinska Institute (Karolinska Institutet)

ROR
https://ror.org/056d84691

Funder(s)

Funder type

Charity

Funder Name
Swedish Heart Lung Fund (Sweden)

Funder Name
King Gustaf V's and Queen Victoria's Freemason Foundation (Sweden)

Funder Name
STROKE-Riksförbundet

Alternative Name(s)
Swedish Stroke Association

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
Sweden

Funder Name
Vetenskapsrådet

Alternative Name(s)
Swedish Research Council, VR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

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	01/08/2020	27/07/2020	Yes	No
Protocol article	protocol	20/08/2015		Yes	No
Protocol article	update to protocol	28/02/2020	02/03/2020	Yes	No
Other publications	statistical and health economic analysis plan	28/12/2017		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes