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Ketamine-ECT Study

Submission date
25/07/2012

Recruitment status
No longer recruiting

Registration date
30/07/2012

Overall study status
Completed

Last Edited
07/04/2017

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Depression is a major cause of disability with many patients failing to recover with current drug and psychological treatments. Electroconvulsive Therapy (ECT), the most effective treatment known for severe depression, can be life-saving but remains controversial. The most serious concerns are problems with memory and other cognitive (thinking) abilities. This can lead to patients stopping ECT before it has improved their mood, and many people report distressing long-term loss of past memories. If these memory and cognitive effects could be prevented, and fewer ECT treatments were needed, this would represent an important advance and would change clinical practice. Ketamine is an anaesthetic drug that blocks the effects of a major brain chemical, glutamate, involved in memory and mood. Preliminary research has found that ketamine protects against the adverse effects of ECT on memory and makes it work more quickly. The proposed study will investigate the benefit of adding ketamine to the usual anaesthetic used for ECT. It will involve enough patients receiving ECT in an NHS setting to be able to assess whether it would be a useful routine treatment.

Who can participate?
160 patients due to receive ECT in 5 NHS Trusts in the North of England, who give informed consent. The 5 trusts are: Manchester Mental Health & Social Care Trust, Northumberland, Tyne & Wear NHS Foundation Trust, Leeds & York Partnership NHS Foundation Trust, Greater Manchester West Mental Health NHS Foundation Trust and Pennine Care NHS Foundation Trust.

What does the study involve?
Patients will be randomised to either receive ketamine injection or saline dummy (placebo) during ECT. The effects of the treatment will be assessed using validated measures of memory, cognitive function and mood improvement during and at the end of treatment, and one and four months after treatment. In depression there are changes in nerve cell connections (neural networks) between brain areas responsible for mood and cognitive function; glutamate is involved in these. We will use brain imaging to investigate whether ketamine a) prevents the ECT-induced impaired working of the front part of the brain (frontal cortex) believed to contribute to cognitive adverse effects, and b) reduces disruption in connections between the frontal cortex and an important memory area of the brain (hippocampus). Given the difficulty in studying severely ill people we will use magnetic resonance imaging (MRI) in a small subgroup to

look at the network connections and brain glutamate levels. We will relate this to results obtained in a majority of patients from a simple, portable, imaging technology, near infrared spectroscopy (NIRS).

What are the possible benefits and risks of participating?
The main possible benefit from taking part is that patients who do get ketamine may have less difficulty with their memory or cognition following ECT than they might have had otherwise. In addition they may also improve more quickly and therefore need fewer ECT treatments to get well. The effects of ECT on patients' mood and memory will be carefully assessed, which may help them and their clinical team plan their care. Also, people who take part in studies like this can get benefit just from taking part. Patients will not know whether they will receive ketamine or not, but, if the study is successful and ketamine is helpful in improving the outcome of ECT treatment, it may help patients in the future. The main risk is due to the fact that both ketamine and ECT increase blood pressure. However, we will not recruit anyone into the study who has heart problems, uncontrolled blood pressure or raised pressure in the head, as well as some other conditions that might increase risks (such as liver damage). Otherwise the risks are the same as for ECT itself and of having a brief anaesthetic. This means that patients having ECT as an outpatient will need to be fully recovered from the anaesthetic and the effects of ECT before leaving hospital.

Where is the study run from?
Neuroscience and Psychiatry Unit, University of Manchester (UK)

When is the study starting and how long is it expected to run for?
September 2012 to August 2014

Who is funding the study?
NIHR Efficacy and Mechanism Evaluation (UK)

Who is the main contact?
Ms Jo Lowe
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2011-005476-41

Protocol serial number
12141

Study information

Scientific Title
Ketamine augmentation of electroconvulsive therapy to improve outcomes in depression

Study objectives
That the addition of ketamine at a sub-anaesthetic dose (versus placebo) to the usual anaesthetic for electroconvulsive therapy (ECT) given for depression will prevent adverse cognitive effects of ECT and speed the improvement in depressive symptoms.

Ethics approval required
Old ethics approval format

Ethics approval(s)
First MREC, 25/01/2012, ref: 12/NW/0021

Study design
Randomised interventional phase IV trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bipolar affective disorder, depression

Interventions
Ketamine, 0.5mg/kg or 0.9% sodium chloride given with the anesthetic induction agent at each ECT treatment session; Study Entry : Single Randomisation only

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ketamine

Primary outcome(s)
Change in memory measured at baseline and end of ECT course

Key secondary outcome(s))
1. Changes in memory measured at baseline and one and 4 month follow up
2. Cognitive changes measured at baseline and a end of ECT, and one and 4 month follow up
3. Evaluation of Memory (GSEMy) symptoms ratings measured at baseline, after 4 ECT treatments, at end of ECT and at one and 4 month follow up

Completion date
31/08/2014

Eligibility

Key inclusion criteria
Patients:
1. Only patients who are referred by their consultant for ECT and who are patients of one of the following 5 participating Trusts will be able to take part: Manchester Mental Health & Social Care Trust, Northumberland, Tyne & Wear NHS Foundation Trust, Leeds & York Partnership NHS Foundation Trust, Greater Manchester West Mental Health NHS Foundation Trust and Pennine Care NHS Foundation Trust (added as of 13/11/2012)
2. Male or female aged 18 years and above
3. Current DSM-IV diagnosis of a major depressive episode, moderate or severe as part of unipolar or bipolar disorder mood disorder diagnosed by the Mini International Neuropsychiatric Interview (MINI)
4. American Society of Anaesthesiologists (ASA) score (excluding mental health considerations in the scoring) of 1, 2 or stable 3, and judged as suitable to receive ketamine by an anaesthetist
5. Verbal IQ = 85, sufficiently fluent in English to validly complete neuropsychological testing
6. Capacity to give informed consent
7. Willing to undertake neuropsychological testing as part of the study.

Healthy control:
1. Aged 18 years or more
2. Currently psychiatrically well, confirmed through MINI interview and no current psychotropic medication
3. In good physical health
4. Male or female participants
5. Aged 18 years and above

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Patients:
1. DSM-IV diagnosis of a primary psychotic or schizoaffective disorder, current primary obsessive compulsive disorder or anorexia nervosa
2. History of drug or alcohol dependence (DSM-IV criteria) within the last year
3. ECT in last 6 months (to avoid confounding the assessment of cognitive outcomes) or has previously received ECT in the current trial
4. Known hypersensitivity or contraindication to ketamine or excipients in the injection; including significant cardiovascular disease, uncontrolled hypertension, glaucoma, cirrhosis or significant liver impairment
5. Known hypersensitivity or contraindication to concomitant medications used for ECT: thiopentone (thiopental), propofol and suxamethonium or excipients in the injections
6. Evidence of organic brain disease including dementia, neurological illness or injury, or medical illness which may significantly affect neuropsychological function
7. Detained under the Mental Health Act (1983 as amended 2007) or unable to give informed consent
8. Pregnancy, or at risk of pregnancy and not taking adequate contraception, breastfeeding
9. Score = 24 on the Mini Mental State Examination (MMSE)
10. In the subgroup receiving MRI based investigation (fMRI, MRS and ASL) contraindication to MRI (eg metal implants or foreign bodies such as from a surgical implant, accident or injury).

Control:
1. Personal history of psychiatric disorder, as revealed by MINI interview
2. First degree family history of major psychiatric illness requiring treatment
3. Significant physical illness including organic brain disease, neurological illness or injury that could interfere with interpretation of results
4. Psychotropic medication or other medication that could interfere with interpretation of results
5. Score = 24 on the Mini Mental State Examination (MMSE)
6. In the subgroup receiving MRI based investigation (fMRI, MRS and ASL) contraindication to MRI (eg metal implants or foreign bodies such as from a surgical implant, accident or injury).

Date of first enrolment
01/09/2012

Date of final enrolment
31/08/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

University of Manchester
Manchester
United Kingdom
M13 9PT

Sponsor information

Organisation
Manchester Mental Health & Social Care Trust (UK)

Funder(s)

Funder type
Government

Funder Name
Efficacy and Mechanism Evaluation Programme (ref: 10/90/04)

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, Efficacy and Mechanism Evaluation (EME), EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2017		Yes	No

Results article	results	01/05/2017		Yes	No
Protocol article	protocol	21/10/2015		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes