

Modifying Delirium Using Simvastatin

Submission date 26/03/2013	Recruitment status No longer recruiting	☐ Prospectively registered ☒ Protocol
Registration date 26/03/2013	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 17/05/2018	Condition category Mental and Behavioural Disorders	☐ Individual participant data

Plain English summary of protocol

Background and study aims

Many different circumstances, such as severe infection or an accident, may result in a person becoming critically ill. For reasons that are unclear, when people are critically ill, their brain function is often impaired – a condition of severe confusion called delirium. Delirium is common, affecting up to two out of every three patients in intensive care units (ICU), and results in a longer hospital stay and a higher risk of death. Importantly, after recovery from the initial illness, following delirium, patients frequently go on to experience the equivalent of a mild or accelerated dementia. There is no proven effective treatment for delirium. It is thought that delirium is often a result of inflammation in the brain. Simvastatin, usually used to reduce cholesterol, has been shown to have significant anti-inflammatory properties. The aim of this study is to test the effectiveness of simvastatin at reducing delirium in the critically ill.

Who can participate?

Patients aged over 18 requiring mechanical ventilation (a machine to support breathing) within 72 hours of admission to intensive care.

What does the study involve?

Patients will be randomly allocated to be given either simvastatin or a dummy drug (placebo). We will count the number of days a patient is delirious, how fast they recover and how well their brain functions at 6 months using a telephone questionnaire.

What are the possible benefits and risks of participating?

Simvastatin is a safe, well-tolerated drug. If simvastatin reduces delirium it would likely decrease ICU stay. Demand for ICU exceeds supply and a treatment that reduced use of ICU resources would result in increased availability of facilities for critically ill patients. The potential impact of an effective treatment for delirium is considerable.

Where is the study run from?

Watford General Hospital (UK)

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

February 2013 to January 2015

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Valerie Page
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-003114-13

Protocol serial number
13988

Study information

Scientific Title
Hydroxymethylglutaryl-CoA reductase inhibition with simvastatin in mechanically ventilated patients at high risk of delirium: a randomised double-blind placebo controlled trial

Acronym
MoDUS

Study objectives
Delirium is common affecting up to 2 out of every 3 patients in ICU, and results in a longer hospital stay and a higher risk of death. Importantly, after recovery from the initial illness, following delirium, patients frequently go on to experience the equivalent of a mild or accelerated 'dementia'. There is no proven effective treatment for delirium. It is thought that delirium is often a result of inflammation in the brain. Simvastatin, usually used to reduce cholesterol, has been shown to have significant anti-inflammatory properties. This study is a randomised, double-blind, placebo controlled trial. 142 patients will randomly allocated to be given either simvastatin or a placebo. Outcomes include number of days a patient is delirious,

how fast they recover and cognitive function at 6 months using an approved telephone questionnaire. If simvastatin reduces delirium it would likely decrease ICU stay. Demand for ICU exceeds supply and a treatment that reduced use of ICU resources would result in increased availability to appropriate facilities for critically ill patients. This study is being funded by a Research for Patients Benefit Grant and run in partnership with ICUSTeps and the Alzheimer's Society.

Ethics approval required

Old ethics approval format

Ethics approval(s)

NRES Committee North East - Newcastle & North Tyneside 1, 06/12/2012, ref: 12/NE/0383

Primary study design

Interventional

Study design

Randomised double-blind placebo-controlled trial, Design type: Prevention, Treatment

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Topic: Generic Health Relevance and Cross Cutting Themes; Subtopic: Generic Health Relevance (all Subtopics); Disease: Critical Care

Interventions

Simvastatin 80 mg or placebo daily for up to 28 days

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Simvastatin

Primary outcome(s)

Alive, delirium free and coma free days; Timepoint(s): 14 days

Key secondary outcome(s)

1. Incidence of delirium
2. Delirium/coma free days in first 28 days
3. Number of ventilator free days at 28 days
4. Length of critical care and hospital stay
5. Mortality at 6 months; (f) Organ failure free days
6. Cognitive Impairment at 6 months
7. Health related quality of life over the 6 month study period using the EQ-5D-5L

8. Quality adjusted life years at 6 months
9. Healthcare resource use and associated costs over the 6 month study period
10. Cost-effectiveness of the intervention at 6 months post-randomisation

Completion date

31/01/2015

Eligibility

Key inclusion criteria

1. Patients requiring mechanical ventilation within 72 hours of admission to intensive care.
2. Male & Female ; Lower Age Limit 18 years

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

Key exclusion criteria

1. Age less than 18 years
2. Patient known to be pregnant
3. Known allergy to statin drugs
4. CK > 10 times upper limit of normal range
5. Alanine aminotransferase (ALT) >8 times the upper limit of normal range
6. Patients currently receiving ongoing and sustained treatment with any of the following; itraconazole, ketoconazole, HIV protease inhibitors, nefazodone, cyclosporine, amiodarone, verapamil or diltiazem
7. Uncomplicated elective surgery
8. Patient expected to be discharged within 48 hours of admission
9. Patients with severe renal impairment (estimated creatinine clearance less than 30ml/minute) not receiving renal replacement therapy
10. Severe liver disease
11. Current or recent treatment (within 2 weeks) with statins
12. Physician decision that a statin is required for proven indication
13. Contraindication to enteral drug administration, e.g. patients with mechanical bowel obstruction. Patients with high gastric aspirates due to an ileus are not excluded.
14. Known participation in investigational medicinal product (IMP) trials within 30 days
15. Consent declined

16. Treatment withdrawal likely within 48 hours

17. Non-English speaking patients or those who do not adequately understand verbal or written information

Date of first enrolment

02/02/2013

Date of final enrolment

31/01/2015

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

West Hertfordshire Hospitals NHS Trust

Watford

United Kingdom

WD18 0HB

Sponsor information

Organisation

West Hertfordshire Hospitals NHS Trust (UK)

ROR

<https://ror.org/03e4g1593>

Funder(s)

Funder type

Government

Funder Name

NIHR (UK) - Research for Patient Benefit (RfPB); Grant Codes: PB-PG-0211-24123

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	01/09/2017		Yes	No
Protocol article	protocol	16/05/2015		Yes	No
HRA research summary			28/06/2023	No	No