ISRCTN11774734 https://doi.org/10.1186/ISRCTN11774734

Does dexamethasone improve outcomes in adults with HSV encephalitis?

Submission date
30/03/2016

Recruitment status
No longer recruiting

Registration date
31/03/2016

Overall study status
Completed

Last Edited
26/07/2021

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Encephalitics is a serious condition in which the brain becomes inflamed (swollen). It usually happens as a direct result of virus, such as herpes simplex virus (HSV). It affects around 1 in every 250-500,000 people in the UK each year and is classed as a “very rare” disease. Its impact is disproportionately large however, with 1 in 10 people dying and survivors being left with serious side effects such as amnesia (memory loss) which puts stain on patients, carers and the health services. HSV encephalitis is often treated with the drug acyclovir (an antiviral drug which slows the growth and spread of HSV in the body). Despite this however, around 2 out of every 3 people will have memory difficulties long term. Dexamethasone is a corticosteroid medication, which works by preventing the release of natural chemicals in the body which cause inflammation. It is possible that dexamethasone could help to reduce in swelling of the brain may improve the recovery of patients with HSV encephalitis. The aim of this study is to find out whether treatment with dexamethasone can improve long-term health outcomes in adults with HSV Encephalitis.

Who can participate?
Adults with confirmed HSV encephalitis across UK hospitals.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are given dexamethasone 10mg through a drip every six hours for four days. Those in the second group do not receive treatment with dexamethasone and continue with usual care alone. Participants in both groups are treated with aciclovir antiviral treatment (10mg/kg aciclovir 8 hourly for at least 14 days). After 26 and 28 weeks, participants in both groups are followed up in order to evaluate the long-term mental health effects, such as memory and cognition (thinking and mental processing) and health effects following their HSV encephalitis.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
The Walton Centre, Liverpool (UK)

When is the study starting and how long is it expected to run for?
January 2015 to September 2021

Who is funding the study?
National Institute for Health Research Efficacy and Mechanism Evaluation Programme (UK)

Who is the main contact?
Mrs Kelly Davis
dexenceph@liverpool.ac.uk

Contact information

Type(s)
Public

Contact name
Mrs Kelly Davies

Contact details
Clinical Trials Research Centre
University of Liverpool
Institute of Child Health
Alder Hey Children's NHS Foundation Trust
Liverpool
United Kingdom
L19 3RB
+44 151 794 9767
dexenceph@liverpool.ac.uk

Additional identifiers

EudraCT/CTIS number
2015-001609-16

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19837

Study information

Scientific Title
DexEnceph: A pragmatic, randomised, controlled, observer-blind trial comparing clinical outcomes in adults who receive Dexamethasone alongside standard treatment versus standard treatment alone for herpes simplex virus Encephalitis

Acronym

DexEnceph

Study objectives
The aim of this study is to evaluate whether dexamethasone improves neuropsychological outcomes in sufferers of HSV encephalitis without allowing uncontrolled viral replication. It will also address whether corticosteroids improve imaging, functional and quality of life outcomes as well as provide a better understanding of the disease mechanisms in HSV encephalitis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West - Liverpool Central, 10/08/2015, ref: 15/NW/0545

Study design
Observer-blind open-label prospective randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Herpes Simplex Virus encephalitis

Interventions
Participants are randomised to one of two groups.

Intervention group: Participants receive dexamethasone 10mg intravenously 6 hourly for 4 days.
Control group: Participants receive standard care and no dexamethasone.

Participants in both groups receviev aciclovir antiviral treatment: as part of standard care: 10mg /kg aciclovir 8 hourly (or at a reduced dose if clinically indicated) for at least 14 days. Continuation of aciclovir is guided by follow-up CSF examination as per national guidelines on the management of HSV encephalitis.

All patients are followed up with Neuropsychology testing, MRI scanning, functional and disability outcome scoring, blood testing and health status and quality of life assessments.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome measure
Verbal memory score, as determined by the Wechsler Memory Scale (WMS-IV) Auditory Memory Index at 26 weeks after randomisation.

Secondary outcome measures
1. Neuropsychological outcome measures (measured at 26 weeks and 78 weeks):
1.1. Visual Memory Index, Immediate Memory Index, and Delayed Memory Index - assessed by the Wechsler Memory Scale version IV (WMS-IV)
1.2. Processing speed and Working Memory - assessed by the Wechsler Adult Intelligence Scale version IV (WAIS-IV)
1.3. Language -assessed by the confrontational naming task of the Language Module in the Neuropsychology Assessment Battery (NAB)
1.4. Higher executive function -assessed by Trail Making Test Parts A and B
1.5. Anxiety and depression -assessed by self-completed Beck Depression Inventory and Beck Anxiety Inventory
1.6. Participant's subjective cognitive complaints- assessed by the Perceived Deficits Questionnaire
2. Cognitive outcomes are measured using the Addenbrooke's Cognitive Assessment (ACE-III) at 30 days/discharge, 26 weeks and 78 weeks)
3. Clinical Outcomes (measured at 30 days, 26 weeks, 78 weeks):
3.1. Incidence of epilepsy
3.2. Time to hospital discharge
3.3. Requirement of HDU/ITU admission up to 30 days post randomisation
3.4. Time to reach 14 days without ventilatory support [if any]
3.5. Time to reach maximum recorded GCS
3.6. Survival
4. Disability & Functional Outcomes are measured at 30 days/discharge, 26 weeks and 78 weeks using the Glasgow Outcome Score Extended (GOS-E), Liverpool Outcome Score (LOS), Barthel Index and the Modified Rankin Scale (mRS)
5. Imaging Outcomes (measured at baseline, 2 weeks, 26 weeks and 78 weeks):
5.1. Temporal lobe volume (as % of intra-cranial volume)
5.2. Whole brain volume (as % of intra-cranial volume)
5.3. Volume of affected region as seen on FLAIR image (as % of intra-cranial volume)
5.4. Volume of affected region as seen on diffusion-weighted image (as % of intra-cranial volume)
6. Biomarker outcomes:
6.1. Transcriptomic and proteomic profiling on CSF at baseline and 2 weeks; on blood at baseline, 2 weeks, and 26 weeks
6.2. Anti NMDA receptor antibody testing at 26 weeks
7. Safety Outcomes
7.1. Proportion of patients with detectable HSV in CSF by PCR at 2 weeks
7.2. White blood cell function at baseline and 26 weeks
8. Health Status and Quality of Life, as measured by the EuroQOL-5D-5L and SF-36 self-completed questionnaires at 26 and 78 weeks

Overall study start date
01/01/2015

Completion date
30/09/2021

Eligibility

Key inclusion criteria
Enrolled patients must fulfil ALL of the following criteria:
1. Suspected encephalitis criteria: New onset seizure OR, new focal neurological signs OR alteration in consciousness, cognition, personality, or behaviour*
2. A positive HSV PCR result from CSF, reported not more than 7 days prior to randomisation
3. Receiving intravenous aciclovir dosed at 10mg/kg TDS or at a reduced dose if clinically indicated
4. Age ≥ 16 years
5. Written informed consent has been given by the patient or their legal representative

* Personality / behaviour change includes: agitation, psychosis, somnolence, insomnia, catatonia, mood lability, altered sleep pattern.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
90 RCT and 90 Non-HSV cohort

Key exclusion criteria
1. Having received oral or injectable corticosteroid therapy in the 30 days prior to the day of admission to hospital**
2. History of hypersensitivity to corticosteroids
3. Immunosuppression secondary to:
3.1. Known HIV infection AND CD4 count under 200cell/mm3
3.2. Currently taking biologic therapy or other immunosuppressive agents [azathioprine, methotrexate, ciclosporin]
3.3. Previous solid organ transplant and currently on immunosuppression
3.4. Previous bone marrow transplant
3.5. Currently undergoing a course of chemotherapy or radiotherapy
3.6. Known primary immunodeficiency syndrome
3.7. Known current haematological malignancy
4. Pre-existing indwelling ventricular devices
5. Peptic ulcer disease in the last 6 months: defined as a peptic ulcer seen at endoscopy or an upper gastrointestinal bleed causing ≥ 2 unit haemoglobin drop in the last 6 months
6. Antiretroviral regime containing rilpivirine as current treatment

**Participants are not excluded if steroids are administered after admission prior to randomisation.

Date of first enrolment
01/04/2016

Date of final enrolment
31/07/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Walton Centre
Lower Lane
Liverpool
United Kingdom
L9 7LJ

Sponsor information

Organisation
University Of Liverpool

Sponsor details
Research Support Office
2nd floor Block D waterhouse Building
3 Brownlow Street
Liverpool
England
United Kingdom
L69 3GL
+44 1517 948739
sponsor@liverpool.ac.uk

Sponsor type
University/education

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
Efficacy and Mechanism Evaluation Programme

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
30/09/2022

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	22/07/2021	26/07/2021	Yes	No
HRA research summary			28/06/2023	No	No