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Emergency treatment with levetiracetam or phenytoin in status epilepticus

Submission date
13/08/2014

Recruitment status
No longer recruiting

Registration date
27/08/2014

Overall study status
Completed

Last Edited
17/11/2020

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Most epileptic seizures and convulsions in children last less than three minutes and will stop on their own accord. However, on occasion, a seizure may continue for longer than three minutes and eventually become what is called convulsive status epilepticus (CSE). This is a medical emergency. To prevent CSE from happening, children are given an antiepileptic medicine called an emergency or rescue medicine (also known as first-line treatment). However, this treatment will only be successful in around half of all children. In those cases where the rescue medicine is not successful, the children need to be taken to the Accident and Emergency Department (AED) of their local hospital. Once there, if the child is still in the seizure, they are given a different rescue medicine. This again will be successful in stopping the seizure in about half of the children. For those that are still in seizure, a different medicine is then given (this medicine is known as second-line treatment). The usual medicine given at this stage is called phenytoin. However, again it only has an about 50% success rate and has to be given very carefully because it can cause very unpleasant and very serious side-effects, including those that may affect the heart, blood pressure and skin. Some early results of a new anticonvulsant called levetiracetam suggest that this medicine may work better and be safer than phenytoin. The aim of this study is to find out whether this is really the case.

Who can participate?
Children between 6 months and 18 years of age in CSE which has not stopped after being given first-line treatment.

What does the study involve?
The children are randomly allocated into one of two groups. Those in group 1 are given intravenous levetiracetam. Those in group 2 are given intravenous phenytoin. The children's progress is then followed for 24 hours. We want to see how long it takes for the seizure to stop after the drugs have been given, whether any further medicine has to be given, whether the child needs to go the intensive care unit, and whether the child develops any unwanted side-effects. Added 17/11/2017: We also now complete a 14 day follow up to see how the children who have taken part are at 14 days after treatment.

What are the possible benefits and risks of participating?
Phenytoin will only stop CSE is about 50-60% of cases and has to be given slowly to avoid a drop in blood pressure and irregular heart beat (cardiac arrhythmias). It may also cause irritation of the veins and inflammation. Levetiracetam may stop CSE in more than 70% of cases. Risks of taking levetiracetam may include dizziness, feeling sleepy and headache. Added 17/11/2017: Levetiracetam side effects can also include: Agitation or a skin reaction including swelling of the tongue and lips and/or a red itchy rash.

Where is the study run from?
Institute of Child Health, Alder Hey Children's NHS Foundation Trust (UK)

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

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

Who is the main contact?
Ms Amy Humphreys
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Study website
http://www.eclipse-study.org.uk/

Contact information

Type(s)
Scientific

Contact name
Ms Amy Humphreys

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Additional identifiers

EudraCT/CTIS number
2014-002188-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 12/127/134

Study information

Scientific Title
Emergency treatment with Levetiracetam or Phenytoin in Status Epilepticus in children (EcLiPSE) – an open-label randomised controlled trial

Acronym
EcLiPSE

Study objectives
1. To determine whether intravenous levetiracetam or intravenous phenytoin is the more effective second-line anticonvulsant for the emergency management of convulsive status epilepticus (CSE) in children
2. To determine if intravenous levetiracetam is associated with fewer adverse side-effects than intravenous phenytoin

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES committee North West – Liverpool central, 03/03/2015, ref: 15/NW/0090

Study design
Multicentre unblinded active comparator randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Status epilepticus

Interventions

Eligible children will be randomised to receive either intravenous Levetiracetam 40 mg/kg administered as an infusion over 5 minutes or intravenous Phenytoin 20 mg/kg administered as an infusion over 20 minutes. Trial intervention is administered as a single infusion of the allocated treatment. Total duration of follow-up is 24 hours.

Added 09/04/2015: Maximum dose of levetiracetam is 2500 mg and maximum dose of phenytoin is 1000 mg.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Levetiracetam, phenytoin

Primary outcome measure
Time to cessation of all visible signs of convulsive seizure activity

Secondary outcome measures
1. Need for further anticonvulsant(s) to manage the seizure after the initial agent
2. Need for rapid sequence induction (RSI) with thiopentone or another agent (e.g. propofol) due to ongoing CSE
3. Need to be admitted to critical care
4. Serious adverse reactions including death, airway complications, and cardiovascular instability (cardiac arrest, arrhythmia and hypotension requiring intervention), extravasation injury ('purple-glove syndrome'), extreme agitation

Overall study start date
01/04/2014

Completion date
01/09/2018

Eligibility

Key inclusion criteria
1. Males and females aged 6 months to 18 years (<18th birthday)
2. Presenting seizure is tonic-clonic, clonic or focal convulsive status epilepticus that requires second-line treatment to terminate the seizure

Added 09/04/2015:
3. Two doses of benzodiazepines administered in order to try and terminate the seizure
Note 1: Patients receiving oral phenytoin or levetiracetam as part of their regular oral anti-epileptic drug regime are eligible for this trial.
Note 2: If more than two doses of benzodiazepines are administered prior to admission to ED then these patients are still eligible for EcLiPSE.

Note 3: A very small number of families will have rectal paraldehyde rather than a rectal or buccal benzodiazepine as their child’s first-line rescue medication. These patients are eligible for EcLiPSE.

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Months

Upper age limit
17 Years

Sex
Both

Target number of participants
308

Total final enrolment
286

Key exclusion criteria
1. Absence, myoclonic or non-convulsive status epilepticus, or infantile spasms
2. Known or suspected pregnancy
3. Known contra-indication or allergy to levetiracetam or phenytoin. This includes where the child's individual rescue (emergency) care plan states that the child never responds to, or has previously experienced a severe adverse reaction to, phenytoin, levetiracetam, or both
4. Known renal failure (patients on peritoneal or haemodialysis or with renal function <50% expected for age)
5. Previous administration of rectal paraldehyde or another second-line antiepileptic drug prior to arrival in the emergency department

Added 09/04/2015:
6. Known to have previously been randomised into EcLiPSE

Date of first enrolment
15/07/2017

Date of final enrolment
10/04/2018

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Alder Hey Children's NHS Foundation Trust
Eaton Road
Liverpool
United Kingdom
L12 2AP

Study participating centre
Birmingham Children's Hospital
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
Royal Alexandra Hospital Brighton
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
Bristol Royal Hospital for Children
Paul O'Gorman Building
Upper Maudlin Street
Bristol
United Kingdom
BS2 8BJ

Study participating centre
Chelsea and Westminster Healthcare NHS Foundation Trust
369 Fulham Road
London

United Kingdom
SW10 9NH

Study participating centre
Derbyshire Children's Hospital (at Royal Derby Hospital)
Uttoexter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
Royal Hospital for Sick Children Edinburgh
9 Sciennes Road
Edinburgh
United Kingdom
EH9 1LF

Study participating centre
Evelina London Children's Hospital
Lambeth Palace Road
London
United Kingdom
SE1 7EH

Study participating centre
Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Royal Hospital for Sick Children Glasgow
Dalnair Street
Yorkhill
Glasgow
United Kingdom
G3 8SJ

Study participating centre
Crosshouse Hospital
Kilmarnock Road
Crosshouse
Kilmarnock
United Kingdom
KA2 0BE

Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Royal Manchester Children's Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Sheffield Children's Hospital
Western Bank

Sheffield
United Kingdom
S10 2TH

Study participating centre
University Hospital Southampton
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
St George’s Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Great North Children's Hospital
Victoria Wing
Royal Victoria Infirmary
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Royal Belfast Hospital for Sick Children
Royal Victoria Hospital
180-184 Falls Road
Belfast
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BT12 6BE

Study participating centre
Royal London Hospital
Whitechapel Road
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E1 1BB

Study participating centre
University Hospital Lewisham
Lewisham High Street
London
United Kingdom
SE13 6LH

Study participating centre
University Hospital of Wales, Cardiff
Heath Park Way

Cardiff
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CF14 4XW

Study participating centre
Watford General Hospital
Vicarage Road
Watford
United Kingdom
WD18 0HB

Study participating centre
Western Sussex Hospitals NHS Foundation Trust
Sussex
United Kingdom
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Sponsor information

Organisation
University of Liverpool (UK) and Alder Hey Children's NHS Foundation Trust

Sponsor details
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Sponsor type
University/education

ROR

https://ror.org/00p18zw56

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
01/03/2019

Individual participant data (IPD) sharing plan
The datasets generated during and analysed during the current study will be available upon request. Further details will be made available at a later date.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	19/06/2017		Yes	No
Results article	results	25/05/2019	23/04/2019	Yes	No
Results article	results	01/11/2020	17/11/2020	Yes	No
HRA research summary			28/06/2023	No	No