

Changing agendas on sleep, treatment and learning in childhood epilepsy

| | | |
|--|--|--|
| Submission date 23/04/2019 | Recruitment status Stopped | <input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol |
| Registration date 15/05/2019 | Overall study status Stopped | <input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results |
| Last Edited 22/03/2021 | Condition category Nervous System Diseases | <input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year |

Plain English summary of protocol

Background and study aims

Rolandic epilepsy (RE) is the most common type of epilepsy. Children with RE have seizures and can often find that their learning, sleep, behaviour, self-esteem and mood are affected.

As part of standard NHS care, children diagnosed with RE may be treated with standard anti-epileptic medicines, like carbamazepine, or no medicine at all. The medicines used to treat epilepsy often slow down a child's thinking and learning. In the past, doctors believed this was an acceptable price to pay to reduce seizures. However, with RE, where the seizures usually stop in teenage years, we do not know if it's better to treat these children with medicines or not, especially if the medicines might have a negative effect on their learning.

A newer medicine called levetiracetam has also been found to work in children with RE and has shown less problems with thinking and learning in adults. However, we still don't know if this is also the case for children and it has not been proven which of the three options (carbamazepine, levetiracetam or no treatment) would be best for RE patients. The CASTLE study aims to find this out.

In addition, it has been found that seizures often happen when a child has had poor sleep and they often come at night or early in the morning. It has been shown that sleep can be improved through practice without the need of medicines. There are established guidelines to help toddlers go to sleep, but nothing available that helps young people with epilepsy and their parents improve their sleep quality. In the CASTLE study, we have developed a sleep training plan for children with epilepsy and would like to find out whether following the sleep training plan results in less seizures than using no sleep training at all.

Who can participate?

Children diagnosed with RE aged ≥ 5 years and < 13 years, currently untreated with antiepileptic drugs can participate.

What does the study involve?

Participants will be randomly selected to receive one of two routine treatments for RE.

Participants and their parents will be asked to visit their local trial centre at 3, 6, and 12 months

so that information can be collected about their health. Some participants will also be asked to wear an actigraph to record sleep and activity levels.

What are the possible benefits and risks of participating?

As CASTLE follows normal NHS practice (both medicines are routinely used in standard care), there are no additional risks of taking part in the study. Both of the medicines used in the study have been shown to improve symptoms of epilepsy but this cannot be guaranteed. We simply don't know which treatment is best or if it is better to receive no treatment.

Where is the study run from?

University of Liverpool Clinical Trials Research Centre, UK

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

June 2019 to June 2022

Who is funding the study?

NIHR (National Institute for Health Research), UK

Who is the main contact?

Dr Agnès Tort,
castle.rct@liverpool.ac.uk

Contact information

Type(s)

Scientific

Contact name

Ms Nadia Al-Najjar

Contact details

University of Liverpool Clinical Trials Research Centre

Institute in the Park

2nd Floor

Alder Hey Children's NHS Foundation Trust

Eaton Road

Liverpool

United Kingdom

L12 2AP

+44 (0) 151 795 8774

Castle.rct@liverpool.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)

2018-003893-29

Protocol serial number

40487

Study information

Scientific Title

Randomised factorial design controlled trial comparing carbamazepine, levetiracetam or active monitoring combined with or without sleep behaviour intervention in treatment naive children with rolandic epilepsy

Acronym

CASTLE TRIAL v1.0

Study objectives

The primary objective of the trial is to test two hypotheses:

- A) To determine if Carbamazepine or Levetiracetam are superior to no AED with respect to time to 6-month seizure remission.
- B) To determine if a Parent-Based Sleep (PBS) intervention is superior to standard care with respect to 3-month sleep problem frequency measured by Children's Sleep Habits Questionnaire (CSHQ).

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 30/04/2019, London - Riverside Research Ethics Committee (Chelsea & Westminster Hospital
369 Fulham Road, London, SW10 9NH; 0207104 8204; nrescommittee.london-riverside@nhs.net)
ref: 19/LO/0452

Study design

Randomised; Interventional; Design type: Treatment, Drug, Psychological & Behavioural, Active Monitoring

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Epilepsy

Interventions

Written informed consent (and assent), Participants will be given ample time to review the patient information sheet. Discussion of objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted will be provided to parents and children by staff who have been trained and have experience informed consent (and are authorised to complete this activity on the trial delegation log).

All participants will have the opportunity to ask questions and time to consider the information prior to agreeing to participate.; Children's Sleep Habits Questionnaire (CSHQ), The parent /primary carer will complete this questionnaire on paper when they attend clinic.; Learning

measured by standardised learning measure - CANTAB, The child will complete this questionnaire /puzzle on an iPad when they attend clinic.; Health-Related Quality of Life Measure for Children with Epilepsy (CHEQOL questionnaire), Both the parent/primary carer and the child (if >8 years) will complete this questionnaire on paper when they attend clinic (each questionnaire is expected to take 5 mins to complete).; Strengths and Difficulties Questionnaire (SDQ), The parent/primary carer will complete this questionnaire on paper when they attend clinic.; Health Utility Measures – adult (EQ-5D-5L), The parent/primary carer will complete this questionnaire on paper when they attend clinic.; Actigraphy, A purposeful sample of 10 dyads (child and primary carer) from each of the 6 final trial subgroups (120 subjects in total) will both wear the watches for 1 week at baseline, 3 and 12 months during the trial.; Qualitative Interviews (for those who consent), Interviews will be conducted by the research team at Edge Hill University and they will either be face-to-face or remotely (via telephone or Skype or equivalent).

The interviews will take place at three timepoints: the first interview will be scheduled at 2-4 weeks post randomisation and the other two at 6 months and 12 months respectively after interview 1.

Interviews will be audio-recorded and transcribed.

Appropriate adults and children with RE who have declined to participate in the trial, will additionally be approached and asked for consent to be interviewed 2-4 weeks after being approached to participate in the trial. Three interviews will also be scheduled for trial decliners: interview 1 will take place at 2-4 weeks after declining trial participation, and the other two interviews will take place at 6 months and 12 months respectively after interview 1.; Health Utility Measures – child (CHU9D questionnaire or EQ-5D-Y questionnaire) , The child will complete this questionnaire when they attend clinic. Children up to 7 years old will complete CHU9D and EQ-5D-Y will be completed by children > 7 years old.; Resource Use Questionnaire, The parent/primary carer will complete this questionnaire on paper when they attend clinic.; Randomisation, The PI or delegated research staff will randomise the patient using a secure (24-hour) web-based randomisation programme. Randomisation will take place at the first clinic visit after all baseline procedures have been done by parent and child.; Prescription of randomised drug intervention (or informing the patient that no treatment was alloc, All treatments will be procured, prescribed and issued as per routine NHS practice.

Following randomisation, the initial IMP dosing (for carbamazepine and levetiracetam arms) will be determined by an authorised medically qualified member of the trial site's research team, who will ideally issue the first prescription to allow trial treatment to commence within 14 days of randomisation. First prescription can also be issued by the GP if this follows routine practice for the site.

Subsequently, repeat prescriptions will be issued by an authorised medical member of the trial site's research team or by the participant's local GP in accordance with the standard care pathway for this population.; PBS intervention , Those randomised to receive the PBS intervention will securely receive an email directly from a CTSC system that will contain a website link, access instructions and unique login details to access the sleep intervention program online. Parents will have access to the system for as long as their child is part of the study.; Review of medical history and EEG results, The PI or delegated medically qualified physician will review the patient's medical history and EEG data before consent to assess eligibility.; Assessment of eligibility criteria and confirmation of full eligibility , The PI or delegated medically qualified physician will confirm eligibility and will record in in the patient's medical notes and on the CRF.; Review of seizure occurrence & hospital admissions, At each clinic visit, the number of seizures, date of first seizure, and date of most recent seizure

experienced since previous visit will be reviewed by the PI or delegated member of staff.;
Assessment of adverse events, At each clinic visit, the adverse events experienced since the previous visit will be reviewed by the PI or delegated member of staff.

Intervention Type

Mixed

Primary outcome(s)

1. To determine if carbamazepine or levetiracetam are superior to no AED with respect to time to 6- month seizure remission measured using time to 6-month seizure remission based on seizure report at 3, 6,12 months and annually thereafter.
2. To determine if a PBS intervention is superior to standard care with respect to 3-month sleep problem frequency measured by CSHQ at baseline and 3 months.

Key secondary outcome(s)

1. To compare time to treatment failure due to inadequate seizure control or unacceptable adverse reactions measured using time taken from randomisation to decision by child, parent or treating physician to be withdrawn from treatment due to inadequate seizure control or unacceptable adverse reactions at 3, 6, 12 months and annually thereafter
2. To compare time to treatment failure due to inadequate seizure control measured using time taken from randomisation to decision by child, parent or treating physician to be withdrawn from treatment due to inadequate seizure control at 3, 6, 12 months and annually thereafter
3. To compare time to treatment failure due to unacceptable adverse reactions measured using time taken from recruitment to decision by child, parent or treating physician to be withdrawn from trial due to unacceptable adverse reactions at 3, 6, 12 months and annually thereafter
4. To compare time to first seizure measured using time to first seizure based on seizure report at 3,6,12 months and annually thereafter
5. To compare time to 12-month remission from seizures measured using time to 12-month seizure remission based on seizure report at 3, 6, 12 months and annually thereafter
6. To determine if a PBS intervention is superior to standard care measured using total sleep problem score as measured by the CSHQ at 12 months and annually thereafter
7. To compare measures of cognition across the different treatment groups measured using total score in three chosen assessments delivered by CANTAB iPad Neuropsychological battery at baseline, 3 and 12 months and annually thereafter
8. To compare Health Related Quality of Life across the different treatment groups measured using CHEQOL score change at baseline and 12 months and annually thereafter
9. To compare measures of children's behaviour across the different treatment groups measured using total score on strengths and difficulties questionnaire (SDQ) at baseline and 12 months and annually thereafter
10. To identify any adverse reactions and their rate measured using records of adverse reactions at 3, 6, 12, 24 months and annually thereafter in clinic
11. To compare selected child quality of life (QOL) utility outcome measures across the different treatment groups measured using score changes in CHU9D and EQ-5D-Y questionnaires at baseline, 3, 12 months and annually thereafter
12. To compare selected adult QOL utility outcome measures across parents in the different treatment groups measured using EQ-5D-5L score change questionnaire at baseline, 3, 12 months and annually thereafter
13. To compare sickness related school absences across the different treatment groups measured using total sickness related school absences (days) at 3, 6, 12 months and annually thereafter
14. To determine the costs to the NHS measured using:

14.1 Resource use questionnaire

14.2 Patient Level Information and Costing System (PLICS) data

14.3 Bespoke Hospital Episode Statistics (HES) questionnaire at 3, 12 months and annually thereafter

15. To determine which sleep and movement parameters change in primary carer and child dyads in different treatment groups measured using summary of actigraphy variables (total sleep time/sleep latency/sleep efficiency) averaged over a 1-week period at baseline, 3 and 12 months

Completion date

23/09/2020

Reason abandoned (if study stopped)

Objectives no longer viable

Eligibility

Key inclusion criteria

1. Children diagnosed with RE
2. EEG showing focal sharp waves with normal background
3. Aged ≥ 5 years and < 13 years at the time of randomisation
4. Currently untreated with antiepileptic drugs
5. Written informed consent received from person with parental responsibility/legal representative.
6. Family have a valid email address and regular internet access (for online sleep intervention)
7. Parent and child are to have a good understanding of the English language.

Parent-child dyads meeting the trial criteria and the following characteristics will be eligible for inclusion in the qualitative sub-study:

- 1 Ability of parent and child to speak conversational English
- 2 Additional consent to main trial: Consent of parent to participate and for their child to participate

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Child

Lower age limit

5 years

Upper age limit

12 years

Sex

All

Key exclusion criteria

1. Known contraindication to any of the trial drugs
2. Previously treated for epilepsy with antiepileptic drugs

Date of first enrolment

07/06/2019

Date of final enrolment

06/06/2022

Locations

Countries of recruitment

United Kingdom

England

Northern Ireland

Study participating centre

King's College Hospital

Denmark Hill

London

United Kingdom

SE5 9RS

Study participating centre

Guy's & St Thomas' NHS Foundation Trust

Great Maze Pond

London

United Kingdom

SE1 9RT

Study participating centre

Northern Lincolnshire and Goole NHS Foundation Trust)

Diana Princess of Wales Hospital

Scartho Road

Grimsby

United Kingdom

DN33 2BA

Study participating centre

NHS North East Essex CCG
Colchester Primary Care Centre
Turner Road
Colchester
United Kingdom
CO4 5JR

Study participating centre
Bolton NHS Foundation Trust
The Royal Bolton Hospital
Minerva Road
Farnworth
Bolton
United Kingdom
BL4 0JR

Study participating centre
Norfolk And Norwich University Hospitals NHS Foundation Trust
Norfolk & Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
Arrowe Park Hospital
Arrowe Park Road
Upton
Wirral
United Kingdom
CH49 5PE

Study participating centre
Southern Health & Social Care Trust
Southern Area College of Nursing
Craigavon Area Hospital
68 Lurgan Road
Portadown
United Kingdom
BT63 5QQ

Study participating centre
North Tees And Hartlepool NHS Foundation Trust
University Hospital of Hartlepool
Holdforth Road
Hartlepool
United Kingdom
TS24 9AH

Study participating centre
Tameside And Glossop Integrated Care NHS Foundation Trust
Tameside General Hospital
Fountain Street
Ashton-under-Lyne
United Kingdom
OL6 9RW

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

Study participating centre
Mid Essex Hospital Services NHS Trust
Broomfield Hospital
Court Road
Chelmsford
United Kingdom
CM1 7ET

Study participating centre
Luton And Dunstable University Hospital NHS Foundation Trust
Lewsey Road
Luton
United Kingdom
LU4 0DZ

Study participating centre

Warrington And Halton Hospitals NHS Foundation Trust

Warrington Hospital
Lovely Lane
Warrington
United Kingdom
WA5 1QG

Study participating centre

East Lancashire Hospitals NHS Trust

Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre

Homerton University Hospital NHS Foundation Trust

Homerton Row
London
United Kingdom
E9 6SR

Study participating centre

West Hertfordshire Hospitals NHS Trust

Watford General Hospital
Vicarage Road
Watford
United Kingdom
WD18 0HB

Study participating centre

Lancashire Teaching Hospitals NHS Foundation Trust

Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre

The Princess Alexandra Hospital NHS Trust
Hamstel Road
Harlow
United Kingdom
CM20 1QX

Study participating centre
East And North Hertfordshire NHS Trust
Lister Hospital
Coreys Mill Lane
Stevenage
United Kingdom
SG1 4AB

Study participating centre
County Durham and Darlington NHS Foundation Trust
Darlington Memorial Hospital
Hollyhurst Road
Darlington
United Kingdom
DL3 6HX

Study participating centre
Nottingham University Hospitals NHS Trust
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Hampshire Hospitals NHS Foundation Trust
Aldermaston Road
Basingstoke

United Kingdom
RG24 9NA

Study participating centre

St Helens And Knowsley Hospital Services NHS Trust

Whiston Hospital
Warrington Road
Prescot
United Kingdom
L35 5DR

Study participating centre

University Hospital Southampton NHS Foundation Trust

Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation

King's College London

ROR

<https://ror.org/0220mzb33>

Organisation

King's College Hospital NHS Foundation Trust

Funder(s)

Funder type

Government

Funder Name

NIHR Central Commissioning Facility (CCF); Grant Codes: RP-PG-0615-20007

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date

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? |
|--------------------------------------|---------------|--------------|------------|----------------|-----------------|
| HRA research summary | | | 28/06/2023 | No | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |