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Changing agendas on sleep, treatment and learning in childhood epilepsy

Submission date
23/04/2019

Recruitment status
Stopped

Registration date
15/05/2019

Overall study status
Stopped

Last Edited
22/03/2021

Condition category
Nervous System Diseases

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] 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,
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Contact information

Type(s)
Scientific

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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 CTRC 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
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United Kingdom
DN33 2BA

Study participating centre

NHS North East Essex CCG
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Turner Road
Colchester
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CO4 5JR

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

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Norfolk And Norwich University Hospitals NHS Foundation Trust
Norfolk & Norwich University Hospital
Colney Lane
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NR4 7UY

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
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CH49 5PE

Study participating centre
Southern Health & Social Care Trust
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United Kingdom
BT63 5QQ

Study participating centre
North Tees And Hartlepool NHS Foundation Trust
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TS24 9AH

Study participating centre
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Study participating centre

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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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes