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Evaluating dietary intervention before surgical treatment for epilepsy

Submission date	Recruitment status	[ ] Prospectively registered
13/11/2014	Stopped	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
13/11/2014	Stopped	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
16/01/2020	Nervous System Diseases	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Focal cortical dysplasia (FCD) is an abnormality of brain development that is a common cause of epilepsy, which results in repeated seizures. The ketogenic diet is a high fat, low carbohydrate, low protein diet designed to mimic the effects of fasting. The aim of this study is to find out whether the ketogenic diet improves seizure control, brain development and quality of life in children with FCD type II who are about to undergo surgery for epilepsy.

Who can participate?
Children aged 5 - 15 with epilepsy that is resistant to drug treatment and believed to be the result of FCD type II, who are considered to be surgically treatable.

What does the study involve?
Participants are randomly allocated to either receive 6 months of treatment with a ketogenic diet before their surgery, or to proceed directly to surgery (no pretreatment).

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

Where is the study run from?
University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
November 2014 to September 2019

Who is funding the study?
EU Seventh Framework Programme

Who is the main contact?
Dr Christiana Papamichael
c.papamichael@liverpool.ac.uk

Study website

http://www.edible.org.uk/

Contact information

Type(s)
Scientific

Contact name
Dr Christiana Papamichael

Contact details
Department of Biostatistics
University of Liverpool
1st floor Duncan Building
Daulby Street
Liverpool
United Kingdom
L69 3GA
-
c.papamichael@liverpool.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT02261753

Secondary identifying numbers
17696

Study information

Scientific Title
Evaluating Dietary Intervention Before surgicaL treatment for Epilepsy (EDIBLE)

Acronym
EDIBLE v1.0

Study objectives
The investigators are undertaking the first European Randomised Controlled Trial (RCT) for epilepsy surgery in children with FCD type II, to prospectively evaluate the role of the KD prior to surgery in improving seizure outcome. The investigators will evaluate the role of the ketogenic diet as a disease-modifying treatment to achieve seizure control and improve neurodevelopment and quality of life. The ketogenic diet is a high fat, low carbohydrate, low protein diet designed to mimic the effects of fasting on the body. It will be administered by calculation as per local standardised classical ketogenic diet protocol with utilisation of long chain fat in a ratio of 2:1 to 4:1 carbohydrate and protein.

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/LO/1885

Study design
Randomised; Interventional; Design type: Prevention

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Topic: Children; Subtopic: All Diagnoses; Disease: All Diseases

Interventions
Children will be randomised to either receive 6m treatment presurgery with a ketogenic diet, or to proceed direct to surgery (no pretreatment).

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Time to 6 month remission; the time to 6 months of seizure freedom from the date of randomisation

Secondary outcome measures
Current as of 19/09/2017:
1. Time to first seizure from date of randomisation;
2. Time to 12 month remission after randomisation;
3. Time to 24 month remission after randomisation (if enough time for follow-up is available);
4. Quality of life at 12 months after randomisation (and at 24 months if enough time for follow-up is available);

5. Adaptive behaviour assessment at 12 months (() after randomisation (and at 24 months if enough time for follow-up is available);
6. Methylation changes in tissue (DNA) from children pre-treated with the ketogenic diet. Tissue will be stored in the EEBB, and further distributed to DESIRE partners (Baker IDI Heart and Diabetes Institute Holdings Ltd, Varionostic GMBH,CEGAT) for further analysis;
7. Changes in peripheral DNA (blood platelets) following treatment with the KD. Tissue will be stored in the EEBB, and further distributed to DESIRE partners (Baker IDI Heart and Diabetes Institute Holdings Ltd, Varionostic GMBH,CEGAT) for further analysis;
8. Proportion of immediate AEs following resective surgery (i.e. surgical complications within 30 days) in the group pre-treated with KD compared to those without.
9. Compare the general AE occurrence between the group pre-treated with KD compared to the group without KD pre-treatment.

Previous secondary outcome meaures:
1. Methylation changes in tissue (DNA); Timepoint(s): At the time of surgery between ketogenic diet pre-treatment group vs non pre-treated group
2. Neuropsychological assessment; Timepoint(s): Neuropsychological assessment at 12 and at 24 months after randomisation
3. Peripheral DNA changes (blood); Timepoint(s): At baseline and at the time of surgery
4. Proportion of immediate AEs following resective surgery; Timepoint(s): Surgical complications within 30 days from surgery
5. Quality of life; Timepoint(s): Quality of life at 12 and at 24 months after randomisation

Overall study start date
01/11/2014

Completion date
26/07/2017

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
Current as of 19/09/2017:
This is applicable to all participating countries with trial approvals working to Protocol V5.0 06 /09/2016 except Austria and Germany (working to Protocol V2.0 17/03/2015)
1. Children aged 3 - 15 years;
2. MRI changes consistent with a diagnosis of FCD type II a or b;
3. History of at least two epileptic seizures in the past 6 months before randomisation;
4. Seizure semiology consistent with focal onset, agreed after pre-surgical discussion to be surgically treatable;
5. Parent/ legal representative willing to give consent.

Previous inclusion criteria:
1. Children aged 5-15 years
2. MRI changes consistent with a diagnosis of Focal Cortical Dysplasia type II a or b
3. History of continuing seizures for less than 5 years
4. History of at least two epileptic seizures in the past 6 months before randomisation
5. Seizure semiology consistent with focal onset, agreed after pre-surgical discussion to be

surgically treatable
6. Failure of at least two antiepileptic drugs to control the seizures
7. Parent/legal representative willing to give consent

Participant type(s)
Patient

Age group
Child

Lower age limit
3 Years

Upper age limit
15 Years

Sex
Both

Target number of participants
Planned Sample Size: 60; UK Sample Size: 60

Key exclusion criteria
1. Previous use of the ketogenic diet
2. Not a surgical candidate for Focal Cortical Dysplasia resection
3. Administration of the ketogenic diet is medically contraindicated

Date of first enrolment
01/11/2014

Date of final enrolment
26/07/2017

Locations

Countries of recruitment
Austria

Czech Republic

England

France

Germany

Italy

Scotland

Switzerland

United Kingdom

United States of America

Study participating centre
University of Liverpool
Liverpool
United Kingdom
L69 3GA

Study participating centre
Krankenhaus Mara Maraweg
Bielefeld,
Germany
33617

Study participating centre
Bristol Royal Hospital for Children
24 Upper Maudlin Street
Bristol
United Kingdom
BS2 8BJ

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

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

Study participating centre
Children's Hospital Meyer
Viale Gaetano Pieraccini, 24
Florence
Italy
50139

Study participating centre
Hôpitaux Universitaires de Genève
Rue Gabrielle-Perret-Gentil 4
Geneva
Switzerland
1205

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
HFME - Hospices Civils De Lyon
3 Quai des Célestins
Lyon
France
69002

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

Study participating centre
Motol University Hospital
150 06, V Úvalu 84 Czechia
Prague
Czech Republic
150 00

Study participating centre
Ospedale Pediatrico Bambino Gesù
Piazza di Sant'Onofrio, 4
Rome
Italy
00165

Study participating centre
Hopital de Hautepierre
1 Avenue Molière
Strasbourg
France
67200

Study participating centre
Schön Klinik Vogtareuth
Krankenhausstraße 20
Vogtareuth
Germany
83569

Study participating centre
Medical University Vienna
Spitalgasse 23
Vienna
Austria
1090

Study participating centre
Johns Hopkins Hospital
1800 Orleans Street
Baltimore
United States of America
21287,

Sponsor information

Organisation
University College London (UK)

Sponsor details
67 Riding House Street
London
England
United Kingdom
W1P 7PN

Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
The results from all the children will be analysed together and published as soon as possible in a peered reviewed scientific journal irrespective of findings. Participants and their parents or legal representative will be able to have collective findings disseminated to them in plain English by their neurologist or paediatrician. A lay summary will be made available on the trial website. Results will also be disseminated through conference presentations.

Intention to publish date

26/07/2018

Individual participant data (IPD) sharing plan

No individual data will be analysed. The identity of participants will remain confidential and results from blood and tissues samples donated for research purposes will not be copied into participants' medical notes.

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No