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Refeeding low weight adolescents with anorexia nervosa

Submission date
14/09/2012

Recruitment status
No longer recruiting

Registration date
16/10/2012

Overall study status
Completed

Last Edited
04/06/2018

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Eating disorders are mental disorders defined by abnormal eating habits that negatively affect physical or mental health. The restoration of normal nutrition after a period of fasting or starvation is called refeeding. Patients are given small amounts of food to eat, with the amount gradually increasing as their body gets used to dealing with normal amounts. Currently refeeding practices vary considerably around the UK. It is vital that refeeding guidelines are established for the nutritional management of these critically unwell children. We need to improve our understanding of the body's response to nutrition during the early stages of refeeding, in order to reduce the risk of complications. The aim of this study is to identify if one refeeding rate is more effective than another with respect to the cardiovascular (heart) response and biochemical response (blood phosphate, potassium, magnesium, calcium and sodium levels).

Who can participate?
Children aged 8 -16 with an eating disorder

What does the study involve?
On admission a detailed nutritional history is taken looking at food and fluid intake over the last three days, followed by monitoring of heart rate, blood pressure, breathing rate and temperature for 48 hours. Thereafter vital signs are monitored once a day before breakfast. A blood sample is taken to monitor levels of phosphate, magnesium, potassium, sodium and calcium, glucose and insulin; and a urine sample is taken to measure ketone levels. A standard electrocardiogram (ECG) is carried out to check for problems with the electrical activity of the heart. Weight and height are also measured. Participants are randomly allocated to be treated with one of two refeeding rates (either 500kcal per day or 1200kcal per day). They are fed by mouth with solid food and/or supplementary sip feeds or via a naso-gastric tube (a tube that carries food through the nose to the stomach). Calorie intake is increased by 200kcal per day until the estimated calorie requirements are met. Further blood samples are collected before breakfast on day 2, 4, 6, 10 and 14. Urine ketone measurements are only repeated if previously positive. The ECG is repeated on day four. Weight and height are measured every three days. Daily nutritional intake is documented on a food record chart.

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

Where is the study run from?
1. Great Ormond Street Hospital, London,
2. Manchester Children's Hospital
3. Sheffield Children's Hospital
4. James Cook University Hospital, Middlesborough
5. Thorneywood Adolescent Unit, Nottingham
6. Marlborough House Unit, Oxford
7. Luton and Dunstable Foundation Trust
8. Royal Devon and Exeter Foundation Trust
9. Poole Foundation Trust

When is the study starting and how long is it expected to run for?
June 2011 to June 2013

Who is funding the study?
Great Ormond Street Children's Charity and the British Dietetic Association (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title
Investigate the physiological response to energy intake in severely malnourished adolescents with anorexia nervosa

Study objectives
1. Identify if one refeeding rate is more effective than another in respect to the cardiovascular acute response to the nutritional load? Focusing on what impact nutrition has on the QT interval and QT dispersion during the initial phase of refeeding malnourished children with anorexia nervosa.
2. Identify if one refeeding rate is more effective that another in respect to the biochemical acute response to nutritional load? Focusing on what impact nutrition has on serum phosphate, potassium, magnesium, calcium and sodium during the initial phase of refeeding malnourished children with anorexia nervosa.
3. Identify if there is a direct relationship between fasting serum insulin and glucose levels and urine ketones with serum phosphate, potassium, magnesium and calcium levels during the initial phase of refeeding?
4. Develop international evidence based refeeding guidelines for children/ adolescents with anorexia nervosa

Hypothesis 1 An initially higher total energy intake (treatment group) will improve the QT measurements more than the lower energy intake (control group) during the early stages of refeeding.

Hypothesis 2 An initially higher total energy intake will increase the glucose load and therefore increase the risk of hypophosphatemia during the early stages of refeeding.

Hypothesis 3 Fasting serum Insulin level and urine ketones may be predictive markers for hypophosphatemia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Central London REC 2, 12/05/2010, REC ref: 10/H0713/15

Study design
Parallel (1:1) randomized control national multi-centre study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

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
Anorexia nervosa

Interventions
Stratified randomization (SIMS computer generated) will assign to the control group of 500kcal/ day or the treatment group 1200kcal/ day. Stratification for %IBW 55-69% and 70 75%, and enteral versus oral feeding.

Children will be fed orally with solid food and/ or supplementary sip feeds or via a naso-gastric tube with a standard polymeric paediatric formula meeting the desired energy requirements. Calorie intake will be increased by 200kcal/day until estimated calorie requirements are met. Estimated calorie requirements will be calculated using Basal Metabolic rate (BMR) (Schofield equation 1985) plus individual activity level 1.2-1.3 (AL). Those patients that have ambiguous or deranged electrolytes or develop the refeeding syndrome should continue and maintain their current calorie regimen; electrolytes should be replaced as outlined in the British National Formulary (2009). Once biochemistry and vital signs are stable total calories can then be increased by 200kcal/day until estimated calorie requirements are met.

Further biochemistry (phosphate, magnesium, potassium, sodium and calcium,) plus glucose and insulin will be collected pre-breakfast on day 2, 4, 6, 10 and 14. Urine ketone measurements should only be repeated if previously positive. A 12 lead ECG should be repeated on day four. If this ECG shows Q-Tc prolongation >0.44s (440ms) an ECG should be repeated regularly until normalised.

Weight, height, weight for height as a percentage of ideal body weight (%IBW) and Body Mass Index [BMI] will be calculated every three days.

Daily nutritional intake should be documented on a food record chart which specific size/ portions or volumes of feed.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Cardiovascular evaluation
QT Interval Baseline pre refeeding (24-48hrs) and then four day post refeeding. QT interval will be measured by a standard 12 lead, adjusted for age. The QT interval will be measured from the initial downward deflection of the QRS complex to the end of the T-wave. QT dispersion will be calculated with a minimum of 9 leads in which the QT interval could be measured.

QT dispersion was defined as the difference between the longest and shortest QT interval in one ECG recording. QT intervals will be corrected by heart rate (QTc) according to Bazetts formula. However, the Bazett formula has flaws when calculating QTc in bradycardic and tachycardic patients, therefore Framingham formula will also calculate QTc.

Power Statement
QT Interval an effect size of 25ms difference between the control and treatment group 4 days post feeding is deemed significant with a standard deviation of 20ms (Cooke 1994, Swenne 2000, Mont 2003, Olivares 2005, Roche 2005, Ulger 2006, Nahshoni 2007, DiVasta 2010).

Altmans Normagram
Standardized difference 1.0 = Target difference 25ms
Standard Deviation 20ms

It was calculated that 20 participants would be required in each arm, using a two sample t-test to compare the two groups, in order to have an 80% chance of detecting a significant difference after four days of refeeding when comparing the two arms to identify a difference of 25ms (Q-T interval) at the 5% level of significance, assuming the standard deviation of 20ms (Q-T interval).

Secondary outcome measures

Biochemical
1. Phosphate: Baseline pre refeeding serum phosphate level is to be obtained by a venopuncture. If serum phosphate is within normal range then fasting serum phosphate will be obtained on days 2, 4, 6, 10 and 14 post refeeding. However, if serum phosphate level is low then biochemistry must be monitored daily.
2. Serum glucose, insulin, magnesium, potassium, calcium, sodium
Serum monitoring of the above biochemistry will be obtained by venopuncture, to be taken pre refeeding. If serum biochemistry is within normal range then fasting biochemistry will be obtained on days 1, 2, 4, 6, 10 and 14 post refeeding. However, if serum biochemistry levels are deranged then biochemistry must be monitored daily until supplementation is effective.

Other Measurements
1. Anthropometrics (weight for height %, BMI) determined by using standard protocol and weight for height computer data system; weight to be measured every 3 days.
2. Resting heart rate Baseline pre-refeeding resting supine heart rate will be measured using the ECG. It is suggested that patients should be rested for 10 minutes and achieve a regular pulsatile waveform for 20seconds prior to the recording.
3. Blood pressure measured at least twice day
4. Temperature daily
5. Urine ketone day 1 and to continue if ketones present

Nutritional Data
The nutritional analysis will be an essential component in the overall data analysis and therefore food record charts must be completed accurately hence the need for appropriate training of research collaborators. Food record charts will be analysed using DietPlan 5 computer system. 15 essential nutrients will be analysed over the 14 days of admission.

Overall study start date

01/06/2011

Completion date

01/06/2013

Eligibility

Key inclusion criteria
1. Children who are admitted to one of the specialist centers and have been diagnosed with an eating disorder (DSM IV, 2005)
2. Aged 8 -16 years old
3. Have a weight for height Ideal Body Weight (IBW) < 75%
4. Have had acute weight loss >0.5kg in the past week
5. Requiring nutritional rehabilitation enteral or oral

Participant type(s)
Patient

Age group
Child

Lower age limit
8 Years

Upper age limit
16 Years

Sex
Both

Target number of participants
32

Key exclusion criteria
1. Excluded if fed via parenteral nutrition
2. Those patients that have any medical condition that may influence biochemistry or cardiovascular parameters above expected in anorexia nervosa i.e. diabetes Type 1

Date of first enrolment
01/06/2011

Date of final enrolment
01/06/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nutrition and Dietetics
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Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
British Dietetic Association (UK) ref:10/06

Funder Name
Great Ormond Street Hospital Charity (ref: V1207)

Alternative Name(s)
Great Ormond Street Hospital Children's Charity, GOSH Charity, GOSH

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2016		Yes	No