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Therapeutic Hypothermia for Birth Asphyxia in a Low Resource Setting

Submission date	Recruitment status	[_] Prospectively registered
28/05/2010	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
28/06/2010	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
20/02/2020	Neonatal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Therapeutic Hypothermia for Perinatal Asphyxial Encephalopathy in a Low Resource Hospital Setting in Equatorial Africa: a Randomised Controlled Trial

Study objectives
In a single site, the Special Care Baby Unit, Mulago Hospital, Kampala,

1. Does the application of a mattress consisting of water bottles filled with room temperature tap water (with the use of cotton blankets over the baby) result in mild whole body cooling to a target core temperature range of 33-34°C in term infants with neonatal encephalopathy? In particular:
1.1. What sort of monitoring and staffing are required for safe cooling to within the target temperature range?
1.2. Is this low tech simple method effective at cooling infants with neonatal encephalopathy in an equatorial African setting and are specific adjustments needed depending on ambient temperature fluctuations?
1.3. Are there specific adverse events related to mild cooling in this African population who may have co-existing morbidities?
1.4. Is it advantageous (in terms of earlier cooling) to enrol on the labour ward? Does enrolment on special care baby unit delay cooling?
2. What is the temperature profile of infants with encephalopathy during the first 80 hours after birth? This is important as recent data from Mulago Hospital suggests that many infants with asphyxia are hypothermic on admission to the special care baby unit; furthermore an intrinsic response to asphyxia in some infants is a drop in core temperature.
3. Is it feasible to recruit infants according to specific inclusion criteria, obtain informed parental consent and randomisation within 3 hrs of birth in a low resource setting and what sort of extra staffing and surveillance procedures are required?

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Research and Ethics Committee of Makerere University Ethics approved on the 24th of July 2007

Study design
Prospective 2 arm randomised controlled parallel group trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Perinatal Asphyxial Encephalopathy

Interventions
1. Randomisation:
Randomisation will be using sealed envelopes in consecutive eligible infants up to a total of 4 study infants at a time. Forty infants will be randomised to undergo either (a) standard care alone or (b) standard care plus cooling (core temperature of 33-34°C).
The maximum number of infants we will be able to study at any one time will be 4. This is due to limited number of data loggers being available and the need to keep the work load to an acceptable level. So if there are 5 encephalopathic infants in one day, only the first 4 can be enrolled and no further enrolments until the study period (80hrs) is over. Infants will be randomised into groups using sealed envelopes.

2. Standard care group:
Infants receiving standard care will be cared for in cots according to usual hospital clinical practice. The rectal, axillary, skin surface (back) and ambient temperatures will be monitored continuously and stored using a 4 channel data logger (Squirrel SQ 2020, Keison Products, Chelmsford, UK). No intervention other than simple measures using cotton blankets will be used to adjust the rectal temperature to 37°C - it will be important to observe for the rectal temperature under 'standard conditions'.

3. Standard care plus cooling:
Infants randomised to standard care plus cooling will be nursed in a cot naked or lightly covered. Active cooling will be by placing a mattress under the infant - the mattress will be 2 commercially available hot water bottles filled with cold tap water (25°C) covered in a cotton sheet. The tap water temperature is generally around 22-25°C. As the tap water temperature can vary during the day and night, a bucket of tap water will be kept in the special care baby unit in the same place at all times to reduce temperature variations. The water bottles will cover as much of the surface area of the infant as possible. The target rectal temperature will be 33-34°C. The rectal, axillary, ambient and surface water bottle temperatures will be monitored continuously and stored using the 4 channel data logger (Squirrel SQ 2020, Keison Products, Chelmsford, UK). It may be necessary to change the water in the water bottle from our pilot work it is likely that the water will need to be changed every 8-12 hours. If warming is required, the infant will be dressed or covered with blankets and sheets as required. Cooling will be concluded 72 hours after randomisation or earlier if clinical circumstances dictate. The rectal temperature will then be allowed to rise by no more than 0.5°C per hour to 37°C, by slowly reducing the contact of the baby with the water bottles.

4. All other aspects of clinical care will be the same in both groups.
4.1. Saturation monitoring:
If a pulse oximeter is available in the neonatal unit the oxygen saturations may be measured 4-12hrly although this is unlikely to be possible for all the period of cooling. If an infant looks cyanotic, supplementary nasal cannulae oxygen should be given if at least 2 recordings of a saturation < 85% have been recorded.
4.2. Blood pressure:
Measured 6-12 hourly
4.3. Administration of Antibiotics:
The current neonatal unit guidelines at Mulago Hospital include the taking of blood cultures and the administration of Ampicillin and Gentamicin to sick infants. All infants in both groups will receive antibiotics after blood cultures.
4.4. Blood glucose and fluid administration:
IV cannulae will be sited and 10% dextrose will be given intravenously at 60ml/kg/day if clinically indicated according to the current neonatal unit guidelines. Blood glucose will be measured 6hrly and recorded on the data collection sheet using glucose test strips (Optimum Medisense H Blood Glucose Test strips and calibrator, Abbott Diabetes Care Ltd, Oxon, UK).
4.5. Sedation:
If an infant in either group appears agitated or unsettled, then sedation will be given as rectal chloral hydrate 25mg/kg 4 hourly as required.
4.6. Head circumference:
Measured at birth, 7 days and 17 days at follow-up clinic and at 1 year
4.7. Temperature monitoring:
The core (rectal) temperature will be monitored and recorded continuously during cooling and re-warming with a rectal temperature monitor with a rectal temperature probe in situ (Squirrel SQ2020 Data Logger, Grant Instruments, Chelmsford, UK). In addition, the axillary, ambient and surface water bottle temperature will be measured and recorded continuously. These data will

provide information on the reliability of temperatures other than rectal for monitoring treatment with whole body hypothermia in centres with fewer resources in the future.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
1. Feasibility of consent, randomisation and induction and maintenance of therapeutic hypothermia in this setting
2. Information which will optimise the design of a phase III RCT in a low resource setting
3. Adverse events

Key secondary outcome(s))
Cranial ultrasound patterns and evolution of injury over the 1st week after birth

Completion date
31/10/2007

Eligibility

Key inclusion criteria
Study infants will be near term or full term infants with:
1. Need for resuscitation with assisted bag and mask ventilation after birth and/or an Apgar score of <6 at 5 minutes (10 minutes
if available)
2. Abnormal neurological assessment between 30 mins and 3 hrs of age
An abnormal neurological examination at 30 mins will be defined as a score >5 on the standardised examination described by
Thompson et al (Thompson et al., 1997).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
36

Key exclusion criteria

1. <35 weeks gestation or birthweight < 2000g
2. Onset of regular breathing delayed > 20 mins or those who remain apnoeic and cyanotic
3. Absent cardiac output > 10 mins
4. > 3 hrs of age at study entry
5. Major malformations
6. Symptomatic infection
7. Metabolic disease suspected at time of randomisation
8. Families who live >20 km radius of Mulago Hospital
9. Out born infants
10. Those parents who do not speak or understand either English or Luganda or any parent who does not understand the study.

Date of first enrolment
27/07/2007

Date of final enrolment
31/10/2007

Locations

Countries of recruitment
United Kingdom

England

Uganda

Study participating centre
Institute for Women's Health
London
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Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
University/education

Funder Name
University College London

Alternative Name(s)
University College London in United Kingdom, Collegium Universitatis Londinensis, UCL

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

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	01/09/2008	20/02/2020	Yes	No
Protocol article	protocol	04/06/2011		Yes	No