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The CoolXenon Study

Submission date	Recruitment status
26/11/2010	No longer recruiting
Registration date	**Overall study status**
26/11/2010	Completed
Last Edited	**Condition category**
19/02/2015	Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.thoresen.org.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2009-014260-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version 1.21 (as of 05/01/2011)

Study information

Scientific Title
A feasibility study of adding xenon to cooling therapy in babies at high risk of brain injury following poor condition at birth

Acronym
CoolXenon

Study objectives
Our experimental work has shown that by adding the inert gas xenon (50%) while undergoing hypothermia treatment the % good outcome doubles (from 35% to 70%) in both small and large survival models. This is the first clinical feasibility study combining xenon inhalation with the established neuroprotective hypothermia treatment in newborn term after moderate and severe perinatal asphyxia.

Further reading:
Dingley J, Tooley J. Porter H, Thoresen M. Xenon provides short term neuroprotection in neonatal rats when administered after hypoxia-ischemia. Stroke 2006; 37(2): 501-6.
http://www.ncbi.nlm.nih.gov/pubmed/16373643

Dingley J, Hobbs C, Ferguson J, Thoresen M. Xenon/hypothermia neuroprotection regimes in spontaneously breathing neonatal rats after hypoxic-ischemic insult: respiratory and sedative effects. Anaesthesia and Analgesia 2008; 106: 916-923.
http://www.ncbi.nlm.nih.gov/pubmed/18292440

Hobbs C, Thoresen M, Tucker AM, Aquilina K, Chakkarapani E, Dingley J. Xenon and hypothermia combine additively offering long term functional and histopathological neuroprotection after neonatal hypoxia-ischemia. Stroke 2008; 39(4): 1307-13.
http://www.ncbi.nlm.nih.gov/pubmed/18309163

Chakkarapani E, Thoresen M, Hobbs C, Aquilina K, Liu X, Dingley J. A closed-circuit neonatal xenon delivery system: technical neuroprotection feasibility study in newborn pigs. Anaesthesia and Analgesia 2009; 109(2): 451-60.
http://www.ncbi.nlm.nih.gov/pubmed/19608817

Thoresen M, Hobbs C, Wood T, Chakkarapani E, Dingley J. Cooling combined with immediate or delayed Xenon inhalation provides equivalent long-term neuroprotection after neonatal hypoxia-ischemia. Journal of Cerebral Blood Flow and Metabolism 2009; 29(4): 707-14.
http://www.ncbi.nlm.nih.gov/pubmed/19142190

Thoresen M. Patient selection and prognostication with hypothermia treatment. Seminars in Fetal and Neonatal Medicine 2010; 15(5): 247-52
http://www.ncbi.nlm.nih.gov/pubmed/20580626

As of 01/03/2011 the target number of participants has been increased from 12 to 14

Ethics approval required
Old ethics approval format

Ethics approval(s)
North Somerset and South Bristol Research Ethics Committee approved on the 16th September 2009 (ref: 09/H0106/64)

Study design
Interventional non-randomised single centre feasibility study

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
GP practice

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: Neurological; Subtopic: Neurological (all Subtopics); Disease: Nervous system disorders

Interventions
Adding xenon to the inspiratory gas of the ventilated infant using a MHRA approved closed loop xenon-delivery system. The xenon, oxygen, carbon dioxide (CO_2) and nitrogen gas concentrations are controlled.

Follow up length: 42 months
Study entry: registration only

Added 01/03/2011: The duration of treatment with Xenon gas has been increased from 12 hours to 18 hours for recruits 12, 13 and 14

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Xenon

Primary outcome measure

Physiological changes, measured within 24 hours after end treatment

Secondary outcome measures
1. Bayley III, measured at 18 or 24 months
2. MRI, measured within 14 days after treatment

Overall study start date
28/03/2010

Completion date
01/03/2013

Eligibility

Key inclusion criteria
Infants will be eligible for xenon if the St Michael's standard inclusion criteria for cooling are met. Standard Hypothermia Treatment Criteria for 72 hours of cooling - all of criteria A, B, and C:

A: Infants greater than 36.0 weeks gestation (clinical assessment) with at least one of the following:
1. Apgar score of less than 5 at ten (10) minutes after birth
2. Continued need for resuscitation, including endotracheal or mask ventilation, at ten minutes after birth
3. Acidosis defined as either umbilical cord pH or any arterial, venous or capillary pH within 60 minutes of birth less than pH 7.00
4. Base deficit greater than or equal to 16 mmol/L in umbilical cord blood sample or any blood sample within 60 minutes of birth (arterial or venous blood)
If the infant meets criterion A then assess for neurological abnormality using criterion B and C (by trained personnel).

B: Moderate or severe encephalopathy as evidenced by:
1. Altered state of consciousness (reduced or absent responses or pathological irritability and hyper responsive
And at least one or more of the following:
2. Hypotonia
3. Abnormal reflexes including oculomotor or pupillary abnormalities
4. Absent or weak suck
5. Clinical seizures, as recorded by trained personnel

C: At least 30 minutes duration of amplitude integrated electroencephalography (aEEG) recording that shows abnormal background aEEG activity. The decision to cool is based on the worst section of the aEEG, not the best (al Naqeeb, et al, 1999) or seizures (clinical or electrical) thus meeting ONE of the following:
1. Normal background with some electrical seizure activity
2. Moderately abnormal activity (upper margin of trace greater than 10 µV and lower margin less than 5 µV)
3. Suppressed activity (upper margin of trace less than 10 µV and lower margin of trace less than 5 µV)
4. Definite seizure activity

Additional inclusion criteria for xenon:
Before being considered for additional inhaled xenon therapy via the breathing gas mixture, the infant would need to meet further additional entry criteria:
1. Intubated, ventilated, sedated, being cooled
2. Any seizures under control
3. Weight greater than 2.3 kg
4. No evidence of infection
5. Stable cardiovascular parameters - mean arterial pressure greater than 45mmHg
6. Oxygen requirement via mechanical ventilator less than 35%
7. Positive end expiratory pressure (PEEP) requirement less than 6 mmHg
8. Arterial pCO2 within the accepted range (4.5 - 6.5 kPa)
9. Postnatal age less than 18 hours, either sex
10. Major congenital abnormalities, imperforate anus and congenital abnormalities suggestive of chromosomal anomaly or other syndromes that include brain dysgenesis

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Added 01/03/2011: 14 (12 at time of registration)

Key exclusion criteria
1. Infants expected to be greater than 12 hours of age at the time of starting cooling treatment
2. Futility; where prognosis is considered to be hopeless, e.g. no cardiac output for 20 minutes
3. Failure to meet the additional inclusion criteria for xenon

Date of first enrolment
28/03/2010

Date of final enrolment
01/03/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
School of Clinical Sciences
Bristol
United Kingdom
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Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust (UK)

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Sponsor type
Hospital/treatment centre

Website
http://www.uhbristol.nhs.uk/

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Charity

Funder Name
Sparks (UK)

Alternative Name(s)
Sparks Charity

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	01/05/2014		Yes	No
HRA research summary			28/06/2023	No	No