

The CoolXenon Study

Submission date

26/11/2010

Recruitment status

No longer recruiting

Registration date

26/11/2010

Overall study status

Completed

Last Edited

19/02/2015

Condition category

Injury, Occupational Diseases, Poisoning

Prospectively registered

Protocol

Statistical analysis plan

Results

Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

2009-014260-19

Protocol serial number

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)

Primary study design

Interventional

Study design

Interventional non-randomised single centre feasibility study

Study type(s)

Treatment

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 (CO₂) 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(s)

Physiological changes, measured within 24 hours after end treatment

Key secondary outcome(s)

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

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 μ V and lower margin less than 5 μ V)
3. Suppressed activity (upper margin of trace less than 10 μ V and lower margin of trace less than 5 μ V)
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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

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**

United Kingdom

England

Study participating centre

School of Clinical Sciences

Bristol

United Kingdom

BS2 8EG

Sponsor information**Organisation**

University Hospitals Bristol NHS Foundation Trust (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

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
Study website	Study website	11/11/2025	11/11/2025	No	Yes