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Erythropoietin, magnesium sulfate and hypothermia for hypoxic-ischemic encephalopathy

Submission date
10/09/2018

Recruitment status
No longer recruiting

Registration date
14/09/2018

Overall study status
Completed

Last Edited
05/04/2019

Condition category
Neonatal Diseases

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

Plain English summary of protocol

Background and study aims
Hypoxic Ischemic Encephalopathy (HIE) is a type of brain damage that occurs when a newborn's brain doesn't receive enough oxygen and blood. It occurs in 1 to 3% of normal births. Nearly 20% of affected infants die during the postnatal period (after birth), while 25% develop central nervous system complications. Therapeutic hypothermia (reduction of body temperature) in newborns with HIE has been tested in six studies and has shown improvements in outcome. However, hypothermia was not always effective and resulted in death or moderate to severe disabilities in more than 40% of the patients. The addition of other strategies may improve the outcome, but it is not known which treatment is most effective in combination or whether these treatments are safe. Both erythropoietin (Epo) and magnesium sulfate are known to improve the outcome of HIE. The safety or effectiveness of Epo and magnesium sulfate in combination with hypothermia has not been studied to date. The aim of this study is to assess the safety and feasibility of the combination in newborns with HIE.

Who can participate?
Newborns with HIE admitted to the Osaka City General Hospital Neonatal Intensive Care Unit (NICU)

What does the study involve?
A combination treatment with Epo, magnesium sulfate and hypothermia is started within 6 hours of birth. Vital signs and side effects are recorded during the treatment. Short-term and long-term developmental outcomes are also assessed.

What are the possible benefits and risks of participating?
The benefit of participating is to receive the new treatment. The risk of participating is the rare possibility to have an unexpected side effect.

Where is the study run from?
Osaka City General Hospital (Japan)

When is the study starting and how long is it expected to run for?
April 2013 to December 2017

Who is funding the study?
Japan Agency for Medical Research and Development (Japan)

Who is the main contact?
Dr Hiroyuki Ichiba
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
UMIN 00003267

Study information

Scientific Title
Erythropoietin, magnesium sulfate and hypothermia for hypoxic-ischemic encephalopathy

Study objectives
Erythropoietin (Epo) and magnesium sulfate in combination with hypothermia is safe and feasible in neonates with hypoxic-ischemic encephalopathy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional ethics committee of Osaka City General Hospital, 21/08/2013, ref: 1306022

Study design
Interventional non-randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Neonatal hypoxic-ischemic encephalopathy

Interventions
A combination therapy with erythropoietin (300 mg/kg every other day for 2 weeks), magnesium sulfate (250 mg/kg for 3 days) and hypothermia was started within 6 hours of birth in neonates who met the institutional criteria for hypothermia therapy. All patients received continuous infusion of dopamine. Vital signs and adverse events were recorded during the therapy. Short-term and long-term developmental outcomes were also evaluated.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Erythropoietin, magnesium sulfate

Primary outcome measure
Mortality and morbidity in neonatal period, measured by clinical records regarding in-hospital death, establishment of oral feeding, establishment of spontaneous respiration and brain MRI findings at 1 month of age

Secondary outcome measures
Neurodevelopmental outcome measured using the Kyoto Scale of Psychological Development (KSPD) at 18 months of age

Overall study start date
01/04/2013

Completion date
31/12/2017

Eligibility

Key inclusion criteria
Neonates admitted to the Osaka City General Hospital Neonatal Intensive Care Unit (NICU) and diagnosed with HIE, meeting institutional criteria for therapeutic hypothermia

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
9

Key exclusion criteria
1. Infants older than 6 hours of birth at the time of initiation of hypothermia therapy
2. Infants with major congenital abnormalities
3. Infants with severe growth restriction with birth weight less than 1800 g
4. Infants who were considered critically ill and unlikely to benefit from neonatal intensive care by the attending neonatologist

Date of first enrolment
07/02/2014

Date of final enrolment
04/06/2015

Locations

Countries of recruitment
Japan

Study participating centre
Osaka City General Hospital
2-13-22 Miyakojima-hondori, Miyakojima-ku
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Sponsor information

Organisation
Osaka City General Hospital

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00v053551

Funder(s)

Funder type
Research organisation

Funder Name
Japan Agency for Medical Research and Development

Alternative Name(s)
, The Japan Agency for Medical Research and Development, AMED

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Japan

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
11/10/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Hiroyuki Ichiba (h-ichiba@med.osaka-cu.ac.jp).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2019		Yes	No