

Erythropoietin, magnesium sulfate and hypothermia for hypoxic-ischemic encephalopathy

Submission date 10/09/2018	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 14/09/2018	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 05/04/2019	Condition category Neonatal Diseases	<input type="checkbox"/> 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
h-ichiba@med.osaka-cu.ac.jp

Contact information

Type(s)
Scientific

Contact name
Dr Hiroyuki Ichiba

Contact details
Department of Neonatology, Osaka City General Hospital
2-13-22 Miyakojima-hondori, Miyakojima-ku
Osaka
Japan
534-0021
+81 (0)669291221
h-ichiba@med.osaka-cu.ac.jp

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

Osaka

Japan

534-0021

Sponsor information

Organisation

Osaka City General Hospital

Sponsor details

2-13-22 Miyakojima-hondori, Miyakojima-ku

Osaka

Japan

534-0021

+81 (0)669291221

h-ichiba@med.osaka-cu.ac.jp

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

Research institutes and centers

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