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Efficacy and safety of methylxanthines in very low birthweight infants

Submission date	Recruitment status	[_] Prospectively registered
05/09/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/09/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
25/04/2017	Neonatal Diseases	

Plain English summary of protocol

Background and study aims
Apnea of prematurity is a condition where premature babies stop breathing for short periods. Methylxanthine drugs such as caffeine are used to prevent or treat apnea of prematurity but it is not known whether methylxanthines have other short- and long-term benefits or risks in infants with very low birth weight. The aim of this study is to clarify whether methylxanthines cause more good than harm in very low birth weight infants.

Who can participate?
Babies during the first 10 days of life with a very low birth weight (500 to 1250 g) who require methylxanthine treatment for apnea of prematurity.

What does the study involve?
Participating babies are randomly allocated to receive either caffeine or placebo (a dummy drug), until drug treatment for apnea of prematurity is no longer needed. Survival and disability rates are compared between the two groups 18 months later.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
McMaster University (Canada)

When is the study starting and how long is it expected to run for?
October 1999 to July 2016

Who is funding the study?
1. Canadian Institutes of Health Research (CIHR) (Canada)
2. MRC Canada
3. NHMRC Australia (supplementary funding to Australian centres only)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00182312

Secondary identifying numbers
MCT-13288; MOP-102601

Study information

Scientific Title
Efficacy and safety of methylxanthines in very low birthweight infants: a randomised controlled trial

Acronym
CAP

Study objectives
Avoidance of methylxanthines (caffeine) to prevent or treat apnea of prematurity reduces the risk of adverse outcomes in very low birth weight infants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
McMaster University Research Ethics Board approved on 21/05/1999
Amendment for MOP-102601 approved on 15/07/2010

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Apnea of prematurity

Interventions
Control arm: caffeine will be administered intravenously or orally (via feeding tube) as follows: Loading dose 20 mg/kg caffeine citrate; maintenance dose 5 mg/kg once every 24 hours. The volume of the maintenance dose will be adjusted every 7 days according to the actual body weight on that day. In case of persistent apnea, the responsible physician will have the option to increase the maintenance dose in two steps to a maximum of 10 mg/kg of caffeine citrate.
Intervention group: an equivalent volume of sterile sodium chloride 0.9% without preservative.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Methylxanthines (caffeine)

Primary outcome measure
Combined rate of mortality and neurodevelopmental disability in survivors at a corrected age of 18 months

Secondary outcome measures
1. Neonatal complications typically associated with respiratory insufficiency and very low birth weight (VLBW):
1.1. Bronchopulmonary dysplasia (BPD) is diagnosed in all infants who still require supplemental oxygen at a postconceptual age of 36 weeks. In addition, quantitative comparisons of the duration of support will be performed (days on positive pressure ventilation via endotracheal tube, days on non-invasive continuous positive airway pressure [CPAP], days in oxygen)
1.2. Intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL) and ventriculomegaly are diagnosed ultrasonographically. Serial cranial ultrasound assessments are routinely performed in VLBW infants to detect hemorrhagic and ischemic changes. The worst scans obtained between days 14 and 28, and between 34-36 weeks post conception, respectively, will be recorded
1.3. Necrotising enterocolitis (NEC) is diagnosed at surgery, at autopsy, or by either the finding of pneumatosis intestinalis, hepatobiliary gas or free intraperitoneal air on abdominal X-ray. In the absence of these findings, suspected NEC is recorded in any infant in whom enteral feeds are withheld for more than 5 days, because of symptoms and signs suggestive of NEC
1.4. Retinopathy of prematurity (ROP) is diagnosed at routine ophthalmologic examinations, beginning at 32 weeks postconceptional age. The severity of ROP will be graded according to the international classification of ROP
2. Weight gain and head circumference will be recorded weekly until discharge from the study centre
3. Functional status at 5 years and at 11-12 years

Overall study start date
01/10/1999

Completion date
31/07/2016

Eligibility

Key inclusion criteria
1. Birth weight 500-1250 g
2. Postnatal age day 1-day 10, either sex
3. Infant considered a candidate for methylxanthine therapy by clinical staff

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
2006

Key exclusion criteria

1. Dysmorphic features or congenital malformations that adversely affect life expectancy or neurodevelopment
2. Unlikely to comply with long-term follow-up
3. Prior treatment with a methylxanthine

Date of first enrolment
01/10/1999

Date of final enrolment
01/10/2004

Locations

Countries of recruitment
Australia

Canada

Germany

Israel

Netherlands

Sweden

Switzerland

United Kingdom

United States of America

Study participating centre
McMaster University
Hamilton
Canada
L8L 2X2

Sponsor information

Organisation
McMaster University Faculty of Health Sciences (Canada)

Sponsor details

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Sponsor type
University/education

ROR
https://ror.org/02fa3aq29

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: MCT-13288 & MOP-102601)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Funder Name
Medical Research Council Canada

Alternative Name(s)
Medical Research Council, Canada, Medical Research Council, Medical Research Council of Canada, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Funder Name
National Health and Medical Research Council (supplementary funding to Australian centres only)

Alternative Name(s)
NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Australia

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	18/05/2006		Yes	No
Results article	results	08/11/2007		Yes	No
Results article	results	01/03/2010		Yes	No
Results article	results	01/06/2017		Yes	No