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The effects of anaesthesia on neurodevelopmental outcome and apnoea in infants: the GAS study

Submission date 23/05/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 03/06/2009	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 09/08/2016	**Condition category** Digestive System	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Anaesthetics are often used during tests and surgical operations. A regional anaesthetic is given to a defined region of your body to stop you feeling pain in that area. A general anaesthetic is often used for more serious operations where you will be totally unconscious and unaware of the procedure. Animal studies have suggested that general anaesthetics harm the developing brain. For example, monkeys exposed to anaesthesia as infants grow up to have slower learning than those not exposed. It is unclear if these findings are relevant to humans but the issue has become a major concern. The aim of this study is to determine whether children exposed to general anaesthesia as a baby have poorer brain development.

Who can participate?
Any baby scheduled for inguinal hernia repair, aged 26 to 60 weeks.

What does the study involve?
The research team will collect some background information about the child's medical and birth history and also some simple details about the child's family and household. A blood sample will also be taken. The child will then be randomly allocated to be treated either with a regional anaesthetic on its own or with both a general and a regional anaesthetic. At 2 years of age, the child will be seen by a paediatrician and psychologist. The paediatrician will do some neurological tests to check the child's development, test the child's hearing and sight, and perform a general check up. The psychologist will conduct some memory testing as well as some tests that will be used to assess the child's attention and processing skills. A paediatrician and psychologist will also assess the child at 5 years of age. The doctor will again conduct some visual and hearing tests as well as a general check up. The psychologist will conduct some tests to assess intellectual ability, processing speed and attention. After both the 2-year and 5-year assessments the psychologist will provide the participant's family with a report.

What are the possible benefits and risks of participating?
Benefits for the child may include receiving closer attention from the researchers looking for complications during and after the anaesthetic. The 2- and 5-year reports may be of some

benefit to the participants' families. The report will have information about school readiness, intellectual abilities and behaviour. If a child is having any problems the family will be offered advice and referrals to an appropriate specialist. This study will give us information about the safety and long-term effects of anaesthetics in babies. There are some risks associated with anaesthesia in babies. Although they may differ slightly in nature, the risks for regional and general anaesthesia are rare but can be serious. For regional anaesthesia there is also a risk of accidentally putting the local anaesthetic into a vein, which may cause a seizure or the heart may beat irregularly, but his is very rare and occurs less than 1 in 10,000 times. There is also a very small risk of damage to nerves or infection and once again the risk is less than 1 in 10,000. In about 1 in 40 babies the regional anaesthetic may not work well enough for the operation and the baby will require a general anaesthetic. There are no extra risks of giving a baby a general anaesthetic after a regional anaesthetic. For both types of anaesthesia there is a risk that the baby may have apnoeas in their breathing (momentarily stop breathing) after their operation. This risk might be greater after a general anaesthetic. The baby will be monitored after the anaesthetic and immediately assisted in their breathing if needed. The exact risk of death or disability from untreated long apnoea is unknown but less than 1 in 100,000. In babies, the risk of death or serious long-term disability resulting from any other cause in either form of anaesthetic is less than 1 in 40,000. For both regional and general anaesthesia there may be additional unforeseen or unknown risks. After the follow-up assessments we will tell the participants' families how their child is doing from a developmental perspective. If there is an indication that the child could benefit from extra help this may be distressing news, but we will discuss this with the family and, if appropriate, the family doctor, who may refer the child to a specialist. In most cases children actually enjoy the assessments, but if for any reason the child becomes distressed during the assessment, then we can stop the assessment and wait until they are calm and ready to continue or we can rebook them for another day.

Where is the study run from?
Royal Children's Hospital, Murdoch Children's Research Institute, Melbourne, Australia

When is the study starting and how long is it expected to run for?
Recruitment for the study started in 2007 and ended in 2012. The assessments will be completed in 2017.

Who is funding the study?
1. National Health and Medical Research Council (Australia)
2. Australian and New Zealand College of Anaesthetists (Australia)
3. NIHR Health Technology Assessment Programme (UK)
4. Canadian Institutes of Health Research (Canada)

Who is the main contact?
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Contact information

Type(s)
Scientific

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IRAS number

ClinicalTrials.gov number
NCT00756600

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HTA 07/01/05; EudraCT 2006-006295-37; ACTRN12606000441516; MCT-98031

Study information

Scientific Title
A multicentre randomised controlled trial comparing regional and general anaesthesia for effects on neurodevelopmental outcome and apnoea in infants

Acronym
GAS

Study objectives
The primary purpose of the GAS study is to determine whether different types of anaesthesia (spinal versus general) given to 660 infants undergoing inguinal hernia repair results in equivalent neurodevelopmental outcomes. The study also aims to describe the incidence of apnoea in the post-operative period after both spinal and general anaesthesia for inguinal hernia repair in infants. This study is important as it will provide the greatest evidence for safety or toxicity of general anaesthesia for human infants.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/070105
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0019/51706/PRO-07-01-05.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)

1. UK: West Glasgow Ethics Committee, 20/02/2007, ref: 07/S0709/20
2. Australia: Royal Children's Hospital Ethics Committee, 21/11/2006, ref: 26135
3. USA: Clinical Investigation Office, Children's Hospital Boston, 23/10/2006, ref: 06-07-0320

Added 15/01/2010:
4. Canada: Local ethics committee in Montreal, 30/08/2007

Study design
Multicentre 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 provided in the interventions field to request a patient information sheet

Health condition(s) or problem(s) studied
Anaesthesia for unilateral or bilateral inguinal hernia repair

Interventions
General anaesthesia:
Sevoflurane (intervention drug) for induction and maintenance of general anaesthesia, dose up to 8% inspired for duration of procedure (approximately 45 minutes) plus bupivacaine local anaesthetic blockade (up to 2.5 mg per kg) administered via caudal or ilioinguinal nerve block.

Regional anaesthesia:
Up to 2.5 mg/kg bupivacaine administered by caudal or subarachnoid routes or both caudal and subarachnoid or subarachnoid and ilioinguinal nerve blockade. Single shot.

Comparator/control treatment:
Comparator treatment is regional anaesthesia (either: spinal block alone, spinal and caudal block, spinal and ilioinguinal block, caudal block alone) with bupivacaine to be administered by caudal and/or subarachnoid routes at the beginning of the surgical procedure.
Spinal dose: 0.2 ml/kg 0.5% bupivacaine
Caudal dose: 2.5 mg/kg bupivacaine

The duration lasts for approximately 90 minutes. Patients are observed for up to 12 hours (if they are in hospital) and parents are telephoned a week after the procedure to see how their child is recovering.

Contact details for patient information material:
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Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Sevoflurane, bupivacaine

Primary outcome measure
Wechsler Pre-school and Primary Scale of Intelligence - Third Edition (WPPSI-III) full scale intelligence quotient (IQ) score. This scale will be used to determine whether different types of anaesthesia (regional versus general) given to infants undergoing inguinal hernia repair results in equivalent neurodevelopmental outcomes at 5 years corrected age.

Secondary outcome measures
1. Bayley neurodevelopmental scale at 2 years corrected age
2. Heart rate, respiration and oxygen saturation post-anaesthesia in order to measure the frequency and characteristics of apnoea in the post-operative period after both regional and general anaesthesia for inguinal hernia repair in infants for up to 12 hours post-anaesthesia

Overall study start date
01/07/2009

Completion date
01/07/2015

Eligibility

Key inclusion criteria
1. Any infant scheduled for unilateral or bilateral inguinal hernia repair (with or without circumcision)
2. Any infant whose gestational age (GA) is 26 weeks or more (GA = 182 days)
3. Any infant whose post-menstrual age (PMA) is up to 60 weeks (PMA = 426 days)

Minimum age: 26 weeks
Maximum age: 60 weeks
Gender: both males and females

Participant type(s)

Patient

Age group
Neonate

Sex
Both

Target number of participants
120 in UK, 660 in total worldwide

Key exclusion criteria
1. Any child older than 60 weeks post-menstrual age
2. Any child born at less than 26 weeks gestation
3. Any contraindication to general or spinal/caudal anaesthesia (for example: neuromuscular disorder or coagulopathy)
4. Pre-operative ventilation immediately prior to surgery
5. Congenital heart disease that has required surgery or will require surgery or which requires ongoing pharmacotherapy
6. Known chromosomal abnormality or any other known acquired or congenital abnormalities (apart from prematurity) which are likely to affect development
7. Children where follow-up would be difficult for geographic or social reasons
8. Families where English (or French for Paris and Montreal sites) is not the language spoken at home
9. Known neurological injury such as cystic periventricular leukomalacia (PVL), or grade 3 or 4 intra-ventricular haemorrhage (IVH) (+/- post-haemorrhage ventricular dilatation)
10. Previous exposure to volatile anaesthesia or benzodiazepines as a neonate or in the third trimester in utero

Date of first enrolment
01/07/2009

Date of final enrolment
01/07/2015

Locations

Countries of recruitment
Australia

Canada

France

Italy

United Kingdom

United States of America

Study participating centre
Royal Children's Hospital
Melbourne
Australia
3052

Sponsor information

Organisation
NHS Greater Glasgow and Clyde and University of Glasgow (UK)

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Sponsor type
Government

Website
http://www.nhsggc.org.uk/content/

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Canadian Institutes of Health Research

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

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
01/05/2019

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	01/07/2015		Yes	No
Results article	results	01/07/2015		Yes	No
Results article	results	16/01/2016		Yes	No