ISRCTN63387871 https://doi.org/10.1186/ISRCTN63387871

Effect-site targeted propofol for anaesthesia in children

Submission date 23/08/2010	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 22/02/2011	**Overall study status** Completed	
Last Edited 09/05/2017	**Condition category** Surgery	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Neil Morton

Contact details
Royal Hospital for Sick Children
Dalnair Street
Glasgow
United Kingdom
G3 8SJ

Additional identifiers

EudraCT/CTIS number
2009-014568-21

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EudraCT number: 2009-014568-21

Study information

Scientific Title
A multicentre open study of the performance of an effect-site targeted infusion of propofol used for induction and maintenance of anaesthesia in children under 16 years

Study objectives
The equilibration of propofol from the plasma compartment to brain can be described using the time to peak effect and keo values for propofol. This is an open study to determine the performance of an effect-site targeted infusion based on the age-dependent values described by Jeleazcov (2008), using the four standard measures of bias, precision, divergence and wobble. These derived parameters estimate quantitatively whether the system over- or under-delivers propofol and how this varies both between patients and for an individual patient over time.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Multicentre open non-randomised non-controlled study

Primary study design
Interventional

Secondary study design
Non randomised study

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
General anaesthesia

Interventions
Patients will be recruited from suitable operating lists and after appropriate consent, will undergo induction and maintenance of general anaesthesia using the effect-site targeted infusion of propofol. Patients will have an intravenous (iv) cannula inserted through topically-anaesthetised skin and a bolus of remifentanil 0.5 µg/kg and lignocaine 0.2 mg/kg will be injected to reduce propofol pain at induction. Bispectral index monitoring will be used to monitor depth of anaesthesia throughout the induction and maintenance period.

During the period of maintenance of anaesthesia, the target effect-site concentration will be lowered and a hysteresis loop of depth of anaesthesia against propofol concentration will be

populated using the BIS data and plasma samples collected from a second venous cannula. From this, an estimate of the keo value for propofol can be calculated. The period of lightening of anaesthesia may be terminated at any point because of clinical or BIS-derived suspicions of a requirement for greater depth of anaesthesia. The main outcome measure of the performance of the infusion algorithm is calculated from propofol sampling performed during the remainder of the period of anaesthesia using non-linear lixed effects monitoring. A maximum of 5 ml blood will be sampled from each patient.

The involvement of each participant concludes at the time of emergence from anaesthesia.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Propofol

Primary outcome measure
Performance of an effect-site target controlled infusion (TCI) pharmacokinetic model for children aged 1 to 12 years and weight 6 - 60 kg, as calculated from the four standard parameters described by Varvel et al. The performance error (PE) is calculated from the concentration of propofol measured in whole blood (Cmeas) and the concentration predicted by the software (Cpred) as follows: PE(%) = ((Cmeas-Cpred)/Cpred) x 100. Four standard measures of performance are derived from this value, namely bias, precision, divergence and wobble. These derived parameters estimate quantitatively whether the system over- or under-delivers propofol, and how this varies both between patients and for an individual patient over time.

Secondary outcome measures
1. Population pharmacokinetics of propofol in children aged 1 to 12 years using non-linear effects modelling (NONMEM). This allows the calculation of volume of distribution and clearance of propofol and potential relationships between these pharmacokinetic parameters and the variables of age, gender and weight to be explored.
2. Pharmacodynamic modelling, using bispectral index as a measure of depth of anaesthesia. This will allow direct estimation of the blood-brain equilibration rate-constant (keo) for propofol in this patient population.
3. Establish a safety profile for effect-site TCI propofol based on the pharmacodynamics of Jeleazcov et al by identifying the rate of adverse events associated with the use of effect-site targeted propofol infusion

Overall study start date
01/12/2010

Completion date
30/11/2011

Eligibility

Key inclusion criteria

1. American Society of Anaesthesiologists (ASA) grade 1 and 2 healthy male and female children aged 1 to 12 years (inclusive)
2. Weight 6 - 60 kg
3. Elective surgery requiring general anaesthesia
4. Surgery or procedure of expected duration of at least 30 minutes
5. Written parental consent or child's consent if competent, for inclusion
6. Child appropriate for intravenous induction and maintenance of anaesthesia with propofol
7. Agreement to undergo intravenous induction of anaesthesia
8. No contraindication to application of topical local anaesthesia prior to cannulation

Participant type(s)
Patient

Age group
Child

Lower age limit
1 Years

Upper age limit
12 Years

Sex
Both

Target number of participants
50

Key exclusion criteria
1. Parental refusal or refusal of child if competent
2. Allergy to propofol or any constituent of propofol
3. Sensitivity to adhesive agents, as used in the Bispectral Index (BIS) measurement strip
4. Refusal of intravenous induction
5. Need for sedative premedication
6. Inadequate topical analgesia for intravenous cannulation
7. Inability to site intravenous cannula within two attempts

Date of first enrolment
01/12/2010

Date of final enrolment
30/11/2011

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Royal Hospital for Sick Children
Glasgow
United Kingdom
G3 8SJ

Sponsor information

Organisation
NHS Greater Glasgow and Clyde (UK)

Sponsor details
Recearch and Development Central Office
Western Infirmary
Glasgow
United Kingdom
G11 6NT

Sponsor type
Government

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

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Research organisation

Funder Name
National Institute of Academic Anaesthesia (NIAA) (UK)

Funder Name
Yorkhill Children's Foundation (UK)

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