ISRCTN02639863 https://doi.org/10.1186/ISRCTN02639863

SLEEPS: Safety profiLe, Efficacy and Equivalence in Paediatric intensive care Sedation

Submission date
24/01/2007

Recruitment status
No longer recruiting

Registration date
25/01/2007

Overall study status
Completed

Last Edited
17/05/2016

Condition category
Other

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

Plain English summary of protocol

Background and study aims
The government have recognised that children are subjected to drugs that have not been adequately assessed for safety and effectiveness. Children are not just small adults and their responses to drugs can be very different. A particular problem area is sedation of the critically ill child where responses to the drugs and ability to deal with the drugs can be greatly affected not just by issues of maturity but also organ function. Midazolam is the most frequently used sedation drug but is associated with poor control, increasing tolerance and persistent distressing behavioural side effects in up to 20% of cases when the drug is withdrawn. Clonidine is a drug with both pain relieving and sedative qualities and may protect critical organs by suppressing stress responses. It is increasingly being used as an alternative drug in the paediatric intensive care unit, but it has not been evaluated for safety and effectiveness. In this study we intend to compare the effectiveness of clonidine with midazolam in terms of quality of sedation and side effects in critically ill children.

Who can participate?
Children aged 30 days to 15 years admitted to the Paedatric Intensive Care Unit (PICU) and likely to require intubation and ventilation for more than 48 hours.

What does the study involve?
Participants are randomly allocated to be treated with either midazolam or clonidine infused intravenously (into a vein) to provide sedation. We measure the quality of sedation and record the changes in drug requirements over their intensive care and subsequent hospital stay to observe drug tolerance, withdrawal behaviours and also collect data on organ function.

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

Where is the study run from?
Bristol Royal Childrens Hospital (UK)

When is the study starting and how long is it expected to run for?
May 2009 to August 2012

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Prof. Andrew Wolf
awolfbch@aol.com

Contact information

Type(s)
Scientific

Contact name
Prof Andrew Wolf

Contact details
Paediatric Intensive Care Unit
Bristol Royal Childrens Hospital
Level 7 Bristol Royal Infirmary
Marlborough Street
Bristol
United Kingdom
BS2 8HQ
+44 (0)11 7928 2163
awolfbch@aol.com

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 05/515/01

Study information

Scientific Title
SLEEPS: Safety profiLe, Efficacy and Equivalence in Paediatric intensive care Sedation

Acronym
SLEEPS

Study objectives

Primary objective:
To determine whether intravenous clonidine can provide equivalent control of sedation in the critically ill child when compared to intravenous midazolam

Secondary objective:
To determine whether clonidine reduces side-effects and improves clinical outcomes due to its effects on reduction of sympathetic outflow, improved organ perfusion and protection in ischaemic reperfusion injury

More details can be found at http://www.nets.nihr.ac.uk/projects/hta/0551501
Protocol can be found at http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0019/51238/PRO-05-515-01.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval pending as of January 2007

Study design
Randomised double-blind parallel-group multi-centre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Quality of life

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

Health condition(s) or problem(s) studied
Children requiring intubation and ventilation for more than 48 hours

Interventions
Clonidine versus midazolam

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Clonidine, midazolam

Primary outcome measure

Adequate sedation defined as at least 80% of total time spent within a comfort score range of 17 to 26

Secondary outcome measures

Current secondary outcome measures as of 09/05/2008:
During study treatment phase:
1. Time to reach the maximum permitted dose of sedation
2. Time to reach the maximum permitted dose of morphine
3. Profile in rise of daily cumulative sedative infusion
4. Profile in rise of daily cumulative morphine infusion
5. Maximum permitted dose of sedative reached
6. Maximum permitted dose of morphine reached
7. Fall in blood pressure judged by clinician to require intervention
8. Increased inotropic support required in 1st 12 hours after randomisation
9. Supplementary analgesia required during sedation
10. Daily urine output
11. Treatment failure defined as inadequate sedation after one hour of maximum doses of sedative and morphine infusions (determined by a COMFORT score above 26)
12. Urinary concentration of gamma glutamyl transpeptidase (Bristol only)
13. Urinary concentration of alkaline phosphatase (Bristol only)

Following study treatment phase:
14. Time from stopping all sedation to being fully awake (recorded by COMFORT score as sustained* values of 22 or more).
15. Rebound hypertension
16. Signs of withdrawal measured using a 11 point assessment for abnormal behaviour
17. Withdrawal symptoms requiring clinical intervention

* Sustained for 2 hours or more.

Throughout the duration of study:
18. Adverse events

Health economics:
19. Cost per additional case of adequate sedation

Previous secondary outcome measures:
1. Treatment failure defined as 3rd hour sedation judged to still be inadequate (determined by a comfort score outside the range 17 to 26)
2. Adverse events
3. Maximum dose of morphine administered
4. Time to reach maximum dose of morphine
5. Maximum sedation infusion rate reached
6. Time to reach maximum dose of sedation
7. Time to recovery, defined as time from stopping all sedation to being fully awake (recorded by COMFORT score as sustained values of 22 or more).
8. Renal function (evaluated with urinary concentration of gamma glutamyl transpeptidase and

alkaline phosphatase in addition to usual measurements)
9. Rebound hypertension
10. Signs of withdrawal measured using a 15 point assessment for abnormal behaviour

Overall study start date
01/05/2009

Completion date
31/08/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 09/05/2008:
1. Children aged 30 days (37 weeks gestation or greater) to 15 years inclusive
2. Admitted to Paedatric Intensive Care Unit (PICU) and likely to require intubation and ventilation for more than 48 hours
3. Recruitment within 48 hours of arrival in PICU
4. Adequately sedated: COMFORT score within the range of greater than or equal to 17 and less than or equal to 26
5. Fully informed written proxy consent

Previous inclusion criteria:
1. Children aged 30 days to 16 years
2. Admitted to PICU and likely to require intubation and ventilation for more than 48 hours
3. Recruitment within 48 hours of arrival in PICU

Participant type(s)
Patient

Age group
Child

Lower age limit
30 Days

Upper age limit
15 Years

Sex
Both

Target number of participants
1000

Key exclusion criteria
Current exclusion criteria as of 09/05/2008:
1. Those patients with open chests following cardiac surgery
2. Those patients chronically treated for raised blood pressure
3. Current treatment with beta blockers

4. Acute traumatic brain injury
5. Those patients requiring haemodialysis
6. Those patients requiring ECMO treatment
7. Those patients with severe neuromuscular problems/impairment
8. Known allergy to either of the trial medications (clonidine, midazolam or morphine)
9. Current treatment with continuous or intermittent muscle relaxants
10. Those patients known to be pregnant
11. Currently participating in a conflicting clinical study or participation in a clinical study involving a medicinal product in the last three months

Previous exclusion criteria:
1. Those patients with open chests following cardiac surgery
2. Those patients chronically treated for raised blood pressure
3. Current treatment with beta blockers
4. Acute traumatic brain injury
5. Known allergy to either of the trial medications (clonidine, midazolam or morphine)
6. Current treatment with continuous or intermittent muscle relaxants

Date of first enrolment
01/05/2009

Date of final enrolment
31/08/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Royal Childrens Hospital
Bristol
United Kingdom
BS2 8HQ

Sponsor information

Organisation
United Bristol Healthcare NHS Trust (UK)

Sponsor details
Trust Headquarters
Marlborough Street
Bristol

England
United Kingdom
BS1 3NU
-
Mary.Perkins@ubht.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.ubht.nhs.uk/

ROR
https://ror.org/04nm1cv11

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

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	01/12/2014		Yes	No