

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

Submission date 24/01/2007	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 25/01/2007	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 17/05/2016	Condition category Other	☐ 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increasing tolerance and persistent distressing behavioural side effects in up to 20% of cases when the drug is withdrawn.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 Paediatric 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
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
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

Primary study design

Interventional

Study design

Randomised double-blind parallel-group multi-centre trial

Study type(s)

Quality of life

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(s)

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

Key secondary outcome(s)

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

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 Paediatric 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

Healthy volunteers allowed

No

Age group

Child

Lower age limit

30 Days

Upper age limit

15 Years

Sex

All

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

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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

United Kingdom

England

Study participating centre

Bristol Royal Childrens Hospital

Bristol

United Kingdom

BS2 8HQ

Sponsor information

Organisation

United Bristol Healthcare NHS Trust (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, Health Technology Assessment (HTA), HTA

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2014		Yes	No