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# The use of melatonin in children with neuro-developmental disorders and impaired sleep; a randomised, double-blind, placebo-controlled, parallel study

**Submission date**
23/01/2007

**Recruitment status**
No longer recruiting

**Registration date**
26/01/2007

**Overall study status**
Completed

**Last Edited**
12/07/2016

**Condition category**
Nervous System Diseases

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

## Plain English summary of protocol

Background and study aims
The management of sleep problems in children with learning difficulties is often less than ideal because the drugs used have unwanted side-effects or behaviour management is very difficult to arrange. Melatonin is a drug which may improve sleep in these children and it seems to have far fewer side-effects than the other drugs used. The aim of this study is to find out how effective and safe melatonin is at improving night-time sleep in children with developmental or learning difficulties.

Who can participate?
Children aged 3 to 15 with developmental or learning difficulties and sleep problems

What does the study involve?
Participants are randomly allocated to receive either melatonin or an inactive treatment (called a 'placebo' or 'dummy'). The study looks at two main outcomes. These are total night-time sleep and the time taken to fall asleep. The study also measures how many times the children wake up during the night. These outcomes are measured using nightly sleep diaries, a simple device worn at the wrist (like a watch), and questionnaires. Some questionnaires are also used to assess quality of life in the children and their families.

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

Where is the study run from?
Alder Hey Children's NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
May 2007 to November 2010

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

Who is the main contact?
Dr Richard Appleton
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# Contact information

### Type(s)
Scientific

### Contact name
Dr Richard Appleton

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# Additional identifiers

### Clinical Trials Information System (CTIS)
2006-004025-28

### Protocol serial number
HTA 05/14/02

# Study information

### Scientific Title
The use of MElatonin in children with Neuro-developmental Disorders and impaired Sleep; a randomised, double-blind, placebo-controlled, parallel study

### Acronym
MENDS

### Study objectives
Current information as of 08/06/10:
Compared with placebo, melatonin treatment will increase total sleep duration.

Initial information at time of registration:
Compared with placebo, melatonin treatment will reduce sleep latency and increase total sleep duration.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/051402
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0015/51162/PRO-05-14-02.pdf

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
North West MREC, 26/05/2007, ref: 07/MRE08/43

## Study design
Randomised double-blind placebo-controlled parallel study

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Neuro-developmental disorders

## Interventions
4 week run in period with sleep hygiene intervention, followed by treatment with either melatonin or placebo.

At the end of 4 weeks (T0), assuming the child continues to fulfil the entry criteria and further consent is provided, the child will be randomised into the study. Each child will be followed up for 12 weeks from date of randomisation, by a combination of home visits, telephone contact and clinic attendance. The active compound (melatonin) and placebo (matching in package and appearance) will be administered at the time that is appropriate to the childs usual bedtime; wherever possible, this time will remain the same throughout the study. The starting dose will be 0.5 mg and will increase every 7 days through 2 mg and 6 mg up to a maximum of 12 mg, depending upon the patients response to the preceding dose.

## Intervention Type
Drug

## Phase
Not Applicable

## Drug/device/biological/vaccine name(s)
Melatonin

## Primary outcome(s)
Current information as of 08/06/2010:
Total night-time sleep

Initial information at time of registration:
1. Total night-time sleep
2. Time to sleep onset (sleep latency)

## Key secondary outcome(s))

Current information as of 08/06/2010:
1. Total night time sleep calculated using actigraphy data
2. Sleep efficiency calculated by (number of minutes spent sleeping in bed/total number of minutes spent in bed) x 100
3. Composite sleep disturbance index scores
4. Daily global measure of parental perception of childs sleep quality
5. Behavioural problems assessed using Aberrant Behaviour Checklist (ABC)
6. Quality of Life of the parent assessed using the Family Impact Module of the PedsQL™
7. Level of daytime sleepiness in caregivers assessed using Epworth Sleepiness Scale
8. Number and severity of seizures evaluated using seizure diaries throughout trial follow-up
9. Adverse effects of melatonin treatment assessed weekly between weeks T0W to T12W using TESS (Treatment Emergent Signs and Symptoms)
10. Salivary melatonin concentrations
11. Associations between genetic variants and abnormal melatonin production
12. Sleep onset latency (the time taken to fall asleep) calculated using actigraphy
13. Sleep onset latency (the time taken to fall asleep) calculated using sleep diaries

Amended as of 28/04/2008:
1. Total night time sleep calculated using actigraphy data
2. Sleep efficiency calculated by (number of minutes spent sleeping in bed/total number of minutes spent in bed) x 100
3. Composite sleep disturbance index scores
4. Daily global measure of parental perception of childs sleep quality
5. Behavioural problems assessed using Aberrant Behaviour Checklist (ABC)
6. Attention and vigilance assessed in care-givers using the car game from the DENEM project
7. Attention and vigilance assessed in children using the Go/No go game from the MARS battery
8. Quality of Life of the parent assessed using the Family Impact Module of the PedsQL™
9. Level of daytime sleepiness in caregivers assessed using Epworth Sleepiness Scale
10. Number and severity of seizures evaluated using seizure diaries throughout trial follow-up
11. Adverse effects of melatonin treatment assessed weekly between weeks T0W to T12W using TESS (Treatment Emergent Signs and Symptoms)
12. Salivary melatonin concentrations
13. Associations between genetic variants and abnormal melatonin production

Initial information at time of registration:
1. Number and severity of seizures evaluated using seizure diaries throughout trial follow-up
2. Level of concentration and severity of learning difficulties and behaviour problems assessed using the Aberrant Behaviour Checklist (ABC)
3. Motor skills and memory assessed using electronic tests (DENEM project and MARS battery items) completed by care-givers and children
4. Quality of life of care-giver assessed using the Kidscreen-10 index and child assessed using the Family Impact Module of PedsQL™
5. Adverse effects of melatonin treatment assessed weekly between weeks T0 to T12W using TESS (Treatment Emergent Signs and Symptoms)
6. Salivary melatonin concentrations

### Completion date
30/11/2010

# Eligibility

### Key inclusion criteria
Current information as of 08/06/2010:
1. Children aged 3 years to 15 years 8 months at screening
All other inclusion criteria remain the unchanged.

Amended as of 29/04/2008:
1. Children aged 5 years to 15 years 8 months at screening
2. Diagnosis of a neuro-developmental disorder that has been made by a community paediatrician, paediatric neurologist or paediatric neurodisability consultant, categorised as:
2.1. Developmental delay alone
2.2. Developmental delay and epilepsy*
2.3. Developmental delay and autistic spectrum disorder* (ASD)
2.4. Developmental delay with other (other is defined as the child having a specific genetic /chromosomal disorder), or
2.5. Any combination of the above
3. Adaptive Behaviour Assessment System (ABAS) questionnaire score with a percentile rank below 7
4. Minimum 5 months history of impaired sleep at screening as defined by:
4.1. Not falling asleep within one hour of 'lights off' or 'snuggling down to sleep' at age-appropriate times for the child**, and/or:
4.2. Less than 6 hours of continuous sleep in three nights out of five
5. Children whose parents are likely to be able to use the actigraph and complete sleep diaries
6. Children who are able to comply with taking the study drug
7. English speaking
8. Children whose parents have completed sleep diaries for an average of 5 out of 7 nights at T0W.

* In coding the presence of epilepsy and ASD diagnoses, we will require sight of documentation from relevant services that demonstrate appropriate diagnostic assessments and investigations have been used

** This will be the child's usual bedtime (recorded in the sleep diary) based upon the familys normal routine

Initial information at time of registration:
1. Children aged 5 years to 15 years 11 months / < 16 years
2. Diagnosis of a neuro-developmental disorder that has been made by a community paediatrician, paediatric neurologist or paediatric neurodisability consultant, categorised as:
2.1. developmental delay alone
2.2. developmental delay and epilepsy*
2.3. developmental delay and Autistic Spectrum Disorder* (ASD)
2.4. developmental delay with other (other is defined as the child having a specific genetic /chromosomal disorder)
3. Vineland assessment score of at least 2 SD below the age standardised reference population mean
4. No plans to commence the following medication:

4.1. Any benzodiazapines
4.2. alimemazine tartrate
4.3. amisulpride (Solian)
4.4. chlorpromazine (Largactil)
4.5. haloperidol (Haldol)
4.6. olanzapine (Zyprexa)
4.7. risperidone (Risperdal)
4.8. sertindole (Serdolect)
4.9. sulpiride (Sulpidil, Sulpor)
4.10. thioridazine (Melleril)
4.11. trifluoperazine (Stelazine)
5. Diagnosis of impaired sleep as defined by:
5.1. not falling asleep within one hour of 'lights off' or 'snuggling down to sleep' at age-appropriate times for the child**, and/or:
5.2. less than 6 hours of continuous sleep in three nights out of five

* In coding the presence of epilepsy and ASD diagnoses, we will require sight of documentation from relevant services, that demonstrate appropriate diagnostic assessments and investigations have been used

** This will be the childs usual bedtime based upon the family's normal routine

## Participant type(s)
Patient

## Healthy volunteers allowed
No

## Age group
Child

## Lower age limit
3 years

## Upper age limit
15 years

## Sex
All

## Key exclusion criteria
Current information as of 08/06/2010:
2. Children who have been taking the following medication for less than 2 months:
2.1. Any benzodiazepines
2.2. Amisulpride (Solian)
2.3. Chlorpromazine (Largactil)
2.4. Haloperidol (Haldol)
2.5. Olanzapine (Zyprexa)
2.6. Risperidone (Risperdal)
2.7. Sertindole (Serdolect)
2.8. Sulpiride (Sulpidil, Sulpor)

2.9. Thioridazine (Melleril)
2.10. Trifluoperazine (Stelazine)
4. Current use of sedative or hypnotic drugs, including Choral hydrate, Triclofos, and alimemazine tartrate (Vallergan) (minimum of 14 days washout required)
All other exclusion criteria remain unchanged.

Amended as of 29/04/2008:
1. Children treated with melatonin within 5 months prior to screening
2. Any plans to commence the following medication:
2.1. Any benzodiazepines
2.2. Alimemazine tartrate (Vallergan)
2.3. Amisulpride (Solian)
2.4. Chlorpromazine (Largactil)
2.5. Haloperidol (Haldol)
2.6. Olanzapine (Zyprexa)
2.7. Risperidone (Risperdal)
2.8. Sertindole (Serdolect)
2.9. Sulpiride (Sulpidil, Sulpor)
2.10. Thioridazine (Melleril)
2.11. Trifluoperazine (Stelazine)
3. Current use of beta blockers (minimum of 7 days washout required)
4. Current use of sedative or hypnotic drugs, including Choral hydrate and Triclofos (minimum of 14 days washout required)
5. Children with a known allergy to melatonin
6. Regular consumption of alcohol (greater than 3 times per week)
7. Children for whom there are suggestive symptoms of Obstructive Sleep Apnoea Syndrome (OSAS) (such as combinations of snoring, gasping, excessive sweating or stopping breathing during sleep), physical signs supportive of OSAS (such as very large tonsils/very small chin), or results of investigations suggesting OSAS (such as overnight pulse oximetry or polysomnography) for which the child should be referred to appropriate respiratory or ENT colleagues for specific assessment and treatment
8. Girls or young women who are pregnant at the time of screening (T-4W)
9. Currently participating in a conflicting clinical study or participation in a clinical study involving a medicinal product within the last 3 months

Previous exclusion criteria:
1. Children treated with melatonin within 6 months prior to screening
2. Children whose parents are unlikely to be able to use the actiwatch or complete sleep diaries, or both
3. Children where there may be a problem with major non-concordance with medication
4. Girls or young women who are pregnant at the time of screening (4 weeks prior to randomisation)
5. Currently participating in a conflicting clinical study or participation in a clinical study involving a medicinal product within the last 30 days

## Date of first enrolment
01/05/2007

## Date of final enrolment
30/11/2010

# Locations

**Countries of recruitment**
United Kingdom

England

**Study participating centre**
**Alder Hey Children's NHS Foundation Trust**
Liverpool
United Kingdom
L12 2AP

# Sponsor information

**Organisation**
Alder Hey Children's NHS Foundation Trust (UK)

**ROR**
https://ror.org/00p18zw56

# 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 | 01/11/2012 | | Yes | No |
| Results article | results | 05/11/2012 | | Yes | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |