Melatonin for children with idiopathic chronic sleep onset insomnia, with or without attention deficit hyperkinesia disorder - A dosefinding trial.
A randomised placebo-controlled double-blind parallel group trial.

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Chronic sleep disorders are associated with dysfunctioning during the day. Circadian rhythm disorders are a frequently occurring cause of chronic sleep disorders. The time at which the endogenous melatonin production starts to rise plays a key-role...

Ethische beoordeling	Positief advies
Status	Werving tijdelijk gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON19948

Bron
NTR

Verkorte titel
MELDOS

Aandoening

Children with chronic sleep onset insomnia without or with ADHD.

Ondersteuning

Primaire sponsor: I.M. van Geijlswijk, ziekenhuisapotheker
Ziekenhuisapotheek Gelderse Vallei
Willy Brandtlaan 10
6716 RP Ede

0318-435693
geijlswijki@zgv.nl
Overige ondersteuning: Pharma Nord

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Actigraphic sleep onset and offset and melatonin onset (defined as the time at which 4 pg/ml melatonin in saliva is reached), diary lights-off time, sleep latency (latency between lights-off and sleep onset), sleep onset, sleep duration, sleep-offset and wake up time, behaviour and health status.

Toelichting onderzoek

Achtergrond van het onderzoek

Background:

Chronic sleep disorders are associated with dysfunctioning during the day. Circadian rhythm disorders are a frequently occurring cause of chronic sleep disorders. The time at which the endogenous melatonin production starts to rise plays a key-role in the synchronisation of circadian rhythms. In adults with sleep-wake rhythm disorders and late melatonin onset, exogenous melatonin, when administered at an appropriate time advances both endogenous melatonin onset and sleep-wake rhythm.
Pharmacokinetics and side effects of melatonin in children might differ from those in adults. Consequently it is necessary to study the effects of melatonin not only in adults but also in children.

Objectives:

The aim of the study is to establish a dose-effect relationship for the efficacy of melatonin treatment as to sleep-wake rhythm in children with chronic sleep onset insomnia without or with ADHD and to acquire information on the melatonin rhythm in these children, before and after treatment.

Study design:

After a baseline week the children receive melatonin 0,1 mg, 0,05 mg/kg, 0,1 mg/kg, 0,15 mg/kg or placebo at 19:00 h. during one week.

Primary outcome criteria:

In the baseline week and in the treatment week sleep is assessed with a diary and an actigraph (a motion-sensing device which is able to evaluate sleep-onset and offset). In the baseline week and during the first night after the treatment week, melatonin onset is measured during one night in saliva, produced hourly between 19:00 and 23:00. No medication is taken at the night at which saliva is produced for melatonin measurements. After the treatment week the study will be considered completed.

Study population:

Elementary school children between 6 and 12 yr., who fall asleep at least one hour later than healthy children of the same age, during more than 4 nights a week during more than 6 months before start of the trial, some fulfilling the DSM-IV-R criteria of ADHD. The insomnia does not improve with sleep-hygiene improving measures.

Number of children to be included. A total of 150 children will be included; 30 per dosing-step.

Inclusion criteria:

1. At inclusion physical examination, medial history and inclusion/exclusion assessments will be performed. The results of a hypnogram, performed within the past two months, showing a normal sleep architecture has to be known at inclusion;

2. The children and their parents have to be motivated to comply the study protocol.

Exclusion criteria:

1. Child-psychiatric or family problems who can explain the sleep onset insomnia;

2. Disturbed sleeparchitecture (hypnogram);

3. Use of MAO inhibitors;

4. Children with known disturbed hepatic or renal function;

5. Patients with the Roter syndrome;

6. Patients with the Dubin-Johnson syndrome;

7. Factors or diseases which can, according to the investigator, inhibit participation to the study;

8. Medical, environmental, psychiatric or other factors, which can cause sleep onset insomnia during the trial;

9. Participation in a study on the efficacy of drugs in the month preceding the inclusion;

10. Mental retardation (IQ<80);

11. Any prior use of melatonin;

12. Use of hypnotics, antidepressants or neuroleptics;

13. Chronic pain;

14. Severe neurological or psychiatric disorder.

Treatment allocation:

By preset randomisation list, patients are randomised in blocks of ten to keep possible time effects to a minimum. Because of the weight-depending dosing, the pharmacist calculates the appropriate dose, which is then prepared and dispensed by the hospital pharmacy.

Efficacy measures:

Primary: actigraphic sleep onset and offset and melatonin onset (defined as the time at which 4 pg/ml melatonin in saliva is reached), diary lights-off time, sleep latency (latency between lights-off time and sleep onset), sleep onset, sleep duration, sleep-offset and wake up time.

Secondary: side effects.

Power analysis:

Sample size calculation with the SPSS Sample power 2.0 program shows that 26 subjects in the melatonin treatment group and 26 subjects in the placebo treatment group are needed to find a significant (P <0.05; power 0.90; 1-tailed) advance (SD) of sleep onset of 67 min. (85 min) compared to an advance (SD) of 10(46) min in the placebo group (These data are based on the study described in appendix 7).

When 4 subjects have to be excluded in each treatment group 30 subjects can be considered to be enough to find a significant advance of sleep onset time.

Burden to the children:

The most important risk consists of the fact that long term effects of melatonin treatment in children have not been described. However animal and human studies of melatonin have shown that melatonin is not toxic. A few slight side effects (slight transient headache and a transient flu-like feeling) have been described. The burden of producing saliva for melatonin measurements and the actigraph registrations is minimal.

Doel van het onderzoek

Chronic sleep disorders are associated with dysfunctioning during the day. Circadian rhythm disorders are a frequently occurring cause of chronic sleep disorders. The time at which the endogenous melatonin production starts to rise plays a key-role in the synchronisation of circadian rhythms. In adults with sleep-wake rhythm disorders and late melatonin onset, exogenous melatonin, when administered at an appropriate time advances both endogenous melatonin onset and sleep-wake rhythm. Pharmacokinetics and side effects of melatonin in children might differ from those in adults. Consequently it is necessary to study the effects of melatonin not only in adults but also in children.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

The study lasts at 2 weeks. One baseline week, followed by 1 treatment week with melatonin 0,1 mg (commercially available OTC product), 0,05 mg/kg, 0,1 mg/kg, 0,15 mg/kg or placebo treatment.

Contactpersonen

Publiek

University Medical Center Utrecht (UMCU), Pharmacy of Faculty Animal Medicine
I.M. Geijlswijk, van
Ede 6716 RP
The Netherlands
+31 (0)30 2532066

Wetenschappelijk

University Medical Center Utrecht (UMCU), Pharmacy of Faculty Animal Medicine
I.M. Geijlswijk, van
Ede 6716 RP
The Netherlands
+31 (0)30 2532066

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. At inclusion physical examination, medial history and inclusion/exclusion assessments will be performed. The results of a hypnogram, performed within the past two months, showing a normal sleep architecture has to be known at inclusion;

2. The children and their parents have to be motivated to comply the study protocol.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Child-psychiatric or family problems who can explain the sleep onset insomnia;

2. Disturbed sleeparchitecture (hypnogram);

3. Use of MAO inhibitors;

4. Children with known disturbed hepatic or renal function;

5. Patients with the Roter syndrome;

6. Patients with the Dubin-Johnson syndrome;

7. Factors or diseases which can, according to the investigator, inhibit participation to the study;

8. Medical, environmental, psychiatric or other factors, which can cause sleep onset insomnia during the trial;

9. Participation in a study on the efficacy of drugs in the month preceding the inclusion;

10. Mental retardation (IQ<80);

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12. Use of hypnotics, antidepressants or neuroleptics;

13. Chronic pain;

14. Severe neurological or psychiatric disorder.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving tijdelijk gestopt
(Verwachte) startdatum:	01-05-2004
Aantal proefpersonen:	150
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	05-09-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL164
NTR-old	NTR200
Ander register	: MELDOS, VERSIE 2.0
ISRCTN	ISRCTN20033346

Resultaten

Samenvatting resultaten
N/A