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Melatonin for nocturia in multiple sclerosis (MS)

Submission date
04/04/2013

Recruitment status
No longer recruiting

Registration date
04/04/2013

Overall study status
Completed

Last Edited
08/08/2018

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Nocturia is a condition that means getting up at night one or more times to pass urine. The bladder is controlled via the brain, spinal cord, and nerves. Therefore, many neurological conditions can also have an effect on bladder function. This can occur in multiple sclerosis, and this can lead to symptoms of frequent urination as well as nocturia. It is a common condition in both men and women and this can have a significant impact on quality of sleep and quality of life. The aim of this study is to investigate the effect of melatonin on nocturia in adults with progressive multiple sclerosis. In multiple sclerosis urinary symptoms are common, including nocturia. Melatonin is a naturally occurring hormone in humans which regulates the normal circadian cycles (the natural pattern of physical and behavioral processes) in each 24-hour period. Melatonin seems to help sleep and control the timing of the sleep period. It is possible that nocturia may be a sign of impaired circadian regulation. In this instance, taking melatonin as a sustained-release tablet may improve nocturia, sleep quality and quality of life in patients with multiple sclerosis.

Who can participate?
Patients aged 18 to 80 with multiple sclerosis and nocturia

What does the study involve?
Participants are asked to attend the clinic for a screening visit (Visit 1) to see if they are suitable to take part in the study. If they are suitable to take part they come back for regular visits to check their progress in the study. It is a crossover study, which means that participants are randomly allocated to receive either melatonin or placebo (dummy drug) in the first treatment period, and in the second treatment period they receive the opposite of they were given (either melatonin or placebo) in the first treatment period. The two treatment periods last 6 weeks each and are separated by a break of 1 month. The number of nocturia episodes per night are measured at the start of the study and at the end of each treatment period. After the second treatment period, participants can continue to take melatonin for 1 year. Participants are interviewed to assess the impact of nocturia on their quality of life.

What are the possible benefits and risks of participating?
Melatonin may reduce how often people with multiple sclerosis have to pass urine during the night, and therefore may reduce urinary symptoms and fatigue, and improve overall quality of life. Melatonin appears to cause very few side effects in the short term, up to 3 months, when

healthy people take it at low doses like the dose used in this study. Unwanted effects in some people, especially at high doses, may include: headaches, nausea, next-day grogginess or irritability, hormone fluctuations, vivid dreams or nightmares, reduced blood flow, and hypothermia. While no large, long-term studies that might reveal side-effects have been conducted, there are reports about patients having taken melatonin for months without problems. Melatonin can cause somnolence (drowsiness), therefore, caution should be shown when driving, operating machinery, or drinking alcohol.

Where is the study run from?
Bristol Urological Institute (UK)

When is the study starting and how long is it expected to run for?
March 2013 to July 2017

Who is funding the study?
Multiple Sclerosis Society (UK)

Who is the main contact?
Prof. Marcus Drake
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2012-004183-21

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13586

Study information

Scientific Title
A randomised, double blind, placebo controlled, crossover trial of melatonin for treatment of nocturia in adults with multiple sclerosis

Study objectives
The aim of this study is to assess the effect of melatonin in patients with Multiple Sclerosis (MS).

Ethics approval required
Old ethics approval format

Ethics approval(s)
National southwest research ethics committee Exeter, 26/02/2014, ref: 12/SW/0322

Study design
Double-blind randomised placebo controlled crossover clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

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
Topic: Renal and Urogenital, Nocturia in adults with multiple sclerosis

Interventions
Sustained-release melatonin ('Circadin' 2mg taken at bedtime) versus placebo in patients with Multiple Sclerosis.

A run-in phase will be followed by two treatment phases (active drug or placebo) of 6 weeks each separated by a washout interval of 1 month. After the second treatment phase, patients will be entitled to participate in an open label, single-arm extension study of duration one year. Qualitative interviews will be undertaken with participants to assess the impact of nocturia on their quality of life.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Added 10/03/2017:
Nocturia episodes per night, measured from a frequency volume chart (FVC) at baseline and at the end of each treatment phase

Secondary outcome measures
Added 10/03/2017:
1. Quality of life, measured with the MS Quality of Life Index (MSQLI), at baseline and at the end of each treatment phase
2. MS disease severity, measured with the MS-specific Expanded Disability Status Scale (EDSS), at baseline and at the end of each treatment phase
3. Urinary tract symptoms, measured with the International Consultation on Incontinence Questionnaires (ICIQ) at baseline and at the end of each treatment phase. ICIQ-MLUTS and ICIQ-FLUTS are gender specific tools for assessing severity and bother of all LUTS
4. Volumes passed when urinating, measured from the FVC at baseline and at the end of each treatment phase
5. Sleep quality, measured with the Pittsburgh Sleep Quality Index (PSQI) at baseline and at the end of each treatment phase

Overall study start date
25/03/2013

Completion date
08/07/2017

Eligibility

Key inclusion criteria
1. Male and female over 18 years old, upper age limit 80 years
2. Confirmed neurological diagnosis of multiple sclerosis.
3. At least 1 episode of nocturia (as defined by International Continence Society criteria [6]) every night.
4. Female subjects of childbearing potential; willing to use an effective method of contraception throughout the study.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
UK Sample Size: 50

Key exclusion criteria
1. Under 18 years old
2. Pregnant patients
3. Symptomatic urinary infection
4. Indwelling urinary catheter
5. Use of desmopressin or investigational medical compounds in the month preceding randomisation
6. Antimuscarinic or diuretic medication, unless used longterm prior to study (at least 3 months) and continued at same dosing regime throughout the study
7. Use of melatonin on prescription, or purchased over the counter/online
8. Use of sleeping tablets on prescription, or purchased overt he counter/ online
9. Diabetes mellitus
10. Diabetes insipidus
11. Unwilling to give informed consent
12. Female subjects of childbearing potential; unwilling to use an effective method of contraception throughout the study

Date of first enrolment
25/03/2013

Date of final enrolment
01/04/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Urological Institute
Bristol
United Kingdom
BS10 5NB

Sponsor information

Organisation

North Bristol NHS Trust (UK)

Sponsor details
Trust Headquarters
Beckspool Road
Frenchay
Bristol
England
United Kingdom
B16 1JE

Sponsor type
Hospital/treatment centre

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

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Charity

Funder Name
Multiple Sclerosis Society (of Great Britain & Northern Ireland) (UK) Grant Codes: 959/11

Alternative Name(s)
Multiple Sclerosis Society of Great Britain and Northern Ireland, The MS Society, MS Society UK, Multiple Sclerosis Society UK, MS Society

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

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?
Protocol article	protocol	27/03/2017		Yes	No
Results article	results	06/08/2018		Yes	No
HRA research summary			28/06/2023	No	No