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Therapy-efficacy of a new mode of Automatic Servo-Ventilation in patients with complicated breathing patterns during sleep

Submission date
12/02/2010

Recruitment status
Stopped

Registration date
15/04/2010

Overall study status
Stopped

Last Edited
13/07/2016

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Among the field of sleep-related breathing disorders (SRBD), there are different kinds of impaired breathing during sleep with different underlying causes. The most common kind of SRDB is obstructive sleep apnea (OSA), in which the upper airways collapse during sleep, preventing air from reaching the lungs, leading to an oxygen shortage and a build-up of carbon dioxide. The body reacts with a short awakening, restoring normal breathing until the next such event. The most effective treatment is continuous positive airway pressure (CPAP). A CPAP device produces positive pressure, applied to the patient's upper airways via a nasal or full-face mask which is worn during sleep. The increase in air pressure within the upper airways keeps them open and enables normal breathing.
Sleep apnea patients with heart failure often exhibit a different kind of SRBD, which may or may not exist in parallel to OSA. This condition is referred to as Cheyne-Stokes respiration (CSR). In CSR, too much breathing (hyperventilation) alternates with pauses in breathing (apneas). Depending on severity, this can occur for just a few minutes during the night or even during the whole night. This breathing disorder, even with co-existing OSA, can be treated with a further development based on CPAP, called auto-servoventilation (ASV). ASV devices apply changing pressure levels for the patient depending on current demand, not only providing a basic pressure to keep the airways open but also adapting pressure levels for inhalation and exhalation separately based on a breath-by-breath analysis of the patient's breathing volume. The aim of this study is to compare three different ASV treatment modes in sleep apnea patients with heart failure. One treatment mode uses the long-established BiPAP autoSV device (ASV2). The other two modes use the next device generation, BiPAP autoSV advanced (ASV3), in which a feature called Bi-Flex was introduced, which aims to provide smoother, more comfortable changes of pressure levels for inhalation and exhalation. ASV3 is used with either Bi-Flex on or off, forming the other two modes of treatment.

Who can participate?
Heart failure patients with central sleep apnea, aged 40 to 80

What does the study involve?
Participants use the three ASV treatment modes in a randomly allocated order during consecutive nights in the study center's sleep lab. During these nights, sleep stages, breathing and other parameters are recorded. After these three treatment nights, the participants return home with the device and treatment mode they used during the last night. They then use the device at home every night and return to the study center after 1 month. At that time, we readout data from the device and ask patients about side effects, sleepiness and their quality of life using questionnaires. After 2 additional months of home use, the participants return to the sleep lab to undergo a final sleep study under treatment.

What are the possible benefits and risks of participating?
Possible benefits include more closely monitored treatment initiation and follow-up. Eligible patients for this study would normally (i.e. without participating in this study) be treated with the same or a similar device which is used in the study. For that reason, the possible risks of study participation essentially do not differ from routine clinical treatment.

Where is the study run from?
Wissenschaftliches Institut Bethanien eV (Germany)

When is the study starting and how long is it expected to run for?
January 2010 to January 2011

Who is funding the study?
Philips Respironics (France)

Who is the main contact?
Prof. Winfried Randerath

Contact information

Type(s)
Scientific

Contact name
Prof Winfried Randerath

Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EAME08ASV01

Study information

Scientific Title
Therapy-efficacy of a new mode of Automatic Servo-Ventilation in subjects with complicated breathing patterns during sleep: a multicentre randomised controlled trial

Acronym
ASV3

Study objectives
The new mode of Automatic Servo-Ventilation (Auto SV) with and without Bi-Flex® is as effective as the established mode of Auto SV in reducing respiratory events and arousals without adversely affecting sleep quality in subjects with heart failure and central sleep apnoea (CSA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. UK: South Birmingham Research Ethics Committee, 04/08/2009, ref: 09/H1207/119. Amendment 1 approved 29/12/2009
2. Germany: Ethik Commision der Univeritat Witten/Herdecke, 02/06/2009, ref: 110/2008. Amendment 1 approved 01/12/2009

Study design
Multicentre randomised controlled double-blind cross-over pilot study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Central sleep apnoea/heart failure

Interventions

Following an expiratory positive airway pressure (EPAP) determination study, subjects will be randomly assigned to one night of the new mode of Auto SV without Bi-Flex (ASV3 without Bi-Flex®), one night of the new mode with Bi-Flex® set at its maximum comfort level (ASV3 with Bi-Flex® set at 3) and one night of the established mode of Auto SV (ASV2) applied on consecutive nights in the sleep laboratory by the PSG technician under full PSG conditions. The first 2 hours of therapy (starting at lights out) will be spent at a sub-therapeutic pressure so that some breathing events are seen (EPAP = 4 cm H2O; IPAPmin/IPAPmax = EPAP). These studies will be performed within 14 days of the EPAP determination study. There will be a fixed follow-up period of 3 months.

Intervention Type
Device

Primary outcome measure
Variables investigated will include:
1. AHI (total, rapid eye movement [REM] and non-rapid eye movement [NREM]) - total, obstructive, central, and mixed (apnoea only) events (apnoea and hypopnoea)
2. Respiratory Disturbance Index (RDI): AHI plus respiratory effort related arousals (RERAs)
3. Cheyne-Stokes Respiration (CSR) Index - total
4. Arousal Index - total, respiratory, RERA and movement related
5. Sleep latency
6. Total sleep time
7. Wake, stages N1, N2, N3 and R sleep (% total sleep time [TST])
8. Wake, stages N1, N2, N3 and R sleep (in minutes)
9. REM latency
10. Number of REM periods
11. Mean REM interval
12. Mean pressure profile (EPAP, minimum inspiratory positive airway pressure [IPAPmin], maximum inspiratory positive airway pressure [IPAPmax])
13. Leak profile

All outcomes will be measured during each of the 3 therapy nights and on waking the following morning.

Secondary outcome measures
1. Comfort will be improved on the new mode of Auto SV and further improved when Bi-Flex® is activated
2. Subjects will rank the new mode of Auto SV higher than the established mode in terms of preference and the new mode of Auto SV highest when Bi-Flex® is activated
3. The breathing event output from the new mode of Auto SV will result in an AHI (total) that is in diagnostic agreement with the apnoea-hypopnoea index obtained from a full clinical PSG
All outcomes will be measured during each of the 3 therapy nights and on waking the following morning.

Overall study start date
24/01/2010

Completion date
20/06/2013

Reason abandoned (if study stopped)

Participant recruitment issue

Eligibility

Key inclusion criteria
1. Apnoea Hypopnoea Index (AHI) greater than 15 (greater than 50% central events including central hypopnoeas) confirmed by full polysomnography (PSG) within last 14 days
2. Heart failure due to ischaemic, non-ischaemic or hypertensive cardiomyopathy (New York Heart Association [NYHA] Class II or III)
3. Aged greater than or equal to 40 - less than or equal to 80 years, either sex
4. Objectively impaired left ventricular ejection fraction greater than or equal to 40%, assessed by echocardiography
5. Stable clinical status and stable optimal medical therapy according to the guidelines of the European Society of Cardiology for at least 4 weeks (www.escardio.org/knowledge/guidelines)
6. Able to provide consent
7. Able to follow the study protocol

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
36

Key exclusion criteria
1. Positive airway pressure (PAP) therapy is otherwise medically contraindicated
2. Acute upper respiratory infection, encephalitis, sinusitis or middle ear infection or surgery of the upper airway, nose, sinus, or middle ear within the previous 90 days
3. Drug abuse (both acute and chronic) according to the Drug Abuse Screening Test (DAST) criteria
4. Alcohol abuse (both acute and chronic) according to the CAGE criteria
5. Intake of opiods or central relevant drugs, sedatives, or other drugs which impair sleep
6. Psychiatric or neurological diseases resulting in impairment of sleep, therapy or compliance
7. Thyroidal dysfunction
8. Any chronic pain syndrome
9. Acute pulmonary, and other internal diseases
10. Chronic pulmonary and other internal diseases resulting in impairment of sleep
11. Untreated, non-obstructive sleep apnoea (OSA)/CSA sleep disorders, including but not limited to; insomnia, periodic leg movements (PLM)/restless legs syndrome (RLS)
12. Previous exposure to positive airways pressure, bi-level or Auto SV therapy
13. Acute dermatitis or other skin lesions or trauma interfering with the application of a mask
14. Unwilling to participate in the study
15. Participation in another clinical study in the past 4 weeks

Date of first enrolment
24/01/2010

Date of final enrolment
20/06/2013

Locations

Countries of recruitment
England

Germany

United Kingdom

Study participating centre
Wissenschaftliches Institut Bethanien eV
Solingen
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42699

Study participating centre
Birmingham Heartland Hospital
Sleep and Ventilation Unit
Department of Respiratory Medicine
Bordesley Green East
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United Kingdom
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Study participating centre
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Leitung Schlaflabor Pneumologie
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Hagen
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Sponsor information

Organisation
Philips Respironics (France)

Sponsor details

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Sponsor type
Industry

Website
http://www.respironics.com

ROR
https://ror.org/05jz46060

Funder(s)

Funder type
Industry

Funder Name
Philips Respironics (France)

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available