Treatment of central sleep apnoea and Cheyne Stokes respiration in patients with heart failure: nasal high-flow oxygen therapy?

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON47575

Source
ToetsingOnline

Brief title
Nasal high flow in heart failure patients with CSAS

Condition

- Heart failures
- Respiratory disorders NEC

Synonym
central sleep apnoea; sleep disorders breathing

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Klinerva B.V. h/o Eurocept Homecare

Intervention

Keyword: Central Sleep Apnea, Heart failure, High Flow Therapy

Outcome measures

Primary outcome

The aim of this study is to investigate whether patients with CHF and CSA would benefit from nHFT with and without oxygen in terms of an improved AHI during sleep while on nHFT, measured after 4 weeks of home nHFT treatment, as compared to the baseline AHI during spontaneous nocturnal breathing.

Secondary outcome

Secondary outcomes are:

• change in oxygen desaturation index (ODI) during sleep while on nHFT, measured after 4 weeks of home nHFT treatment, as compared to the baseline ODI during spontaneous nocturnal breathing.

• sleep quality, assessed by polysomnography, after 4 weeks of home nHFT treatment compared to baseline.

• exercise tolerance, measured with the 6-minute walking test, after 4 weeks of home nHFT treatment compared to baseline.

• Symptoms of sleepiness, assessed by validated questionnaires, after 4 weeks of home nHFT treatment compared to baseline.

• Cardiac functioning; LVEF, heart rate variability and N-terminal natriuretic peptide (NTproBNP), after 4 weeks of home nHFT treatment compared to baseline.

• Compliance with the nHFT

Furthermore, with a titration night at baseline, we will investigate mechanisms of action and optimal settings of nHFT in this group of patients. We will investigate effects of different flow rates and oxygen percentage on the pressures in the circuit and in the pharynx. As this pressure is expected to have effects on the breathing drive and the work of breathing, we will also investigate these parameters with the use of surface electromyography (EMG) and transdiaphragmatic pressure measurements.

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Study description

Background summary

Chronic heart failure (CHF) is a common health problem affecting 38 million people worldwide. The treatment of heart failure is in general aimed at reducing dyspnoea but is it is often overlooked that up to 62% of the patients with heart failure have some moderate to severe sleep disordered breathing (SDB). SDB leads to serious health complaints and worsens clinical outcomes and may even be an antecedent risk factor for the development of overt heart failure.
The 2 most common patterns of SDB are obstructive sleep apnoea (OSA) or central sleep apnoea (CSA). In patients with heart failure, both may occur.
Furthermore, especially patients with severe CHF may exhibit a special form of CSA with relative long cyclic episodes of crescendo/decrescendo respiration, called Cheyne Stokes respiration (CSR).
Treatment of SDB in patient with heart failure is challenging. OSA is, in general, adequately treated with a treatment that maintains upper airway patency. The pathophysiological mechanisms and treatment of CSA/CSR, however, are more complex. Hypocapnia, increased chemosensitivity, an higher apnoea threshold, and a circulatory delay all contribute to ventilatory instability and CSA/CSR in patients with heart failure.7
The goal of CSA treatment is to stabilise ventilation. Several treatment options, ranging from pharmacological treatment with acetazolamide to nocturnal

oxygen therapy (NOT) and positive airway pressure therapies as continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) or adaptive servo ventilation (ASV)) have been investigated, but interpretation of the results of the studies is difficult to draw as these studies were small, short-term and/or showed conflicting results in terms of improvement in clinical outcomes. Secondly, to be even more cautions, some therapies might even harm. In patients with a reduced left ventricular ejection fraction, ASV therapy decreased the AHI index but increased mortality.16 It was suggested that application of inspiratory and expiratory pressure levels, thereby increasing intrathoracic pressure, might be harmful for an already diseased heart.Furthermore, it was hypothesized that CSR is some sort of protective mechanism in CHF patients.16 This suggests that a therapy probably should not focus on total abandonment of CSR. Furthermore, the effects of CPAP and or non-invasive ventilation or often hampered by a limited compliance with the therapy. Overall, the optimal treatment of patients with CHF and CSA is currently unknown.
Nasal high-flow therapy (nHFT) is the application of humidified heated high-flow air, with or without the mixture with additional oxygen, through a nasal catheter. This therapy combines the positive effects of a certain level of continuous positive pharyngeal/airway pressure with application of additional oxygen. We hypothesise that nHFT results into enough positive airway pressure to maintain upper airway patency, to reduce pulmonary oedema because of positive alveolar pressure, and to reduce left ventricular afterload. On the other hand, the positive pressure achieved with nHFT is in comparison with CPAP levels much lower and therefore a reduction in cardiac output because of high intrathoracic pressure is not expected to occur. NOT has been hypothesized to dampen the ventilatory overshooting characteristic of CSA due to a reduction in peripheral chemosensitivity and may positively affect the heart as (deep) repetitive oxygen desaturations are prevented. So, combining both modalities with NFT might be beneficial. However, despite these theoretical potential positive effects, however, nHFT may also promote hyperventilation due to the high flow of air and thereby promote ventilatory instability.
A second advantage of nHFT that might be of importance is that compliance rates of this therapy are shown to be very promising, as the nasal pillows of this system are more comfortable compared to wearing a mask.CPAP results have been shown to be limited because compliance rates were low. In this respect, the mean disease alleviation, which is the product of therapeutic efficacy and adjusted compliance expressed as percentage, might be better with nHFT and might be of importance in affecting clinical outcomes.
To summarize, the effects of nHFT on CSA are unknown.
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Study objective

The aim of the present pilot study is to investigate whether nHFT of different settings (with different flow rates and additional amounts of oxygen) stabilizes respiration and thus improves AHI index and promotes compliance

with the therapy in patients with known heart failure and CSA/CSR.

Study design

The study is a one-arm intervention pilot study, exploring the effects of 4-weeks home nHFT in 10 patients with CHF and CSA.

Intervention

High Flow Therapy which is the application of humidified heated high-flow air, with or without the mixture with additional oxygen, through a nasal catheter. This therapy combines the positive effects of a certain level of continuous positive pharyngeal/airway pressure with application of additional oxygen.

Study burden and risks

Initiation of nHFT is considered as safe for several reasons. First, no serious side effects of this therapy have been described in prior studies, although in different, but also frail, patient groups. Secondly, patients are initiated on the HFT during a titration night under direct supervision of the principle researcher, which is a nurse specialist in the home mechanical ventilation center in Groningen specialized on the treatment of patients with sleep apnea. When there are problems with the nHFT, the patients can consult the principle researcher and changes could immediately be made in the settings after evaluation. For safety reasons, we will decide not to continue nHFt once during the titration night AHI increases by more than 50%, regardless of the setting applied.
Thirdly, patients with heart failure and CSA are not dependent of the therapy for 24 hours. Although we advise to use the nHFT during the night, it is safe to discontinue the therapy as long and often as they want to. Thereby, we carefully take care that patients are able to remove the nasal catheter any time when they are left alone with the high-flow device. Since it is easy to remove the nasal catheter and patients with heart failure have adequate hand functioning, we believe that patients are able to stop the therapy any moment he/she wants. Therefore, we expect that the use of nHFT will be utmost safe.
Finally, the only invasive measurement that we will include are the measurement of transdiaphragamtic pressure with the balloon catheters. These measurements give some discomfort but are shown to be save in several patient groups. All other measurements are noninvasive.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Moderate to severe central sleep apnoea (CSA)/Cheyne Stokes respiration (apnoea/hypopnoea index>15), in which CSA is defined when at least 50% of the apnoea*s are central apnoea*s
• Heart failure diagnosed by cardiologist

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Other diseases affecting respiration during sleep (COPD GOLD 3 or 4, neuromuscular disorders, thorax cage deformities)
• At the moment of the inclusion, the patient does not have a therapy to treat the CSA, such as CPAP, oxygen, BiPAP or acetazolamide.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-08-2017
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Nasal high flow therapy
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	26-07-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL61187.042.17
Other	UMCG trial register 201700147