Treatment of chronic Respiratory failure in COPD patients with non-invasive ventilation: starting at home and selecting the right patient

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Primary Objective: The aim of the present study is to investigate whether home initiation of chronic NIV in stable COPD patients with CHRF is non-inferior to inpatient initiation Secondary Objective(s): The secondary objective of the study is to…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON43384

Source
ToetsingOnline

Brief title
Initiation of long-term non-invasive ventilation in COPD.

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Lung emphysema

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Longfonds;projectnummer 5.2.15.057JO,Respironics Inc., Murrysville, PA, USA

Intervention

Keyword: Chronic Obstructive Pulmonary Disease, Home initiation, Non-invasive ventilation, Patient selection

Outcome measures

Primary outcome

Non-inferiority of home initiation of NIV will be assesed in terms of

improvement in PaCO2 (at daytime without NIV or additional oxygen) after 6

months.

Secondary outcome

Secondary outcomes are change in lung function (forced expiratory volume in 1

second (FEV1), lung volumes (total lung capacity (TLC), residual volume (RV)

and RV%TLC), and diffusion capacity (DLCO (%predicted)), change in HRQoL,

compliance, exercise tolerance and costs including cost-effectiveness analyses

Study description

Background summary

COPD is a chronic disease with high mortality and morbidity worldwide. Patients with end-stage COPD frequently develop CHRF associated with end-of-life. In that stage of disease, treatment options are limited.
Long-term nocturnal NIV has been applied in patients with chronic alveolar hypoventilation for decades. While there is no doubt that applying chronic nocturnal NIV improves outcomes in patients with restrictive and neuromuscular diseases, the evidence in COPD patients has long been controversial.
At the HMV centre Groningen, the majority of patients treated with NIV therefore still concerns patients with neuromuscular diseases.
Initial trials investigating chronic NIV in COPD showed no relevant benefits, neither in terms of improvement in gas exchange nor in improvements in patient-centred outcomes as HRQoL. However, most of these trials used low

inspiratory pressures so that improvement of alveolar hypoventilation was not or only partially achieved. Consequently, little improvement in clinical outcomes could be expected.
More than 10 years ago, the concept of high-intensity NIV in COPD was introduced. By applying higher inspiratory pressures and breathing frequencies aimed at a more controlled form of ventilation and improvement in gas exchange, clinically relevant improvements in HRQoL and lung function were observed, without undue loss of patient comfort. Recently, a German group conclusively showed that high-intensity NIV improves survival in severe COPD patients with CHRF. These positive results with high-intensity NIV have changed our view towards the use of chronic NIV in stable COPD. Nowadays, we believe that the evidence for long-term nocturnal NIV is convincing and justifies the application of this therapy in patients with severe stable COPD patients with CHRF. Nevertheless, for a broader implementation of this treatment in a potentially large group of severe COPD patients, important issues have to be solved.

First, we need to reconsider the current inpatient NIV initiation process, which despite tight titration based on arterial blood gases, does not always lead to good patient compliance, is inconvenient for patients and is expensive. While it might be thought that high-intensity NIV necessitates inpatient titration to gain adequate reversal of hypoventilation, different in hospital set ups of NIV initiation (on a general ward, medium care unit or on an intensive care unit), with different ways of titration (guided by transcutaneous carbon dioxide (PtCO2) or arterial blood gases (PaCO2)), have not resulted in different outcomes or a different compliance at the long-term. Also, these inpatient options are expensive as initiation of NIV in COPD routinely requires 5-14 days. Recently, our group of the HMV centre Groningen has shown that, in patients with neuromuscular and restrictive thoracic diseases, initiation of NIV can safely be performed at home. Initiation of NIV at home was preferred by the patients, was equally effective and saved costs compared to inpatient initiation. Importantly, COPD patients have been excluded in this randomised controlled trial (RCT), as at the start of that study chronic NIV in COPD was not considered a regular standard treatment option in the Netherlands. Furthermore, initiation of NIV in COPD patients at that time was thought to be probably too difficult to be performed at home, because high-intensity NIV is needed in this patient group to improve outcomes. However, challenges with the initiation of high-intensity NIV require attention, but do not necessarily have to be solved in-hospital. On the one hand, patients with COPD need higher inspiratory pressures and higher backup breathing frequencies as it is more difficult to correct alveolar hypoventilation in lung parenchyma diseases compared to diseases in which the lungs are not primarily affected, such as in neuromuscular disease. On the other hand, we believe that careful high-intensity NIV initiation and titration should not only focus on maximal improvement in PaCO2 but also on patient comfort. The consequence of high-intensity might be that COPD patients need even more time and attention from caregivers to get used to the high pressures

and high backup frequencies before our target can be reached, i.e. improvement in gas exchange and respiratory muscle unloading, before the conditions also for a good long-term compliance can be satisfied.
Finding the individual high-intensity setting leading to sufficient improvement in objective physiological parameters is challenging in this group of patients. This process therefore probably requires more frequent and more intensive monitoring. At home, we will optimise monitoring of the patients with the use of frequent non-invasive monitoring of gas exchange with transcutaneous measurements (SenTec DM®, Software V-STATS 4.0; SenTec AG; Therwil, Switzerland). Secondly, analysis of data read from the ventilator software (Respironics A30 or A40®, Philips, the Netherlands) will be used to provide information about compliance and the actual provided ventilation. Finally, we will aid measurements of respiratory muscle activity by means of surface electromyography (EMG) as a relatively new tool which can aid in optimising NIV initiation.17-18 Surface EMG is a new tool that might help to optimise NIV initiation. It has been shown that especially high-intensity NIV is able to unload the respiratory muscles (Duiverman, work in progress). This might importantly add to the achievement of clinical relevant benefits. Until now, no studies have used non-invasive measurements of respiratory muscle unloading to optimise initiation of NIV. In the last decade, I have developed and validated a surface EMG technique for use in COPD patients, measuring respiratory muscle activity as a surrogate of respiratory neural drive and thus muscle loading. As this method is non-invasive, it can easily be applied at home. Furthermore, surface EMG can be used to asses patient-ventilator asynchrony (PVA). Especially with higher inspiratory pressures and/or high breathing frequencies PVA may arise. PVA is important as it leads to increased work of breathing, decreased patient comfort and less effective ventilation. During the traditional in-hospital NIV initiation, one might suggest that an indication of respiratory muscle (un)loading and patient-ventilator synchrony is received through observation of the patient. However, observation by the respiratory nurses is mostly of limited time and detects only events leading to a huge excess of respiratory muscle loading, such as during severe PVA. During home initiation, direct observation is far less easy and less frequent. In concordance with a recent study showing that parasternal EMG can be used to assess PVA in a mixed group of patients initiated on home NIV,20 we have shown in a recent pilot project that also our surface EMG is feasible to measure respiratory muscle unloading and detect PVA, of note, during different settings, also high-intensity NIV (submitted work). As the use of surface EMG for optimising NIV initiation is relatively new, we will extend the monitoring of patients in both groups including surface EMG as a surrogate marker of respiratory muscle unloading and to detect PVA during NIV.
For the second issue, the necessity for acclimatisation time and caregiver attention, very elegant solutions are available to provide this at home too. A longer initiation period can better be met at home, in a trusted environment for the patient, saving the disadvantages and costs of a prolonged hospital stay. With modern technologies the necessary caregiver attention can also be provided at home. Monitoring data can be sent to caregivers on daily basis by

telemonitoring. This proven technology enables caregivers to make on daily basis, on distance, decisions regarding the NIV initiation process, which will be discussed with the patient by frequent telephone calls. This so called telemedicine has already been shown to be a valuable and promising tool to monitor and to adjust treatment of patients already established on chronic NIV at home. In our home NIV initiation pilot project in neuromuscular patients, we were the first to show in a RCT that this technology was very feasible to use for NIV initiation at home.

The second important issue to be solved regards better patient selection. By collecting the baseline and follow-up data of the COPD patients initiated on NIV, we aim to find predictors of a favourable response to NIV. We know, from clinical practice and from studies, that not all patients respond favourably. Until now, data have shown that patients with CHRF benefit Furthermore, benefits at least in terms of improvement in gas exchange, seem to be more prominent in patients with severe stable hypercapnia. In contrast, our group has shown that patients that remain hypercapnic after an exacerbation do not uniformly benefit.23 An individual COPD phenotype benefiting most from this demanding therapy has not been identified.

Study objective

Primary Objective:
The aim of the present study is to investigate whether home initiation of chronic NIV in stable COPD patients with CHRF is non-inferior to inpatient initiation

Secondary Objective(s):
The secondary objective of the study is to collect patient demographics (age, weight, height, social status, HRQoL, anxiety and depression scores, data on comorbidities and medication use), respiratory function (lung function as well as measures of respiratory muscle activity, arterial blood gases), and inflammatory blood markers, in order to analyse how differences in baseline parameters are related to changes in HRQoL after 6 months.

Study design

A 1:1 randomised controlled trial of non-inferiority design with minimisation for rehabilitation status will be employed in order to test the hypothesis that home initiation of chronic NIV is not inferior to inpatient initiation in COPD patients with CHRF. Outcomes will be assessed after 3 and 6 months.

Additionally, from this cohort of patients, data will be collected in a prospective manner in order to predict the response to NIV in terms of improvement in HRQoL after 6 months of treatment

Intervention

Home initiation of long-term non-invasive ventilation in COPD patients with CHRF

Study burden and risks

Home NIV is regarded extremely safe in our patient group as these patients are not 24-hour ventilator dependent, and with adequate hand function can always switch off the machine and remove the mask once technical issues occur. For a safe home initiation, as investigated in this study, we consider patient eligible once they fulfil the same criteria as used currently for home application of NIV, namely that patients have adequate understanding of the machine and are capable of removing the mask. As so, we believe also initiation of NIV at home is extremely safe.
On the other hand, we believe the benefits of home initiation of NIV can be huge. NIV initiation which is currently performed during an hospital stay of 5-14 days which is very demanding for these end-stage COPD patients with severe disabilities. Furthermore, for the home initiation group more noninvasive monitoring possibilities will be used instead of invasive procedures, such as repeated sampling of arterial blood gases.

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

- Indication to initiate chronic NIV in COPD patients (GOLD stage III or IV: FEV1/ FVC< 70% and FEV1< 50% predicted; PaCO2 > 6.0 kPa in stable condition, which means no COPD exacerbation for 4 weeks and a pH > 7.35)
- Age > 18 years
- Existence of a sufficient social support network making initiation of HMV at home possible and safe.
- Written informed consent is obtained

Exclusion criteria

- Instable severe cardiac comorbidities (left ventricular ejection fraction below 45%, instable angina pectoris complaints)
- Patients admitted to a nursing home

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-06-2016
Enrollment:	62
Type:	Actual

Medical products/devices used

Generic name:	Non-invasive ventilation
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	11-04-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-12-2016
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	NL56412.042.16
Other	UMCG research register 201600008 en Clinical Trials.Gov