The use of heated humidified nasal high flow oxygen (NHF) in patients with COPD

John Fraser, Amy Spooner, Kimble Dunster, Chris Anstey, Amanda Corley

Background

Chronic obstructive pulmonary disease (COPD) is a leading cause of death worldwide [1]. In addition to generating high healthcare costs [2], COPD imposes a significant burden in terms of disability and impaired quality of life [3]. Unlike many leading causes of death and disability, COPD is projected to increase in much of the world as smoking frequencies rise and the population ages [4, 5].

Oxygen as a therapeutic agent was first introduced by Alvin Barach [6] in 1922 and since then it has become an important form of home therapy for hypoxic chronic obstructive pulmonary disease (COPD). Its use has increased dramatically over the last 20 years since two pivotal studies demonstrated improved survival in hypoxic COPD patients receiving continuous oxygen [7,8].

Domiciliary long term oxygen therapy (LTOT) is usually delivered via loose fitting nasal cannulae, which allow room air to be breathed around the cannula. This room air dilutes the oxygen, providing the inspired oxygen concentration required by the patient. The oxygen is neither warmed nor humidified and high flows of cold dry gas are uncomfortable and may lead to airway obstruction by thickened secretions.

An alternative therapy now available is a nasal high flow (NHF) of humidified air, which can be enriched with oxygen, and delivered at up to 60L/min by a comfortable nasal cannula (Airvo and Optiflow, Fisher & Paykel Healthcare, Auckland, NZ). NHF therapy has been successfully trialled in a long-term study in New Zealand on COPD patients [8] which showed a lowering of exacerbations, improved lung function and quality of life, and high compliance.

This randomised crossover observational study aims to assess the short term physiological respiratory changes caused by using NHF versus the currently used LTOT.

Aims

We aim to establish if NHF:

- reduces respiratory rate
- improves oxygenation
- improves subjective scoring of dyspnoea
- increases tidal volume and end expiratory lung volume

Study Population

Thirty male COPD patients attending the respiratory clinic of The Prince Charles Hospital. Patients will be selected by the respiratory physician in collaboration with the research nurse.

Inclusion Criteria

- Male COPD patients requiring home oxygen
- ≥18 years
- able to attend hospital for a 2.5-3 hour data collection period

Exclusion Criteria

- previous lung resections
- hemidiaphragm palsy
- active respiratory infection (diagnosed by treating physician)
- frequent purse-lip breathing or anxiousness using an alternate respiratory device

Withdrawal Criteria

- Anxiety during the study
- Oxygen saturation falling by more than 10% below baseline
- Transcutaneous carbon dioxide level rising by more than 50% above baseline
- Tachypnea more than 50% above baseline

Identification of patients and consent

In collaboration with the respiratory physician, the research nurse will identify suitable patients from the respiratory clinic of The Prince Charles Hospital. All patients registered for home oxygen will be screened for suitability. The research nurse will approach the patient at the respiratory clinic, explain the study and obtain informed consent to undertake the study at the patient's next clinic visit.

Study Procedures

The research nurse and scientist will prepare and calibrate the research equipment (as per the checklist below). The respiratory physician will confirm that the patient is otherwise well and fit to undertake the study.

All patients will be placed on a bed in a semi-recumbent position, using their own LTOT at their usual oxygen flow rate.

The following physiological monitoring equipment will be attached. Before each is attached, the purpose will be explained to the patient.

- Radiometer TCM4 transcutaneous oxygen and carbon dioxide monitor will be attached to the inner forearm using the supplied adhesive attachment ring.
- 504 Criticare systems pulse oximeter will be placed on a finger tip to measure oxygen saturation.
- Dräger Electrical impedance Tomography (EIT) electrode belt will be placed around the chest at nipple level to monitor end-expiratory lung volumes.
- Viasys Respitrace bands will be placed around the chest and abdomen to monitor breath volumes. The Respitrace system will be calibrated by having the patient breath through a low resistance pneumotacograph for two minutes.
- Continuous ECG monitoring will be applied to measure heart rate
- A video camera will be used to record from the mouth to above the waist during the study in order to identify any "glitches" in the recorded data, such as coughs, sneezes or sighs. It is imperative to monitor this to exclude any erroneous data which will affect the final analysis.

<u>Measurements</u>
A 20 minute baseline recording will be performed (on LTOT). After the baseline period the patient will be randomised using sealed opaque envelopes to either: NHF followed by LTOT OR LTOT followed by NHF. Twenty minutes of data will be recorded using each device with a 20 minute washout period between the two modes of oxygen delivery. During the washout period, the patient will be on their own cannulae.

Data collected during each measurement period is as follows:

- EIT measurements will be undertaken at 18 minutes into the study period
- all other physiological data will be recorded continuously
- dyspnoea level using a Visual analogue scale (a scale of 0-10) 15 minutes into the treatment period

The patient will remain monitored on their own LTOT for another twenty minute period as a safety precaution. At the end of the period, the patient will again breathe through a low resistance pneumotacograph for two minutes to validate the calibration of the Respitrace system. If the patient meets any of the pre-specified withdrawal criteria or if the patient does not wish to continue with the study for any reason, the study will be immediately stopped.

Pre-Study Equipment Checklist

- Emergency equipment in place and staff aware of study
- AIRVO system disinfection cycle completed.
- AIRVO circuit in place, set for 30L/min and warmed up
- AIRVO cannulae in multiple sizes
- Oxygen flowmeter and tubing
- Masimo Radical 7 oximeter – test probe on researcher's finger
- Radiometer TCM4, calibrated
- TCM4 attachment rings and contact fluid
- Respitrace system on and working
- Respitrace bands in various sizes
- EIT system self-tests passed
- EIT bands and electrodes in various sizes
- Face mask and pneumotach
- All data acquisition systems performing satisfactorily

Ethics

This study will be performed in accordance with the ethical principles of the Declaration of Helsinki (June 1964 and amended 1975, 1983, 1989, 1996, 2000, 2008 and Note of Clarification 2002 and 2004), ICH GCP Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95) annotated with Therapeutic Goods Administration comments and NHMRC National Statement on Ethical Conduct in Research Involving Humans (March 2007).

Data Management

Demographic data will be recorded on prepared forms and kept in a locked filing cabinet in the CCRG. Physiological data and video recordings will be stored on personal computers not connected to networks. Data files will be flagged as "read only" and only remain on the password protected data collection PCs until the end of the study.

On a case-by-case basis, these files will be copied to a password protected external hard drive that will be kept in a locked filing cabinet in the CCRG and to a directory of the QH network with appropriate security and backup.

Following analysis of the data and the use of the video files to identify any "glitches", the video files will be deleted from all storage media.

Only unidentified data will be given to statisticians or others performing data analysis.

Statistical Considerations

All statistical analyses will be performed by the CCRG's visiting statistician, Dr Chris Anstey who will be blinded to whether the patient is receiving LTOT or NHF. The sample size calculation is based on our previous studies using NHF and a reduction in respiratory rate of 4 breaths per minute in the NHF group is estimated. To find this difference with 80% power using a 5% significance level requires a sample size of 30 patients. Two-way (paired) comparisons by treatment group will be performed. Paired t-tests will be used for normally distributed data and results will be presented as mean and standard deviation. For non-normally distributed data, a Wilcoxon signed rank test will be used and results will be presented as median and interquartile range.

Adverse events

Adverse events (AEs) are defined as any untoward medical occurrence in a patient or clinical investigation subject administered an investigational intervention and which does not necessarily have to have a causal relationship with this treatment (adapted from the Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95 July 2000).

It is recognised that the patient population with COPD will experience aberrations in physiology due to the severity of their underlying disease. These will not necessarily constitute an adverse event unless they require significant intervention or are considered to be of concern in the investigator's clinical judgement.

Serious adverse events

Serious Adverse Events (SAE) are defined in accordance with the Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95) (July 2000) as any untoward medical occurrence that: results in death Is life-threatening; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; is an important medical event which may require intervention to prevent one of the previously listed outcomes.

References

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