Is Outpatient Control of Long-Term Non-Invasive Ventilation Feasible in Chronic Obstructive Pulmonary Disease Patients?

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Keywords

Home mechanical ventilation · Health-related quality of life · Outpatient setting · Chronic obstructive pulmonary disease · Respiratory failure

Abstract

Background: Long-term non-invasive ventilation (NIV) is an established and increasingly used treatment option for patients with chronic hypercapnic chronic obstructive pulmonary disease (COPD). Following inpatient NIV establishment, inpatient control visits regularly occur thereafter. However, it remains unclear whether such control visits can also be performed in an outpatient setting, which, in turn, would reduce costs, patient burden and the complications related to hospitalization. **Objectives:** To investigate an outpatient setting with predefined criteria for hospitalization for patients with chronic hypercapnic COPD. **Methods:** An outpatient clinic located within the hospital in the vicinity of the respiratory care unit provided predefined criteria for hospitalization of COPD patients receiving long-term NIV therapy. The results of this setting were retrospectively analysed. **Results:** A total of 130 outpatient visits (80 patients) were analysed. In 93 cases (71.5%), hospital admission was not necessary,

while hospitalization was performed in 37 cases (28.5%). Out of these, 7 cases with acute conditions required prompt hospitalization. Patients without hospitalization had better PaCO₂ values (45.40 ± 5.27 vs. 50.05 ± 8.04 , $p = 0.002$) and Severe Respiratory Insufficiency Questionnaire Summary scores (55.54 ± 19.74 vs. 41.82 ± 19.59 , $p = 0.012$). **Conclusion:** Outpatient control of long-term NIV in a hospital setting is feasible and has the capacity to identify stable COPD patients in whom NIV therapy is sufficient according to predefined criteria. These patients may not require hospitalization and may account for more than two thirds of cases.

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Introduction

Nocturnal long-term non-invasive ventilation (NIV) is a well-established, increasingly used modern therapeutic option for patients with chronic hypercapnic respiratory failure that arises from end-stage chronic obstructive pulmonary disease (COPD) [1, 2]. While early random-

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ized controlled trials (RCTs) concluded that there was insufficient evidence to support recommendation of routine NIV use in COPD patients [3–7], two recent RCTs have clearly shown that when NIV is administered with the aim of improving elevated PaCO₂ values, it has the capacity to improve outcome and health-related quality of life (HRQL) [8, 9]. Higher than usual ventilator settings are necessary to augment alveolar ventilation and, in turn, improve blood gases. This approach has been defined as high-intensity NIV [10–13].

Based on these findings, and given the increasing incidence and prevalence of COPD, the number of COPD patients receiving long-term NIV is steadily rising [14–16]. These patients require regular follow-up visits, which are inevitably needed to control for NIV efficiency, adherence to treatment, and problems – technical or otherwise – that are associated with NIV [16, 17]. In Germany, this is usually performed on a regular basis in the inpatient hospital setting, allowing for nocturnal measurements of gas exchange and sleep quality while NIV is running [16, 18]. In addition, the recommendation for hospitalizing these patients is based not only on the severity of the disease, but also on the fact that modifications to the ventilator settings have a strong physiological influence and hence need to be evaluated for their potential impact on nocturnal ventilation efficiency.

In contrast, regular hospitalization is a burden for these patients and has been linked to an increased risk of nosocomial infections in ICU patients [19]. In addition, there is increasing evidence for successful outpatient management in non-COPD patients requiring long-term NIV [20–24]. However, most of these patients receive long-term NIV due to neuromuscular and chest wall diseases and therefore the results are not comparable to COPD patients.

Furthermore, the increasing number of COPD patients treated with long-term NIV is likely to be associated with higher costs, while the need for regular hospitalization can significantly limit bed availability for other patients. In addition, some patients are stable and do not require any change in NIV during hospitalization, questioning the necessity for regular inpatient treatment.

As a consequence, the time has come to evaluate the impact of outpatient care in COPD patients undergoing long-term NIV therapy. Other European countries already provide outpatient NIV clinics for example Great Britain or the Netherlands. Especially in the Netherlands, it is standard that NIV patients are visited at home and also receive nocturnal transcutaneous carbon dioxide measurements in the home environment [25]. The aim of

the current trial was therefore to evaluate the results of an outpatient clinic pilot project for long-term NIV-treated COPD patients. Such findings are expected to be valuable for designing future RCTs on the role of outpatient management in COPD patients receiving long-term NIV therapy.

Methods

Subjects and Study Design

This was an investigator-initiated single-centre retrospective trial. Data were collected from all COPD patients treated between January 2016 and January 2017 in the outpatient NIV unit of the Department of Pneumology, Cologne Merheim Hospital, Witten/Herdecke University, Faculty of Health/School of Medicine. Prior to the analysis, the ethics committee of the University of Witten/Herdecke were contacted regarding the need for ethical approval, which was not required in this retrospective trial. All patients suffered from COPD GOLD stage IV according to the GOLD guidelines [7] and had previously been hospitalized for the establishment of long-term NIV prior to the analysis. Documented information on ventilator settings, blood gas values, demographic data, and HRQL measurements was selected for analysis.

For hospital admission, two categories were defined according to hospitalization priority: prompt admission (same day) versus short-term hospitalization (defined as hospital admission within <2 months).

Measurements and Ventilator Settings

NIV was applied using either assisted pressure-controlled ventilation, pressure-supported ventilation or pressure-controlled ventilation. NIV was delivered via nasal or full-face masks. Daytime blood gases were measured at rest and obtained from the arterialized earlobe as previously described (ABL 800 flex, Radiometer, Denmark) [26]. The Severe Respiratory Insufficiency Questionnaire (SRI) was designed and validated for HRQL in patients receiving long-term NIV therapy [27, 28]. Transcutaneous PCO₂ (PtcCO₂) (SenTec Digital Monitoring System; VStats-Software®: 4.00; SenTec AG, Therwil, Switzerland) measurements were performed during daytime ventilation in selected patients [29, 30].

Therapy adherence was evaluated from readings generated by the built-in ventilator software. Read-outs from each of the ventilators were performed by individual ventilator software (ResScan: 5.5, ResMed Limited, San Diego, CA, USA; VENTiViews: 1.0, Weinmann GmbH + Co. KG, Hamburg, Germany; Vivo PC Software: 4.01, Breas medical AB, Mölnlycke, Sweden; Vivo 50 PC Software: 3.1, Breas medical AB; DirectView: 1.3, Philips Respironics, Koninklijke, the Netherlands; EncoreBasic: 2.8, Philips Respironics).

Outpatient Setting

As a pilot project, the Cologne Merheim Hospital offers long-term NIV patients an outpatient care service that is located next to the Respiratory Care Unit. Hereby, two beds equipped with modalities for full polysomnography, PtcCO₂ measurements as well as the option for invasive and non-invasive cardiovascular and respiratory monitoring were provided for outpatient NIV manage-

Fig. 1. Outpatient clinic setting. SRI, Severe Respiratory Insufficiency Questionnaire; NIV, non-invasive ventilation; PtcCO₂, partial pressure of transcutaneous carbon dioxide.

ment. A flowchart describing the outpatient NIV set-up is illustrated in Figure 1.

Prompt hospitalization was recommended if at least one of the following major criteria was identified: severe hypercapnia (PaCO₂ ≥ 55 mm Hg), respiratory acidosis (pH ≤ 7.35) or acute exacerbation of COPD defined as an acute worsening of respiratory symptoms which results in additional therapy [7]. In addition, minor criteria were defined as follows: PaCO₂ 50–54 mm Hg, low adherence to therapy defined by ≤ 4 h/day of ventilator use, problems with equipment, or clinical issues such as progression of dyspnoea. In the case of two minor criteria being identified, short-term hospital admission was recommended, even though daytime ventilation with PtcCO₂ monitoring was performed in parallel to reduce problems and determine the level of urgency for hospitalization.

In the case of one minor criterion being identified, daytime ventilation (min. 1 h, max. 4 h) with PtcCO₂ monitoring was carried out with the aim of addressing the problem at hand. Short-term hospital admission was recommended if this strategy was unsuccessful. In the remaining cases where neither major nor minor criteria were met, or problems were resolved, patients were not hospitalized and instead planned for routine outpatient control every ≥ 2 months.

Data Collection and Statistical Analysis

The following data were collected: sex, birth date, date and circumstances of NIV initiation (initiation because of chronic hypercapnia, after acute hypercapnic exacerbation or after weaning), smoking status and index, time remaining until next control visit,

Fig. 2. Flowchart showing the distribution of study cases. NIV, non-invasive ventilation.

long-term oxygen therapy, ventilator settings, duration of NIV application per day and further treatment recommendations.

Statistical analysis was performed using Sigma-Plot® (Version 12.3, Systat Software, Inc., Point Richmond, CA, USA). Means and standard deviations are reported for demographics, ABG results and ventilator settings. Unpaired *t* tests for continuous variables were used to compare patient characteristics between the two groups (inpatient versus outpatient), and the Mann-Whitney rank sum test was used for non-normally distributed data.

Results

A total of 130 outpatient visits by 80 patients were analysed. Demographics, ventilator settings and diagnostic data are given in Table 1. A flowchart summarizing the design of the study cases is illustrated in Figure 2.

In 84 cases (64.6%), NIV was continued without hospital admission. In contrast, hospitalization was carried out in 37 cases (28.5%), with the aim of optimizing treatment and solving problems associated with NIV. Amongst these hospitalized patients, prompt hospitalization was required in 18.9% (*n* = 7) and short-term hospital admission was recommended for the remaining 81.1% (*n* = 30), even though 12 out of these patients were admitted later

Table 1. Patient characteristics and ventilator settings (*n* = 80)

Males, <i>n</i> (%)	32 (40)
Age, years	67.11±8.44
Body mass index	26.97±7.27
Smoking status (active;prior)	22:58
Smoking index, pack years	54.23±23.45
Time under NIV, years	2.28±2.52
Supplemental oxygen (yes:no)	75:5
LTOT (L/min during rest; <i>n</i> = 80)	1.54±1.19
NIV initiation, <i>n</i> (%)	
Following acute NIV	36 (45)
Chronic elective NIV	30 (37.5)
NIV following prolonged weaning	9 (11.25)
Unknown	5 (6.25)
Ventilator settings	
IPAP, cmH ₂ O	23.90±4.39
EPAP, cmH ₂ O	5.65±1.20
BF per min	16.55±2.22
Adherence, hours per day	6.58±3.65

LTOT, long-term oxygen therapy; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure; BF, breathing frequency.

Table 2. Daytime blood gases and oxygen flow rates in patients who required hospitalization (inpatient care) versus those who did not (outpatient care)

	Outpatient care (<i>n</i> = 84)	Inpatient care (<i>n</i> = 37)	<i>p</i> value
PaCO ₂ , mm Hg	45.40±5.27	50.05±8.04	0.002
PaO ₂ , mm Hg	65.97±10.98	61.79±12.08	0.034
pH	7.40±0.03	7.39±0.03	0.050
HCO ₃ ⁻ , mmol/L	26.99±2.44	27.98±3.17	0.040
LTOT, L/min	1.47±1.52	1.73±1.54	0.239

PaCO₂, arterial partial pressure of carbon dioxide; PaO₂, arterial partial pressure of oxygen; HCO₃⁻, bicarbonate; LTOT, long-term oxygen therapy.

than 2 months following outpatient control. In 9 cases (6.9%), no follow-up was necessary because NIV was terminated prior to control visits, due to successful withdrawal trial with no further indication for this therapy. Five out of the 9 cases (55.6%) were initiated following acute exacerbation. Termination of NIV was based on now obsolete indication criteria. These patients were therefore excluded from the final analysis.

Most recommendations for hospital admission were based on the results of the blood gas analysis. Consequently, blood gas values differed significantly between

Table 3. Severe Respiratory Insufficiency Questionnaire scores in patients who required hospitalization (inpatient care) versus those who did not (outpatient care)

	Outpatient care (<i>n</i> = 84)	Inpatient care (<i>n</i> = 37)	<i>p</i> value
Respiratory complaints	34.72±20.20	32.25±25.04	0.678
Physical functioning	63.61±16.71	50.29±17.49	0.005
Attendant symptoms and sleep	65.24±20.63	64.11±19.52	0.835
Social relationships	55.69±25.22	44.89±25.21	0.114
Anxiety	53.55±19.94	46.30±16.35	0.151
Psychological well-being	49.79±21.84	40.61±20.31	0.111
Social functioning	54.02±15.83	45.75±14.59	0.048
Summary scale	55.54±19.74	41.82±19.59	0.012

Fig. 3. Length of hospital stay.

patients who required hospitalization and those who did not, as specified in Table 2.

Daytime ventilation with PtcCO₂ monitoring was performed in 10% (*n* = 13) of outpatient visits; 8 of these did not need recommendations for hospitalization, since problems with NIV related to the predefined criteria could be managed successfully.

Clear differences in SRI scores were observed between patients who required hospitalization versus patients who did not (Table 3). The length of inpatient stay is illustrated in Figure 3, showing that only short hospital stays of 2 days or less were necessary in 22 cases (70%) of hospitalized patients. In contrast, 4 cases (13% of the hospitalized patients) were hospitalized for 6 days or longer. Reasons for this prolonged hospital stay were as follows: acute exacerbation (*n* = 2), severe hypercapnia (PaCO₂ 60 mm Hg, *n* = 1), and symptoms of angina pectoris with known coronary heart disease (*n* = 1).

Discussion

This is the first study to carry out an analysis of a specialized outpatient care system for COPD patients already receiving long-term NIV therapy at home. The main findings of this trial are as follows:

Firstly, 72% (*n* = 93) of all the cases evaluated in a clearly defined outpatient setting were not hospitalized. Out of these patients continuing home NIV, 84 were deemed not to require inpatient care, according to predefined criteria based on blood gas analysis, subjective parameters such as exacerbation, dyspnoea or problems related to NIV, and adherences to NIV. In contrast, 9 patients no longer required long-term NIV.

Secondly, only less than one third of patients who were scheduled for regular outpatient control visits eventually required in-hospital treatment. Here, the major proportion of these patients requiring hospitalization were scheduled for short-term admission within 2 months following outpatient control, while only a small number of patients required prompt hospitalization on the same day that they visited the outpatient clinic.

Thirdly, as a consequence of the algorithm that determined the need for hospitalization, patients who did not require hospital admission not only had better blood gas analysis results, but also better SRI-assessed HRQL.

There were some limitations to the present analysis. Firstly, the study was retrospectively performed and hence needs further validation by prospective RCTs; however, the advantage of this study is that the findings may help to design future prospective trials. Secondly, the study did not include data for lung function, as current lung function measurements were not available in some patients. Thirdly, there was no analysis of follow-up visits.

Therefore, the outcome of outpatient management of long-term NIV remains to be elucidated.

Despite these limitations, the present study has some important clinical implications for the management of long-term NIV in COPD patients. Most importantly, our findings suggest that a significant number of patients with COPD can indeed be managed in an outpatient setting, without inpatient control visits. These patients have acceptable blood gases and SRI scores that are comparable to those from patients who in previous studies were re-evaluated following a hospital admission [31]. This is an important observation given that outpatient management of these patients can indeed reduce costs as well as hospitalization-related complications such as nosocomial infections, even though this has not yet been investigated and therefore remains speculative.

Most hospitalized patients can be managed during a short in-hospital period of 2 days or less. The frequent reason for hospitalization in the present study cohort was to manage significant hypercapnia and clinical problems. Another important issue, however, refers to the observation that some patients required prompt hospitalization and a few patients also required longer stays in hospital. Therefore, any future outpatient clinics designed for monitoring long-term NIV should also allow the possibility of admitting the patient to hospital immediately. The most optimal outpatient setting for this would be within the NIV unit of a hospital specialized for NIV.

On the other hand, the present study shows that while nearly half of the patients received long-term NIV following acute NIV in hospital, NIV could be terminated there-

after in at least some of these patients. Therefore, both oversupply and undersupply need to be avoided, and any setting, whether it be in- or outpatient, should be capable of addressing this important issue. Thereby, it remains questionable whether NIV should be automatically continued once patients are established on long-term NIV after repeated inpatient control visits.

In conclusion, outpatient control of long-term NIV is feasible and has the capacity to identify stable COPD patients whose NIV therapy suffices to the extent of precluding the need for hospitalization. In addition, outpatient settings for long-term NIV monitoring should also have the means to provide prompt hospitalization for unstable patients or those with insufficient NIV treatment. Further prospective trials are needed to clearly define the criteria for in- and outpatient care of COPD patients receiving long-term NIV therapy.

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