Palliation of dyspnea with mouthpiece ventilation in patients with COPD – a pilot feasibility study

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Abstract

Background: Mouthpiece ventilation (MPV) reduces hypoventilation, but its efficacy in relieving dyspnea in patients with acute chronic obstructive pulmonary disease exacerbation (AECOPD) is unclear.

Objective: To assess the feasibility of MPV in relieving dyspnea among patients with AECOPD.

Methods: In this prospective single arm pilot study, the change in dyspnea on numeric rating scale (NRS) after using MPV and side-effects of the treatment was studied in eighteen patients with AECOPD.

Results: The median decrease in dyspnea was 1.5 (95% confidence interval = 0.0 - 2.5, p = 0.006) on NRS after the intervention lasting a median of 16.9 minutes. Of the patients, 61% found MPV beneficial. The use of MPV did not increase the sense of anxiety or pain.

Conclusions: Mouthpiece ventilation is feasible and may relieve dyspnea in patients with AECOPD, but the intervention needs further evaluation.

Introduction

In patients hospitalized for obstructive pulmonary disease exacerbation (AECOPD) the response to the conventional treatments (e.g. bronchodilators) towards dyspnea is limited [1,2] and thus new therapies are urgently needed.

The use of noninvasive ventilation (NIV) with facial mask in acute hypercapnic respiratory failure in AECOPD is a standard care to normalize hypoventilation [3] but relief of dyspnea through NIV during AECOPD remain poorly reported. [4,5] NIV has been shown to reduce dyspnea in patients with end-stage diseases in general, [6–8] but the use of NIV with facial mask may cause discomfort, pain and claustrophobia. [9,10]

Noninvasive ventilation via open-circuit mouthpiece has been reported to relieve dyspnea and decrease the work of breathing [11] and even to improve the quality of life in patients suffering from neuromuscular diseases. [12] This mouthpiece ventilation (MPV) has also been shown to decrease dyspnea in a small study population in palliative care setting. [13] Preliminary data suggests that NIV via mouthpiece helps to normalize hypoventilation equally well as NIV via face mask in AECOPD, [14] but MPV´s efficacy on subjective feeling of dyspnea in patients with COPD remains unknown. [5] The aim of this study was to assess the feasibility and the effectiveness of mouthpiece ventilation in relieving dyspnea in patients with non-hypercapnic AECOPD.

Material and Methods

Patients

The patients were recruited between January 2017 and August 2020 from the pulmonary and geriatric wards in the Tampere University Hospital after they had been admitted to hospital

through emergency room and followed up until death or the end of December 2021. Inclusion criteria were a hospitalization due to AECOPD with dyspnea ≥ 4 on numeric rating scale without significant hypoventilation (blood pH ≥ 7.35 and partial pressure of carbon dioxide in arterial or capillary blood (pCO_2) ≤ 6.0 kPa), age ≥ 18 years and capability to give written informed consent. Patients with decreased level of consciousness, insufficient co-operation, hypercapnia, a treatable cause of dyspnea (i.e. pleural effusion) or chronic respiratory insufficiency treated by NIV and/or continuous positive airway pressure (CPAP) before hospitalization were excluded.

Intervention

The patients used mouthpiece ventilation for a minimum of 15 minutes, but it was possible to continue to use MPV as long as they preferred. After this intervention period, the patients were allowed to use the ventilator as they wanted during the next 24 hours. All the other treatments of COPD exacerbation and dyspnea were allowed.

Mouthpiece ventilation was provided using a Trilogy 100® (Philips Respironics, Murrysville, PA, USA) ventilator with an angled or straw-type mouthpiece (Figure 1). Inspiratory pressure (IPAP), inspiratory time (TI) and rise time (RT) were adjusted according to each patient's preference. The starting settings were 10 cmH_2O for IPAP, 1.2 s for TI and 300 ms for RT. The patients were taught to inhale through the mouthpiece and exhale either by taking the mouthpiece out from their mouth or by loosening their lips around the mouthpiece.

Assessments

Intensity of dyspnea, pain and anxiety were measured by numeric rating scale (NRS) from 0 (no symptom) to 10 (the worst possible symptom) right before the intervention, right after the intervention period and after 24 hours. The wording of each question was "Please circle the number 0 (no symptom) to 10 (the worst possible symptom) for the intensity of symptom that

best describes how you feel right now". The effectiveness of MPV was measured by the primary end point of the study, which was the change in the severity of dyspnea on NRS after the intervention period on MPV. Dryness of mouth, accumulation of air into stomach, sense of panic and other possible adverse events (AE) were measured by NRS after the intervention. Serious AEs leading to death or serious deterioration of the patient were also assessed. [15] The patients' opinion on the benefits, adverse events and compliance of mouthpiece ventilation were asked by using a Likert scale ranging from 1 (totally disagree) to 5 (totally agree). The feasibility of the MPV was defined as a proportion of patients able to use MPV, agreeing completely or partly with MPV with statements concerning mouthpiece ventilation and reporting AEs and their severity right after the intervention. Oxygen saturation, gas exchange parameters, breathing frequency, and heart rate were measured as well.

Statistics

As this was a pilot study, we did not have good a prior information for the sample size calculation. We did aim for a higher number of patients but due to difficulties in recruitment, we were able to include 18 patients. The current sample size of 18 patients has a statistical power of 90% (with alpha error of 5%) to detect a change in NRS equal to 80% of standard deviation (large effect size). Wilcoxon test was used to test the difference of symptoms severity before and after the treatment and confidence intervals for median were calculated using bootstrap method. Statistical significance was set as $p < 0.05$. Analyses were performed with IBM Statistics version 26.0 (IBM Corp, Armonk, NY, 2019).

Ethical considerations

The study was approved by the Ethics Committee of Tampere University Hospital (R16148; 11 October 2016), Tampere, Finland and all the subjects gave their written informed consent. Before initiation, this study was registered at clinicaltrials.gov (study number: NCT03025425).

Results

Eighteen patients, who had been hospitalized for AECOPD without hypercapnia, were recruited (Table 1). Twelve patients (68%) had emphysema, but only one used long-term oxygen therapy. Six of the patients (33%) needed concomitant supplementary oxygen with oxygen flow of 1.0-1.5 l/min during the study period. All patients had inhalation therapy for COPD, but none used opioids for dyspnea before hospitalization. Of the patients, 100 %, 83 % and 61 % received bronchodilators, systemic steroids and antibiotics for their AECOPD, respectively. At the time of MPV intervention, four patients received morphine as rescue medication for dyspnea.

Do Not Resuscitate (DNR) order was recorded in four (22%) patients. Eight patients (44%) had a history of frequent exacerbations leading to hospitalization. Twelve patients (67%) died during the follow-up period and the median survival time of the patients was 2.1 years (IQR 1.5-NA).

In MPV settings the median IPAP was 10 cmH_2O (range 8-12), the median inspiratory time was 1.2 s (range 1.2-1.5), and the median rise time was 300 ms (range 300-400). All the patients were able to use mouthpiece ventilation for intervention period and the median time of use was 16.9 minutes (IQR 15.0 - 19.8). After the intervention period, all the patients used mouthpiece ventilation with a total median time of 30.0 min (IQR 2.6 - 82.7) during the next 24 hours.

All the patients had dyspnea intensity of ≥ 4 on numeric rating scale (NRS) during the inclusion, but in three patients, the dyspnea score decreased to 3 at the initiation of MPV. The median NRS scores at the initiation of MPV were 5.0 (range 3.0 - 8.0), 0.5 (range 0.0 - 8.0) and 4.0 (range 0.0 - 9.0) for dyspnea, pain and anxiety, respectively. Further, the median NRS scores right after the intervention were 4.0 (range 0.0 - 8.0), 0.5 (range 0.0 - 7.0) and 2.0 (range 0.0 - 7.0) in dyspnea, pain and anxiety, respectively. Change in dyspnea after mouthpiece

ventilation in each patient is shown in Figure 2. Median decrease in dyspnea after the intervention period for a minimum 15 minutes was 1.5 (95% CI 0.0 – 2.5, p = 0.006) measured by NRS. Two patients with increased mucus in airways reported to have increased dyspnea after the mouthpiece ventilation. Severity of pain or anxiety did not significantly change during the intervention. Median decrease in pain after the intervention was 0.0 (95% CI 1.0 - 0.0, p = 0.102) and in anxiety 1.0 (95% CI 2.0 - 0.0, p = 0.47) measured by NRS.

Patients´ opinions concerning the mouthpiece ventilation are presented in Table 2. Almost half of the patients found that mouthpiece ventilation relieved their dyspnea. Dry mouth was the most common adverse event (Table 3), but no serious adverse events occurred. There was no significant change in oxygen saturation, breathing frequency or heart rate during the intervention. None of the patients developed significant hypoventilation during the next 24 hours after the study intervention.

Discussion

In this pilot study, most of the patients with COPD complied with mouthpiece ventilation without serious adverse events at the time of non-hypercapnic AECOPD. There was a statistically significant decrease in dyspnea after the mouthpiece ventilation.

There are only a few studies available concerning the use of NIV via mouthpiece in patients with COPD. To our knowledge there are no previous studies in COPD focusing primary on the relief of dyspnea by MPV. Our finding that the use of mouthpiece ventilation during the acute COPD exacerbation did not cause significant deterioration of gas exchange is in line with previous studies. [14,16] In the study of Nicolini et al. [14] patients with AECOPD found MPV more comfortable than conventional NIV with mask which supports our finding that MPV is well tolerated. One third of our patients reported air accumulation into stomach which was also

seen in the study of Nicolini et al. [14] The usage of MPV requires co-operation so the frail patients may have difficulties in adapting to MPV therapy as seen in our previous study on patients with advanced diseases. [13]

The advanced stage of the disease is often poorly recognized among patients with COPD and, thus, advance care planning and palliative care are delayed. [17] Identification of end stage disease and implementation of palliative care earlier may lead to better symptom control. [17–19] This could allow providing treatment options causing less suffering, like MPV versus conventional NIV with mask, when focusing on the symptom control instead of normalizing physiological parameters like blood gases. In addition, as the use of MPV requires active co-operation by the patients, it probably won't prolong the possible process of dying.

Strengths and limitations

Previous studies on MPV in AECOPD have focused mainly on gas exchange parameters instead of symptom relief but we descripted how mouthpiece ventilation can be used primarily to relieve dyspnea in AECOPD. However, we do realize that we are presenting the results of a pilot study. We measured change in dyspnea over time (before vs. after the intervention) and lacked control group. Thus, our results may partly reflect regress towards the mean or change in dyspnea due to other factors than MPV. We instructed the physicians of the study wards to screen all the consecutive patients admitted due to AECOPD for eligibility, but we cannot rule out selection bias. Even though this study was aimed for a greater number of patients, we were able to recruit only 18 patients with inclusion criteria because most of the patients treated in University Hospital are hypercapnic and hence treated with NIV via conventional face mask. A short-term use of MPV in our study also limits the conclusions regarding possible benefits and feasibility of the treatment in longer term. Further studies including control group are

needed for the evaluation of MPV. One possibility would be to compare MPV with low and higher pressures and another to compare MPV to usual care in palliative care settings.

Conclusions

Mouthpiece ventilation is feasible and safe among patients with non-hypercapnic AECOPD, and it may alleviate dyspnea. MPV might be a rational treatment option for palliation of dyspnea also during the end-of-life care in patients with suffering from advanced COPD and MPV can be considered as an add-on therapy to other symptom management. Further studies are needed in patients with end stage COPD suffering multiple symptoms to determine the efficacy of mouthpiece ventilation in relieving refractory dyspnea also outside exacerbation and in early palliative care settings.

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Authors´ contributions

S.L.-K., J.T.L. and L.L. were responsible for the study design, but all the authors participated in this. S.L.-K. recruited the patients. All the authors contributed to the analyses and interpretation of the data and writing and drafting of the manuscript. All authors approved the final version of the manuscript.

Authors Disclosure Statement

The authors report no conflict of interest.

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Tables

TABLE 1. Patient characteristics

Total, n	18
Male, n (%)	12 (66.7)
Age, years, median (range)	78.0 (58.0-92.0)
Living conditions, n (%)	
At home without help	7 (38.9)
At home with help	10 (55.6)
Nursing home	1 (5.6)
Smoking status, n (%)	
Ex-smoker	7 (38.9)
Current smoker	11 (61.1)
Pack years, median (range)	40 (25-80)
FEV_1	
Median (range) L	0.89 (0.46-1.85)
Median (IQR) % of predicted (%) (range)	31.5 (14.0-55.0)
Diffusion capacity (%), median (range)[a]	53 (25-82)
Comorbidities, n (%)	
Cardiovascular diseases	15 (83.3)
Other respiratory diseases[b]	10 (55.6)
Cancer	6 (33.3)
Depression	5 (27.8)
Diabetes	4 (22.2)
Measurements at the time of inclusion	
Oxygen saturation[c] (%), median (range)	93.5 (89.0-98.0)
Blood gases[d]	
pH, median (range)	7.44 (7.42-7.46)
PCO_2 (kPa), median (range)	5.3 (4.0-5.8)
BE, median (range)	1.50 (-2.90 – 7.50)
Respiratory rate (per minute), median (range)	22 (12-36)

[a]Data missing in 6 patients
[b]Asthma (5), bronchiectasis (1), asbestosis (1), sleep apnoea (2)
[c] Measured with a pulse oximeter
[d] Arterial (1) or capillary (17) sample
FEV_1, forced vital capacity in one second; IQR, interquartile range; DNR, do not resuscitate; pH, potential of hydrogen; PCO_2, partial pressure of carbon dioxide; BE, base excess

TABLE 2. Proportion of patients agreeing completely or partly with statements concerning mouthpiece ventilation right after the intervention period.

Statements on mouthpiece ventilation	n (%)
Mouthpiece ventilation relieved my dyspnea	8 (44.4)
Mouthpiece ventilation was beneficial for me	11 (61.1)
I complied well with mouthpiece ventilation	14 (77.8)
Mouthpiece ventilation was unpleasant	6 (33.3)
I would like to use mouthpiece ventilation again for my dyspnea	8 (44.4)

TABLE 3. Proportion of patients reporting adverse events and their severity right after the intervention.

Adverse events after mouthpiece ventilation	n (%)	Median NRS (range)
Dry mouth	12 (66.7)	5.5 (1.0-9.0)
Air accumulation into stomach	7 (38.9)	3.0 (2.0-8.0)
Sense of panic	7 (38.9)	3.0 (1.0-8.0)
Increased respiratory secretions	3 (16.7)	8.0 (6.0-8.0)

NRS, numeric rating scale

Figure 1. Ventilator with the equipment for the mouthpiece ventilation.

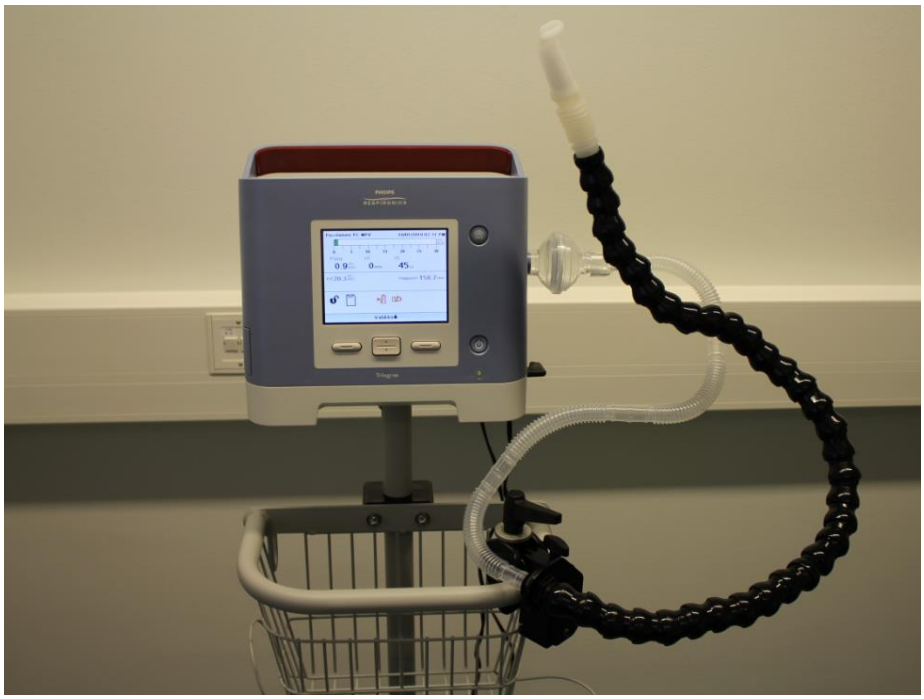

Figure 2. Change in the severity of dyspnea on numeric rating scale (NRS) right after the intervention period on mouthpiece ventilation.