

Effects of Nasal High Flow on Ventilation in Volunteers, COPD and Idiopathic Pulmonary Fibrosis Patients

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Key Words

Nasal high flow · Tidal volume · Hypercapnia · Idiopathic pulmonary fibrosis · COPD

Abstract

Background: A high flow of air applied by large bore nasal cannulae has been suggested to improve symptoms of chronic respiratory insufficiency. In pediatric patients, nasal high-flow (nHF) ventilation was similarly effective compared to noninvasive ventilation with a face mask. **Objectives:** The aim of this study was to describe changes in respiratory parameters. **Methods:** We measured pressure amplitudes during the respiratory cycle and mean pressures in patients with idiopathic pulmonary fibrosis (IPF) and COPD. In order to achieve tidal volume and minute volume measurements, we used a polysomnography device. Capillary blood was taken for blood gas analysis before and after nHF breathing (8 h). **Results:** nHF led to an increase in pressure amplitude and mean pressure in healthy volunteers and in patients with COPD and IPF in comparison with spontaneous breathing. In COPD, nHF increased tidal volume, while no difference in tidal volume was observed in patients with IPF. Interestingly, tidal volume decreased in healthy volunteers. Breathing

rates and minute volumes were reduced in all groups. Capillary pCO₂ decreased in patients with IPF and COPD. **Conclusions:** nHF resulted in significant effects on respiratory parameters in patients with obstructive and restrictive pulmonary diseases. The rise in pressure amplitude and mean pressure and the decrease in breathing rate and minute volume will support inspiratory efforts, helps to increase effectiveness of ventilation and will contribute to a reduction in the work of breathing. A CO₂ wash-out effect in the upper airway part of the anatomical dead space may contribute to the beneficial effects of the nHF instrument.

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Introduction

Noninvasive ventilation has become a main stay of the therapy of respiratory insufficiency in various conditions. It is also applied in COPD patients, although its efficacy is less well demonstrated in this disease. However, the method is inapplicable to some patients with poor mask tolerance and other well-known factors [1]. Recently, high flow rates of room air or room air/oxygen gas mixtures have been tried in situations of sleep apnea and

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respiratory insufficiency [2, 3]. These flow rates (range 16–40 liters/min) are tolerable because the air is warmed and humidified and because nasal cannulas are designed in order to avoid creating a jet directed to mucosal surfaces. Various terms have been used for the new method such as ‘high-flow nasal cannula’, ‘mini-CPAP’ or ‘trans-nasal insufflation’ (TNI). The terms ‘nasal high flow’ (nHF) or ‘nasal high-flow ventilation’ are the most descriptive and precise terms from our point of view and are therefore used in this study.

nHF has been employed in pediatric settings with some success [2]. Shoemaker et al. [3] compared ventilator support via nHF and via nasal CPAP. Compared to infants managed with nCPAP, no increase in adverse outcomes were observed with nHF. Patient days on a ventilator were decreased (19.4 down to 9.9 days) with nHF. Benefits were also observed in pediatric sleep apnea when nasal CPAP was compared to nHF: episodes of obstructive apnea decreased from 11 ± 3 to 5 ± 2 events per hour with nHF therapy. The reduction in apnea-hypopnea index with nHF was comparable to that in nCPAP. A positive airway pressure during nHF was suggested to be the predominant mechanism [4–7].

nHF has also been used in obstructive sleep apnea [4, 7, 8]. In a study by Nilius et al. [8] the respiratory disturbance index decreased from 22.6 ± 15.6 to 17.2 ± 13.2 events per hour in patients treated with nHF (20 liters/min). The respiratory disturbance index significantly dropped by 27% in obstructive sleep apnea patients treated with nHF. In this study subgroup, analysis revealed that patients with obstructive hypopnea and rapid eye movement-associated events benefited the most [8].

The differences between nasal low (3.9 ± 1.8 liters/min) and high flow (20 liters/min) in patients with COPD were analyzed by Chatila et al. [9]. These authors observed increased exercise capacity (10 ± 2.4 vs. 8.2 ± 4.3 min) with improved oxygenation using an unloaded bicycle ergometer (12 min for every flow with a 30 min rest between measurements) with nHF compared to spontaneous breathing.

Several groups have described elevated end-expiratory pressures with various nHF settings [10, 11]. Roca et al. [12] compared an nHF-system with conventional oxygen application via mask (30 liters/min via nasal ‘high flow’ vs. 15 liters/min via mask). The nHF group exhibited higher flows following 30 min under nHF ventilation. This was associated with lesser dyspnea, a decreased breathing rate and an elevated pO_2 .

Materials and Methods

nHF Ventilation

For this study, the TNI20s oxy device was used (TNI medical AG, Freiburg, Germany). The system is able to provide a flow of up to 30 liters/min and allows the admixture of oxygen up to 16 liters/min. The air stream delivered is warmed and humidified with some degree of individual regulation of temperature. nHF was applied via nasal prongs with larger bore outlets (in comparison to regular oxygen supplementation with nasal prongs) to accommodate the intended flow (fig. 1a). We used the BiPAP synchrony system when CPAP was applied (Philips/Respironics, Andover, Mass., USA).

Volunteers and Patients

The 16 healthy volunteers were 18–64 years old (32.8 ± 13.6 years; 6 males, 10 females). Tidal volumes were measured with elastic sensor belts in 12 individuals out of the group of 16 volunteers (4 males, 6 females). Patients with COPD and idiopathic pulmonary fibrosis (IPF) were recruited among the patients from the respiratory wards at the university hospital, Leipzig. Pressure measurements were completed in 15 patients with COPD (67.7 ± 14 years; 8 males, 7 females) and in 13 patients with IPF (62.6 ± 6 years; 7 males, 6 females). Additional tidal volume measurements were done in 12 of the patients with COPD and in 12 of the patients with IPF (66.7 ± 10.4 years; 3 males, 4 females). Finally we recruited 8 additional patients with COPD (66.7 ± 10.4 years; 4 males, 4 females) and 8 patients with IPF (58.5 ± 15.7 years; 3 males, 5 females) who suffered from a global respiratory insufficiency with hypercapnia. These patients were used in the pilot trial to investigate pCO_2 changes with nHF therapy. The study was approved by the local ethics committee and patients gave their informed consent to participate (No. 123-2009-25052009).

Measurement of Airway Pressure

A water-filled flexible tube (inner diameter 1 mm, Original Perfusor®-cable type standard; B. Braun, Meisungen, Germany), placed in the nasopharyngeal space was used as a pressure transducer. A pressure transformer (Infinity Haemo 4; Draeger Medical Systems, Lübeck, Germany), an amplifier and analogue chart writer (L200E; Linseis Messgeräte GmbH, Selb, Germany) were used to record the signal (fig. 1b). Ten breaths were recorded each during spontaneous breathing, nHF (24 liters/min) and nCPAP breathing (4 mbar; fig. 1c). These measurements were done for both prone and supine body positions. For calibration of the system, a pressure detector (GMH3111; Greisinger Electronic GmbH, Regenstauf, Germany) was used.

Measurement of Tidal Volume, Breathing Rates and Minute Volume

A polysomnograph (Respirace; Care Fusion, Höchberg, Germany) was used to measure tidal volume. Elastic sensor belts were placed 10 cm below the jugular notch and 10 cm below the xiphoid process in all individuals in whom tidal volume measurements were performed. Subsequently, we calibrated the device individually for each volunteer/patient starting at quiet breathing recorded with standard lung function equipment (Master Screen Body; CareFusion GmbH, Höchberg, Germany). While measuring tidal volumes of 10 breaths and simultaneously registering the sensor signal, we were able to calibrate the sensor belt signal to changes

in lung volume. Following calibration, volume measurements during nHF (20 liters/min) and spontaneous breathing were started. Chest and abdominal excursions were recorded and volumes were calculated.

Measurement of I-E Ratio

Thoracic wall excursions during inspiration and expiration were used to calculate the I-E ratio for all breaths.

Capillary $p\text{CO}_2$

Sixteen patients (8 COPD and 8 IPF) were identified with little variability in $p\text{CO}_2$ values. Capillary blood gas analysis was done in the morning and afternoon at the hyperemic earlobe (Capsamol; Wörwag Pharma GmbH, Böblingen, Germany). The following day patients received nHF ventilation at 20 liters/min. Gas checks were repeated prior to nHF ventilation ($t = 0$) and 8 h of nHF breathing.

Statistics

Data were analyzed using Student's t test (Sigma Plot; Systat Software GmbH, Ekrath, Germany). A probability level for the null hypothesis (no difference) of 5% or below ($p < 0.05$) was accepted for significance.

Results

Elevation of Pressure Amplitude and Mean Pressure

The pressure amplitude of breathing cycles, describing the difference between minimal and maximal pressures during nHF breathing was significantly elevated in healthy volunteers compared to spontaneous breathing (fig. 2a). Similar results were observed in patients with COPD (fig. 2b) and IPF (fig. 2c). At the same time, mean pressures were also elevated during nHF ventilation in healthy volunteers (fig. 2d) as well as in COPD (fig. 2e) and in IPF patients (fig. 2f). No differences between prone and supine body position were observed (data not shown).

We also compared nHF with nCPAP therapy, which is supposed to achieve the chosen pressure in the pharynx. The nCPAP device was set to 4 mbar in order to allow for pharyngeal pressures within the vicinity of the pressures reached with the nHF device. We realized that this pressure is lower than that chosen for most patients using nCPAP, e.g. for obstructive sleep apnea. The pressure set at 4 mbar was not achieved in the pharynx, instead, lower values were recorded in the nasopharyngeal space. A face mask was firmly occluded in order to validate our experimental setup in terms of pressure measurements. The occluded system was also set at 4 mbar and this pressure was recorded. Thus, the nCPAP system was able to keep up the set pressure level of 4 mbar.



Fig. 1. **a** nHF device with thick nasal prong. **b** Setup for measurement of pressure changes, with nHF device (left), amplifier (lower right), Hämobox and pen recorder (upper right). **c** Example of pressure diagram. SA = Spontaneous breathing; TNI = nHF device; pressure amplitude = peak to trough; mean pressure increase = shift to the left.

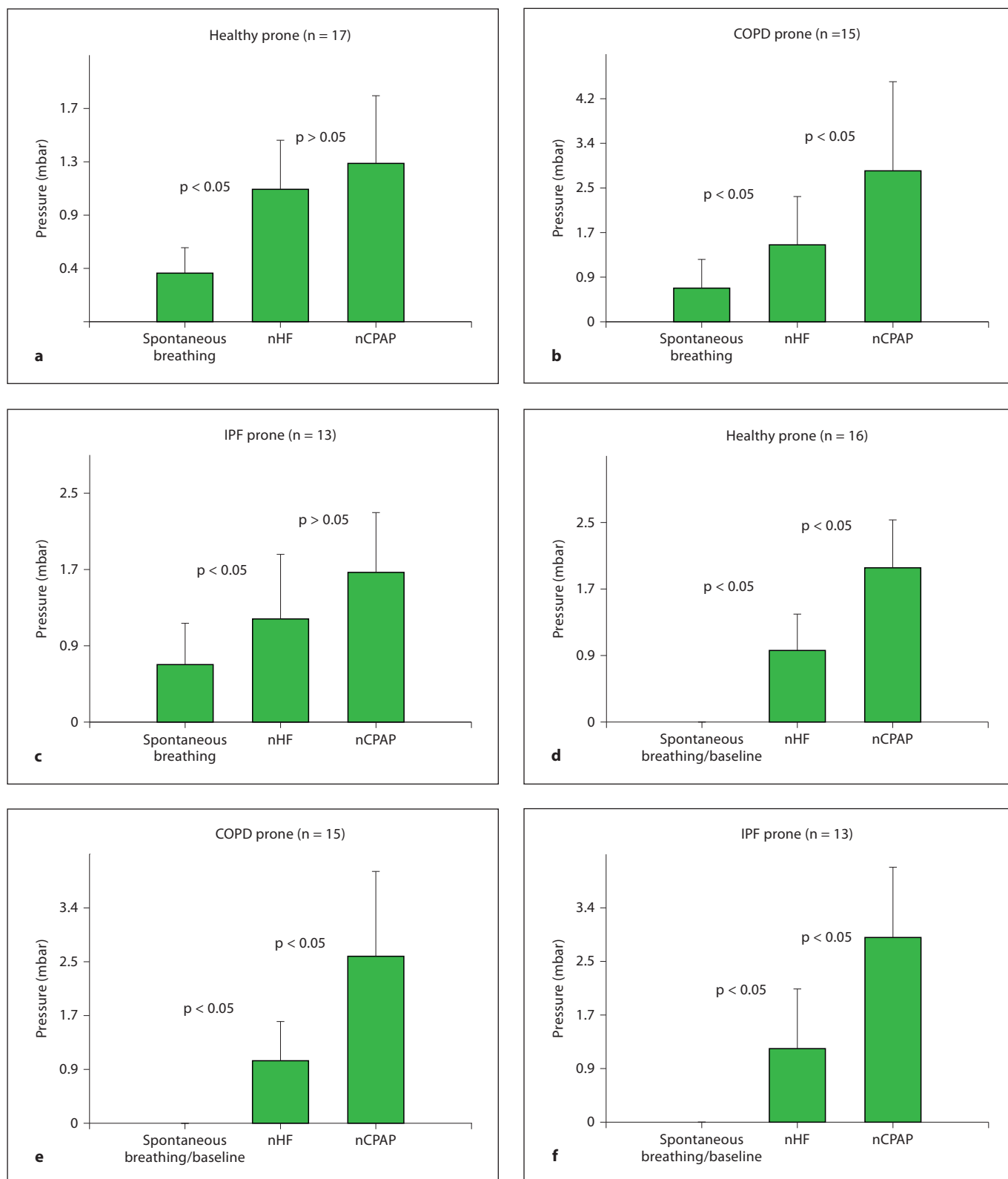


Fig. 2. Changes in pressure amplitude (a–c) and mean pressure (d–f) in healthy volunteers, COPD and IPF patients.

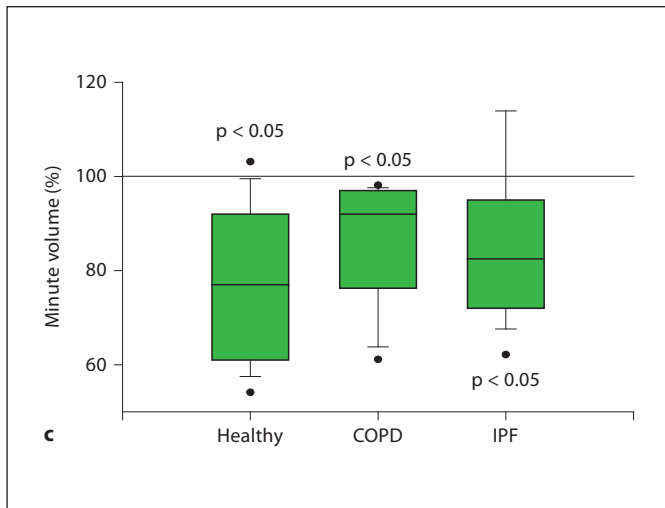
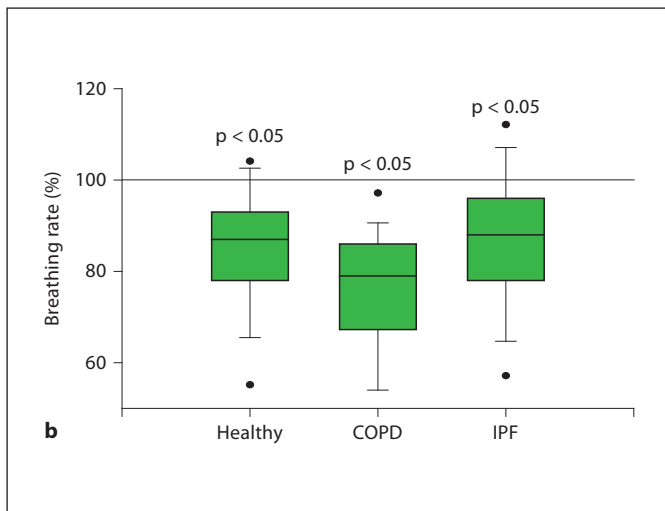
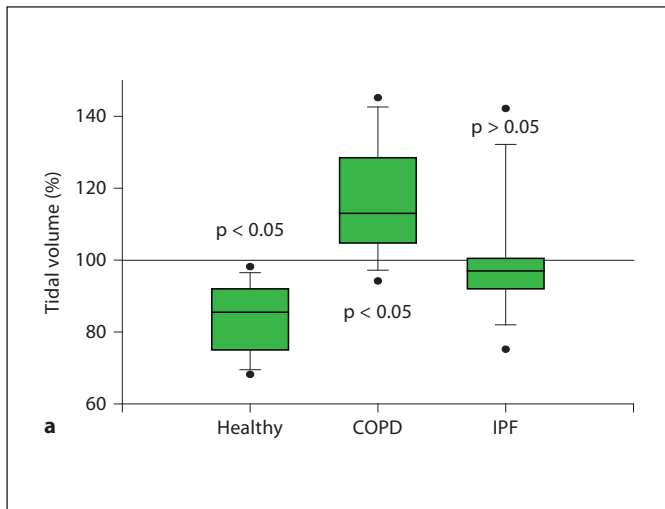


Fig. 3. Changes in tidal volume (a), breathing rate (b) and minute volume (c) in healthy volunteers, COPD and IPF patients (n = 12 for each).

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Tidal Volumes

Tidal volumes in healthy volunteers were reduced by 82.8 ± 57.6 ml ($13.2 \pm 9.9\%$) during the use of nHF. However, in patients with COPD tidal volume was increased during nHF ventilation by 87.8 ± 88.6 ml ($20.5 \pm 18\%$). In patients with IPF, however, no changes in tidal volume were noticed (fig. 3a).

Breathing Rate

Breathing rates during nHF breathing were reduced in healthy volunteers by 2.7 ± 1.6 bpm ($15.3 \pm 9.1\%$), in patients with COPD by 2.4 ± 2.3 bpm ($22 \pm 11.3\%$) and in IPF patients by 2.6 ± 1.5 bpm ($13 \pm 7.5\%$; fig. 3b). These were all significant changes.

Minute Volume

Minute volumes with nHF ventilation were similarly reduced in healthy volunteers by 2.3 ± 1.8 liters ($23 \pm 18\%$), in COPD patients by 1 ± 0.9 liters ($15 \pm 13.5\%$) and also in IPF patients by 1.5 ± 1.4 liters ($14 \pm 13.1\%$; fig. 3c). Again all of these changes were significant.

I-E Ratio

In healthy volunteers, patients with COPD and patients with IPF, the I-E ratio did not differ with nHF versus spontaneous breathing.

Capillary pCO₂

Sixteen patients with chronic respiratory insufficiency due to COPD (n = 8) and IPF (n = 8) were investigated for changes in capillary pCO₂ with nHF. During 8 h of spontaneous breathing none of these patients showed significant changes in pCO₂. However, following 8 h of nHF breathing (20 liters/min) we observed a significant fall in pCO₂ in patients with COPD by 0.69 ± 0.2 kPa ($9.9 \pm 2.2\%$). In patients with IPF, pCO₂ decreased by 0.47 ± 0.34 kPa ($6.1 \pm 4.4\%$; fig. 4). This represents a significant fall in pCO₂ in COPD patients by 7.42 ± 0.81 to 6.73 ± 0.69 kPa and in IPF patients by 6.86 ± 0.7 to 6.39 ± 0.53 kPa.

Discussion

We investigated the effects of nHF ventilation on pharyngeal pressures, tidal volumes, breathing rates and minute volumes in healthy volunteers as well as in patients with obstructive as well as restrictive lung disease. In order to compare changes with nHF to more established means of ventilator support, nHF was compared to nCPAP at 4 mbar.

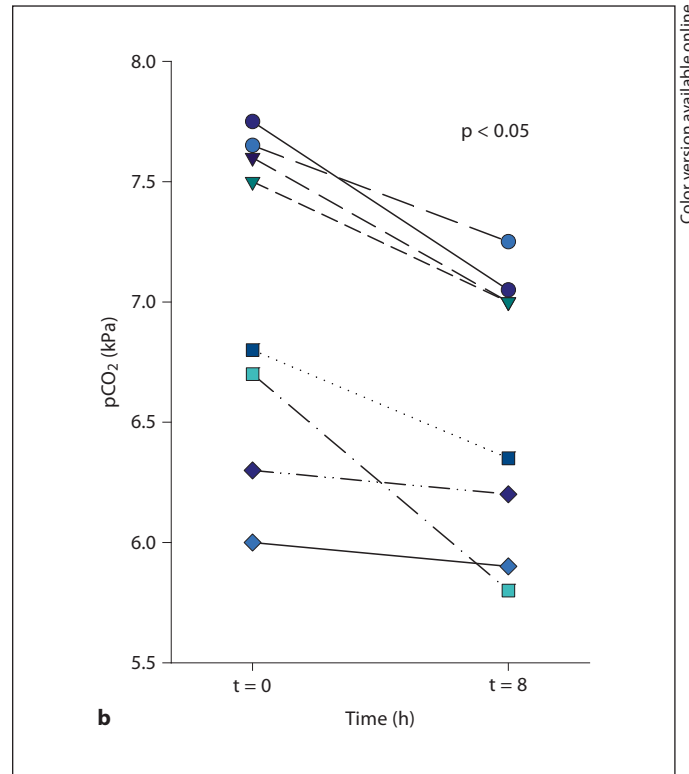
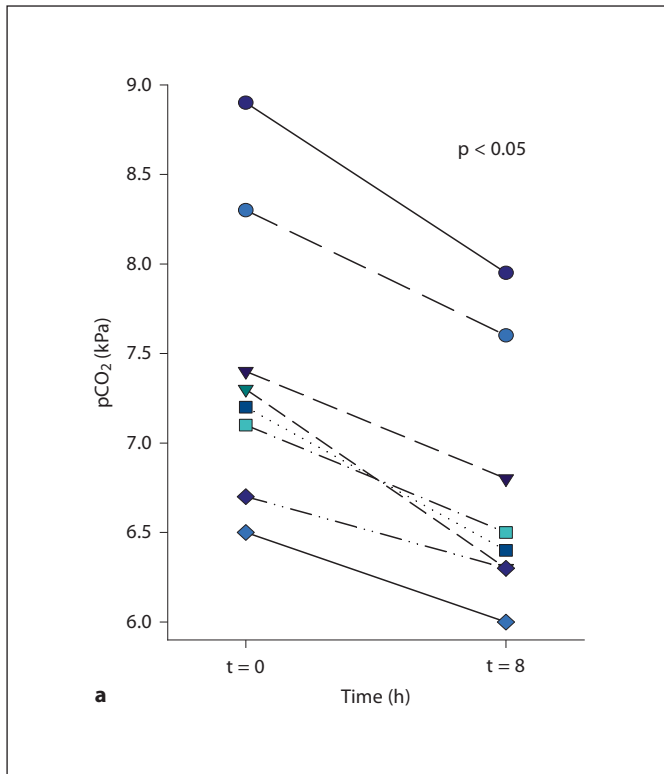


Fig. 4. Changes in pCO₂ in patients with COPD (a) and IPF (b), 20 liters/min (n = 8 for both).

A significant increase in pressure amplitude and in mean pressure was observed in healthy volunteers, in patients with obstructive and restrictive lung disease during nHF breathing compared with spontaneous breathing.

The effects on pressure described in this study confirm and expand on the results of other authors who suggested increased pressure during nHF as an indication of relief of breathing-related work [7, 12] and also observed a flow-dependent increase in pharyngeal pressure which was greater with the mouth closed than with the mouth open.

Tidal volume was observed to be increased in patients with COPD during nHF breathing. In contrast, tidal volume was decreased in healthy volunteers during nHF breathing. It is possible that COPD patients on nHF support were reenabled to hyperventilate in order to compensate for COPD-related pulmonary deficits. An increase in tidal volume was also observed in patients with COPD following the initiation of NIV [13]. Without any ventilatory support, severe COPD patients demonstrate a decrease in ventilation and concomitant hypercapnia.

Ventilator support provided with nHF ventilation may thus support the achievement of compensatory hyper-ventilation.

In contrast to the increased tidal volume in COPD patients, we observed a reduction in breathing rates and also in minute volumes in all groups including COPD patients. Thus the efficiency of breathing appears to be increased by nHF and this increase will in turn need less work of breathing for a given respiratory result. Indeed, an effect on breathing efficiency and breathing-related work might come by one of three factors: (1) positive pressure support, (2) constant flushing of the upper respiratory tract with oxygen-enriched air, or (3) a component of tracheal gas exchange brought about by the air streaming over the laryngeal opening.

Ventilation is primarily adapted to pCO₂ and a more efficient elimination of pCO₂ in the upper airways may therefore result in a reduced ventilatory drive. Thus the rate of breathing decreases and will result in a decreased minute volume. Increased elimination of CO₂ is the prerequisite for a stable pCO₂ or even a decrease in pCO₂ with a decrease in minute ventilation.

This possible explanation was supported very recently by Frizzola et al. [14]. A more direct measurement of an increase in tracheal pressures with nHF was described in an experimental animal setting. The piglets ventilated in this study following acute lung injury exhibited similar increases in directly measured tracheal pressure. Interestingly, pCO₂ decreases were not correlated to tracheal pressures but were correlated to nHF flow rate. Since high-leak nasal prongs led to improved pCO₂ in comparison with low-leak nasal prongs it was suggested that pCO₂ improvement was more likely to be caused by constant flushing of the upper respiratory tract than by tracheal pressure.

nHF appears to emerge as an interesting alternative way of supporting ventilation. It is well tolerated and easy to use. The additional effect of an improvement of inspiratory efforts by some increase in tracheal pressure and supporting of inspiration may depend on the flow chosen. Tolerance of the flow will depend on the extent of humidification and on adequate warming of the airstream, which are important prerequisites of nHF therapy. However, effects in healthy individuals as well as patients with COPD and patients with IPF are encouraging and larger studies should expand on these observations.

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Limitation of the Study

Our study is a pilot study investigating basic alterations in ventilatory pattern and in pharyngeal pressure with nHF. The number of volunteers and patients in each group is low. The groups were not age matched since pressure differences and ventilatory responses to nHF breathing were thought to be basically similar, but an influence of age cannot be excluded. The observed pCO₂ differences vary within groups, meaning the extent of ventilatory support by nHF cannot be estimated reliably. We did not measure respiratory muscle activity or force and thus can merely suggest that our observations are consistent with a partial relief in respiratory muscle load with nHF.

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Financial Disclosure and Conflicts of Interest

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