Change in pulmonary mechanics and the effect on breathing pattern of high flow oxygen therapy in stable hypercapnic COPD

ABSTRACT

We studied the effects of high flow oxygen therapy (HFOT) versus non-invasive ventilation (NIV) on inspiratory effort, as assessed by measuring transdiaphragmatic pressure, breathing pattern and gas exchange. Fourteen patients with hypercapnic COPD underwent five 30-min trials: HFOT at two flow rates, both with open and closed mouth, and NIV, applied in random order. After each trial standard oxygen therapy was reinstituted for 10 min. Compared with baseline, HFOT and NIV significantly improved breathing pattern, although to different extents, and reduced inspiratory effort; however, arterial carbon dioxide oxygen tension decreased but not significantly. These results indicate a possible role for HFOT in the long-term management of patients with stable hypercapnic COPD.

Trial registration number NCT02363920.

INTRODUCTION

High flow oxygen therapy (HFOT) is a new technique for delivering oxygen. In patients with acute respiratory failure, compared with standard oxygen therapy, HFOT was repeatedly shown to improve comfort, avoid mucosal dryness and injury, and deliver a more reliable and stable fraction of inspired oxygen (FiO_2).[1] In a study performed in patients with stable COPD, HFOT reduced the arterial carbon dioxide oxygen tension ($PaCO_2$), increased end-expiratory and tidal volumes (VTs), and decreased respiratory rate.[2] This makes HFOT an appealing form of treatment in patients with stable chronic hypercapnic respiratory failure (CHRF). In this setting, HFOT could be used in place of non-invasive ventilation (NIV) in the least tolerant and compliant patients, or in association with NIV, to reduce mask-related side effects.

In this randomised short-term physiological investigation we compare the physiological effects of standard oxygen therapy, NIV and HFOT in patients with stable hypercapnic COPD, as assessed at two flow rates with open and closed mouth. In addition to breathing pattern and arterial blood gases (ABGs), we measured the inspiratory effort by measuring the transdiaphragmatic pressure (Pdi).

MATERIALS AND METHODS

We enrolled 14 consecutive patients with COPD and CHRF. Patient characteristics and inclusion criteria are shown in the online supplementary table 1R and figure 1R. The study was approved by the Institutional Ethical Committee and written informed consent was signed by each patient.

Data were recorded during five 30-min trials applied according to a predetermined computer-generated random sequence. After each trial standard oxygen therapy through a nasal cannula was reinstituted for 10 min.

NIV and HFOT (Airvo 2; Fisher & Paykel Healthcare, Auckland, New Zealand) settings during the experimental procedure are illustrated in the online supplement. FiO_2 was kept constant.

ABGs were obtained at baseline and at the end of each trial. During baseline and HFOT trials VT was obtained by integrating the flow signal. Flow and VT could not be determined during the open mouth HFOT trials. Inspiratory and expiratory breath durations were determined from Pdi tracing, as previously described.[3] The patient's own respiratory rate (RRp) was also determined from the Pdi.[3] The last 5 min of each trial was recorded and averaged for data analysis.

In the online repository we provide detailed information on the inclusion and exclusion criteria, study procedures and statistical analysis.

RESULTS

As shown in table 1, compared with baseline, breathing frequency was significantly reduced in HFOT trials with the mouth closed and with NIV. Patient's own expiratory time (TE,p) was significantly prolonged and VT higher compared with baseline for all the settings. The patient's own inspiratory time (TI,p) was no different between trials.

Pdi swing and diaphragm pressure time product (PTPdi) were reduced compared with baseline in all trials. However, the reductions observed during NIV were significantly larger, as opposed to all of the HFOT trials. Dynamic intrinsic positive end expiratory pressure (PEEPi, dyn) was significantly reduced compared with baseline in all trials.

Breathing frequency, TI,p and TE,p, did not change between the different HFOT trials with the mouth closed or open, while Pdi at HFOT 20 L/min, was statistically higher with the mouth closed compared with open.

As shown in table 2, the $PaCO_2$ level decreased but not significantly with HFOT at 30 L/min and NIV compared with standard oxygen.

Also shown in table 2, comfort did not vary among the different trials.

DISCUSSION

We have demonstrated that compared with low oxygen flow, HFOT and NIV both reduce the respiratory muscle load on the respiratory system, resulting in a change in breathing pattern, increasing Te and reducing respiratory rate, suggesting a change in the pressure–volume curve.

Therefore, HFOT is an appealing technique as a potential alternative to NIV because it is less of a burden, it provides a more physiological humidification and heating of the airways, and a more 'easy to fit' interface.

Two studies in normal[4] controls and patients with COPD[2] have also shown that HFOT led to a marked increase in VT that was offset by a reduction in respiratory rate.

The most likely explanation for this response seems to be related to the increase in the expiratory resistance, with a mechanism different from that of CPAP.[4]

The respiratory pattern elicited by HFOT resembles pursed lip breathing which is, however, associated with increased work of breathing and patients cannot maintain this pattern over a longer time period.[5] In contrast, during HFOT we could demonstrate for the first time that inspiratory effort was reduced.

Several mechanisms have been advocated to explain the effect of HFOT on work of breathing, such as minimisation of inspiratory resistance,[4] attenuation of the activation of cold receptors or osmoreceptors in the nasal mucosa[6] and reducing the anatomical dead space in the upper airways.[7] Indeed the prolonged expiratory time may also reduce the amount of PEEPi, which may increase the inspiratory load.[8]

Furthermore, HFOT generates a modest degree of positive pressure, unlikely to be above 5–6 cmH_2O,[9] which may also partially counteract the threshold load imposed by the presence of PEEPi.[10]

The reduction in transcutaneous CO_2 in Fraser's study[2] and in $PaCO_2$, despite not being statistically significant, in our investigation, support the hypothesis that it is possible to reduce hypercapnia using HFOT. Indeed, carbon dioxide directly controls the activity of inspiratory muscles alone and therefore its reduction may lead to a decrease in diaphragmatic effort. We cannot rule out the effect of a higher PaO_2/FiO_2 ratio as explanation for the

Table 1 Breathing pattern, inspiratory effort and lung mechanics in different settings

	Baseline	HFOT 20 (closed)	HFOT 20 (open)	HFOT 30 (closed)	HFOT 30 (open)	NIV
TI,p (seconds)	0.95±0.2	0.85±0.4	0.96±0.2	0.94±0.3	0.92±0.3	1.00±0.2
TE,p (seconds)	1.94±0.4	2.35±0.4*	2.19±0.5*	2.30±0.5*	2.20±0.3*	2.61±1.0*
Breathing frequency (breaths/min)	24.8±2.3	19.01±5.2†	20.8±5.8	18.7±3.6†	19.64±2.8	17.8±3.8†
Tidal volume (mL)	314.50±84	391.22±106‡		364.22±66		456.20±100‡
Pdi swing (cmH_2O)	13.5±6.7	8.7±4.1§	12±5.8	8.2±3.7§	10.2±5.2§	5.1±2.2§¶
PTPdi/min (cmH_2Oxs/min)	238.3±82.1	164.2±51.3**	172.7±45.4**	143.2±48.9**	157.3±56.9**	101.7±42.9**††
PEEPi,dyn (cmH_2O)	2.12±0.9	1.48±0.7‡‡		1.03±0.6‡‡		0.9±0.02‡‡

*p=0.006 HFOT 20 closed versus baseline; p=0.01 HFOT 20 open versus baseline; p=0.007 HFOT 30 closed versus baseline; p=0.02 HFOT 30 open versus baseline; p=0.002 NIV versus baseline.
†p=0.022 HFOT 20 closed versus baseline; p=0.007 HFOT 30 closed versus baseline; p=0.002 NIV versus baseline.
‡p=0.015 HFOT 20 closed versus baseline; p=0.007 NIV versus baseline.
§p=0.005 HFOT 20 closed versus baseline; p=0.005 HFOT 30 closed versus baseline; p=0.03 HFOT 30 open versus baseline; p=0.001 NIV versus baseline.
¶p<0.003 NIV versus HFOT 20 closed; p=0.003 NIV versus HFOT 20 open; p=0.007 NIV versus HFOT 30 closed; p=0.005 NIV versus HFOT 30 open.
**p=0.005 HFOT 20 closed versus baseline; p=0.002 HFOT 20 open versus baseline; p=0.004 HFOT 30 closed versus baseline; p=0.015 HFOT 30 open versus baseline; p=0.001 NIV versus baseline.
††p<0.004 NIV versus HFOT 20 closed; p=0.006 NIV versus HFOT 20 open; p=0.016 NIV versus HFOT 30 closed; p=0.02 NIV versus HFOT 30 open.
‡‡p=0.01 HFOT 20 closed versus baseline; p=0.003 HFOT 30 closed versus baseline; p=0.001 NIV versus baseline.
Data are presented as mean±SD.
HFOT, high flow oxygen therapy; NIV, non-invasive ventilation; Pdi, transdiaphragmatic pressure; PEEPi,dyn, intrinsic dynamic positive end expiratory pressure; PTPdi, pressure–time product of the transdiaphragmatic; TE,p, patient's expiratory time; TI,p, patient's inspiratory time.

Table 2 Arterial blood gas values and comfort scores at different settings

	Baseline	HFOT 20 (closed)	HFOT 30 (closed)	NIV
pH	7.40±0.03	7.42±0.04	**7.43±0.04**	**7.44±0.04**
$PaCO_2$ (mm Hg)	61.2±9.2	57.2±11.7	**55.7±10.6**	**55.2±11.9**
PaO_2 (mm Hg)	70.6±12.6	70.3±17.3	61.5±11.1	**83.3±33.2**
Comfort score	7 (5–8)	5.5 (5–8)	5.5 (2–8)	**5 (3–5)**

Data are presented as mean±SD unless indicated otherwise.
Comfort score was assessed with a scale where 0 is the worst comfort and 10 the best. The data are presented as the median (interquartile 25–75).
HFOT, high flow oxygen therapy; NIV, non-invasive ventilation.

$PaCO_2$ increase during baseline conditions. Moreover baseline conditions consisted of breathing oxygen through nasal cannula, and under these conditions, FiO_2 cannot be controlled depending on the breathing pattern, the patient's inspiratory flow and whether patients breathe predominantly through the mouth or the nose. Therefore, the decrease in PaO_2 during HFOT can be explained by a higher actual FiO_2 under nasal oxygen therapy compared with HFOT.

We have further explored the physiological changes induced by mouth or nasal breathing, since it is totally unrealistic to assume that patients recruited for long-term treatment will always breathe with their mouth perfectly 'sealed'. It has been shown[9] that breathing with the mouth open negatively influences the generation of a positive pressure. Despite this, we were unable to demonstrate any 'detrimental' effect of this behaviour on the breathing pattern and inspiratory effort compared with breathing with the mouth closed.

The results of this study show overall similar acute physiological changes between HFOT and NIV, and support the need for further investigations to assess the effectiveness of domiciliary HFOT versus NIV in patients with stable hypercapnia. Obviously our findings could not be translated to the situation of an acute exacerbation of COPD.

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Competing interests None declared.

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