ONLINE SUPPLEMENT

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

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MATERIAL and METHODS

Patients

Fourteen consecutive COPD patients with stable chronic hypercapnic respiratory failure (CHRF), referring to our outpatient clinic for periodical controls, were enrolled in the study. Patients' characteristics are shown in table R1. The study was approved by the Sant'Orsola Malpighi Hospital. Written informed consent was obtained before enrolment. The study is registered with ClinicalTrials.gov, number NCT02363920. Clinical stability was defined as lack of 1) exacerbations in the previous three months, and 2) changes in the medications, as assessed from electronic records. Enrolment criteria were pH>7.35<7.45 and a PaCO2>45 mmHg with PaO2/FiO2> 200. Patients with cancer, neuromuscular disease or chronic heart failure were excluded.

Protocol

The patients were studied in a semi-recumbent position. They were asked to breathe for a few minutes through a standard nasal cannula (baseline). Data were recorded during five 30-minute 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 (baseline). In all of the trials the oxygen was administered to maintain SaO2 between 91% and 94%, keeping the FiO2 constant for the NIV and HFOT trials.

Non-invasive ventilation

Non-invasive ventilation (NIV) was administered using ventilators equipped with a dedicated NIV software (Vivo 50 Breas, Molnlycke, Sweden) or V60 (Respironics

V60 ventilator, Philips), through a full-face mask (PerforMax Face Mask, Philips Respironics). Great care was taken to avoid any possible air leaks. Correct positioning of the mask was reassessed at the beginning of each trial. The expiratory pressure (EPAP) was set by default to 4 cmH20 (the minimum allowed by the ventilators), while the peak inspiratory pressure (IPAP) was set according to the patient's tolerance and to avoid tidal volumes (VTs) >7 ml/Kg.

High Flow Oxygen Therapy (HFOT)

HFOT was delivered at two flow rates, 20 and 30 L/min. At each flow rate we performed two separate trials, asking the patients to breathe with their mouth open or closed. For this purpose, the patient was requested and instructed to breathe through both the nose and mouth in one trial and with the nose only in the other trial. The presence or absence of flow at the mouth was assessed using a pneumotachograph connected to a mouthpiece. The two flow rates used for the investigation had been previously defined by assessing patient comfort during HFOT, on a flow range between 10 and 50 L/min, using a visual analog scale, in eight different COPD patients with CHRF. It is worth mentioning that six patients scored the highest comfort at 30 L/min, which was then selected as the highest flow rate for the study.

HFOT was delivered using an AIRVO through an Optiflow nasal interface (Fisher & Paykel Healthcare, Auckland, New Zealand). With this system, the gas mixture is routed through a circuit to be delivered to the patient via short, large bore nasal prongs at 37°C with 100% relative humidity.

Measurements

Esophageal (Pes) and gastric (Pga) pressures were measured using separate balloon-

tipped catheters (Microtek, Medical B.V., Zutphen, Netherlands) positioned in the mid-esophagus and in the stomach respectively and connected to two differential pressure transducers (Micro Switch, Honeywell, USA). Esophageal and gastric balloons were filled with 0.5 and 1 ml of air, respectively [E1]. Correct positioning of the catheters was evaluated as previously described [E2]. Transdiaphragmatic (Pdi) pressure was obtained by subtracting Pes from Pga. The inspiratory efforts generated by the diaphragm was assessed by the inspiratory swing in Pdi , i.e., baseline to peak. The Pdi-time product was calculated as the integral of inspiratory Pdi over one minute, as already described[E3].

Flow was measured using a pneumotachograph (Hans Rudolph, Model 3700; Shawnee, KS, USA) connected to a mouthpiece during the baseline and HFOT trials with a closed mouth, and at the airways opening, between the mask, and the Y-piece during trials with an open mouth. Tidal volume (VT) was obtained by the integration of the flow in the NHF trials with the mouth open. Flow and VT were obviously not determined in the two HFOT sessions with open mouth. The patient's own inspiratory time (TI,p) and expiratory time (TE,P) were obtained from the Pdi tracing. TI,p was determined as the time lag between the onset of the positive Pdi swing above baseline (i.e., start of inspiratory effort) and the point where Pdi started to fall toward baseline. While TE,p was determined as the time distance between this latter point and the onset of the following inspiration[E4]. The patient's respiratory rate (RRp) was also determined from the Pdi tracing[E4].

PEEPi (PEEPi,dyn) was obtained from the Pdi signal, as the value of Pes at the point of zero flow, only in the trials where flow was measured [E5].

Patient comfort was assessed during each trial using a visual analogue scale from 0 to

10, where the former is the worst comfort and the latter the best. At the end of each run, just before ABG assessment, the patient was asked to score her/his comfort on the scale. [E6].

Statistical Analysis

The results are expressed as mean ± standard deviation (SD). Differences between the different trials were determined using the Friedman test. The difference between the two HFOT trials with the mouth open and closed interfaces was assessed using the Wilcoxon signed-rank test. P values < 0.05 were considered statistically significant. Comparison between groups, were adjusted for multiplicity in post-hoc analysis using the Bonferroni's test. All of the analyses were performed using statistical package Stata Intecooled for Windows, version 12.0 (STATA, College Station,TX).

REFERENCES

E1. Tobin MJ. Monitoring respiratory mechanics in spontaneously breathing patients. In: Tobin MJ, ed. Principles and Practice of Intensive Care Monitoring. Columbus, McGraw-Hill, 1998; pp. 621–628.

E2. Baydur A, Behrakis PK, Zin WA et al. A simple method for assessing the validity of the esophageal balloon technique. *Am Rev Respir Dis*.1982;126:788-91.

E3. Sassoon CS, Light RW, Lodia R, et al. Pressure-time product during continuous positive airway pressure, pressure support ventilation, and T-piece during weaning from mechanical ventilation. *Am Rev Respir Dis* 1991; 143:469-75.

E5. Appendini L, Purro A, Gudjonsdottir M et al. Partitioning of inspiratory muscle workload and pressure assistance in ventilator-dependent COPD patients. *Am J Respir Crit Care Med* 1996;154:1301-9

E6. Navalesi P, Fanfulla F, Frigerio P et al. Physiologic evaluation of noninvasive mechanical ventilation delivered with three types of mask in patients with chronic hypercapnic respiratory failure. *Crit Care Med* 2000; 28:1785–1790.

Table. 1R Baseline characteristics of the patients

	n=14
Age, yrs	73.5± 5.2
Sex (M/F)	9/6
Body Mass Index (BMI)	26.65±4.8
FEV1 (% pred)	44.29 ± 13.59
LTOT duration (months)	37.3±12.
Previous "acute" NIV (n/total)	5/14
Actual Smokers (n/total)	6/14
Ex-Smokers (n/total)	8/14
Charlson Index	2-11
Secretions	2 ± 1.1 (30) 0-3

Data are presented as mean ± SD, minimum and maximum value
NIV=Non-invasive ventilation, FEV1= Forced expiratory volume in the 1st second, LTOT=Long Term Oxygen Therap

Fig.1 Consort diagram of the study