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Efficacy of temporary positive expiratory pressure (TPEP) in patients with lung diseases and chronic mucus hypersecretion. The UNIKO® project: a multicentre randomized controlled trial

Elena Venturelli[1], Ernesto Crisafulli[2], Assunta DeBiase[2], Daniela Righi[2], Daniele Berrighi[3], Pier Paolo Cavicchioli[3], Guido Vagheggini[3], Francesco Dabrosca[4], Bruno Balbi[4], Mara Paneroni[5], Luca Bianchi[5], Michele Vitacca[5], Vittoria Galimberti[6], Michele Zaurino[6], Giorgio Schiavoni[6], Andrea Iattoni[1], Nicolino Ambrosino[3] and Enrico M Clini[1,2]

Abstract

Objective: To evaluate whether temporary positive expiratory pressure provides benefit in patients with lung diseases and chronic hypersecretion.

Design: Single blind multicentre randomized trial.

Setting: Five Italian rehabilitation centres.

Participants: Ninety-eight patients with chronic obstructive pulmonary disease and/or chronic bronchitis (*n*=78), or bronchiectasis (*n*=20), with a peak cough expiratory flow >150 l/min and sputum production >30 ml/day, randomly included into two treatment groups.

Interventions: For 10 consecutive days, the active group performed twice a day 20-minute cycles of manually assisted breathing techniques in sequence with the addition of 15 minutes of temporary positive expiratory pressure, while the control group was treated by manually assisted breathing techniques alone.

Measures: Within and between group changes of arterial oxygenation index, lung volumes and respiratory muscles strength were recorded at enrolment and after 3 and 10 treatment sessions.

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Pre-to-post treatment change of sputum volume and bronchial encumbrance (Δ-visual analog scale), sputum density and purulence were compared daily within the study period.
Results: No significant changes were recorded for the oxygenation index, while dynamic lung volumes and respiratory muscle strength significantly (P <0.05) improved in the active group. The group comparison analysis of the pre-to-post change showed that inspiratory capacity was significantly higher in the active than in the control group (+19.5% and +2.2%, P=0.044) at day 10. A greater improvement in Δ-visual analog scale was recorded in the active group at day 3 and 8.
Conclusions: These preliminary data suggest that temporary positive expiratory pressure improves lung volumes and speeds up the improvement of bronchial encumbrance in patients with lung diseases and hypersecretion.

Keywords
Hypersecretion, bronchial drainage, temporary positive expiratory pressure, cough, rehabilitation

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Introduction

Chronic mucus hypersecretion is frequently observed in many respiratory diseases, such as chronic airway obstruction in chronic obstructive pulmonary disease, including chronic bronchitis and bronchiectasis,[1] with a negative impact on both function and survival.[2,3]

To date, chest physiotherapy techniques by manually assisted breathing techniques remain the gold standard for those patients with normal cough reflex.[1] In addition, positive expiratory pressure delivered by hand-held devices is considered a valid technique to manage excessive airway secretion, enhancing expectoration and modifying muco-rheological properties.[4] However, results supporting the use and the effectiveness of these tools to assist airways clearance are still controversial in literature.

Recently, a new modality to mechanically deliver a low positive expiratory pressure level at the mouth during spontaneous breathing, so-called temporary positive expiratory pressure, has become available in the market, and it has been proposed in assisting patients with chronic mucus hypersecretion. This technique produces a 1 cmH_2O increase in airway pressure along the respiratory cycle until immediately before the end of expiration. Although the level of applied pressure with temporary positive expiratory pressure is several times lower than that (5 to 15 cmH_2O) used and considered effective with other positive expiratory pressure and/or oscillatory-positive expiratory pressure devices,[1] preliminary results have shown that an expiratory pressure ≤1 cm H_2O applied for a fraction of the expiratory phase may improve the distribution of alveolar ventilation and prevent mechanical stress injury, which is expected to occur in the bronchial tree or lung parenchyma at a higher pressure.[5]

The aim of our study was to evaluate the clinical effectiveness of temporary positive expiratory pressure as a new positive low-pressure technique to clear excessive mucus in stable patients with hypersecretion and normal cough reflex. We therefore tested the hypothesis that temporary positive expiratory pressure may provide additional clinical benefits over conventional manually assisted breathing techniques, considered as the reference techniques in this condition.

Methods

Patients

We prospectively recruited 98 chronic mucus hypersecretion patients admitted from July 2008 to December 2010 to five Italian centres (Villa Pineta Hospital, Pavullo n/F, Auxilium Vitae Rehabilitation Center, Volterra, IRCCS Maugeri Foundation, Centres of Veruno and Lumezzane, and San Giuseppe

Hospital, Milano) for an inpatient pulmonary rehabilitation. Villa Pineta Hospital acted as the study coordinator.

The institutional review board and ethical committee at each hospital approved the study, which was conducted according to the declaration of Helsinki.[6]

All patients were in a stable clinical condition and free from any acute exacerbation for least four weeks at the time of inclusion; chronic mucus hypersecretion was specifically related to chronic obstructive pulmonary disease or bronchiectasis. Forty per cent of them had concomitant chronic respiratory failure leading to regular domiciliary oxygen therapy (long term oxygen therapy) (see Table 1) but not precluding them from participation in the trial. Diagnosis and severity of chronic obstructive pulmonary disease were confirmed on a clinical basis and by means of spirometry.[7,8]

Chronic mucus hypersecretion was defined as a sputum volume production of greater than 30 ml/day.[1] A peak cough expiratory flow >150 l/min confirmed the patients were able to cough without the need of any additional support.[9]

Patients with limitations regarding exercise or with other associated conditions (i.e. severe concomitant cardiovascular disease or cancer) which may have limited or impaired the response to training, and those patients under domiciliary mechanical ventilation or taking any active drugs supposed to have a mucoregulatory action (i.e. aminophyllines, N-acetyl-cysteine), were excluded from the study. Finally, patients who were deemed unable to use the temporary positive expiratory pressure device were also excluded.

Patients were considered as having dropped out of the study when clinical signs of a new exacerbation occurred. Patients dropping out were nonetheless included in the analysis as being registered and part of the trial.

Design

This was a single blind randomized trial with randomization list by blocks for each centre; each centre had a randomization list provided, which indicated the group for each patient's allocation. The protocol was recorded on the ClinicalTrial.gov website with identification code NCT00700388.

Rehabilitation program

Appropriate selection of patients and the program content were according to the American Thoracic Society/European Respiratory Society joint statement on pulmonary rehabilitation.[10,11] All the eligible patients were instructed to use temporary positive expiratory pressure for acclimatization in a 2-hour training period in the lung laboratory before inclusion into the trial.

The study group (active) performed twice a day 20-minute cycles of manually assisted breathing techniques plus 15 minutes of temporary positive expiratory pressure (UNIKO®, Medical Products Research, Legnano, Italy) each day.

Controls were treated by manually assisted breathing techniques alone with the same modalities as in the active group. In all patients intervention lasted 10 consecutive days, within the period of the in-hospital rehabilitation course starting at least 48–72 hours following admission and initial assessment.

Manually assisted breathing techniques consisted of a cycle of assisted exercises; among these we performed Expiration Lente Totale avec Glotte Ouverte en Infralateral and forced expiration,[1,5] which were delivered in sequence to all patients up to the time limit; a short preliminary description of the procedure was given by the attending physiotherapist. Temporary positive expiratory pressure, when appropriate, was delivered continuously to the subjects throughout the programmed period. Spontaneous cough to eliminate secretions following treatment periods was not assisted by personnel, and patients were instructed to collect sputum in a single plastic pot (changed on a daily basis) to calculate the total volume per day. The temporary positive expiratory pressure device (UNIKO® Medical Products Research, Legnano, Italy) delivered a fixed positive pressure (1 cmH_2O or 0.0977 kPa) only in the expiratory phase. This increase in low pressure was created through a pulsatile flow approximately 42 Hz in frequency.

Table 1. Anthropometric, demographic and physiological characteristics of the population in study.

Variables		Active (*n*=53)	Control (*n*=45)	*P*-value
Age	Years	70.0 (10.8)	71.6 (8.7)	0.448
Sex	M/F	29/24	35/10	**0.017**
BMI	kg/m^2	26.3 (7.0)	25.7 (5.8)	0.690
Smoker	Smoker/Ex/No	13/18/22	15/16/14	0.560
Drop-out	Yes/No	9/44	6/39	0.617
Diagnosis	COPD/COPD and CB/ Bronchiectasis	40/0/13	36/2/7	0.185
LTOT		19	20	0.386
pH		7.42 (0.03)	7.42 (0.04)	0.733
$PaCO_2$	mmHg	44.7 (10.4)	42.7 (8.5)	0.817
PaO_2	mmHg	72.3 (10.5)	68.9 (9.5)	0.510
PaO_2 /FiO_2		318.6 (60.0)	296.6 (69.7)	0.123
$SPaO_2$ /FiO_2		313.2 (57.3)	280.7 (67.7)	0.087
$SatO_2$	%	94.7 (2.3)	94.0 (1.6)	0.520
FEV_1	Litres	1.29 (0.60)	1.11 (0.54)	0.149
	% predicted	61.9 (25.0)	50.3 (24.8)	0.069
FVC	Litres	2.14 (0.74)	2.25 (0.79)	0.345
	% predicted	79.7 (23.2)	75.8 (26.3)	0.848
FEV_1/FVC	%	52.7 (15.6)	44.2 (13.7)	0.006
CV	Litres	2.43 (0.71)	2.52 (0.72)	0.444
	% predicted	85.2 (22.3)	83.7 (27.5)	0.588
IC	Litres	1.56 (0.55)	1.58 (0.59)	0.680
	% predicted	83.7 (34.1)	73.6 (29.9)	0.883
RV	Litres	2.97 (1.19)	3.52 (1.65)	0.162
	% predicted	131.6 (48.8)	150.5 (64.4)	0.307
TLC	Litres	5.41 (1.31)	6.10 (1.81)	0.075
	% predicted	102.1 (22.1)	106.6 (27.1)	0.658
MIP	cm H_2O	57.8 (25.9)	55.0 (17.5)	0.463
	% predicted	60.9 (26.1)	51.0 (19.3)	0.131
MEP	cm H_2O	83.0 (29.9)	81.9 (37.3)	0.921
	% predicted	74.9 (47.0)	56.9 (31.7)	0.099
PCEF	Litres /min	247.3 (83.6)	223.3 (67.8)	0.065

Data are presented as mean (SD).
BMI, body mass index; CB, chronic bronchitis; COPD, chronic obstructive pulmonary disease; CV, current volume; F, female; FEV_1, forced expiratory volume in 1 s; FiO_2, fraction of inspired oxygen; FVC, forced vital capacity; IC, inspiratory capacity; LTOT, long term oxygen therapy; M, male; MEP, maximum expiratory pressure; MIP, maximum inspiratory pressure; $PaCO_2$, carbon dioxide tension; PaO_2, oxygen tension; PaO_2 /FiO_2, arterial oxygenation; PCEF, peak cough expiratory flow; RV, residual volume; $SatO_2$, oxygen saturation; TLC, total lung capacity.

Physiotherapists from each centre and involved in this research were previously instructed to standardize the type and duration of all activities. They knew which group each patient was in, but none of them was aware of the study purpose.

Measurements and outcomes

At enrolment, patients' anthropometric and physiological characteristics and main diagnosis were recorded. Cough peak expiratory flow by a hand-held device

was recorded in all patients to confirm their cough competence and reflex initially.[9]

Outcome measures were taken at study entry (day 0), and after three and 10 days of treatment. Data on sputum volume and characteristics, and individuals' perceived symptoms, were recorded on a daily basis.

One physiotherapist, different from those who treated the patients and unaware of the study purpose, was in charge in each centre for all the measurements at each time point.

Primary outcome – Arterial blood gas analysis was obtained from an arterial blood sample taken from the radial artery with the patient in resting condition and breathing room air or oxygen (when appropriate) at the prescribed flow rate: parameters were corrected by the Mays' graph.[12]

The derived arterial oxygen tension to inspiratory oxygen fraction ratio (PaO_2/FiO_2) was considered as the primary outcome based on previous data using a device to treat a condition of chronic mucus hypersecretion in severely affected patients.[13]

Secondary outcomes – Lung function was assessed by means of an automated spirometer: dynamic and static volumes were expressed as % of their predicted value.[14] Respiratory muscle strength (maximal inspiratory and expiratory pressure) was then performed by means of a specific module recording maximal pressures against an occlusive mouth resistance at both total lung capacity (for maximal expiratory pressure) and functional residual volume (for maximal inspiratory pressure); values were recorded as absolute and as a percentage of predicted values according to the reference equations.[15] Both measures of lung function were recorded with the patient in a sitting position; the best of three measurements was recorded.

The perceived sensation of bronchial encumbrance was reported by patients as a discomfort and/or appearance of substantial amount of secretions leading to dyspnoea; it was measured each day by a visual analogic scale[16] (days 1 to 10). The change in sputum volume and percent visual analogic scale were recorded as study outcomes.

Sputum density and purulence were also recorded on a daily basis by means of a specific three-point semi-quantitative scale (where 0=fluid for density or light for purulence, 1= dry for density or yellowish for purulence, 2= thick for density or dark for purulence).[17] The patients were instructed to collect their secretions in a small container every day in the morning and following the chest physiotherapy (120 minutes after the second daily session) in both groups and for the whole study period. The same nurse, not involved in the study aims, recorded these variables.

Statistical analysis

Sample size. Although this study addresses several outcome measures, only one was considered for sample size determination. Changes in daytime oxygenation ratio (PaO_2/FiO_2) under usual breathing conditions was the outcome selected to determine a minimum sample able to ensure powerful testing of treatment effect.[13] In order to ensure 80% power to detect a group difference ≥25 points in oxygenation ratio after treatment period as significant at the 0.05 level, 42 patients per group were needed for the study. Considering a probability of 15% drop-out rate of randomized patients, the minimum target sample size was fixed at 49 patients per group.

Efficacy analysis. Analyses were carried out using SPSS software (SPSS 8.0 for Windows; SPSS, Chicago, Illinois, USA) and applied according to the current methodology.[18]

Qualitative and quantitative variables are presented as count, percentage (%), and mean (± standard deviation, SD), respectively. A preliminary test for normal distribution of data was made by the Kolmogorov–Smirnov test.

Absolute values and changes (Δ) in each outcome variable were compared by means of ANOVA and Student *t*-test. Wilcoxon and Kruskal–Wallis tests were applied for non-parametric variables. Comparisons among groups and times were performed following the intention to treat model; last observation carried forward was used as the method of analysis and data are presented accordingly.

A further analysis for confirming results has been added; indeed, the general linear model for repeated measures (mixed-model ANOVA) was

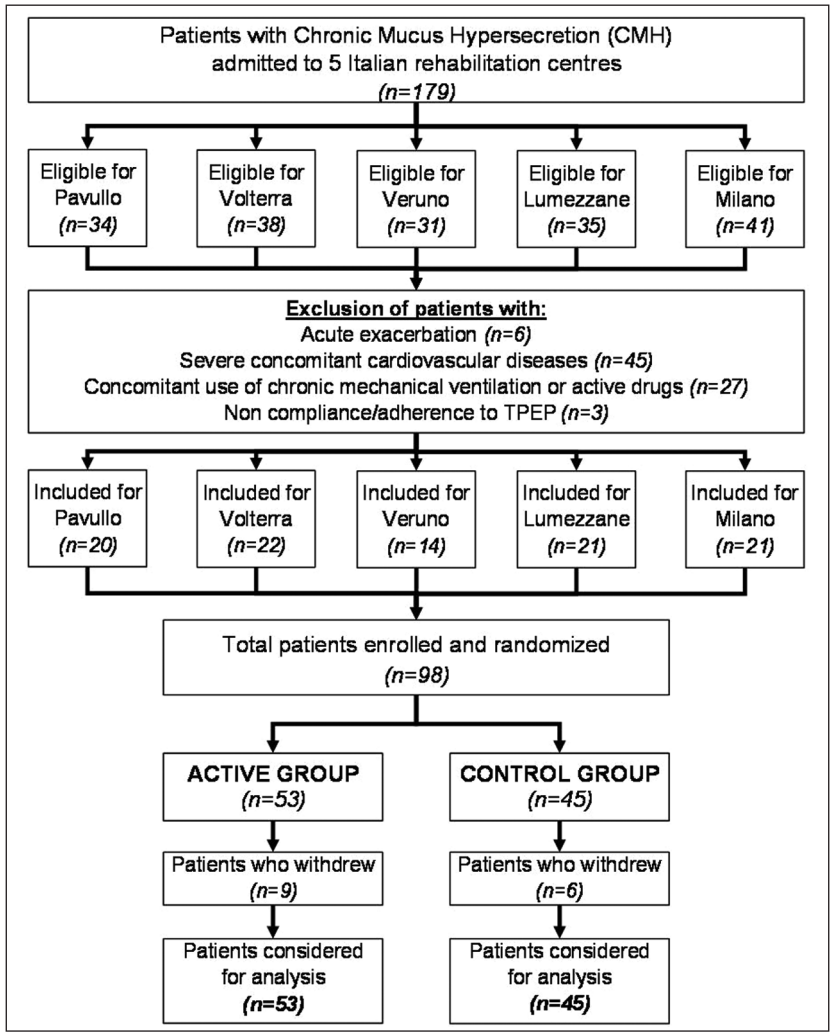

Figure 1. Flow chart of the study.

applied to all the variables in the study to calculate the statistical interaction between groups, time and groups at each time point.

All results were considered to be statistically significant at a level of $P < 0.05$.

Results

The study flow diagram is depicted in Figure 1. Main descriptive anthropometric, clinical and functional characteristics of patients included are shown in Table 1; no differences among centres were reported. Sixty-four patients were male (65%) and 15 of the whole population presented a Body Mass Index >30 kg/m^2, with no difference between groups. Gender distribution was different among groups. Chronic respiratory failure needing long term oxygen therapy occurred in 39 patients (40%). Overall, the study population was characterized by a moderate airflow obstruction with concomitant hyperinflation. The drop-out rate from the study

Table 2. Absolute changes of gas exchange, lung volumes, muscle strength and bronchial encumbrance at each time point in the study groups.

		Active			Control		
		Day 0	Day 3	Day 10	Day 0	Day 3	Day 10
$PaCO_2$	mmHg	44.7 (10.4)	41.9 (7.4)	42.8 (7.7)	42.7 (8.5)	42.1 (7.1)	41.3 (8.4)
PaO_2	mmHg	72.3 (10.5)	74.4 (8.2)	73.5 (9.8)	68.9 (9.5)	70.1 (11.7)	70.3 (9.7)
$SPaO_2$	mmHg	70.8 (10.6)	71.2 (8.1)	71.3 (10.1)	65.5 (10.5)	67.1 (11.2)	65.9 (10.3)
PaO_2/FiO_2		318.6 (60.0)	328.2 (52.6)	327.1(63.5)*	296.6 (69.7)	305.2 (81.7)	303.0 (62.7)
$SatO_2$	%	94.7 (2.3)	95.1 (1.9)	95.1 (2.0)	94.0 (1.6)	93.7 (2.6)	94.3 (2.2)
FEV_1	% predicted	61.9 (25.0)	61.2 (29.1)	64.9 (27.0)*	50.3 (24.8)	51.5 (24.4)	51.2 (23.5)
FVC	% predicted	79.7 (23.2)	81.9 (24.1)	84.1 (24.4)	75.8 (26.3)	78.8 (24.9)	78.2 (21.4)
FEV_1/ FVC	%	52.7 (15.6)*	44.0 (13.4)*	53.7 (16.6)**	44.2 (13.7)	42.9 (14.6)	43.8 (15.2)
CV	% predicted	85.2 (22.3)	88.1 (24.9)	89.4 (23.8)	83.7 (27.5)	86.5 (27.3)	85.6 (24.2)
IC	% predicted	83.7 (34.1)	95.4 (40.2)	103.3 (38.0)	73.6 (29.9)	78.5 (27.7)	75.8 (24.3)
MIP	% predicted	58.2 (26.4)	58.5 (26.0)	64.2 (25.9)	49.7 (21.1)	61.1 (28.9)	59.1 (30.8)
MEP	% predicted	77.8 (49.5)	72.2.6 (39.7)	80.1 (49.4)	50.3 (29.5)	57.6 (32)	61.6 (34.9)
Bronchial encumbrance	%VAS	48.1 (23.1)	48.3 (25.0)	37.4 (21.4)	38.5 (25.2)	37.1 (25.3)	30.1 (26.5)

Data are presented as mean (SD).
CV, current volume; FEV_1, forced expiratory volume in 1 second; FiO_2, fraction of inspired oxygen; FVC, forced vital capacity; IC, inspiratory capacity; MEP, maximum expiratory pressure; MIP, maximum inspiratory pressure; $PaCO_2$, carbon dioxide tension; PaO_2, oxygen tension; PaO_2/FiO_2, arterial oxygenation; $SatO_2$, oxygen saturation; VAS, Visual Analog Scale.
*$P < 0.05$ between groups at the same time.
**$P < 0.01$ between groups at the same time.

was 17% (n=9) and 11% (n=6) in active and control groups respectively (not significant); in all cases, patients withdrew due to a recurrent exacerbation of their respiratory condition.

Table 2 shows the changes in arterial blood gases, lung volumes, muscle strength and bronchial encumbrance (visual analogic scale %) over time. No significant changes were observed for the blood gases or for the oxygenation ratio in both groups. There were significant ($P < 0.05$) increases by T10 in forced expiratory volume in the first second (+3.0%), forced vital capacity (+4.4%), current volume (+4.2%), and inspiratory capacity (+19.6%) in the active but not in the control group.

However, in the group comparison analysis of the pre-to-post change for the same variables only inspiratory capacity was more significantly increased in the active than in the control group (see Table 3).

The same statistical results in terms of group and time comparison as in Tables 2 and 3 have been obtained by means of the general linear model for repeated measures (data not shown).

Figure 2 shows the daily trend of sputum variables and symptoms during the study period. Δ-volume (sputum) and Δ-visual analog scale showed similar behaviour in the two groups over time; however, a greater improvement in Δ-visual analog scale after intervention was recorded at day 3 and 8 in the active group (Figure 2, panel B). Sputum density and purulence showed a similar and significant trend to improvement over time in both groups; however, lower (=better) scores were recorded at several time points in the active but not in the control group (Figure 2, panels C and D).

Discussion

The present study suggests that temporary positive expiratory pressure, added to conventional

Table 3. Group comparison analysis of the pre-to-post change of blood gases, lung volumes and muscle strength in the study groups.

		Active	Control	*P*-value
Δ FEV_1	% predicted	3.0 (10.4)	0.8 (7.7)	0.295
Δ FVC	% predicted	4.3 (12.9)	2.3 (12.9)	0.495
Δ FEV_1 / FVC	%	1.90 (7.7)	−0.20 (6.51)	0.214
Δ CV	% predicted	3.7 (10.8)	2.2 (10.1)	0.537
Δ IC	% predicted	19.5 (20.6)	2.2 (17.0)	**0.044**
Δ MIP	% predicted	6.0 (11.0)	9.4 (17.0)	0.541
Δ MEP	% predicted	2.3 (21.5)	11.3 (13.1)	0.233
Δ $PaCO_2$	mmHg	−1.8 (9.0)	−1.6 (6.9)	0.915
Δ PaO_2	mmHg	1.6 (8.2)	0.4 (11.4)	0.571
Δ $SPaO_2$	mmHg	0.1 (7.7)	−0.03 (10.6)	0.785
Δ PaO_2 /FiO_2		10.0 (37.9)	2.0 (50.9)	0.424
Δ $SPaO_2$ /FiO_2		3.3 (36.8)	−1.5 (46.9)	0.610
ΔSAT O_2	%	0.53 (1.73)	0.13 (2.22)	0.371

Data are presented as mean (SD).

Δ, difference pre-to-posttreatment; CV, current volume; IC, inspiratory capacity; FEV_1, forced expiratory volume in 1 second; FiO_2, fraction of inspired oxygen; FVC, forced vital capacity; MEP, maximum expiratory pressure; MIP, maximum inspiratory pressure; $PaCO_2$, carbon dioxide tension; PaO_2, oxygen tension; PaO_2/FiO_2, arterial oxygenation; $SATO_2$, oxygen saturation.

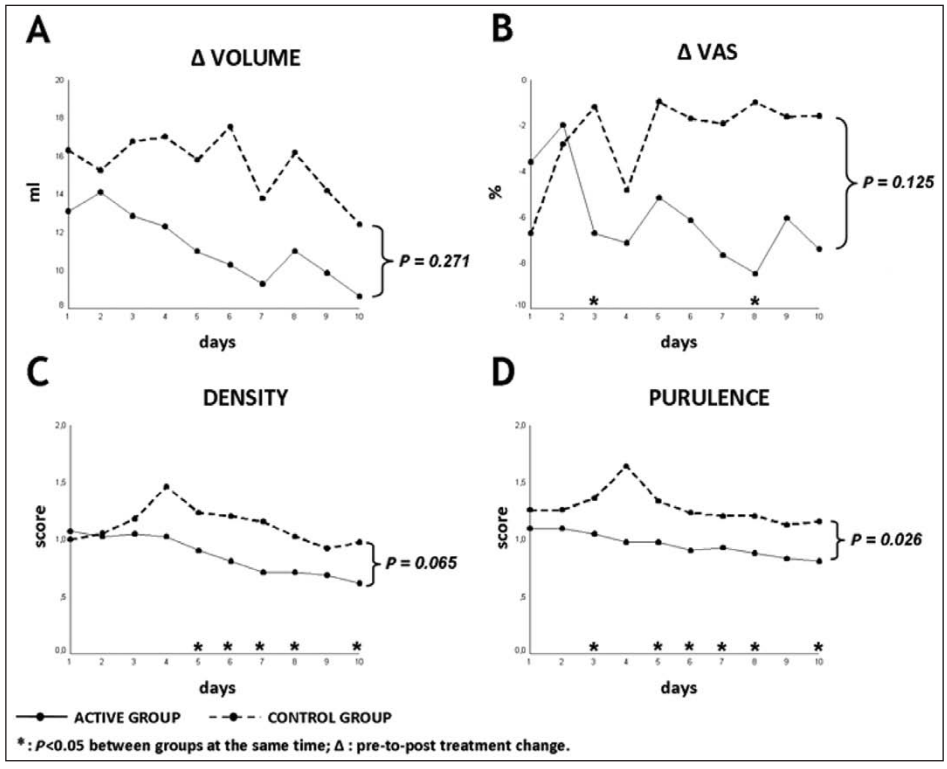

Figure 2. Daily trend of variables assessed during the study period: sputum volume production (Δ volume – panel A), bronchial encumbrance (Δ visual analog scale – panel B), sputum density (panel C) and sputum purulence (panel D).

manually assisted chest physiotherapy to clear excessive mucus in patients with lung diseases and chronic hypersecretion, improves ventilatory function and speeds up the improvement of perceived bronchial encumbrance.

Airway clearance can be effectively performed through different manually assisted or unassisted methods.[19] Recently, temporary positive expiratory pressure, as a positive pressure device, has been developed for those patients having a valid cough reflex. This is the first controlled study assessing the short-term (10 days) clinical effectiveness of temporary positive expiratory pressure in a consistent population of patients with lung diseases and chronic mucus hypersecretion.

The preliminary and experimental use of temporary positive expiratory pressure in pathology has been performed in chronic respiratory diseases, including chronic obstructive pulmonary disease, asthma and cystic fibrosis, showing that symptoms and static and dynamic lung volumes improved after two weeks of treatment.[20] In addition, temporary positive expiratory pressure has been successfully used for 30 minutes twice a day for five days in the preparation of 28 chronic obstructive pulmonary disease patients for major abdominal surgery.[21] According to those findings,[20,21] it has been speculated that lung ventilation was less inhomogeneous and arterial blood gases significantly improved in patients treated by temporary positive expiratory pressure, who also reported a significant and progressive reduction in mucus production and in perceived bronchial encumbrance.

Our results have confirmed those preliminary observations in terms of lung ventilation, but not the expected effect on gas exchange. The lack of improvement in the primary outcome is possibly due to two main problems. First, the expected change PaO_2/FiO_2 ratio was estimated on the basis of a previous study using a different mechanical device to remove secretions;[13] indeed, expected changes in arterial blood gases with temporary positive expiratory pressure were lacking based on the available data. Second, it is more likely that, due to the previous reason, the sample size was underpowered to show any significant difference in oxygenation ratio between the two groups.

Notably, we have found that temporary positive expiratory pressure causes a significant change in pulmonary function, as documented by the significant improvement of most variables at T10 (see Table 3) in the active but not in the control group. In particular, the analysis of group difference in variable changes confirmed the significant effect of temporary positive expiratory pressure on the increase in inspiratory capacity (see Table 3), which is likely to prove both the reduction in airway obstruction and the recruitment of collapsed or obstructed peripheral airways and lung parenchyma.

This beneficial effect on lung function has also so far been assessed by clinicians aiming at evaluating the effectiveness of different types of positive expiratory pressure techniques.[22,23] The theoretical benefit of these techniques, indeed, is the ability to enhance mucus clearance by either stenting the airways and preventing airway collapse, or increasing intrathoracic pressure and collateral ventilation distal to retained secretions, or decreasing functional residual capacity of the lung.[24]

Another relevant finding in our study was the effect following the use of temporary positive expiratory pressure on the characteristics of mucus in the population treated. Indeed, a trend towards a greater reduction of sputum over time in the active group compared with the control group was reported (see Figure 2, panel A). The use of temporary positive expiratory pressure also enhanced the improvement of the score for density and for purulence in the active group at several time points (see Figure 2, panels C and D). It is likely that, for a given reduction in the overall volume of sputum produced over the study period, the reduction in sputum density may reflect and parallel the reduction of perceived bronchial encumbrance that patients experienced early, three days after beginning temporary positive expiratory pressure (see Figure 2, panel B).

Previous studies have challenged the effect of conventional chest physiotherapy and different positive expiratory pressure techniques on the individual's ability to expectorate, and found a likely benefit, probably due to change in the operational lung volumes and flow.[4] Some authors have specifically tested positive expiratory pressure mask and

manually assisted breathing techniques in improving lung function and maintaining the effect over a one-year period when compared with postural drainage.[25,26] However, the significant advantage of one technique over another was not clear, even if used for a long period.[27]

Although this study reports some interesting and new findings in relation to the use of temporary positive expiratory pressure, some limitations should be carefully taken into account by readers. First, the study failed to test the hypothesis that the addition of temporary positive expiratory pressure may gain in terms of oxygenation, and this was probably due to a type-2 statistical error for an under-powered sample size (see discussion above). Second, temporary positive expiratory pressure was delivered for only a 10-day period and we cannot exclude the possibility that a longer period would have enhanced and/or sustained the positive effects; this preliminary study is unlikely to show the optimal regimen of temporary positive expiratory pressure in terms of either frequency or duration. Third, despite the low level of pressure delivered by temporary positive expiratory pressure, we cannot exclude that a different effect could have been generated in patients with chronic obstructive pulmonary disease or bronchiectasis; however, the limited population in the study does not allow this question to be answered. Therefore, our clinical findings can only generate hypotheses that should be further tested in physiological studies with an appropriate design and aim.

Finally, we did not study any functional outcome (e.g. the six minute walk test) to see whether the recorded improvements might have been related to a better general clinical condition of these patients.

Despite this, the trial has the strength of being based on a multicentre randomized controlled design that guarantees an elegant and correct scientific method of research. Moreover, the population in the study is quite representative of patients suffering from lung diseases and chronic mucus hypersecretion in *real life*, thus making this research a realistic base for future studies in the same field.

Clinical messages

- Temporary positive expiratory pressure improves lung function and symptoms in patients with chronic lung disease and mucus hypersecretion.
- The clinical advantage of temporary positive expiratory pressure over conventional chest physiotherapy consists in a faster recovery from symptoms during treatment.

Authors' contributions

Conception and design of the study: EV, EC, EMC
Drafting the article: EV, EC
Analysis of data: EC, EV
Acquisition of data: DR, AD, DB, PC, FD, MP, VG, MZ, GS, AI
Revising paper and the final draft: BB, NA, EMC

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