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Effects of Positive Expiratory Pressure (PEP), Continuous Positive Airway Pressure (CPAP) and Hyperventilation in COPD Patients with Chronic Hypercapnea

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Abbreviations: ABG, Arterial blood gases; COPD, Chronic obstructive pulmonary disease; CO_2, Carbon dioxide; CPAP, Continuous positive airway pressure; CPT, Chest physiotherapy; FEV_1, Forced expiratory volume in one second; FRC, Functional residual capacity; LTOT, Long-term oxygen therapy; $PaCO_2$, Arterial carbon dioxide tension; PaO_2, Arterial oxygen tension; PEP, Positive expiratory pressure; PLB, Pursed-lips breathing; $PtcCO_2$, Transcutaneous carbon dioxide tension; $PtcO_2$, Transcutaneous oxygen tension; SaO_2, Arterial oxygen saturation; SpO_2, Oxygen saturation by pulse oximeter; TC, Thoracic compressions.

ABSTRACT

We have studied the effects of positive expiratory pressure (PEP), continuous positive airway pressure (CPAP) and hyperventilation on 9 hypoxemic and hypercapnic chronic obstructive pulmonary disease (COPD) patients. All the patients were in a stable condition and received continuous oxygen. PEP and nasal CPAP were each given for 3 days in random order once every hour during the day and 3 times overnight. The effects of treatment were compared with a 3-day period in which the patients had no treatment for CO_2 elimination. The effects were based on transcutaneous measurements of PO_2 ($PtcO_2$), PCO_2 ($PtcCO_2$) and SO_2 (SpO_2) and arterial blood gas measurements. The transcutaneous measurements showed that the PEP treatment reduced the $PtcCO_2$ in COPD patients by 0.5 kPa and the CPAP treatment reduced it by 0.1 kPa ($p<0.05$). The hyperventilation maneuver caused a decrease in the $PtcCO_2$ of 0.7 kPa. The nocturnal treatments and measurements were all similar to the daytime measurements; the $PtcCO_2$ decreased by 0.6 kPa using PEP and by 0.3 kPa using CPAP ($p<0.01$). This indicated that all 3 methods reduced the $PtcCO_2$, but only in the short term as the effects lasted for less than 4 min. COPD patients had no "late response" after any form of treatment. Arterial blood gases in COPD patients showed an elevation in $PaCO_2$ (1.2 kPa) and a decrease in PaO_2 and SaO_2 during the night (11 pm to 7 am) without treatment. After 3 days of treatment with PEP and CPAP, the same pattern was noticed. The $PaCO_2$ increased with both therapies, 1.3 kPa with PEP and 0.6 kPa with CPAP. Our data indicate that the effects were not of clinical significance and there is no justification for treating stable hypercapnic COPD patients with these methods.

INTRODUCTION

Patients with far-advanced chronic obstructive pulmonary disease (COPD) often become unable to maintain ventilation which is sufficient to prevent hypoxia and hypercapnia. Long-term oxygen treatment (LTOT) is often an effective treatment for these patients, but in some cases oxygen supplementation induces a further increase in arterial oxygen tension ($PaCO_2$). This may prevent

the administration of oxygen in amounts sufficient to maintain an adequate level of oxygenation. To overcome this problem it is desirable to find methods preventing the CO_2 tension to increase e.g. by increasing the CO_2 elimination. One of the aims of chest physiotherapy (CPT) is to improve ventilation and gas exchange. Several studies have shown that pursed-lips breathing (PLB) can reduce PCO_2 (9,21,29,30). We have previously evaluated two physiotherapy methods, thoracic compressions (TC) and positive expiratory pressure (PEP), and found that they reduce PCO_2 (17). These were short-term studies and showing a decrease in PCO_2 only during the maneuvers. Another treatment method, continuous positive airway pressure (CPAP), is known to increase PaO_2 and SaO_2 (11,25) but it is not known whether it influences hypercapnia. Nor is it known if CPAP increases the work of breathing resulting in greater hypercapnia (25).

The present report investigates the clinical effectiveness in hypercapnic COPD patients of two forms of CPT given for 3 days. Positive expiratory pressure and nasal continuous positive airway pressure were evaluated with respect to their effectiveness in lowering the PCO_2 in the long term.

Methods increasing the intrabronchial pressure, such as pursed lips breathing, have been shown to increase the tidal volume (22), the functional residual capacity (FRC), the PO_2 (6) and in a few cases to decrease the PCO_2. On the other hand there is one study observing an increased PCO_2 in connection with CPAP treatment (3). The respiratory drive is known to be downregulated by increased levels of PCO_2 (14). Decreasing this value might result in an increased sensitivity in the respiratory center. The effects of methods increasing the intrabronchial pressure have only been observed in short term. Our aim was to investigate if repeated applications of these methods had any long lasting effects on patients with advanced COPD.

PATIENTS AND METHODS

Study design. All the patients were admitted to the inpatient ward of the Department of Lung Medicine for 10 days. The study was divided into 3 periods, each of 3 days (Fig 1).

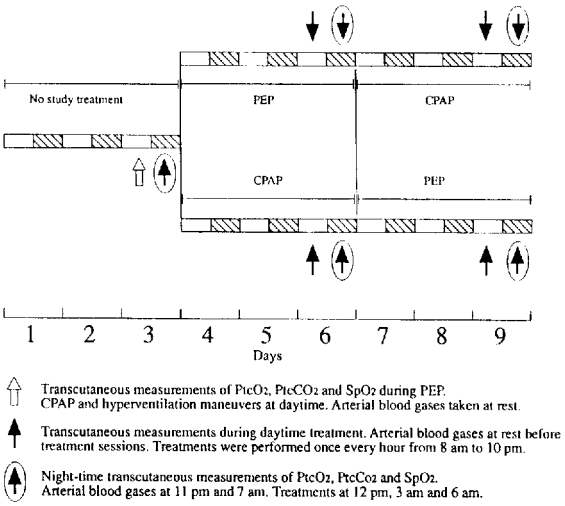


Fig 1: Study design

During the first 3 days the patients had no specific treatment for hypercapnia. They were receiving continuous oxygen and the same flow-rate was maintained throughout the study and they were allowed to sleep undisturbed during the night. After 3 days, the patients were randomized into two groups. Six patients started with PEP treatment for 3 days and then changed to CPAP treatment for another 3 days. Three patients started with CPAP and changed after 3 days to PEP. In PEP treatment, the positive pressure is applied only during the expiration phase (19). The patients expired smoothly through a plastic tube, the end of which was placed in a bottle containing 10 cm of water. Expirations were repeated without force 30 times at a comfortable rate (17). This maneuver lasted for 5 to 10 min.

The CPAP system applies positive pressure to spontaneously breathing patients during both inspiration and expiration (19). In this study the CPAP treatment was administered through a Sleep Easy II System airflow generator and a tight-fitting nose-mask (Respironics, Monroeville, PA) (26). A constant pressure of 7.5 cm H_2O was used for all patients. The CPAP treatment was given for 10 min each time and the oxygen supply was changed from nasal prongs to the nose-mask. The flow rate was unchanged. The PEP and CPAP treatments were administered once every hour during the daytime (from 8 am to 10 pm), and 3 times overnight (12 pm, 3 am, 6 am). The duration and frequency of the treatments were chosen from our preliminary experience with the aim to give as much treatment as possible without interfering unacceptably with the sleep and daily life of the patients. Hyperventilation was performed for 2 min, taking 20 maximal breaths per min. A metronome was used and the maneuver was carried out on the third day of the first period. The patients were treated in a sitting/half-sitting position. Every treatment session was supervised. Instructions and practice with PEP and CPAP equipment and hyperventilation were given before the study.

Subjects. Ten patients were studied; one patient was excluded owing to an exacerbation of her disease during the first treatment period. The remaining 9 patients, 4 men and 5 women, had a mean age of 69 years (range 60-81 years) (Table 1).

Table 1. *Patient characteristics*. FEV_1, Forced expiratory volume in one second; RV, Residual volume; PaO_2, Arterial oxygen tension; $PaCO_2$, Arterial carbon dioxide tension; SaO_2, Arterial oxygen saturation.

Case No	Sex	Age years	FEV_1 % of predicted	RV	PaO_2 kPa (during long-term oxygen therapy)	$PaCO_2$ kPa	SaO_2 %	O_2 l/min
1	M	65	32	71	7.5	9.8	86	0.5
2	F	77	27	170	5.7	10.1	79	0.5
3	M	61	14	372	9.0	7.2	91	2.5
4	F	60	18	397	9.2	10.2	92	1.0
5	F	72	17	334	12.4	6.0	97	1.0
6	F	62	29	293	8.8	8.2	91	1.5
7	M	75	28	121	7.8	8.1	89	0.5
8	F	72	27	326	9.4	9.7	92	1.5
9	M	81	25	215	7.6	8.6	87	2.5
Mean		69	24	250	8.6	8.6	89	1.3
SD		8	6	123	1.8	1.4	5	0.8

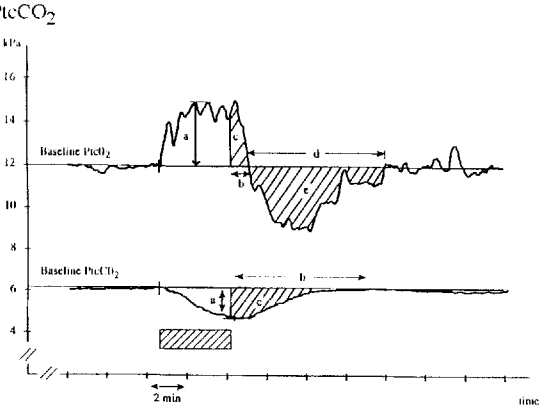
All the patients suffered from severe COPD with respiratory insufficiency and had LTOT at home. The forced expiratory volume in 1 s ($FEV_{1.0}$) was less than 32% of the predicted value. Patients were treated with low-flow oxygen by nasal prongs (0.5 to 2.5 l/min) for hypoxia. Arterial blood gases when breathing oxygen showed hypoxemia with mean PaO_2 values of 8.6 kPa and hypercapnia with $PaCO_2$ values of 8.6 kPa. All patients had normal pH. At the time of the study all the patients were in a stable condition with respect to their disease. No changes in medication were made during the study. Variables reflecting the patients' pulmonary function are listed in Table 1. All patients gave their informed consent. The study protocol was approved by the Ethics Committee of the Medical Faculty of Uppsala University.

Measurements. Transcutaneous partial pressures of oxygen ($PtcO_2$) and CO_2 ($PtcCO_2$) were measured and recorded on a paper recorder (speed 2 cm/min) using the System E 5230 (Radiometer, Copenhagen) as described previously (17,20,33). The transcutaneous O_2 saturation (SpO_2) was measured using a Biox 3700 (Ohmeda, Colorado) or Radiometer Oxy (Copenhagen) pulse oximeter (32) and was recorded on a paper recorder (speed 5 cm/min). The probe was attached to the patient's finger. Arterial blood gases, PO_2 and PCO_2 were analyzed with a blood gas analyzer ABL 300 (Radiometer, Copenhagen) and SO_2 was analyzed with an OSM 3 analyzer (Radiometer, Copenhagen). Samples were taken in the radial or femoral artery. The body position was determined individually, either sitting or supine, but was the same on all occasions during the study. During the third day of the first period (without specific treatment) patients were continuously recorded transcutaneously during repeated PEP and CPAP and during one hyperventilation maneuver. The $PtcO_2$, $PtcCO_2$ and SpO_2 were also recorded during the last day of PEP and CPAP treatments. Repeated treatments were performed during monitoring. Arterial blood gases were measured at rest, before the treatment sessions. An overnight monitoring (8 hours) was made during the last night of each 3-day period. Treatments were carried out as described. Arterial blood gas levels were measured at the beginning and at the end of each recording night (11 pm and 7 am) (Fig 1).

Analyses of transcutaneous measurements. The start and end of each maneuver and treatment were carefully noted on the strip charts during the recordings. The $PtcCO_2$, $PtcO_2$ and SpO_2 tracings were analyzed with an Apple digitizer. The variables which were calculated are shown in Fig. 2.

Fig.2: Schematic illustration of $PtcO_2$ and $PtcCO_2$ tracings in a normal subject performing PEP (shaded box)

a. Initial response (kPa)
b. Duration of change (min)
c. Remaining effect (mm^2)
d. Duration of late response (min)
e. Area size of late response (mm^2)



Initial response (a); the greatest decrease in $PtcCO_2$ (kPa) and greatest increase in $PtcO_2$ (kPa) and SpO_2 (%) measured during treatment. *Duration of change* (b): the time in min that the decrease ($PtcCO_2$) and increase ($PtcO_2$,SpO_2) lasted after treatment before reaching the baseline value. *Remaining effect* (c) after treatment was measured as the area under the curve (mm^2) between the end of the treatment and the return to baseline.The variables were analyzed separately for each patient and treatment occasion. The additional variables which were calculated, when appearing, were the *duration of the late response* (d) after treatment and the *area size of the late response* (e).

Statistical methods. Data were presented as mean ± SD or range. Student's t-test was used for paired data for differences between treatment methods and treatment sessions. Differences were considered significant if the p value was < 0.05.

RESULTS

Both therapies were generally tolerated well. One patient developed a unilateral, purulent conjunctivitis, a possible complication of the nasal CPAP treatment (27).

Immediate effects.

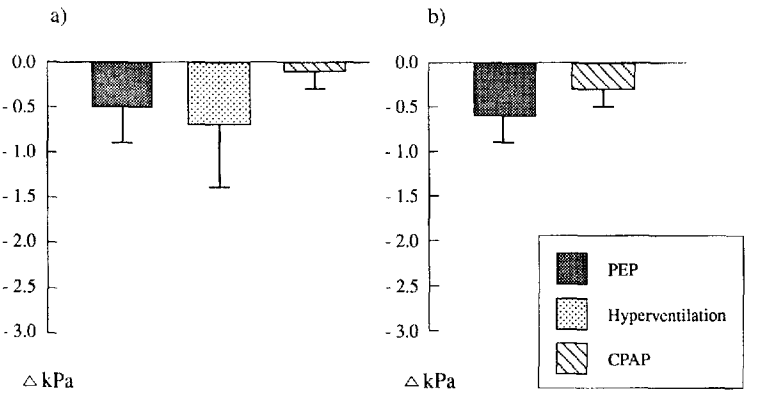


Fig 3: Initial response to treatment (mean - SD) in $PtcCO_2$ in COPD patients a) during the day and b) at night.

In COPD patients it was possible temporarily to lower the $PtcCO_2$ by treatment with PEP, CPAP or hyperventilation. The mean initial response was largest with hyperventilation (0.7 kPa, range 0.2-2.2) followed by PEP (0.5 kPa, 0.3-1.5) and CPAP (0.1 kPa, 0-0.4) (Fig 3a). The response to CPAP was significantly lower ($p< 0.05$) than the response to the other two treatments. There was no significant difference between PEP and hyperventilation.

The duration of the $PtcCO_2$ decrease (Fig 4) displayed basically the same pattern, as did the "remaining effect" (PEP 77 mm^2, hyperventilation 68 mm^2 and CPAP 13 mm^2). The CPAP treatment significantly ($p<0.01$) differed from the effect of the other treatments. The initial response and the duration of $PtcO_2$ (Fig 5) and SpO_2 both increased when the patients were treated, but there was no difference between the 3 types of treatment.

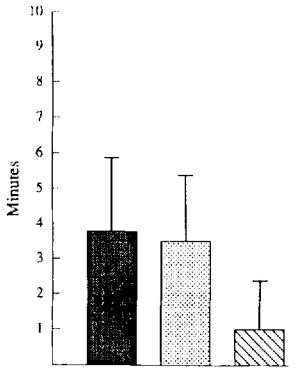


Fig 4. Duration of change (mean+SD) in $PtcCO_2$ after treatment in COPD patients.

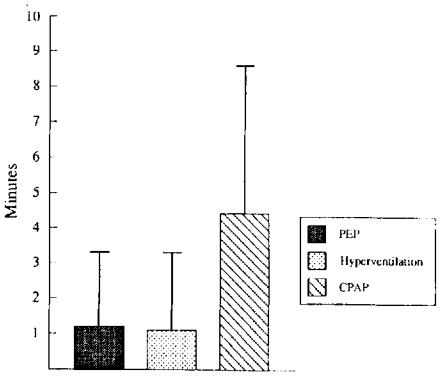


Fig 5. Duration of change (mean+SD) in $PtcO_2$ after treatment in COPD patients

The recordings during the night-time treatments with PEP and CPAP were analyzed separately. PEP produced a higher initial response in $PtcCO_2$ than CPAP during the day ($p<0.05$) as well as during the night ($p<0.01$). There was no significant difference between the initial response for either treatment between day and night (Fig 3). No "late response" was seen in any form of treatment.

Effects of treatment periods. The overnight changes in resting arterial blood gases (ABG) are shown in Table 2.

Table 2: Changes in mean arterial blood gases in COPD patients during nights (from 11 pm to 7 am) with and without Chest physiotherapy (CPT). PEP, Positive expiratory pressure; CPAP, Continuous positive airway pressure

	No treatment	PEP treatment	CPAP treatment
$\Delta PaCO_2$ (kPa)	+ 1.2	+ 1.3	+ 0.6
ΔPaO_2 (kPa)	- 0.6	+ 0.4	- 0.2
ΔSaO_2 (%)	- 2.2	- 0.8	- 2.8

When measurements were made on the third day without specific treatment for hypercapnia, the mean $PaCO_2$ value was 8.6 (±1.4) kPa at 11 pm and 9.8 (±1.7) at 7 am the next morning ($p<0.001$). The PaO_2 and SaO_2 were significantly ($p<0.01$) lower in the morning than in the evening. After 3 days of treatment with PEP, the mean morning value of $PaCO_2$ was significantly higher, 10.4 (±1.9) kPa, than without treatment. The morning value obtained after CPAP treatment was about the same (9.7 ±1.6 kPa) as that seen without treatment. The overnight increase in $PaCO_2$ was significant for the PEP treatment but not for the CPAP treatment at night (Table 2). The only significant overnight difference in the oxygenation parameters was the decrease in SaO_2 during the CPAP treatment.There was no statistically significant difference between the overnight changes in blood gases during any of the treatment periods in comparison with the period without treatment.

DISCUSSION

COPD is a disabling condition and few effective treatments are available. Continuous oxygen therapy is essential in the treatment of respiratory failure, but in hypercapnic patients a balance should be obtained between the correction of hypoxia and a dangerous increase in $PaCO_2$. Several methods for reducing hypercapnia have been investigated for their short-term effects. Pursed-lips breathing (PLB) is commonly used in an attempt to improve ventilatory pattern and gas exchange. Mueller and associates found that PLB increased tidal volume and decreased $PaCO_2$ in patients with COPD (22,29). Other studies have noted an improvement in vital capacity and arterial oxygen saturation (6,21,30). Still others have noted none of these benefits (1). In a longterm study (6 months) Christensen et al found no change in $PaCO_2$ in COPD patients using PEP mask (10). However, the study was conducted to increase mucus secretion and not to eliminate CO_2. Therefore, the PEP treatment, which was used only for 45 min a day could not suffice a longterm change in PCO_2.

In the present study we used the PEP and CPAP methods in order to decrease CO_2 tension. PEP has been described in the literature as improving the distribution of ventilation by re-expanding collapsed lung tissue, presumably by collateral reinflation, and thereby increasing functional residual capacity (FRC) (2). Garrard and Stock also found that both PEP and CPAP increased FRC in healthy subjects and in diseases combined with reduced lung volume (15,28). In a previous short-term study, we found that PEP reduced CO_2 accumulation (17), presumably by increasing the minute ventilation. Fluctuations of arterial blood gases in day-to-day values and values during the night have been studied. Changes in normal subjects during sleep have been demonstrated by desaturation (5) and elevation in CO_2 (7). The cyclic rise in PCO_2 is supposed to be caused by a change in the responsiveness of the respiratory center and decreased ventilation (4). Several studies have shown that these fluctuations also occur in many COPD patients. Fletcher et al showed that significant oxygen desaturation was seen in 27% of cases during sleep despite adequate daytime oxygenation (13). Some of these patients demonstrated nocturnal desaturation despite the use of long-term oxygen therapy (8). The same results have been reported by other authors (12,31). Beerel et al reported a significant elevation in CO_2 tension between the evening and the morning hours in patients with emphysema (4).

When using noninvasive monitoring the question of measurement accuracy and delay in transcutaneous measurements arises. The precision of transcutaneous apparatuses has been evaluated and accepted as having sufficient accuracy in several studies (9,16). In our study all the patients decreased their $PtcCO_2$ with hyperventilation and PEP. Only 5 patients decreased it using CPAP. The difference between PEP and CPAP was significant, but not between PEP and hyperventilation. On the other hand, more patients increased their $PtcO_2$ and SpO_2 using CPAP than using PEP. Six patients experienced a decline in $PtcO_2$ and SpO_2 using hyperventilation.The nocturnal treatments and measurements showed that PEP decreased the $PtcCO_2$ somewhat more than CPAP. The effects were all similar to the daytime measurements and there was no difference between the effects of night-time and day-time treatment. The SpO_2 increased more with CPAP. This indicated that all 3 methods decreased CO_2 but only in the short term as the effect lasted for

less than 4 min. The fact that SpO_2 increased more with CPAP may be partly due to an increase in inspired oxygen concentration, when oxygen was changed from nasal prongs to the CPAP mask. We have observed (unpublished) that when normal subjects were hyperventilating or using PEP they had a "late reaction" with a period of a decrease in $PtcO_2$ and SpO_2. None of the COPD patients had any "late reaction". This reaction in normal subjects was tentatively due to a reduction in the respiratory drive as a result of the induced decrease in CO_2 tension. The mechanism was obviously not present in our patients who had a habitual increase in CO_2 tension.

In our study, arterial blood gases taken after 3 days without treatment showed an elevation in $PaCO_2$ during the night (11 pm to 7 am). A concomitant decline in PaO_2 and SaO_2 was also seen. Despite 3 days of treatment with PEP or CPAP, the same pattern was seen. The $PaCO_2$ showed an elevation during the night with both therapies, although the difference was smaller than without treatment. In CPAP, the difference was not significant. The present study showed that PEP and CPAP both decreased PCO_2 in stable COPD patients, but this effect lasted only for a few minutes. An intensive treatment period over 3 days did not produce any clinically-important improvement in arterial blood gases during the day or night. In our opinion there is no justification for treating stable COPD patients with chronic hypercapnia with these methods.The results relate to patients in a stable condition and it remains unclear which effect COPD patients during an acute exacerbation would experience using these treatments.

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