

Acute effects of external negative pressure ventilation in chronic obstructive pulmonary disease compared with normal subjects

C.B. Cooper, N.D. Harris, P. Howard

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ABSTRACT: This study compares the acute physiological effects of external negative pressure ventilation (ENPV) in normal subjects and patients with chronic obstructive pulmonary disease (COPD). The equipment consisted of an airtight jacket (Pneumosuit) and vacuum pump. Minute ventilation (\dot{V}_E) was recorded using a light-emitting turbine transducer. Oxygen uptake (\dot{V}_{O_2}) and carbon dioxide output (\dot{V}_{CO_2}) were calculated every 30 s. Measurements were made at rest and during ENPV with pressures of -20 cmH₂O and -40 cmH₂O. The ventilator rate was fixed at $16 \cdot \text{min}^{-1}$. In 10 normal subjects, \dot{V}_E increased from 8.6 to 22.9 $l \cdot \text{min}^{-1}$ ($p < 0.01$) accompanied by an increase in \dot{V}_{CO_2} from 0.25 to 0.39 $l \cdot \text{min}^{-1}$ ($p < 0.01$). In 10 normocapnic COPD patients (arterial carbon dioxide tension (P_{aCO_2}) ≤ 6.0 kPa) \dot{V}_E increased from 11.5 to 17.1 $l \cdot \text{min}^{-1}$ ($p < 0.01$) whilst in 10 hypercapnic patients ($P_{aCO_2} > 6.0$ kPa) \dot{V}_E increased from 9.7 to 12.4 $l \cdot \text{min}^{-1}$ ($p < 0.01$). A change in \dot{V}_{CO_2} was not detected in the COPD patients, and \dot{V}_{O_2} did not change in any group. Arterial blood samples were obtained in eight hypercapnic patients. Baseline mean physiological deadspace ventilation (\dot{V}_D) was calculated to be 4.9 $l \cdot \text{min}^{-1}$ (56% of \dot{V}_E) whilst \dot{V}_E was 8.8 $l \cdot \text{min}^{-1}$ in this subgroup. During ENPV, arterial oxygen tension (P_{aO_2}) increased from 6.8 to 8.2 kPa ($p < 0.01$) whilst P_{aCO_2} decreased from 6.8 to 5.8 kPa ($p < 0.01$) suggesting that despite the large physiological deadspace, a significant increase in alveolar ventilation had occurred. In advanced COPD, thoracic compliance falls and limits the ventilatory response to ENPV. Despite this, useful improvement of blood gases was obtained using modest external negative ventilatory pressures of -20 cmH₂O. Maintenance of these changes over longer periods of ENPV has yet to be proven. *Eur Respir J.*, 1991, 4, 63-68.

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The tank or body respirator was introduced by DRINKER and SHAW [1] in 1929. It readily gained acceptance as a means of treating patients with poliomyelitis and other neuromuscular disorders. The description in 1958 of the Tunnicliffe breathing-jacket [2] contributed to the development of a variety of cuirass ventilators but the principle of the apparatus remained the same, that is a negative pressure cycle is applied outside the body whilst ambient pressure is maintained at the mouth.

Studies during the 1950's described the use of body-type respirators in chronic obstructive pulmonary disease (COPD) and restrictive diseases. In COPD the results were not consistently favourable [3, 4] although BOUTOURLINE-YOUNG and WHITTENBERGER [5] reported long-term improvement in arterial oxygen saturation with correction of hypercapnia and recovery of CO_2 responsiveness in one patient.

Respiratory muscle fatigue has been considered as a contributory factor in the genesis of hypercapnic respiratory failure in COPD [6]. Attention has been focused on the need to rest the respiratory muscles as well as to increase alveolar ventilation and this might be achieved by external negative pressure ventilation (ENPV). Assisted ventilation with body respirators reduced respiratory muscle electromyogram (EMG) activity in patients with chronic respiratory failure supporting the concept of respiratory muscle rest [7] whilst daily intermittent ENPV in COPD improved pulmonary function and reduced hospital admissions [8]. The mechanical and physiological changes responsible for such beneficial effects have not been fully explored. This study attempts to identify these changes and to highlight the limitations of the technique in COPD by comparison with normal subjects.

Methods

Subjects

Three groups of subjects were studied, their characteristics are shown in table 1. The first group consisted of 10 normal subjects, the other two groups consisted of patients attending an out-patient clinic with clinically stable COPD and forced expiratory volumes in the first second (FEV_1) less than 50% of normal predicted values. The COPD subjects were divided into two groups according to resting arterial blood gas tensions, breathing air. Ten were normocapnic (arterial carbon dioxide tension ($Paco_2$) <6.0 kPa) and 10 were hypercapnic ($Paco_2 >6.0$ kPa).

Table 1. - Characteristics of the three groups of subjects

	Normal subjects	Normocapnic patients	Hypercapnic patients
n	10	10	10
Age yrs	29 (9)	67 (8)	63 (11)
Height m	1.79 (0.07)	1.64 (0.08)	1.72 (0.08)
Weight kg	71.8 (5.7)	62.4 (14.0)	70.6 (17.8)
FEV_1 l	4.50 (0.72)	0.88 (0.28)	0.69 (0.10)
% pred FEV_1 *	-	36 (14)	23 (4)
FVC l	5.47 (0.93)	1.71 (0.46)	1.45 (0.53)
Pao_2 kPa	-	9.5 (1.0)	6.4 (1.4)
$Paco_2$ kPa	-	4.9 (0.4)	6.8 (0.8)

FEV_1 : forced expiratory volume in one second; FVC: forced vital capacity; Pao_2 : arterial oxygen tension breathing air; $Paco_2$: arterial carbon dioxide tension breathing air. *: European predicted values [9]. Values are means with standard deviations in parentheses.

Apparatus

The subjects were studied in a semi-recumbent position (fig. 1) wearing an airtight jacket respirator with backplate and adjustable front shell (Pneumosuit; Thomas Respiratory Systems, London, UK). Cyclical negative pressures were generated by a vacuum pump with a flow capacity of $1,000$ l·min⁻¹ and an electrically operated rotary valve (Newmarket Pump; Si Plan Electronics Research Ltd, UK). The ventilator rate was fixed at 16·min⁻¹ for all subjects, with equal inspiratory and expiratory times. Measurements were made at rest and then during two periods of ENPV with pressures of -20 cmH₂O and -40 cmH₂O. These pressures were set by electronic feedback from a pressure transducer within the pump.

Ventilation was recorded using a turbine transducer (Ventilometer MK2; PK Morgan, Gillingham, Kent, UK). The accuracy of this instrument is known for different patterns of breathing [10]. Fractional concentrations of mixed expired gases were measured using a para-magnetic oxygen analyser (Servomex 580A; Sybron Taylor Instrument Analytics Ltd, Crowborough, Sussex, UK) and infra-red capnograph (Gould capnograph IV; Gould Medical Ltd, Lutterworth, Leics, UK). Minute ventilation (\dot{V}_E), oxygen uptake ($\dot{V}O_2$) and carbon dioxide output ($\dot{V}CO_2$) were calculated at 30 s intervals. \dot{V}_E is expressed in litres per minute (BTPS), $\dot{V}O_2$ and $\dot{V}CO_2$ are expressed in litres per minute (STPD). Subjects were judged to have reached an equilibrium when fractional concentrations of mixed expired gases became constant over 90 s. The duration of the studies was about 15 min at each ENPV setting. Mean values for \dot{V}_E , $\dot{V}O_2$ and $\dot{V}CO_2$ were calculated during the final 90 s.

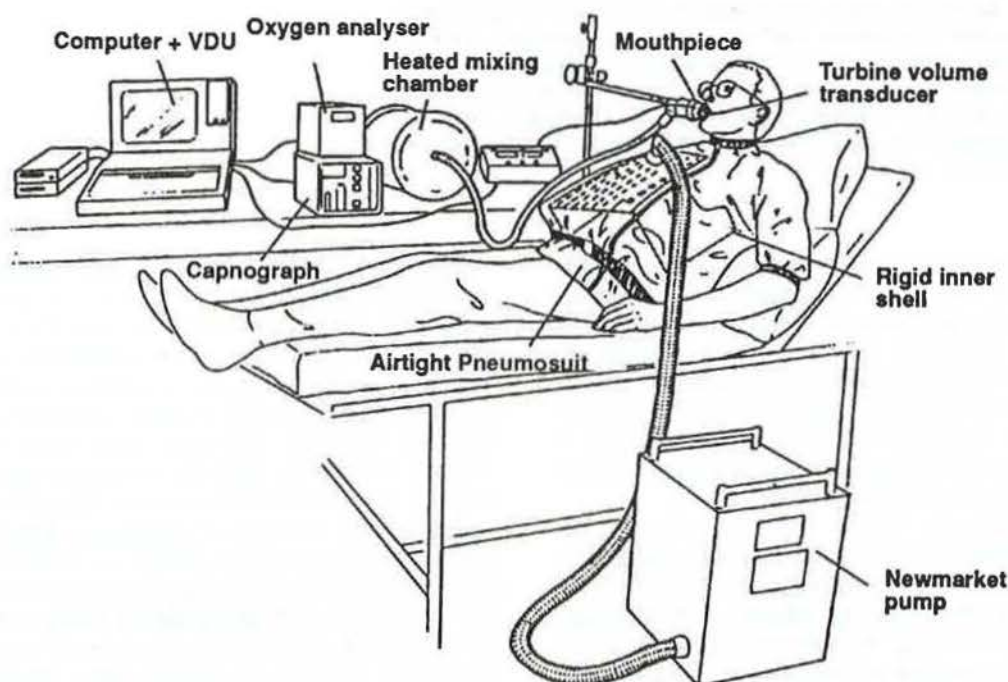


Fig. 1. - Diagram of the apparatus. The turbine is connected to a microprocessor which corrects for inertia and overrun.

Serial arterial blood samples were obtained in eight hypercapnic COPD subjects from a radial artery cannula. Arterial oxygen and carbon dioxide gas tensions (P_{aO_2} and P_{aCO_2}) were measured at rest and used in the calculation of physiological deadspace ventilation (\dot{V}_D);

$$\dot{V}_D = \left(\frac{P_{aCO_2} - P_{eCO_2}}{P_{aCO_2}} \cdot \dot{V}_E \right) - (\dot{V}_{Di} - fR)$$

Where P_{eCO_2} is the mixed expired carbon dioxide tension, \dot{V}_E is the overall minute ventilation, fR is the breathing frequency and \dot{V}_{Di} is the instrument deadspace which was 90 ml for this apparatus.

Statistical analysis

The differences in measured variables was assessed using analysis of variance for repeated measures and Student's t-test for paired data with Bonferroni corrections [11]. A probability of 5% or less was considered significant.

Results

Figure 2 shows changes in \dot{V}_E for the three groups and figure 3 shows \dot{V}_{CO_2} . During ENPV in normal subjects there was an increase in \dot{V}_E from 8.6 to 22.9 $l \cdot min^{-1}$ ($p < 0.01$) accompanied by an increase in \dot{V}_{CO_2} from 0.25 to 0.39 $l \cdot min^{-1}$ ($p < 0.01$). In patients with hypercapnic COPD, ventilation increased from 9.7 to 12.4 $l \cdot min^{-1}$ ($p < 0.01$). A significant change in \dot{V}_{CO_2} was not detected in either group of COPD patients and \dot{V}_{O_2} did not appear to change in COPD patients or controls.

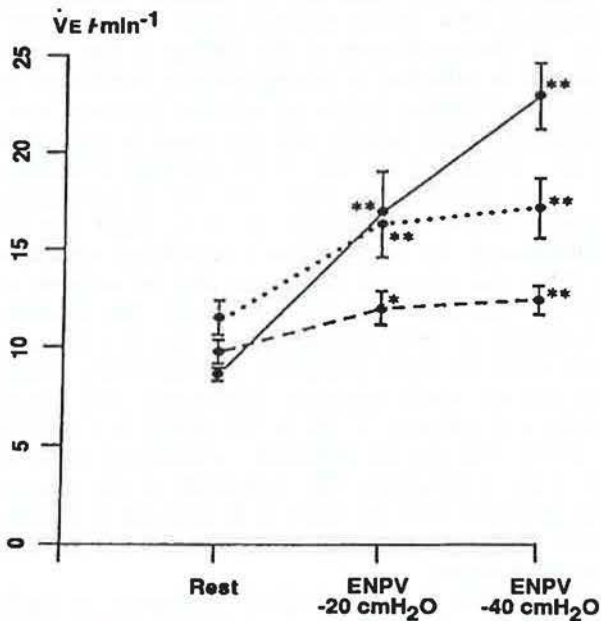


Fig. 2. - Minute ventilation (\dot{V}_E) for the 3 groups of subjects (—) normal subjects, (.....) normocapnic patients, (- - -) hypercapnic patients. Values are means with standard error bars. ENPV: external negative pressure ventilation.

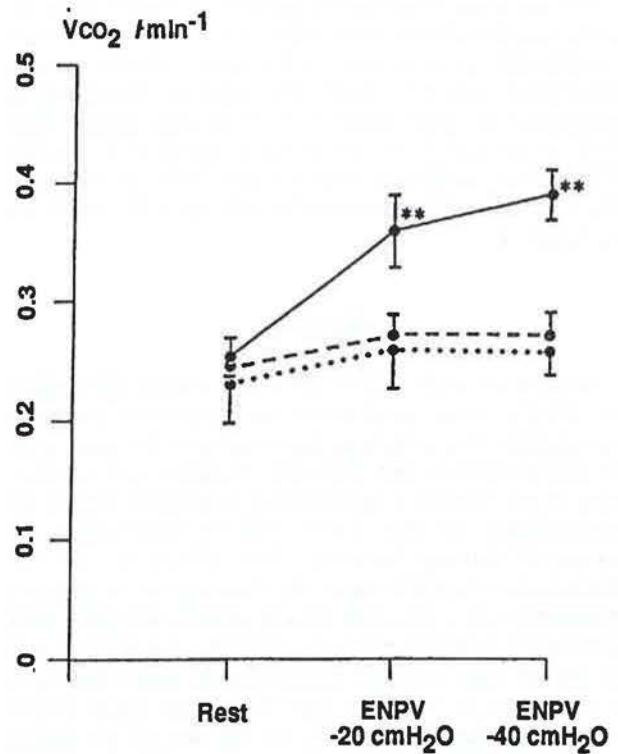


Fig. 3. - Carbon dioxide output (\dot{V}_{CO_2}) for the 3 groups of subjects. (—) normal subjects, (.....) normocapnic patients, (- - -) hypercapnic patients. Values are means with standard error bars. ENPV: external negative pressure ventilation.

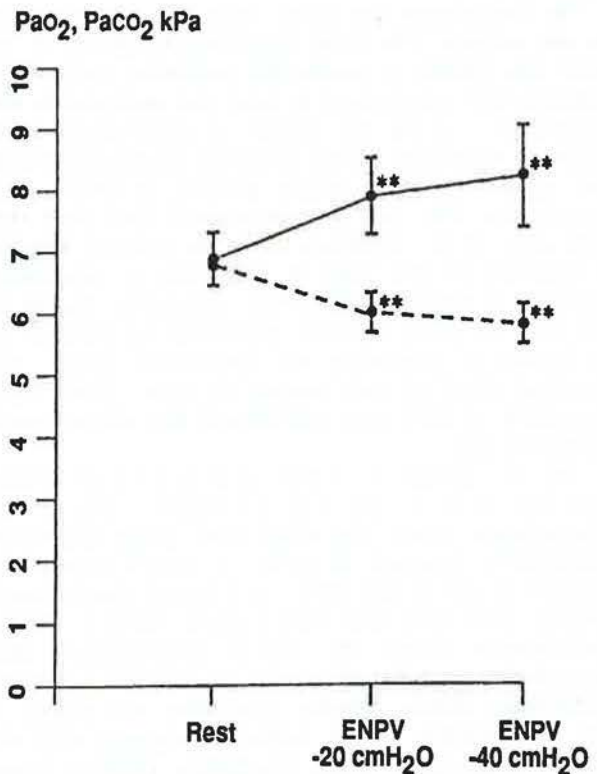


Fig. 4. - Arterial oxygen and carbon dioxide blood gas tensions (P_{aO_2} , P_{aCO_2}) for 8 hypercapnic patients. (—) arterial oxygen tension, (- - -) arterial carbon dioxide tension. Values are means with standard error bars. ENPV: external pressure ventilation.

For the eight hypercapnic patients in whom serial arterial blood samples were taken \dot{V}_D during steady-state conditions at rest was $4.9 \text{ l}\cdot\text{min}^{-1}$ whilst minute ventilation was $8.8 \text{ l}\cdot\text{min}^{-1}$. The ratio of physiological deadspace to tidal volume (V_D/V_T) was greater than 50% in all cases, the mean value being 56%. During ENPV, P_{aO_2} increased from 6.8 to 8.2 kPa ($p < 0.01$) and P_{aCO_2} decreased from 6.8 to 5.8 kPa ($p < 0.01$) as shown in figure 4.

Discussion

In patients with COPD there are several advantages of ENPV over intubation and positive pressure ventilation. The technique does not carry the same risks of pneumothorax and infection. Sedation and suppression of the subject's spontaneous respiratory efforts are unnecessary so that ENPV can be interrupted, for example during feeding. The efficiency of the Pneumosuit depends upon the distribution of negative pressures over a maximal area of unimpeded chest wall. Efficiency is improved by covering the abdomen as well as the rib cage [12] and supporting the inner shell with a back-plate [13]. ENPV may exacerbate upper airway obstruction during sleep [14, 15] but this did not appear to be a problem in our awake subjects. When it occurs in subjects with restrictive disease having ENPV this disadvantage can be overcome by use of nasal continuous positive airway pressure (CPAP) or protriptyline [16].

The Pneumosuit was easily fitted and well-tolerated in our subjects. The fixed ventilation frequency of 16 min^{-1} was chosen to capture the ventilatory cycle. The subjects were encouraged to relax and surrender to the ventilator. During the period of observation each subject's respiratory efforts remained synchronized with the apparatus. With longer periods of ENPV this synchrony may not be maintained and thus the efficiency of the apparatus would be reduced. Precise evaluation of this type of respirator is especially difficult in patients with severe respiratory disease at the time of acute infective exacerbations because of difficulty in capturing the respiratory cycle. We therefore chose to study patients in stable clinical state focussing on short-term mechanical and physiological improvements.

The two groups of COPD subjects were of similar age but body weight was predictably less in the normocapnic group. The hypercapnic group had worse respiratory function in terms of forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). They were also more hypoxic (table 1). These differences reflect the overall deterioration that accompanies progression of COPD towards respiratory failure. Resting ventilation was higher in the normocapnic COPD subjects compared with the other 2 groups. This probably results from increased respiratory drive in subjects who maintain a normal P_{aCO_2} despite an increase in the work of breathing.

Worsening airflow obstruction limits the ventilatory response to ENPV as shown in figure 2. In normal subjects with compliant respiratory systems there was a progressive increase in \dot{V}_E with two stages of ENPV. This response is reduced as pulmonary function deteriorates and may be explained in two ways. The slope of the relationship between \dot{V}_E and applied negative pressure is inversely proportional to airflow resistance and is therefore reduced in COPD. Abnormal airway and lung mechanics are the most likely cause of difficulty in ventilating COPD patients. On the other hand, JAMESON *et al.* [3], observing that cuirass ventilators were effective in normal subjects but less efficient in severe emphysema, suggested that this was due to rigidity of the chest wall. This view was not supported by SHARP *et al.* [17] who demonstrated normal chest wall compliance in paralysed COPD patients. In both groups of COPD subjects that we studied the limited ventilatory response was seen with pressures of $-20 \text{ cmH}_2\text{O}$ and the additional gain in ventilation with pressures of $-40 \text{ cmH}_2\text{O}$ was small. This is interesting since it shows that more negative pressures do not necessarily produce a greater ventilatory response and may indicate that the limitation is indeed due to loss of chest wall compliance resulting from failure of complete relaxation of the respiratory muscles during ENPV. We did not have electromyography and therefore we can only make assumptions about the state of activation of the respiratory muscles but the lack of fall in \dot{V}_{O_2} supports the concept of persistent muscle activity. An alternative explanation is that the effect of ENPV may be self-limiting because as higher lung volumes are achieved during respiration, the compliance of the respiratory system falls.

In normal subjects the increase in \dot{V}_E was accompanied by an increase in \dot{V}_{CO_2} whereas in COPD subjects a change in \dot{V}_{CO_2} could not be detected, mean \dot{V}_{CO_2} being $0.25 \text{ l}\cdot\text{min}^{-1}$ before and $0.27 \text{ l}\cdot\text{min}^{-1}$ during ENPV (fig. 3). The implication of this finding is that ENPV may not be effective in raising alveolar ventilation in this type of patient despite an increase in overall ventilation in certain subjects and this could be explained by an increase in the ratio of physiological deadspace to tidal volume. In eight of the hypercapnic subjects, whilst an increase in \dot{V}_{CO_2} could not be demonstrated, but nevertheless a significant reduction in P_{aCO_2} was observed suggesting that an increase in alveolar ventilation had been achieved. The apparent discrepancy in these findings may be due to a type two error where the actual changes in ventilation were small and did not reach statistical significance with small numbers of subjects. A fall in \dot{V}_{O_2} would be expected if ENPV relieved the respiratory muscles of some of the work of breathing. The magnitude of this change may also have been too small to be detected or alternatively the effect may not have occurred for reasons discussed above.

Calculation of physiological deadspace in eight hypercapnic subjects demonstrated a severe disturbance in obstructive airways disease. V_D/V_T was greater than 50% in all cases. This finding supports the conclusion

of MARTHAN *et al.* [18] that ventilation/perfusion (V_A/Q) heterogeneity is the main factor underlying gas exchange disturbance in COPD. Ventilation of the physiological deadspace clearly accounts for a considerable portion of the work of breathing in these subjects. The improvement in arterial blood gas tensions which we observed (fig. 4) suggests that an increase in \dot{V}_A occurred during ENPV. However, the fall in P_{aCO_2} , although significant, was small compared with the increase in minute ventilation which we observed. It is likely, therefore, that an important change in \dot{V}_D had also occurred making a substantial contribution to any increase in \dot{V}_E . We were unable to determine \dot{V}_D or \dot{V}_A during ENPV because of the uncertainty of achieving steady-state conditions within the relatively short duration of this study.

Our findings indicate that there is potential for, at least short-term, improvement in blood gas tensions of some COPD subjects with ENPV. The report of BRAUN and MARINO [8] suggested improvement in pulmonary function and reduction in hospital admissions with five months of daily intermittent ENPV at home but these findings have yet to be substantiated. We believe that ENPV may find a useful role as a means of domiciliary support for some subjects with COPD but that they require careful evaluation to determine what degree of physiological improvement is possible and to evaluate their mechanical limitation. Future studies need to define whether physiological improvement can be maintained.

References

1. Drinker P, Shaw L. - An apparatus for the prolonged administration of artificial respiration. *J Clin Invest*, 1929, 7, 229-247.
2. Spalding JMK, Opie L. - Artificial respiration with the Tunnicliffe breathing-jacket. *Lancet*, 1958, i, 613-615.
3. Jameson AG, Ferrer MI, Harvey RM. - Some effects of mechanical respirators upon respiratory gas exchange and ventilation in chronic pulmonary emphysema. *Am Rev Respir Dis*, 1959, 80, 510-521.
4. McClement JH, Christianson LC, Hubaytar RT, Simpson DG. - The body type respirator in the treatment of chronic obstructive pulmonary disease. *Ann NY Acad Sci*, 1965, 121, 746-750.
5. Boutourline-Young HJ, Whittenberger JL. - The use of artificial respiration in pulmonary emphysema accompanied by high carbon dioxide levels. *J Clin Invest*, 1951, 30, 838-844.
6. Roussos C, Macklem PT. - Diaphragmatic fatigue in man. *J Appl Physiol*, 1977, 42, 189-197.
7. Rochester DF, Braun NMT, Laine S. - Diaphragmatic energy expenditure in chronic respiratory failure. *Am J Med*, 1977, 63, 223-232.
8. Braun NMT, Marino W. - Effect of daily intermittent rest of respiratory muscles in patients with chronic airflow limitation. *Chest*, 1984, 85, 59S (Abst).
9. Cooper CB, Harris ND, Howard P. - Evaluation of a turbine transducer in the measurement of human ventilation. *Thorax*, 1987, 42, 240 (Abst).
10. Glantz SA. - *In: Primer of biostatistics*, 2nd edn, McGraw Hill Inc, New York, 1981.
11. Collier CR, Affeldt JE. - Ventilatory efficiency of the cuirass respirator in totally paralysed chronic poliomyelitis patients. *J Appl Physiol*, 1954, 6, 531-538.
12. Scales JT, Kinnier-Wilson AB, Holmes-Sellors T *et al.* - Cuirass respirators - their design and construction. *Lancet*, 1953, i, 671-674.
13. Scharf SM, Feldman NT, Goldman MD. - Vocal cord closure. A cause of upper airway obstruction during controlled ventilation. *Am Rev Respir Dis*, 1978, 117, 391-397.
14. Splaingard ML, Jefferson LS, Harrison GM. - Survival of patients with respiratory insufficiency secondary to neuromuscular disease treated at home with negative pressure ventilation. *Am Rev Respir Dis*, 1982, 125 (Suppl. 4), 139.
15. Goldstein RS, Molotiu N, Scrastins R *et al.* - Reversal of sleep-induced hypoventilation and chronic respiratory failure by nocturnal negative pressure ventilation in patients with restrictive ventilatory impairment. *Am Rev Respir Dis*, 1987, 135, 1049-1055.
16. Sharp JT, van Lith P, Nuchprayoon CV, Briney R, Johnson FN. - The thorax in chronic obstructive lung disease. *Am J Med*, 1968, 44, 39-46.
17. Marthan R, Castaing Y, Manier G, Guernard H. - Gas exchange alterations in patients with chronic obstructive lung disease. *Chest*, 1985, 87, 470-475.
18. Quanjer PH. - Standardized lung function testing. Report Working Party. Standardization lung function testing. *Bull Eur Physiopathol Respir*, 1983, 19 (Suppl. 5).

Effets aigus d'une ventilation externe à pression négative dans la maladie pulmonaire chronique obstructive, par comparaison avec les sujets normaux. C.B. Cooper, N.D. Harris, P. Howard.

RÉSUMÉ: Cette étude compare les effets physiologiques aigus d'une ventilation externe à pression négative chez les sujets normaux et chez les patients atteints de bronchopneumopathie chronique obstructive. L'équipement consiste en une jaquette étanche à l'air (Pneumosuit) et en une pompe à vide. La ventilation minute (\dot{V}_E) a été enregistrée en utilisant un traducteur de turbine à émission lumineuse. La consommation d'oxygène (\dot{V}_{O_2}) et le débit de CO_2 (\dot{V}_{CO_2}) ont été calculés toutes les 30 secondes. Les mesures ont été faites au repos et au cours de la ventilation externe, avec des pressions de -20 à -40 cmH₂O. Le rythme du ventilateur a été fixé à 16·min⁻¹. Chez 10 sujets normaux, \dot{V}_E a augmenté de 8.6 à 22.9 l·min⁻¹ (p<0.01), ce qui s'est accompagné d'une augmentation de \dot{V}_{CO_2} de 0.25 à 0.39 l·min⁻¹ (p<0.01). Chez 10 patients atteints de BPCO et normocapniques (P_{aCO_2} <6.0 kPa), \dot{V}_E a augmenté de 11.5 à 17.1 l·min⁻¹ (p<0.01), alors que chez 10 sujets hypercapniques (P_{aCO_2} >6.0 kPa), \dot{V}_E augmentait de 9.7 à 12.4 l·min⁻¹ (p<0.01). Une modification du \dot{V}_{CO_2} n'a pas été détectée dans le groupe des patients BPCO, et la \dot{V}_{O_2} ne s'est modifiée dans aucun groupe. Des échantillons de sang artériel ont été obtenus chez 8 patients hypercapniques. La ventilation moyenne de base de l'espace mort physiologique (\dot{V}_D) a été calculée à 4.9 l·min⁻¹ (56% de \dot{V}_E) alors que \dot{V}_E était de 8.8 l·min⁻¹ dans ce sous-groupe. Au cours de la ventilation externe, la P_{aO_2} a augmenté de 6.8 à 8.4 kPa (p<0.01), alors que la P_{aCO_2} diminuait de 6.8 à 5.8 kPa (p<0.01), suggérant que malgré une espace mort physiologique

important, un augmentation significative de la ventilation alvéolaire était survenue. Dans les BPCO avancées, la compliance thoracique diminue et limite la réponses ventilatoire à la ventilation externe. Malgré ceci, une amélioration utile des gaz du sang a été obtenue au moyen du

pressions ventilatoires négatives externes modestes (-20 cmH₂O). La persistance de ces modifications sur des périodes plus longues de ventilation externe doit encore être démontrée.

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