

"Intrinsic" positive end-expiratory pressure in stable patients with chronic obstructive pulmonary disease

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ABSTRACT: We have assessed "intrinsic" positive end-expiratory pressure (PEEPi), during quiet breathing in 18 patients with chronic obstructive pulmonary disease (COPD) in stable condition. Ventilatory flow, lung volume, oesophageal (Poes), gastric (Pga), and transdiaphragmatic pressure (Pdi) were measured. PEEPi was measured as the pressure difference (Δ Poes) between the onset of the inspiratory effort, indicated by the start of the Pdi swing, and the point corresponding to zero flow. PEEPi was present in all of the 18 COPD patients, and averaged 2.4 ± 1.6 cmH₂O. The maximum transdiaphragmatic pressure (Pdi,max) was also measured and averaged 81.5 ± 17.4 cmH₂O. Following a randomized sequence, ten patients then inhaled an adrenergic agonist (fenoterol 1.6 mg), and eight patients the corresponding placebo. Fenoterol, but not placebo, caused a significant increase in forced expiratory volume in one second (FEV₁) (+34%, on average), associated with a significant decrease in PEEPi (-63%, on average) and a significant improvement in Pdi,max (+19%, on average). We conclude that: 1) intrinsic PEEP can be present in stable COPD patients due to increased airflow resistance; 2) fenoterol improved diaphragmatic strength (Pdi,max) in our COPD patients, possibly due to a decrease in lung volume.
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Pulmonary hyperinflation, due to the loss of lung elastic recoil, is a well-recognized consequence of chronic obstructive pulmonary disease (COPD), and is an important cause of decreased mechanical efficiency of the inspiratory muscles [1]. Dynamic factors such as increased airflow resistance, respiratory frequency, or the post-inspiratory activity of the inspiratory muscles can further enhance the end-expiratory lung volume (EELV) above the elastic equilibrium volume of the respiratory system (Vr) [2]. In COPD patients with acute respiratory failure (ARF) a systematic corollary of dynamic hyperinflation is the "intrinsic" positive end-expiratory pressure (PEEPi), which is due to the end-expiratory elastic recoil pressure of the respiratory system [3-11]. It has been suggested that the magnitude of PEEPi can play an important role in the development of ARF as well as in the difficult weaning of COPD patients [12-14]. In fact, PEEPi is an "inspiratory threshold load" which has to be offset by the inspiratory muscles before inflating the lung.

In recent years, PEEPi has been measured in intubated, critically ill, COPD patients during mechanical [5-8] as well as spontaneous ventilation [10, 11]. However, it has not yet been investigated whether PEEPi is also present in stable, spontaneously breathing, non-intubated, COPD patients. This might be suspected because COPD patients

are often flow-limited even during tidal ventilation [15]. However, MARTIN and DE TROYER [2] have shown that in some instances, e.g. during histamine induced bronchoconstriction, hyperinflation is not merely passive, but also active, because of the post-inspiratory tonic contraction of inspiratory muscle.

We undertook this study to assess PEEPi in stable COPD patients. We also administered an inhaled adrenergic agonist in order to assess the contribution of bronchoconstriction on the magnitude of PEEPi. Since we measured changes in the intrathoracic (oesophageal) and abdominal (gastric) pressure, this protocol enabled us to measure the effects of an inhaled sympathomimetic agent on transdiaphragmatic pressure in stable COPD patients, which had not yet been reported.

Patients and methods

Eighteen COPD patients were recruited for this study from our out-patient clinic and gave their informed consent. The study was approved by the Ethics Authorities.

The diagnosis of COPD at the time of inclusion in the study was based essentially on measurement of lung

volume (table 1) [16]. Selection criteria included: age above 18 yrs; history of chronic shortness of breath; evidence of airflow obstruction, namely forced expiratory volume in one second (FEV_1) and $FEV_1/VC\%$ (VC: slow vital capacity) below 60% predicted [16], and the need for long-term bronchodilator therapy. Exclusion criteria included cardiovascular diseases (e.g. cardiac arrhythmias, high blood pressure) and acute exacerbation of the chronic airway obstruction in the preceding month. Patients were, therefore, examined in a steady state period. All patients were male and had a positive smoking history. No patient had atopy. At the time of the study no patient was taking steroids.

Procedure

All measurements were performed in the morning. Oral theophylline and inhaled sympathomimetics had been suspended for more than 24 and 12 h, respectively. The patients were studied in the sitting position. The average length of the procedure was about two hours. Following local anaesthesia (xylocaine 2%), the patients were asked to swallow the two balloons. The balloons were then inflated with 1 ml of air and a positive pressure swing synchronous with the inspiratory flow as well as with manual pressure of the belly indicated that they were in the stomach. The oesophageal balloon was then

Table 1. - Patients' characteristics and lung volumes

Group n	Age yrs	Height cm	Weight kg	VC		FEV ₁		FEV ₁ /VC	FRC/TLC
				l	% pred	l	% pred		
Fenoterol 10	57 ±7.8	171 ±8.7	81.0 ±13.1	3.07 ±1.00	57.9 ±20.7	1.35 ±0.56	39.3 ±13.2	0.43 ±0.08	0.64 ±0.10
Placebo 8	60 ±8.2	172 ±5.3	71.2 ±19.4	2.69 ±0.90	61.0 ±16.9	1.39 ±0.70	39.7 ±16.1	0.49 ±0.11	0.64 ±0.09

VC: vital capacity; FEV₁: forced expiratory volume in one second; % pred: percentage of predicted from [16]; FRC: functional residual capacity; TLC: total lung capacity. Fenoterol and placebo refer to two groups of patients.

We did not differentiate between chronic bronchitis and emphysema as the predominant cause of the disease. The patient's responsiveness to bronchodilators was not among the inclusion criteria of this study. Five of the 18 patients (all ex-smokers) had periodic dyspnoea and wheezing in their history, which could suggest bronchial asthma as the cause of chronic airflow obstruction, although they did not have a clear pre-established diagnosis of asthma. This peculiarity has been taken into account in data analysis.

Ventilatory flow (\dot{V}) was measured with a Fleisch no. 2 pneumotachograph connected to a Hewlett-Packard 47304A flow transducer, and volume (V) was obtained from electrical integration of the flow signal. Oesophageal and gastric pressures (Poes and Pga, respectively) were measured according to standard recommendations [17], with two balloon-catheter systems connected to two differential pressure transducers (Honeywell 143PCO3D). Another catheter similar to the oesophageal one was inserted into the mouthpiece with a needle and was connected to the other port of the same differential transducer where Poes was measured, to obtain transpulmonary pressure (Ptp). The proximal tips of the polyethylene tubings coming from the stomach and the oesophagus, were also connected, by means of small Y tubes, to the two ports of another differential pressure transducer (Honeywell 143PCO5D) for direct recording of transdiaphragmatic pressure (Pdi). Signals were recorded throughout the experiment on a four channel pen recorder (Gould Instruments s.a.f., model 8188.4400.0X). Ptp was recorded only during the occlusion test [17]. Ventilatory flow, Poes, and Pga, were recorded continuously. Volume and Pdi were recorded on paper alternatively on adjacent series of breaths during steady state tidal breathing.

deflated and withdrawn into the middle third of the oesophagus, and inflated with 0.5 ml of air. The occlusion test was performed and was satisfactory in every instance. Once the subject felt comfortable with the experimental setting (mouthpiece and catheters) and appeared to be relaxed, tidal breathing was recorded for a few minutes at low paper speed (1 mm·s⁻¹) to ensure a steady state, and then at higher speed (10 and 25 mm·s⁻¹).

Inspiratory and expiratory time (Ti and Te), total cycle duration (Tr), and duty cycle (Ti/Tr) were measured from the flow record; tidal volume (Vt) was obtained from the integrated flow signal in order to compute minute ventilation (VE). Dynamic lung compliance (Cdyn) was measured as the ratio between Vt and the ΔPoes between the two points of zero flow [16]. Pdi during tidal breathing was measured as mean Pdi (Pdi) [18, 19]. All measurements during quiet breathing were averaged from five consecutive tidal breaths, and the mean value of each variable was used for further analysis.

Maximum transdiaphragmatic pressure (Pdi,max) was obtained, in each subject, from three manoeuvres: the maximal sniff [20], the classical Mueller manoeuvre, and the two-step manoeuvre, in which the subject was instructed to generate and maintain a maximal expulsive effort while, in addition, a maximal inspiratory (Mueller) manoeuvre was superimposed [21]. During this manoeuvre a visual feed-back from the paper record was provided as suggested by LAPORTA and GRASSINO [21]. The three manoeuvres were randomly performed by the patient until no further increase in Pdi was observed in any manoeuvre, and the difference between two maximum Pdi was less than 10%. The highest value of Pdi,max obtained with this procedure was used for further analysis [19]. Adequate rest was allowed between Pdi,max

efforts, and great attention was paid for the inspiratory efforts to start from end-expiratory tidal volume. This was achieved by close observation of the flow, and pressure (*i.e.* Pdi, Poes, Pga) tracings as well as of the patients' breathing movement. The Pdi,max manoeuvre was obtained while the patients were breathing regularly, at the end of the expiration. The tension time index of the diaphragm (TTdi) was computed according to BELLEMARE and GRASSINO [18, 19].

According to a randomized sequence, ten patients then inhaled 0.8 and 1.6 mg of fenoterol (a beta₂ selective adrenergic agonist) in a cumulative dose-response fashion, and eight patients inhaled the corresponding puffs of placebo from a pocket nebulizer. All measurements during quiet breathing, as well as measurement of Pdi,max, and FEV₁, were repeated 15 min after the end of each administration.

Neither the patient nor the physician in charge of the experiments knew whether they were using fenoterol or placebo for the inhalation. However, it has to be mentioned that the patients who received the drug, and not those who received placebo, exhibited tremor at the highest dose. No patient had significant change in cardiac rhythm or blood pressure.

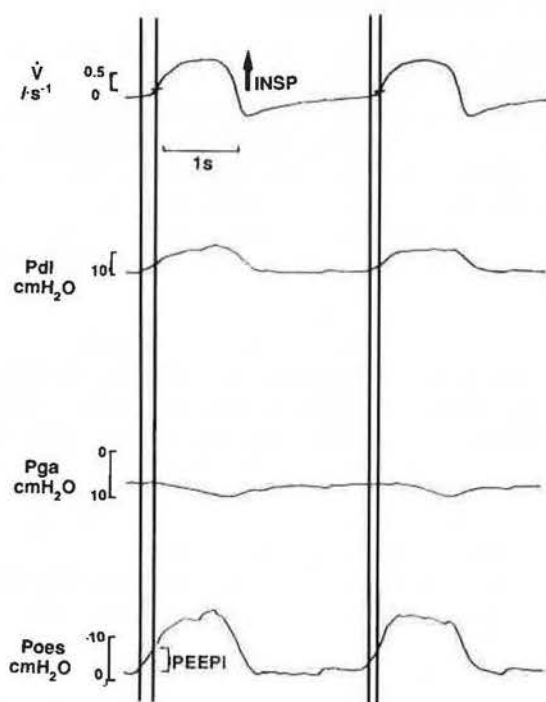


Fig. 1. — From top to bottom: tracings of ventilatory flow (\dot{V}), transdiaphragmatic (Pdi), gastric (Pga), and oesophageal pressure (Poes) in a representative chronic obstructive pulmonary disease (COPD) patient during tidal breathing. Tidal volume was 0.75 l. The first vertical line indicates the point corresponding to the onset of the inspiratory effort (Pdi swing). The second vertical line indicates the point corresponding to the start of inspiratory flow. Note that expiratory flow abruptly ends before inspiration, whilst the Pdi and Poes swing has already begun and Pga has remained constant in that interval. The difference between the point corresponding to the onset of the Pdi swing and the point of zero flow on the Poes tracing represents the end-expiratory elastic recoil pressure, *i.e.* the "intrinsic" positive end-expiratory pressure (PEEPi), which had to be counterbalanced by the inspiratory muscles in order to start inspiration (see Appendix).

Statistically significant differences between groups of data were tested with paired and unpaired Wilcoxon rank tests. A $p < 0.05$ was accepted as significant.

Results

A representative record from one of our COPD patients during quiet breathing is shown in figure 1. It can be seen that slow flow continued throughout expiration and that it abruptly ended at the end of expiration. The onset of inspiratory flow was preceded by the onset of the swing in Poes and Pdi, while Pga did not change in that interval and started synchronously with the inspiratory flow. This pattern of breathing was observed in all of the 18 COPD patients examined. These features indicate that the patients were dynamically hyperinflated and that the inspiratory muscles had to initially counterbalance the elastic pressure present at end-expiration before initiating expiratory flow. The end-expiratory recoil pressure was named "intrinsic" positive end-expiratory pressure (PEEPi) [6]. PEEPi was measured on the Poes tracing as the pressure difference (Δ Poes) between the point corresponding to the onset of the Pdi swing (*i.e.* the start of the inspiratory effort) and the point corresponding to zero flow (*i.e.* the start of inspiratory flow). Individual values of PEEPi, measured as illustrated in figure 1 are reported in table 2. Individual values of VT, Ti, Te, and Pdi,max are also reported in table 2.

Table 2. — Pattern of breathing, intrinsic PEEP and maximum transdiaphragmatic pressure

Patient no.	VT l	Ti s	Te s	PEEPi cmH ₂ O	Pdi,max cmH ₂ O
1	0.61	1.2	1.9	1.2	71.6
2*	0.72	1.0	3.4	2.3	105.0
3	0.78	1.8	2.6	3.5	67.2
4	0.83	1.2	2.2	2.1	59.0
5	1.07	1.7	3.0	1.1	70.0
6	0.39	1.1	1.4	3.3	64.4
7*	0.60	1.4	2.6	1.0	98.0
8	0.58	1.6	2.5	5.0	70.0
9	0.60	1.4	2.2	1.4	98.0
10	0.48	1.4	2.2	2.0	70.0
11*	0.72	1.3	2.2	2.0	99.0
12*	0.92	2.3	4.3	1.0	91.0
13	0.48	1.4	1.9	0.9	99.7
14	0.48	0.9	1.6	3.0	74.9
15	0.85	1.1	2.6	6.0	108.0
16	0.41	0.7	1.5	5.2	51.2
17*	0.59	1.2	2.3	0.9	84.0
18	0.56	1.2	1.7	1.6	86.0
mean	0.65	1.3	2.3	2.4	81.5
SD	0.18	0.4	0.7	1.6	17.2

VT: tidal volume; Ti: inspiratory time; Te: expiratory time; PEEPi: intrinsic positive end-expiratory pressure; Pdi,max: maximum transdiaphragmatic pressure; *: patients with wheezing in their clinical history.

Table 3 shows that inhalation of fenoterol caused a significant increase in FEV₁ (+34% on average) and a marked decrease of PEEPi (-63% on average). T_E averaged 2.4±0.7 s and 2.2±0.6 s before and after fenoterol, respectively (no significant change). C_{dyn} did not change significantly following fenoterol. Since there was no significant difference between the effects of 0.8 and 1.6 mg of fenoterol on lung mechanics and transdiaphragmatic pressure, results in table 3 pertain to the last highest dose, which includes the learning effect as well as the patients' fatigue. No significant difference was observed between the two control conditions or between control and placebo. P_{di,max} improved significantly following inhalation of fenoterol (+19% on average), whereas it did not change with placebo (fig. 2). However, P_{di,max} did not change in one patient and decreased by 7 cmH₂O after fenoterol in another; in the remaining eight patients the improvement of P_{di,max} ranged from 7–37 cmH₂O.

Despite a significant increase in \dot{V}_E (+23% on average), tidal P_{di} was slightly lower after fenoterol (-10% on average) possibly due to bronchodilatation. These changes caused a significant decrease in P_{di}/P_{di,max} and in TT_{di}, i.e. an improvement in diaphragmatic force-reserve [19]. No such changes were observed in patients who received placebo (table 3).

Three and two of the five patients with wheezing in their clinical history were in the fenoterol and in the placebo group, respectively. Their response to fenoterol or placebo was no different from that of the other patients either in terms of bronchodilatation (FEV₁ and PEEPi) or in terms of P_{di,max}. However, it has to be noted that we used larger doses than normal therapeutic doses (i.e. 1.6 mg instead of 0.4 mg) and also that these five patients had a positive smoking history.

Table 3. – Breathing pattern, lung mechanics, and transdiaphragmatic pressure, before (control) and after treatment with fenoterol or placebo

		Control	Fenoterol	Control	Placebo
V _T	l	0.66±0.19	0.76±0.30	0.63±0.18	0.61±0.16
f	b·min ⁻¹	17.4±4.2	19.2±4.1	18.6±5.5	18.6±3.8
T _I /T _T		0.40±0.07	0.40±0.07	0.36±0.05	0.40±0.07
\dot{V}_E	l·min ⁻¹	11.5±3.4	14.2±3.7*	10.9±1.8	10.8±1.3
FEV ₁	l	1.35±0.56	1.82±0.93**	1.39±0.70	1.23±0.65
PEEPi	cmH ₂ O	2.5±1.5	0.9±1.3**	2.4±2.2	2.9±2.6
C _{dyn}	l·cmH ₂ O ⁻¹	0.238±0.095	0.278±0.106	0.199±0.085	0.154±0.062
\bar{P}_{di}	cmH ₂ O	8.4±2.3	7.6±2.5	10.8±4.4	10.5±5.1
P _{di,max}	cmH ₂ O	77.3±16.4	91.1±15.8*	86.7±17.7	87.4±21.5
P _{di} /P _{di,max}		0.11±0.03	0.08±0.03**	0.13±0.06	0.14±0.12
TT _{di}		0.040±0.014	0.031±0.015*	0.045±0.019	0.046±0.034

V_T: tidal volume; f: frequency of breathing; T_I: inspiratory time; T_T: total breath duration; T_I/T_T: duty cycle; \dot{V}_E : minute ventilation; PEEPi: intrinsic positive end-expiratory pressure; C_{dyn}: dynamic lung compliance; \bar{P}_{di} : mean P_{di} during tidal breathing; P_{di,max}: maximum transdiaphragmatic pressure; TT_{di}: tension time index of the diaphragm; *: p<0.05; **: p<0.01.

Discussion

This study shows that PEEPi, although amounting only to a few cmH₂O, was present in all of the 18 stable COPD patients examined, and that it was due to airway narrowing, since it was significantly decreased by bronchodilatation. Also that inhalation of an adrenergic agonist (fenoterol 0.8–1.6 mg) caused a significant improvement in the strength (P_{di,max}) and force reserve (P_{di}/P_{di,max} and TT_{di}) of the diaphragm, in the COPD patients.

The method of quantification of PEEPi in this study is indirect. Direct measurement of PEEPi, by means of a brief end-expiratory airway occlusion, can be performed quite easily in mechanically ventilated patients, whereas it is difficult during spontaneous breathing [5, 6]. Indeed, the respiratory muscles are often relaxed during mechanical ventilation, and during airway occlusion, airway pressure exhibits a positive plateau which provides the value of the end-expiratory recoil pressure, i.e. PEEPi, when present [5, 22]. By contrast spontaneously

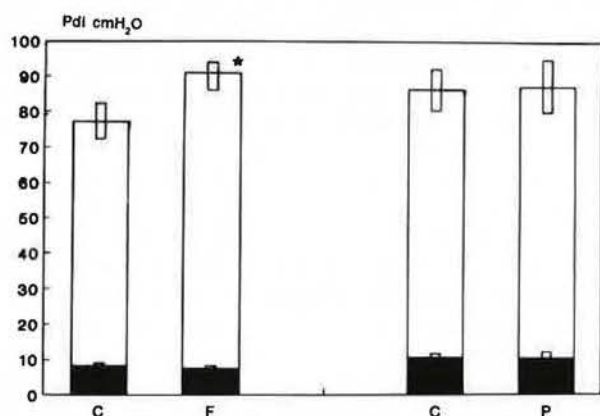


Fig. 2. – Changes in transdiaphragmatic pressure (P_{di}) after drug and placebo (two groups of patients). Columns are means and bars are SD. The shaded area represents mean transdiaphragmatic pressure (P_{di}), and the top of the column is P_{di,max}. C: control; F: fenoterol; P: placebo; *: p<0.05. P_{di}/P_{di,max} was significantly lower after fenoterol (p<0.01).

breathing patients often react to airway occlusion, and a satisfactory plateau in mouth pressure can seldom be obtained. Rossi *et al.* [6] measured PEEPi in mechanically ventilated patients as the pressure difference between the onset of the positive pressure swing for the mechanical lung inflation and the point of zero flow on the continuous record of flow and pressure at the airway opening (Pawo). They showed good agreement between the values of PEEPi obtained from the Δ Pawo and the values provided by the end-expiratory airway occlusion [6]. We used a similar approach in our spontaneously breathing COPD patients by measuring PEEPi as the Δ Poes between the points corresponding to the onset of the inspiratory effort and the onset of the inspiratory flow (fig. 1). In fact, in spontaneously breathing patients, PEEPi, when present, must be offset by the contraction of the inspiratory muscles (see Appendix). Our interpretation of the Δ Poes in figure 1 as representing PEEPi, *i.e.* the end-expiratory recoil pressure, is probably valid provided that the expiratory muscles are relaxed during expiration. In fact, the expiratory muscles could contract until almost the end of expiration and then relax suddenly. Under these conditions, the initial decrease in Poes might be due to relaxation of expiratory muscles rather than contraction of inspiratory muscles. However, we have measured gastric pressure, and that possibility is made unlikely, in our patients, by the lack of change in Pga throughout most of the expiration (*i.e.* after the initial post-inspiratory decay) as well as during that interval (fig. 1). On the other hand, the initial constancy of Pga suggests that the diaphragm was acting more as a fixator at the very beginning of inspiration. Our conclusion is further supported by the fact that PEEPi was significantly decreased by bronchodilatation, which is likely to improve the rate of lung emptying, but which is unlikely to change the action of the respiratory muscles.

The presence of PEEPi in stable COPD patients, and the fact that it is essentially the consequence of increased airflow resistance, can have important implications. Firstly, PEEPi represents a load for the inspiratory effort, which is neglected in the usual concept about the work of breathing. The contraction of the inspiratory muscles to offset the end-expiratory elastic recoil, *i.e.* PEEPi, is an isometric contraction which increases the energy demand for ventilation, but it determines neither a displacement of lung volume (elastic work) nor inspiratory flow (resistive work). Secondly, any event affecting the bronchial calibre (*e.g.* acute exacerbation) or the expiratory duration (*e.g.* the increased ventilatory demand during exercise, or the rapid shallow breathing during ARF) will enhance PEEPi. Indeed in COPD patients with ARF due to acute exacerbation, the EELV was well above the relaxed functional residual capacity (FRC) and was systematically associated with high values of PEEPi, during mechanical [5–9] as well as spontaneous ventilation [10, 11]. During mechanical ventilation, PEEPi can have adverse cardiovascular consequences [5], whereas during spontaneous breathing, PEEPi can become an unbearable extra-load for the inspiratory muscles, the efficiency of which as pressure generators is already

impaired by pulmonary hyperinflation [9, 11]. DODD *et al.* [23] have shown that COPD patients are hyperinflated during exercise. However, to our knowledge, the presence and magnitude of PEEPi in COPD patients during exercise is unknown, although PEEPi could become a significant portion of the increased inspiratory effort during exercise, and could play an important role in determining the patients' exercise limitation.

Our baseline measurements of Pdi,max are similar to those reported by other authors in stable COPD patients, and confirm that Pdi,max can be low in COPD patients because of pulmonary hyperinflation as well as other factors [19, 21, 24]. Measurement of Pdi,max is commonly accepted as an index of diaphragmatic strength, at least for clinical purposes [18–21]. The lack of significant changes of Pdi,max in the patients who inhaled placebo indicates that this measurement, in our COPD patients, was rather reproducible. On the other hand, since the patients were randomly assigned to the fenoterol or placebo group, the significant improvement of Pdi,max after fenoterol inhalation strongly suggests that it was not due to a learning effect, but to the action of the drug. A likely explanation for the improvement in Pdi,max is a decrease in lung volume due to the bronchodilatation, as would be suggested by the marked decrease of PEEPi. Alternatively, a direct effect of fenoterol on the diaphragmatic contractility, though controversial, could be hypothesized [26–28]. It has been shown that fenoterol can have systemic effects, even when administered by inhalation, related to the quantity of the drug absorbed into the circulation in an active form through the bronchial mucosa [29]. That part of fenoterol was absorbed and active, in our COPD patients, is supported by the fact that all patients who inhaled fenoterol exhibited tremor, a well-known systemic effect of beta₂ agonists. To our knowledge, the direct effects of adrenergic agonists on diaphragmatic contractility have been studied in animals [26, 27] and in normal humans [28], but not yet in stable COPD patients.

In the majority of COPD patients bronchoactive drugs result in little improvement in FEV₁, although it is known that COPD patients with a long history of cigarette smoking can exhibit a pronounced response to inhaled bronchodilators, [30, 31]. In this study, the improvement in FEV₁ after fenoterol was higher than 15% in all patients and higher than 20% in seven. This response is widely accepted as significant [30, 31]. However, it has to be remembered that the doses of fenoterol used in this study are four times higher than the common therapeutic doses, although without important side-effects. In terms of clinical benefits, it may be of interest to note that a higher V_E was obtained with a lower inspiratory effort (table 3), whilst the contemporary increase in Pdi,max, caused a significant improvement in the diaphragmatic force-reserve [19]. Therefore, the action of beta₂ adrenergic agonists, can become an important part of a strategy to prevent diaphragmatic fatigue in COPD patients who are at risk of developing it.

In conclusion PEEPi is not only present in COPD patients during ARF, but also in the stable state, as a

consequence of increased airflow resistance. Implications of PEEPi, in COPD patients, have been discussed here and elsewhere [12]. We have also shown that, in stable COPD patients, inhalation of 1.6 mg of a beta₂ adrenergic agonist (fenoterol) can improve diaphragmatic contractility.

Appendix

The method of quantification of PEEPi used in this study is probably valid, although we make two assumptions: 1) that the transdiaphragmatic pressure represents the pressure applied to inflate the lung during quiet breathing; 2) that the expiratory muscles are relaxed during tidal expiration. The latter is supported indirectly by our measurement of Pga.

The equation of motion to inflate the lung (neglecting inertia), is represented by [32]:

$$\text{Papp}(t) = V(t)/C_{\text{dyn}} + R\dot{V}(t) \quad (1)$$

where Papp is the pressure applied by the inspiratory muscles at any given time (t); V is the change in volume; C_{dyn} is the dynamic compliance; R is airflow resistance, and \dot{V} is the inspiratory flow. This equation is valid provided that expiratory flow had become nil before the end of expiration, such that inspiration starts from the elastic equilibrium volume of the respiratory system, which represents zero volume for the purpose of our analysis. This is not unusual in normal subjects during tidal breathing. By contrast, in COPD patients, even in stable conditions like the patients of this study, this is seldom the case. Complete expiration at the end of the ventilatory cycle is prevented by increased airflow resistance and expiratory flow limitation. Flow continues throughout expiration and a positive end-expiratory pressure is present at the alveolar level due to the elastic recoil pressure which is driving the expiratory flow.

Clearly, the positive end-expiratory alveolar pressure (*i.e.* PEEPi) has to be offset by the inspiratory muscles before inspiratory flow can start. Under these circumstances, equation 1 becomes:

$$\text{Papp}(t) = \text{PEEPi} + \Delta V(t)/C_{\text{dyn}} + R\dot{V}(t) \quad (2)$$

where ΔV is the change in lung volume from the end-expiratory tidal volume. At end-expiration, V is zero and change in lung volume has not yet begun, so that equation 2 becomes:

$$\text{Papp} = \text{PEEPi} \quad (3)$$

We used this approach to measure PEEPi, indirectly, in our spontaneously breathing COPD patients (fig. 1). We did not compare our results with the end-expiratory occlusion method as was done in a previous study [6]. However, that comparison may also not be fully satisfactory. In fact, the "end-expiratory occlusion" PEEPi is obtained in static condition, *i.e.* after equilibration between alveolar units with different time constant

(pendelluft) and stress relaxation phenomena. In contrast, "dynamic" PEEPi as it was measured in this study can be different because alveolar units with shorter time constant can start filling whilst other units with longer time constant are still emptying, and there was not enough time for equilibration as well as for stress relaxation phenomena.

Clearly, our method of quantification of PEEPi has some limitations. However, it seems to us a reasonable approach in spontaneously breathing COPD patients. In these patients, the presence of PEEPi can be qualitatively suspected by the pattern of the end-expiratory flow.

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Pression positive "intrinsèque" en fin d'expiration chez les patients atteints d'affection pulmonaire obstructive chronique en état stable. L. Dal Vecchio, G. Polese, R. Poggi, A. Rossi.

RÉSUMÉ: Nous avons apprécié la pression positive "intrinsèque" en fin d'expiration (PEEPi) chez dix-huit patients atteints de bronchopneumopathie chronique obstructive (COPD) en état stable, au cours de la respiration calme. Le débit, le volume, et les pressions oesophagiennes (Poes), gastriques (Pga) et transdiaphragmatiques (Pdi) ont été mesurés. PEEPi a été mesuré comme le Δ Poes entre le début de l'effort inspiratoire, indiqué par le commencement du mouvement de Pdi, et le point correspondant au débit nul. PEEPi était présent chez les dix-huit patients COPD de cette étude, et atteignait en moyenne 2.4 ± 1.6 cmH₂O. La pression transdiaphragmatique maximum (Pdi, max) a été mesurée également et atteignait en moyenne 81.5 ± 17.4 cmH₂O. Ensuite, selon une séquence randomisée, dix patients ont inhalé un agoniste adrénergique (Fenoterol 1.6 mg), et huit le placebo correspondant. Le Fenoterol mais non le placebo a déterminé une augmentation significative du VEMS (+34% en moyenne), associée à une diminution significative du PEEPi (-63% en moyenne), et à une amélioration significative de Pdi,max (en moyenne, +19%). Nous concluons que: 1) le PEEP intrinsèque peut être présent chez des patients COPD en état stable, par suite d'une augmentation de la résistance au débit aérien; 2) le Fenoterol améliore la force diaphragmatique (Pdi, max) chez nos patients COPD, peut-être par le canal d'une diminution des volumes pulmonaires.

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