ORIGINAL ARTICLE

Breathing frequency and use of expiratory muscles do influence the dynamic positive end-expiratory pressure

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Abstract

End-expiratory air trapping due to obstructive airway disease can be estimated through the measurement of intrinsic positive end-expiratory pressure $PEEP_i$. The influence of breathing-frequency and use of expiratory muscles on $PEEP_i$ were measured in 10 normal and 10 chronic bronchitic patients (COPD). Insignificant control values of $PEEP_i$ increased to measurable values at high breathing rate in normal subjects. Control values were higher in COPD patients and increased at fast breathing rate. When corrected for the use of expiratory muscles according to simultaneous gastric pressure drop, $PEEP_i$ decreased in COPD, but still increased at high rate. We conclude that modifying the respiratory rate can increase $PEEP_i$ values independently of the severity of airway obstruction and the use of expiratory muscles. Before estimating the pathological value of a $PEEP_i$ measurement or evaluating the effects of a treatment, we always need to know the simultaneous breathing frequency.

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Keywords breathing rate; gastric pressure; normal subjects; chronic bronchitis; end-expiratory pressure.

INTRODUCTION

Patients suffering from chronic obstructive pulmonary disease(COPD) do present end-expiratory air trapping especially during acute exacerbation. This causes an increase of their inspiratory work and can precipitate respiratory failure. The pressure needed to counteract this airway closure is called the intrinsic positive end-expiratory pressure ($PEEP_i$) and can be measured through the negative deflection of oesophageal pressure preceeding the start of the inspiratory flow (dynamic $PEEP_i$) (1). This measurement can be used in clinical situations when the efficacy of mechanical ventilation has to be estimated (2). These external positive pressure ventilatory helps can overcome the $PEEP_i$, but also have an influence on the breathing frequency. Decreasing or increasing the respiratory rate should modify the expiratory time (T_e) and then the $PEEP_i$. We intended to measure the influence of varying the respiratory rate on $PEEP_i$ measurements in normal and COPD subjects during spontaneous breathing. As COPD patients need a longer T_e to blow out their expiratory tidal volume, they use their expiratory muscles. The positive expiratory pressure induced by this muscular action interferes with $PEEP_i$ measurement: it can be estimated through simultaneous gastric pressure measurement that can be subtracted from the dynamic $PEEP_i$ to approach the true $PEEP_i$ value (2). Furthermore, the increase of respiratory rate modifies T_e and should increase the use of the expiratory muscles in COPD patients and their interference with $PEEP_i$ measurement. So we studied the influence of varying the respiratory rate on $PEEP_i$ measurements with and without correction by gastric pressure in normal and stable COPD patients.

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MATERIALS AND METHODS

Population

First group of normal subjects: 14 healthy volunteers were asked to participate at the protocol but only 10

were able to perform all the measurements due to an intolerance to the oesophageal catheter or to the loss of a signal during the procedure or to tremendous artefacts. Second group of patients suffering from COPD: out of 11 COPD patients, the results were complete in 10. In the 10 normal volunteers (age 34 $\pm$ 8 SD years old; height 1 m 80 $\pm$ 0.07; weight 80 $\pm$ 7 kg), the respiratory function tests were within normal values (3) : forced expiratory volume in 1 s(FEV_1) 109 $\pm$ 14 SD% of normal values, forced vital capacity (FVC) 113 $\pm$ 10 SD%, functional residual capacity (FRC) 119 $\pm$ 30%, lung diffusion test (DLCO) 98 $\pm$ 12%. No blood gas measurements have been performed in normal subjects for ethical reasons. In the 10 stable COPD patients (age 60 $\pm$ 12 SD years old, height 1 m 71 $\pm$ 0.07, weight 73 $\pm$ 16 kg), respiratory function results were: FEV_1 41 $\pm$ 26SD%, FVC 78 $\pm$ 22%, FRC 191 $\pm$ 54%, DLCO 46 $\pm$ 26%. Blood gases before experiments: pH 7.42 $\pm$ 0.04, $PaCO_2$ 42 $\pm$ 6 mmHg; PaO_2 65 $\pm$ 14 mmHg. All subjects gave informed consent to the protocol approved by the institution's ethics committee.

Measurements

Static and dynamic lung volumes were measured using a MEDISOFT 5500 PART'NAIR (Dinant, Belgium) body plethysmograph. Single-breath DLCO was measured by using a MEDISOFT 5200 PART'NAIR. Predicted values for lung function variables are those proposed by the European Community for Coal and Steel (3). Arterial blood gases tensions were measured with an Instrumentation Laboratory IL BG3 analyzer. Respiratory flow was measured at the opening of the mouth piece with a Fleisch pneumotachograph connected to a differential transducer VALIDYNE DP45 $\pm$ 5 cmH_2O. The flow was integrated into volume, and signals sent to a computing ANADAT system 5.2 (INFODAT, Montréal, Canada). Minute ventilation (V_E), tidal volume (V_T), inspiratory flow (V_T/T_I), duty cycle (T_I/T_{tot}) and respiratory rate (F) were computed. Pressure at the airway opening (P_{ao}) was measured directly in the mouth piece using a differential transducer Validyne DP 732 $\pm$ 2 psi. Oesophageal and gastric pressures were measured with a GAELTEC catheter (Dunvegan, U.K.) with two sensors situated 15 cm one from the other and connected to a MEDATEC amplifier (Brussels, Belgium). This system has been shown to be reliable for acute changes in respiratory pressures and studies of respiratory muscle strength (4). One sensor was positioned in the oesophagus (P_{oes}) and the other in the stomach (P_{gas}): electrical subtraction gave transdiaphragmatic pressure P_{di}. Correct position was confirmed using an occlusion test as described by Baydur (5). Total inspiratory work (WOB) was computed from P_{oes} and volume by using the Campbell's diagram (6) on the ANADAT system for every respiratory cycle (WOB/cy), and then computed according to volume (WOB/l) and minute ventilation (WOB/min). A transdiaphragmatic work W_{di} was computed from P_{di} and volume with the same system and results equally given as W_{di}/cy, W_{di}/l and W_{di}/min. Dynamic intrinsic positive end-expiratory pressure ($PEEP_i$) was computed as the negative deflection of Poes preceeding the start of the inspiratory flow (1). In a second time, it was also corrected according to the concomitant decrease of P_{gas} when present ($PEEP_{i\,corr}$) according to Appendini *et al*. (2).

Experimental protocol

All subjects were studied in the sitting position while breathing through the mouth piece; they were asked to relax completely and instructions were given to keep their lips closed around the mouth piece. Measurements were performed when ventilatory parameters were stable, during periods of 1 min of spontaneous breathing at a relaxed respiratory rate; two periods of measurements were acquired in control conditions to attest the stable state; measurements were repeated at their maximal breathing frequency during periods of 1 m after stabilization of the respiratory parameters.

Data analysis

Numerical values are expressed as mean $\pm$ SD. Parameters at low and high breathing frequencies were compared by a two-way analysis of variance (ANOVA) with one repeated (frequency) and one independent (normal *vs*. COPD) factor. Pearson coefficients were used to assess the correlation between changes in T_E and $PEEP_i$ or $PEEP_{i\,corr}$ and were compared by Hotelling test. All statistical tests are two-tailed.

RESULTS

Populations and control measurements: normal subjects were significantly younger and taller than COPD patients ($P < 0.01$), but with no different weight. All functional parameters (volumes and diffusion) were significantly different ($P < 0.005$). Statistical analysis of the various measurements showed no significant difference between the two control periods in both populations and the mean of the two controls has been used for comparison with measured values during maximal breathing frequency.

The ventilatory behaviour did not change in the same way in the two groups during tachypnea. In normal subjects, tidal volume increased from 663 ml $\pm$ 142 SD to 1040 $\pm$ 346 ($P < 0.001$) when breathing frequency increases from 16.4 $\pm$ 1.1 to 29.9 $\pm$ 3.4/min while it did not differ significantly in COPD patients (570 $\pm$ 252 to 428 $\pm$

213 ml) when breathing frequency varied from 19.4 ± 8.7 to 31.7 ± 6.0/min. The difference between V_t of the two groups at high frequency was significant ($P < 0.001$). As a consequence, minute ventilation increased much more in normal subjects (from 10.8 ± 2.6 to 31 ± 10.3 l/min) than in COPD patients (from 10.8 ± 5.8 to 14 ± 8.6 l/min) ($P < 0.001$). V_t/T_I increased much more in normal subjects (from 519 ± 167 to 1288 ± 451 ml/s) than in COPD patients (from 475 ± 199 to 596 ± 328 ml/s) ($P < 0.001$), but T_I/T_{tot} increased in normals only (from 0.36 ± 0.06 to 0.41 ± 0.04) ($P = 0.002$). Expiratory time T_e decreased similarly and significantly in both groups ($P < 0.001$) (see Fig. 1). This increase of flow and ventilation in normal subjects was concomitant to a huge increase of inspiratory WOB/cy (0.24 ± 0.19 J to 0.81 ± 0.67; $P = 0.002$), WOB/l (0.36 ± 0.24 to 0.69 ± 0.43 J/l; $P = 0.002$), and WOB/min (4.2 ± 3.4 to 24.4 ± 21.0 J/min; $P < 0.001$); no significant change was observed in COPD patients (WOB/cy 0.40 ± 0.20 J, WOB/l 0.73 ± 0.35 J/l, WOB/min 7.6 ± 5.1 J/min) but the control values of WOB/l were significantly higher in COPD respective to normal subjects ($P = 0.021$). Inspiratory work computed on transdiaphragmatic pressure showed similar results: higher W_{di}/l values in COPD patients in control measurements (1.95 ± 1.51 J/l *vs*. 0.72 ± 0.47 in normals; $P = 0.023$), but no increase at high frequency in these patients; on the contrary, a significant increase of W_{di}/cy ($P = 0.004$), W_{di}/l ($P = 0.033$) and W_{di}/min ($P < 0.001$) in normal subjects at high frequency. Very small insignificant control values of $PEEP_i$ were measured in normal subjects (0.6 ± 0.4 cmH_2O) and higher values in COPD (4.8 ± 3.0) ($P < 0.001$) : $PEEP_i$ increased significantly at high frequency in both groups (2.1 ± 1.1 and 6.4 ± 3.1 cmH_2O) ($P < 0.001$) (Fig. 1). When corrected according to gastric pressure, control $PEEP_{i\,corr}$ was also smaller in normals *vs*. COPD (0.5 ± 0.4 *vs*. 3.9 ± 1.8 cmH_2O) and both values increased at high breathing frequency (1.9 ± 1.0 and 5.6 ± 2.6 cmH_2O; $P < 0.001$). The correlations between changes in T_e and $PEEP_i$ and between changes in T_e and $PEEP_{i\,corr}$ do not differ significantly, for normal and for COPD subjects (Fig. 1).

DISCUSSION

Measuring the dynamic $PEEP_i$ during acute respiratory failure can be helpful to evaluate the end-expiratory air trapping and to test the efficacy of the medical treatment and of the external ventilatory supports (2). The severity of the obstructive disease and the effects of these therapies can modify the activity of the expiratory muscles and the breathing frequency. Both factors could influence the measured value of $PEEP_i$ independently of flow limitation (7–10). We intended this study to measure the influence of both respiratory rate and expiratory muscle activity on dynamic $PEEP_i$ in healthy and stable emphysematous subjects.

Very small insignificant values of $PEEP_i$ were measured in normal subjects at their control breathing frequency. A previous study had not found any evidence for $PEEP_i$ during quiet breathing in normal subjects (11). In normal subjects at rest, end-expiratory lung volume corresponds indeed closely with the elastic equilibrium point of the respiratory system (12). During high-rate minute ventilation, it can occur that the lungs do not have time enough to reach their equilibrium point during passive expiration. Our results show a small but significant increase of $PEEP_i$ at high frequency in normal subjects: auto-$PEEP_i$ and dynamic hyperinflation occurred then without flow limitation. We had expected that an abdominal muscle activity during expiration could have prevented an increase in lung volume by increasing expiratory flow in these normal subjects (13), but we did not observe any limitation of this increase of $PEEP_i$ value by correcting it with the concomitant expiratory gastric pressure change. The increase of dynamic $PEEP_i$ at high

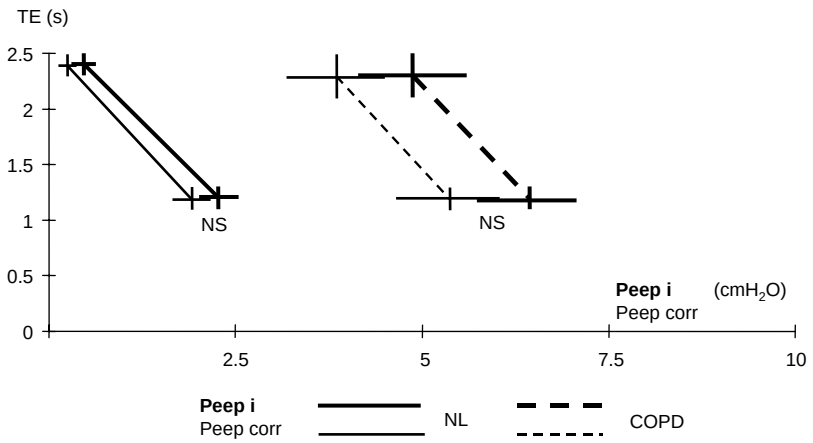

Fig. 1. Variations of $PEEP_i$ and $PEEP_{i\,corr}$ corrected according to gastric pressure drop in normal subjects (NL) and COPD patients during variations of expiratory time T_e.

breathing frequency seems then to be due only to the shortening of the expiratory time T_e in normal subjects.

A flow limitation can usually occur in these normal subjects only with maximal forced manoeuvres but it can occur during tidal breathing in stable COPD patients(1). As previously described, significantly higher values of $PEEP_i$ have been measured in our stable COPD patients during spontaneous respiration in control conditions (11,14). In these patients, the rate of lung emptying becomes impaired because of increased expiratory resistance and expiratory flow limitation (15). The end-expiratory lung volume therefore is higher than the elastic equilibrium point of the respiratory system (dynamic pulmonary hyperinflation) and a positive pressure $PEEP_i$ is present at end expiration (16). The auto-PEEP is then a result of the critical closure of the airways (17).

A further increase of these high values of $PEEP_i$ has been observed at high breathing frequency in our COPD patients. The relationship between the shortening of T_e and the increase of $PEEP_i$ has been similar in normal and COPD subjects. A part of the positive $PEEP_i$ observed in COPD can be explained by expiratory muscle contraction during expiration (2). When expiratory muscles are recruited during expiration, a positive value of alveolar pressure may persist throughout expiration without increasing lung volume. Provided that flow continues to the end of the expiratory cycle, there will be an end-expiratory gradient of alveolar to central airways pressure (auto-PEEP effect) without a corresponding increase in lung volume (18). After subtraction of the simultaneous gastric pressure drop (2,7,8,10), we observed a small decrease of the $PEEP_i$ value in both control and high-frequency conditions in COPD patients, but this difference was not significant. Some recent studies in acute respiratory failure suggest that the estimate of the actual $PEEP_i$ by subtracting P_{gas} decay restricted between the onset of inspiratory effort and the point of zero flow, from $PEEP_i$, could overestimate the actual $PEEP_i$ proportionally to the intensity of expiratory muscles recruitment (10). That should not have influenced our results since a similar pressure drop was observed at both frequencies. The using of expiratory muscles at high breathing rate seems then to have only a small influence on $PEEP_i$ measurement in that condition.

In both normal and stable COPD groups, the shortening of the expiratory time T_e seems then to be the main factor of increasing $PEEP_i$. Despite large differences in ventilation at high respiratory rate, the expiratory time decreased in the same way in both groups. Having regard to their higher inspiratory works at spontaneous breathing rate, the COPD patients seem to have been able to increase their breathing frequency but unable to increase their inspiratory works and ventilation. It should be pointed out that these measurements have been performed in stable patients and that different respiratory behaviours could occur in patients with acute respiratory insufficiency.

We conclude that modifying the respiratory rate alters the measurement of dynamic $PEEP_i$ independently of the airway obstruction and of the use of expiratory muscles. An appreciation of the pathological value of a $PEEP_i$ measurement, or its use in evaluating the effects of a treatment, needs always to know the concomitant breathing frequency.

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