Shape change of the occlusion-pressure wave during exercise

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ABSTRACT: In conscious subjects, the occlusion pressure measured in the initial part of the inspiration (up to 200 ms) appears to be a valid index of output of the respiratory centres. To interpret any relative change in occlusion pressure, the shape of the occlusion-pressure wave must remain absolutely constant. The purpose of this study was to test the hypothesis that the shape of occlusion-pressure wave does not change during exercise. However, we found that the shape changed significantly during cycle incremental-load exercise in five healthy subjects and in 12 of 17 patients with chronic obstructive pulmonary disease. The major change appeared during the second half of the exercise and mainly during the last workloads. This study shows that it is necessary to take into consideration this form change to interpret any relative change in shape of pressure traces during exercise.

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In conscious subjects, the initial part (200 ms) of the inspiratory occlusion-pressure wave is not altered by conscious or reflex reactions and no major change has been found [2, 3]. The waveform is not generally verified and interpretation errors may result, mainly from analysis of change in mechanical transformation of neural output as assessed by pressure at 0.1 s (P1) and mean inspiratory flow (Vt/TI) or their ratio. This finding confirms, in direct fashion, the expected form change from previously published data in which P1 is thought to measure the rate of change in chest wall muscle pressure (Pmus) over a segment somewhat removed from the onset of neural inspiration.


The aim of the present study was to verify the validity of the hypothesis of shape constancy in the occlusion-pressure wave during exercise in healthy subjects as well as in patients with chronic obstructive pulmonary disease. We found that the shape changed significantly during exercise in most of the subjects, and thus that any relative change in P1 and P1/Vt/TI during exercise should be interpreted with caution.

Methods

Population

Five healthy subjects (N) and 17 out-patients with chronic airflow obstruction (CAO) were studied. Healthy subjects were nonsmokers and had no previous history of pulmonary or cardiovascular disease. We selected patients with clinical and physiological evidence of chronic airflow limitation according to the American Thoracic Society [7]. The CAO group was composed of various patients suffering from chronic bronchitis (CB) (n=7), emphysema (roentgenologic evidence) (EMP) (n=5) and post-tuberculous fibrosis (PT) (n=5). Patients with acute bronchial infection or history of asthma were excluded. All patients were familiar with pulmonary function testing and gave informed consent for this study. The physical characteristics and lung...
function tests of healthy subjects and patients are given in table 1. The predicted values for lung function tests are those of Quanjer et al. [8]. At exercise on cycle ergometer, maximum workload in patients ranged from 30–180 W, and maximal ventilation ranged from 17–85 l min⁻¹.

Material and protocol

Static lung volumes were measured with a water-sealed spirometer (Spirotest 3, Jaeger, West Germany); functional residual capacity (FRC) was measured by helium dilution technique. Blood gases were determined from an arterialized ear lobe blood sample at rest (Corning 170, Corning, France). Exercise was performed using a bicycle ergometer (Gauthier EPC 7701, Paris France). After a 3 min rest, each subject performed an incremental exercise (30 W/3 min) until exhaustion (subject unable to maintain cycling frequency above 40 rpm). Inspiratory mouth occlusion was performed with an electromagnetic valve (6655, Mecalectro, Paris, France) which could be closed or opened by a command sent on line to a peripheral interface adapter (PIA6821, MID, Paris, France) via an analogue driver that amplified the PIA signal and slowed down valve closure during expiration. Another line for the same PIA was used to connect or disconnect the mouth pressure transducer back to the atmosphere. This reset procedure was performed automatically after expiration. For each level of workload, the mean and the variance of occlusion pressure measurements and calculated variables (time-derivatives) were considered. The shape of the inspiratory rising part of the occlusion-pressure (Po be) wave was analysed by fitting the data with a power function: Po ≈ b time⁻a where b is a dimensionless constant and a is the ratio of occlusion pressure to inspiratory flow. When a command was given from the computer keyboard for occlusion, it was memorized and the respiratory phase was verified. When the occlusion pressure valve was closed and it was maintained for 200 ms following the onset of inspiration. Then, the occlusion valve was opened and the mouth pressure transducer valve reversed, connecting the transducer to the atmosphere. A few ms later (to avoid switching noise) the mouth pressure value was taken as a new zero reference point on the pressure recording. The occlusion pressure value was based on its accuracy. From these data, occlusion pressures at 100, 150 and 200 ms were compared.

Table 1. – Physical characteristics and lung function tests in healthy subjects and CAO patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Sex</th>
<th>Age yrs</th>
<th>Height cm</th>
<th>Weight kg</th>
<th>VC %pred</th>
<th>FEV₁/VC %</th>
<th>RV/TLC %</th>
<th>TLC % pred</th>
<th>PaO₂ mmHg</th>
<th>PaCO₂ mmHg</th>
<th>SaO₂ %</th>
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<tbody>
<tr>
<td>N</td>
<td></td>
<td>3 ±2</td>
<td>26</td>
<td></td>
<td>10 ±3</td>
<td>103</td>
<td>107 ±9</td>
<td>105 ±25</td>
<td>109 ±10</td>
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<td></td>
</tr>
<tr>
<td>n=5</td>
<td></td>
<td>±1.3</td>
<td>±11.6</td>
<td>±13.2</td>
<td>±9.6</td>
<td>±5.1</td>
<td>±12.2</td>
<td>±9.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CB</td>
<td>7 0</td>
<td>56</td>
<td>171</td>
<td>66 66</td>
<td>36 36</td>
<td>104 59</td>
<td>136 60</td>
<td>136 ±8.1</td>
<td>136 ±8.1</td>
<td>43 53 43 53</td>
<td>94.0</td>
</tr>
<tr>
<td>n=7</td>
<td></td>
<td>±17.8</td>
<td>±6.7</td>
<td>±13.9</td>
<td>±14.5</td>
<td>±13.3 ±5.9</td>
<td>±8.1</td>
<td>±19.4</td>
<td>±3.5</td>
<td>±4.2 ±1.58</td>
<td></td>
</tr>
<tr>
<td>EMP</td>
<td>3 2</td>
<td>56</td>
<td>169</td>
<td>57 75 28</td>
<td>60</td>
<td>104 67</td>
<td>136 69</td>
<td>35.5</td>
<td>4.2</td>
<td>±5.5 ±5.68</td>
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<tr>
<td>n=5</td>
<td></td>
<td>±7.6</td>
<td>±5.1</td>
<td>±14.4</td>
<td>±13.9</td>
<td>±5.9 ±8.1</td>
<td>±19.4</td>
<td>±3.5</td>
<td>±1.58</td>
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<tr>
<td>PT</td>
<td>3 2</td>
<td>58</td>
<td>167</td>
<td>59 46 53</td>
<td>50</td>
<td>104 67</td>
<td>136 69</td>
<td>41</td>
<td>92.4</td>
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</tr>
<tr>
<td>n=5</td>
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<td>±12.9</td>
<td>±9.7</td>
<td>±17.2</td>
<td>±12.4</td>
<td>±7.9 ±13.1</td>
<td>±14.5</td>
<td>±12.3</td>
<td>±5.5 ±5.68</td>
<td></td>
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</tr>
</tbody>
</table>

Means ±sd. N: healthy subjects; CB: chronic bronchitis; EMP: emphysema; PT: posttuberculous fibrosis; % pred: percentage of predicted value; VC: vital capacity; FEV₁/VC: forced expiratory volume in one second as percentage of VC; RV/TLC: residual volume as percentage of TLC; TLC: total lung capacity; PaO₂: arterial oxygen tension; PaCO₂: arterial carbon dioxide tension; SaO₂: arterial oxygen saturation; CAO: chronic airflow obstruction.

Statistical analysis

For each level of workload, the mean and the variance of occlusion pressure measurements and calculated variables (time-derivatives) were considered. The shape of the inspiratory rising part of the occlusion-pressure (Po be) wave was analysed by fitting the data with a power function: Po be ≈ b time⁻a where b is a dimensionless constant and a is the ratio of occlusion pressure to inspiratory flow. When a command was given from the computer keyboard for occlusion, it was memorized and the respiratory phase was verified. When the occlusion pressure valve was closed and it was maintained for 200 ms following the onset of inspiration. Then, the occlusion valve was opened and the mouth pressure transducer valve reversed, connecting the transducer to the atmosphere. A few ms later (to avoid switching noise) the mouth pressure value was taken as a new zero reference point on the pressure recording. The occlusion pressure value was based on its accuracy. From these data, occlusion pressures at 100, 150 and 200 ms were compared.
Fig. 1. - Occlusion pressure-time course during incremental cycle exercise (30 W/3 min) in healthy subjects. Each graph point represents the mean of occlusion pressure measured at rest (R) and during each 30 W increment in workload. Pocc: occlusion pressure.

Fig. 2. - Change in time-derivative ratio of occlusion pressure between rest and exhaustion (Ex.) in healthy subjects and CAO patients. \( \frac{dP}{dt_{[0.10, 0.15]}} \)/\( \frac{dP}{dt_{[0.15, 0.20]}} \); time-derivative of occlusion pressure on the [0.10, 0.15] time interval; \( \frac{dP}{dt_{[0.10, 0.15]}} \); time-derivative of occlusion pressure on the [0.15, 0.20] time interval; ●: emphysema, ○: chronic bronchitis; △: posttuberculous fibrosis; bars represent the 95% confidence interval of mean. CAO: chronic airflow obstruction.
end-exercise periods. This method has the advantage of being independent of the accuracy of inspiration beginning point. These comparisons were performed in each group (healthy subjects and CAO patients) by using paired t-test, and subject by subject using unpaired t-test. The $P_{0.1}/P_{0.2}$ ratio was also considered to illustrate the change in pressure waveform as a function of workload increase during exercise in healthy subjects.

Results

The variability of occlusion-pressure measures (in term of variation coefficient) was equal to 25 and 19% at rest and to 11 and 10% at exhaustion for $P_{0.1}$ and $P_{0.2}$, respectively.

The shape of the initial (200 ms) inspiratory part of the occlusion-pressure wave during exercise in the healthy subjects is illustrated in figure 1. As seen from this figure, the pressure-time course exhibits a slight upward concavity or a quasi-linearity at rest whereas it is obvious that an upward convexity appears at end-exercise. The analysis of the occlusion-pressure wave by fitting a power function showed wide variability in shape between subjects as assessed by the form index (b parameter) which ranged from 1.11–1.39 at rest and from 0.63–0.71 at exhaustion. For patients, b values ranged from 0.81–2.13 at rest and from 0.42–1.26 at exhaustion.

The analysis of the shape after 100 ms at rest and at end-exercise by means of the time-derivatives of occlusion pressure revealed a significant change in both healthy subjects (p<0.01) and CAO patients (p<0.001) (fig. 2). Detailed analysis, subject by subject, revealed a significant departure from the basal shape in all healthy subjects and in all but five CAO patients. In these two groups of subjects, the change in pressure-time course was characterized by the passage from a concave or quasi-linear relationship to a convex shape or by an accentuation in the convexity. The patients did not present any special shape of occlusion-pressure wave as compared to healthy subjects but the variability of pressure waveform between patients was larger both at rest and at end-exercise (fig. 2).

It was difficult to determine precisely at which workload the shape of the pressure wave changed during the incremental exercise because the intrasubject variability of occlusion pressure ($P_{a1}$ and $P_{a2}$) between workloads was relatively large (fig. 3). Nevertheless, the major change in $P_{0.1}/P_{0.2}$ ratio appeared during the second half-exercise and mainly for the last workloads as illustrated in figure 3 from the data of healthy subjects. In patients, the maximum workload was reduced and thus this analysis was not possible.
Discussion

The time course of inspiratory activity stems from the work of Von Euler et al. [9] who introduced the concept that a distinction has to be made between intensity of inspiratory activity and its timing. Actually, the factors determining the rising phase shape of inspiratory neural output are not known. Several observations suggest that the shape of inspiratory rising output is not affected, except in amplitude, by either hypercapnia or hypoxia whereas changes in body temperature, as well as different anaesthetics and narcotics can cause shape alterations [10].

Pressure is the first level in respiratory output at which the action of various muscles are combined to give a single output. Assessment of the pressure losses due to the force-velocity and force-length relationships of the respiratory muscles and to distortion of the respiratory system during active breathing presents a major problem that can be avoided at least partly from measurements of airway occlusion pressure [11]. The wave shape of occlusion pressure closely reflects the shape of the inspiratory neural drive [12] and, in conscious subjects, the initial part (the first 200 ms) appears to be an index of output of the respiratory centres which depends only on the neuronal discharge and on the effectiveness of the contraction of the respiratory muscle [1]. Thus, to interpret any relative change in occlusion pressure in the first part of inspiration, it is absolutely necessary that the shape of pressure wave remain constant. The shape of occlusion pressure wave has been controlled during CO₂ rebreathing and no major change has been found [2, 3] except in anaesthetized dogs, in which the constant relationship between pressure peak and P₆₃ was abolished as the result of a shortening of inspiratory time [13]. In the case of exercise-induced hyperventilation, this shape constancy is not generally considered and qualitative or quantitative errors in interpretation may result, mainly from analysis of the change in mechanical transformations (P₆₃ and V₉/T₉) or their ratio termed “effective inspiratory impedance” [14]) of inspiratory neural drive when the occlusion-pressure wave changes in form.

The relatively large variability in occlusion pressure measurements was accounted for by considering the mean and variance determined from several respiratory cycles at each workload level. Thus, only mean shapes were to be considered. The crucial offset problem in these measurements was prevented by automatic reset of mouth pressure after each measurement of occlusion pressure. The concordance of our results (occlusion pressure measures at rest and during exercise in healthy subjects and CAO patients, observed shape of occlusion-pressure wave at rest) with those in the literature [1, 15, 16] argues against any particular bias in our measurements. The shape change of occlusion-pressure wave in early time of inspiration during exercise was obvious from our data, both by visual judgement and after statistical analysis.

Others studies relate variation in the pressure wave shape under various particular conditions: ventilation under positive pressure in anesthetized healthy subjects [17], suppression of hypoxic stimulus in patients with acute respiratory failure [18], and different anaesthetics and narcotics [10]. In a study by Szkowinska et al. [16], the P₆₃/V₉₂ (volume at 0.2 s) did not change significantly during exercise whereas ventilation did not parallel change in P₆₃, in healthy subjects or in patients with chronic obstructive pulmonary disease. These results also suggest a form change in pressure wave during exercise by factors involved in P₆₃/V₉₂ or P₆₃/V₉/T₉: the effectiveness of contraction of the inspiratory muscles (active impedance) and passive component of the ventilatory system.

The experimental determination of factors determining the shape of pressure wave (and thus its change) is very difficult because the inspiratory muscles (diaphragm and accessory muscles) interact and work at different phases of respiration to produce breathing movements. A full analysis of breathing movements requires measurement of the collective spatial distribution and temporal activity of the entire pool of respiratory α-motoneurones. Thus, the factors being unknown, any discussion can be only speculative according to anatomical, physiological and experimental data. A change in pressure waveform from central origin is not to be excluded, but remains to be elucidated.

The changes in arterial oxygen and carbon dioxide tension (Pao₂ and Paco₂) during exercise in healthy subjects are moderate and no hypoxic or hypercapnic stimulus appears. The anaerobic mechanisms did not seem to be involved in the shape change because two patients presented a form change in occlusion-pressure wave despite their exercise being insufficient (30 W) to reach anaerobic threshold and, inversely, in two patients the pressure waveform remained unchanged despite maximal workload reached being 90 W.

A change in occlusion-pressure waveform from a peripheral level could be explained by a change in the mode of temporal recruitment of inspiratory muscles and/or muscular fibre types. Simultaneous measurements of oesophageal and gastric pressures and of volume changes of the rib cage and abdomen, allow the analysis of the contribution of the various respiratory muscles (intercostal-accessory, diaphragmatic and abdominal) to the tidal volume change both at rest and during exercise [19]. At rest, the diaphragm acts as the main generator of pressure and the intercostal-accessory muscles are not active. During exercise, there is evidence of intercostal-accessory muscle recruitment during inspiration and abdominal muscle recruitment during expiration. These findings are supported by electromyographic evidence of increased intercostal and abdominal activity as ventilation increases above resting levels [20, 21]. Similarly, in patients with chronic obstructive pulmonary disease (COPD) and marked hyperinflation, most of the increase in ventilation during cycle exercise is achieved by recruitment of intercostal-accessory muscles during inspiration [22]. Furthermore, the diaphragm should not be treated as
one muscle: the mechanical linkage of its costal and crural parts may change during exercise particularly if the volume of the chest wall changes [23]. These changes in respiratory muscle recruitment are not the only modification that appears during exercise. Indeed, Critchlow and co-workers [24, 25] have found that inspiratory muscle fibres are selectively activated according to the inspiratory rate. Their results indicate a shift from slow to fast fibres which provide a greater power per unit stimulus. These recruitment changes in various inspiratory muscles and muscular fibres modify the muscular mechanical transformation of respiratory neural drive during exercise and thus could induce change in the pressure waveform. The inspiratory neuromuscular drive also depends on the change in the end-expiratory volume and in the abdominal-chest wall configuration that can be modified during exercise.

Agoston and Torsu [26] demonstrated that the chest wall undergoes considerable distortion at high levels of ventilation. These observations also apply to exercise during which Grimby et al. [27] found substantial departures of both the rib cage and abdominal walls for their relaxation characteristics. Grassino et al. [4] showed that when end-expiratory volume is lowered through recruitment of expiratory activity, the pressure generated in the first 100 ms will overestimate inspiratory muscle pressure because of release of the elastic energy involved in reducing end-expiratory volume. This would tend to cause a change in pressure waveform since the increase in pressure between 0 and 100 ms will be contributed to by both inspiratory and expiratory muscles, whereas the rate of rise later on is primarily a reflection of inspiratory muscle activity.

More recently, the time course of dP/dt throughout inspiration at rest [5] and during exercise [6] has been defined: advancing the point of equilibrium between elastic recoil and chest wall muscle pressure (Pmus), and thus advancing the segment exposed by P0, would result in measured P0, being lower even in the absence of any change in Pmus waveform. Thus, the occlusion-pressure between 0 and 200 ms looks at different time segments of the neural activity and phase lags between onset of neural inspiration and onset of mechanical inspiration appear. Hence, particularly at high levels of exercise, a change in occlusion pressure waveform is to be expected.

Thus, various peripheral factors may be involved in the mechanical transformation of the inspiratory neural drive and may induce a particular pressure waveform. Further complex studies are needed to determine the central or peripheral origin of the change in waveform and the causal factors. When carrying out such studies, this shape change must be taken into consideration when interpreting any relative change in P0, or derived indices such as P0VTVT during exercise. Our findings demonstrate the expected results from previous data [4–6] in which P0 is thought to measure the rate of change in chest wall muscle pressure (Pmus) over a segment somewhat removed from the onset of neural inspiration.

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