An evaluation of $P_{0.1}$ measured in mouth and oesophagus, during carbon dioxide rebreathing in COPD

M.W. Elliott*, D.A. Mulvey†, M. Green†, J. Moxham**

An evaluation of $P_{0.1}$ measured in mouth and oesophagus, during carbon dioxide rebreathing in COPD. M.W. Elliott, D.A. Mulvey, M. Green, J. Moxham. ©ERS Journals Ltd 1993.

ABSTRACT: The pressure generated 100 ms after the onset of an occluded inspiratory effort ($P_{0.1}$) is advocated and used as a measure of respiratory centre drive. We have re-examined $P_{0.1}$ measured simultaneously in the mouth ($P_{m0.1}$) and the oesophagus ($P_{oes0.1}$) during carbon dioxide rebreathing, in eight patients with severe chronic obstructive pulmonary disease, to see whether either indicates central respiratory drive. $P_{m0.1}$ was identical to $P_{oes0.1}$ in 4 out of 61, greater than $P_{oes0.1}$ in 18 out of 61, and less than $P_{oes0.1}$ in 39 out of 61 measurements (overall $P_{m0.1} - P_{oes0.1}$ median +0.075, range -0.175 to +1.01 kPa). Within a rebreathing run in an individual patient, there was considerable variability in the relationship $P_{m0.1}/P_{oes0.1}$ (0.89±0.24), coefficient of variation (%CoV) 14.4±3.7%, in the end-expiratory oesophageal pressure (0.7±0.54 kPa, CoV 16.5±10.6%), and in the time delay between the onset of a fall in oesophageal pressure ($P_{oes}$) from the end-expiratory level to the beginning of inspiration, defined as starting when mouth pressure ($P_{mo}$) fell below atmospheric pressure (129±25 ms, %CoV 22.5±5.3%).

We conclude that the problem of determining the true onset of inspiratory muscle activity from pressure data, and the likelihood that breaths are taken from different lung volumes, makes it unlikely that $P_{oes0.1}$ accurately represents central respiratory drive during rebreathing in chronic obstructive pulmonary disease. Furthermore, $P_{m0.1}$ differed from $P_{oes0.1}$ during rebreathing, and their relationship was not constant, so that $P_{m0.1}$ is even less likely to be a useful reflection of central nervous system output or respiratory centre drive in such patients.

The pressure generated 100 ms after the onset of an occluded inspiratory effort ($P_{0.1}$) was devised as a test of respiratory centre output [1]. In acutely ill patients with chronic obstructive pulmonary disease (COPD), $P_{0.1}$ measured at the mouth ($P_{m0.1}$) is considerably lower than that measured in the oesophagus ($P_{oes0.1}$) and trachea [2]. During carbon dioxide rebreathing, the slope of $P_{0.1}$ against end-tidal carbon dioxide tension ($EtCO_2$) has been shown to be less in the mouth than the oesophagus, and it has been suggested that the latter may be a better measure of respiratory centre output [3]. Despite these limitations, $P_{m0.1}$ is still used as a measure of respiratory drive [4-10]. We have re-examined the relationship between $P_{m0.1}$ and $P_{oes0.1}$ during carbon dioxide rebreathing in patients with COPD.

Patients and methods

Eight out-patients with severe, but stable, COPD participated in the study, which was approved by the Ethics Committee of the Brompton Hospital. All patients gave informed consent. Functional details are given in table 1.

Oesophageal ($P_{oes}$) pressure, reflecting pleural pressure, was measured using a balloon-tipped catheter, 100 cm in length (PK Morgan, Rainham, Kent, UK), positioned in the standard manner [11]. Mouth pressure was measured by a needle puncturing the valve box. Both catheters were connected to Validyne MP45-1 differential pressure transducers (range ±25.0 kPa; Validyne Corp., Northridge, CA, USA), calibrated before each study and referenced to atmospheric pressure. The 10-90% response time of the entire system (balloon - catheter - transducer - recorder) was 0.0175 s, and the frequency response approximately 20 Hz, assessed from the pressure generated by a square wave input obtained by bursting a pressurized balloon with a hot wire [12].

All studies were performed with the patient seated. The oesophageal and mouth occlusion pressure response to $CO_2$ was determined using a modification of the rebreathing method of Read [13]. Patients inhaled from a 6 l anaesthesia bag, which had been filled with a concentration of $CO_2$ approximating to the patient’s predetermined $EtCO_2$, and an oxygen concentration of at least 90%.
The rebreathing bag remained flaccid, so that the pressure within it was atmospheric. Inhaled O₂ concentration and EtCO₂ were measured with a Hewlett Packard 78356A gas parameter monitor. The patient breathed on a mouthpiece, with a noseclip, through a low resistance one-way valve (Hans Rudolph, Kansas City, MO, USA). The resistance of the circuit at flow rates of 0.5 and 3 l·s⁻¹ was 0.11 and 0.27 kPa·l⁻¹·s⁻¹, respectively, for the inspiratory limb, and 0.15 and 0.26 kPa·l⁻¹·s⁻¹, respectively, for the expiratory limb.

A fast reacting pneumatically-driven shutter, situated in the inspiratory limb, was used to occlude airflow. The shutter was closed during expiration, and opened again 200–300 ms after the onset of inspiration. Patients were unable to see the operator activate the shutter, and listened to a radio programme through headphones. Questioning at the end of the study confirmed that these measures had been successful in preventing anticipation of shutter occlusions. Airway occlusions were made approximately every 30 s, during a 4 min CO₂ rebreathing run. In common with other studies, inspiration was considered to start when mouth pressure fell below atmospheric pressure, and Pm₀₁ and Poe₀₁ were measured as the pressure change over the next 100 ms. The end-expiratory oesophageal pressure (EEP₀) and the time from its initial fall to the onset of inspiration, as defined above, were measured.

All signals were recorded on paper by a Mingograf 800 ink-jet recorder (Siemens-Elema AB, Stockholm, Sweden), at a paper speed of 5 cm·s⁻¹.

**Results**

The relationship between simultaneous measurements of mouth and oesophageal occlusion pressures is demonstrated by plotting the mean against the difference of Pm₀₁ and Poe₀₁ [14] (fig. 1). Pm₀₁ and Poe₀₁ were identical (i.e. difference=0) in 4 out of 61 measurements, and in a further 16 instances the difference was ±0.1 kPa. Poe₀₁ was greater than Pm₀₁ in 18 out of 61, and less than Pm₀₁ in 39 out of 61 measurements. In three patients (nos 1, 3 and 4) there was a significant positive correlation between Pm₀₁ - Poe₀₁ and the mean (r=0.72, 0.81 and 0.7, respectively, p<0.05), and in two others (Nos. 2 and 6) the correlation did not quite reach statistical significance (r=0.59, p=0.13, and 0.68, p=0.09, respectively), suggesting that in these patients the difference between Poe₀ and Pm₀ increased as the end-tidal CO₂ increased. There was no relationship to the severity of airway obstruction. Within a rebreathing run in each patient, there was considerable variability in the ratio Pm₀₁ / Poe₀₁ (0.89±0.24, CoV% 14.4±3.7), and also in the EEP₀ (+0.7±0.54 kPa, CoV% 25.5±5.3%), and in the time delay (TD) between the fall in oesophageal pressure from the end-expiratory level to the fall in mouth pressure (Pm₀) below atmospheric pressure (129±25 ms, CoV% 22.5±5.3%) (table 2).

Figure 2 shows an example of a recording from patient No. 2 showing a positive EEP₀, and the TD from its initial fall to the onset of "inspiration", as would be judged from the point where mouth pressure falls below atmospheric pressure.
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Table 2. - Ratio Pmo₀.₁ to Poes₀.₁, end-expiratory oesophageal pressure (EEPoes), and time delay between the fall in Poes from the end-expiratory level to the fall in Pmo below atmospheric pressure.

<table>
<thead>
<tr>
<th>Pt no.</th>
<th>Ratio Pmo₀.₁/Poes₀.₁</th>
<th>CoV %</th>
<th>EEPoes kPa</th>
<th>CoV %</th>
<th>Time delay ms</th>
<th>CoV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.86 (0.64–1.07)</td>
<td>19</td>
<td>+0.09 (-0.35–0.35)</td>
<td>332</td>
<td>120 (100–170)</td>
<td>17</td>
</tr>
<tr>
<td>2</td>
<td>0.98 (0.76–1.11)</td>
<td>12</td>
<td>+1.8 (1.3–2.4)</td>
<td>18</td>
<td>110 (80–140)</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>0.44 (0.29–0.50)</td>
<td>15</td>
<td>+0.73 (0.25–1.60)</td>
<td>68</td>
<td>180 (140–290)</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
<td>1.00 (0.87–1.17)</td>
<td>10</td>
<td>+0.45 (0.0–0.85)</td>
<td>76</td>
<td>100 (60–120)</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>0.94 (0.75–1.13)</td>
<td>15</td>
<td>+0.73 (0.4–1.5)</td>
<td>55</td>
<td>140 (120–230)</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>0.67 (0.47–0.75)</td>
<td>14</td>
<td>+0.93 (0.3–1.1)</td>
<td>31</td>
<td>120 (80–140)</td>
<td>19</td>
</tr>
<tr>
<td>7</td>
<td>1.21 (0.81–1.52)</td>
<td>20</td>
<td>+0.15 (0.3–0.2)</td>
<td>195</td>
<td>120 (80–150)</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>0.99 (0.88–1.16)</td>
<td>10</td>
<td>+0.75 (0.5–2.05)</td>
<td>62</td>
<td>145 (120–260)</td>
<td>32</td>
</tr>
<tr>
<td>Mean</td>
<td>0.89</td>
<td>14.4</td>
<td>±0.7</td>
<td>105</td>
<td>129</td>
<td>22.5</td>
</tr>
<tr>
<td>±sd</td>
<td>±0.24</td>
<td>±3.7</td>
<td>±0.54</td>
<td>±106</td>
<td>±25</td>
<td>±5.3</td>
</tr>
</tbody>
</table>

Data are presented as median and range in parenthesis. Pmo₀.₁ and Poes₀.₁: pressure generated 100 ms after the onset of an occluded inspiratory effort measured at the mouth and oesophagus, respectively; CoV: coefficient of variation; Poes: oesophageal pressure; Pmo: mouth pressure.

Discussion

Our results confirm that there is a difference in Pₒ.₁ measured simultaneously at the mouth and in the oesophagus in patients with COPD.

Differences in the measurement technique might be one explanation, since Poes was measured using a balloon catheter, and Pmo by a needle puncturing the valve box. If this was the case, a systematic difference would have been seen, but the relationship was not constant, and varied in an individual patient during a single rebreathing run. This suggests that Pmo₀.₁ and Poes₀.₁ are modified by different and independent factors.
The finding that Poeso was less than Pmoo in 18 out of 61 measurements was surprising. There are two possible mechanisms to explain this. Firstly, Pmoo may be greater than Poeso if the glottis is closed and the patient exerts a negative pressure with pharyngeal or cheek muscles [15]. Secondly, Poeso may not be representative of global, and hence driving, pleural pressure. MURCIANO et al. [2] found no difference in Poeso measured at two different levels in the oesophagus in patients with COPD. However, the oesophagus only represents the central part of the pleura, and pleural pressure is known to vary at different sites because of the effects of gravity on the lung and the chest wall, and because of the different shapes of these two structures [16]. This may be accentuated by airways obstruction and hyperinflation.

MARAZZINI et al. [3] attributed the difference in Pmoo and Poeso in patients with COPD to a delay in equalization of pressure within the airways, because of lung units with differing time constants. However, MURCIANO et al. [2] found no difference between P0.1 measured in the oesophagus and trachea in patients with COPD, and concluded that the difference between Pmoo and Poeso could be attributed to the compliance of the upper airway. JAGER [17] found that the distensibility of the upper airway ranged between 0.01–0.001 fcm H2O-1 in normal subjects, and proposed that, in COPD this could cause an underestimation of Pmoo of the order of 30%. However, the upper airway is not a fixed structure, and its compliance may change from breath to breath. Changes in upper airway or cheek muscle tone, due for instance to variation in the way that patients grip the mouthpiece, may thus alter compliance and modify the relationship between Pmoo and Poeso within a rebreathing run.

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The time delay (TD) in the fall of Poeso from EEPOeso to the onset of "inspiration" judged from Pmo also affects P0.1 as a measure of central drive, since it suggests that the inspiratory muscles may be active some time before "inspiration" begins. This is further complicated by the fact that TD varied in each patient during a rebreathing run. The degree of activation of the inspiratory muscles depends, in part, upon when in inspiration the measurement is made, and this is also true of Poeso, which does not change linearly. This variability in TD means that P0.1 was measured at different times after activation of the inspiratory muscles and, therefore, P0.1 may change independently of the intensity of overall neural drive. Taking the point when Poeso falls from the end-expiratory level may be more representative of the onset of inspiratory muscle activity, but again the difference between inspiratory muscle contraction and expiratory muscle relaxation cannot be inferred from pressure changes. Additionally, this point is often not easy to determine (fig. 3). Recording of the electromyogram (EMG) might help to clarify the start of inspiration, but to do this when using P0.1 in a clinical or experimental situation defeats the object of using P0.1 as a simple and noninvasive test of central drive. In addition, EMG electrodes only record from the underlying muscle groups, and different muscle groups may be activated at different times, again confounding the definition of the onset of inspiration.

**Conclusion**

In patients with severe COPD the relationship between Pmoo and Poeso is not constant during a single rebreathing run. The problem of identifying the true onset of inspiratory muscle activity, and the likelihood of breaths being taken from different lung volumes, make it unlikely that either Pmoo or Poeso reliably represent central respiratory drive in these patients during rebreathing.
References


