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TECHNICAL NOTE

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

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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 ($Pmo_{0.1}$) and the oesophagus ($Poes_{0.1}$), during carbon dioxide rebreathing, in eight patients with severe chronic obstructive pulmonary disease, to see whether either indicates central respiratory drive.

$Pmo_{0.1}$ was identical to $Poes_{0.1}$ in 4 out of 61, greater than $Poes_{0.1}$ in 18 out of 61, and less than $Poes_{0.1}$ in 39 out of 61 measurements (overall $Poes_{0.1}$ - $Pmo_{0.1}$, 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 $Pmo_{0.1}/Poes_{0.1}$ (0.89±0.24), coefficient of variation (CoV%) 14.4±3.7%), in the end-expiratory oesophageal pressure (0.7±0.54 kPa, CoV% 105±106%), and in the time delay between the onset of a fall in oesophageal pressure (Poes) from the end-expiratory level to the beginning of inspiration, defined as starting when mouth pressure (Pmo) 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, make it unlikely that $Poes_{0.1}$ accurately represents central respiratory drive during rebreathing in chronic obstructive pulmonary disease. Furthermore, $Pmo_{0.1}$ differed from $Poes_{0.1}$ during rebreathing, and their relationship was not constant, so that $Pmo_{0.1}$ is even less likely to be a useful reflection of central nervous system output or respiratory centre drive in such patients.

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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 ($Pmo_{0.1}$) is considerably lower than that measured in the oesophagus ($Poes_{0.1}$) 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, $Pmo_{0.1}$ is still used as a measure of respiratory drive [4–10]. We have re-examined the relationship between $Pmo_{0.1}$ and $Poes_{0.1}$ 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 (Poes) 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%.

Table 1. – Patient functional data

Pt no.	Age yrs	Sex	FEV_1 ml	FEV_1 % pred	FVC ml	FVC % pred	FEV_1/FVC %	TLC ml	TLC % pred	RV ml	RV % pred	RV/TLC %	Pao_2 kPa	$Paco_2$ kPa
1	62	F	350	16	940	36	37	4580	95	3410	180	74	6.5	7.4
2	53	M	640	22	2180	58	29	5660	104	3460	188	61	7.5	6.4
3	51	M	600	17	2790	66	22	7020	106	4380	205	62	6.6	8.9
4	50	M	570	19	1770	46	32	5020	91	3120	170	62	8.6	5.5
5	64	M	650	25	2590	71	25	6660	117	4240	198	64	7.6	6.9
6	62	F	260	13	1130	42	23	5550	125	4400	261	79	5.9	8.1
7	64	M	1000	34	2660	65	38	–	–	–	–	–	6.7	7.1
8	50	F	560	26	1690	68	33	4180	109	2440	190	58	7.4	7.7

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume; Pao_2: arterial oxygen tension; $Paco_2$: arterial carbon dioxide tension.

The rebreathing bag remained flaccid, so that the pressure within it was atmospheric. Inhaled O_2 concentration and $Etco_2$ 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 $l \cdot s^{-1}$ was 0.11 and 0.27 $kPa \cdot l^{-1} \cdot s$, respectively, for the inspiratory limb, and 0.15 and 0.26 $kPa \cdot l^{-1} \cdot s$, 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 CO_2 rebreathing run. In common with other studies, inspiration was considered to start when mouth pressure fell below atmospheric pressure, and $Pmo_{0.1}$ and $Poes_{0.1}$ were measured as the pressure change over the next 100 ms. The end-expiratory oesophageal pressure (EEPoes) 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 $cm \cdot s^{-1}$.

Results

The relationship between simultaneous measurements of mouth and oesophageal occlusion pressures is demonstrated by plotting the mean against the difference of $Poes_{0.1}$ and $Pmo_{0.1}$ [14] (fig. 1). $Pmo_{0.1}$ and $Poes_{0.1}$ were identical (*i.e.* difference=0) in 4 out of 61 measurements, and in a further 16 instances the difference was ±0.1 kPa. $Pmo_{0.1}$ was greater than $Poes_{0.1}$ in 18 out of 61, and less than $Poes_{0.1}$ in 39 out of 61 measurements. In three patients (nos 1, 3 and 4) there was a significant positive correlation between $Poes_{0.1}$ - $Pmo_{0.1}$ 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 Poes and Pmo increased as the end-tidal CO_2 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 $Pmo_{0.1}$/$Poes_{0.1}$ (0.89±0.24, CoV% 14.4±3.7), and also in the EEPoes (+0.7±0.54 kPa, CoV% 105±106%), and in the time delay (TD) between the fall in oesophageal pressure from the end-expiratory level to the fall in mouth pressure (Pmo) 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 EEPoes, 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.

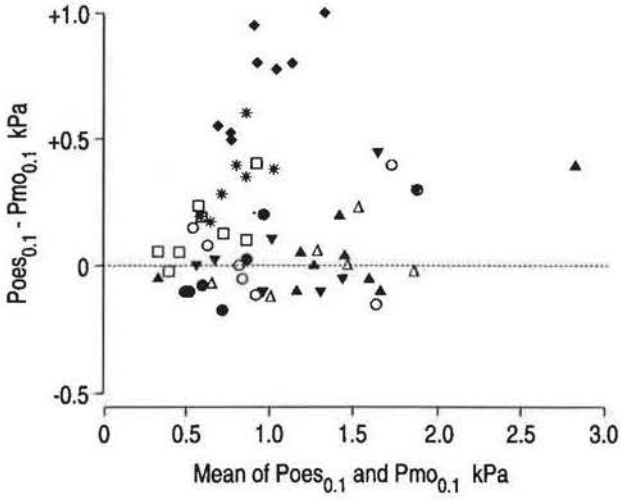

Fig. 1. – The difference ($Poes_{0.1}$ - $Pmo_{0.1}$) plotted against the mean of $Poes_{0.1}$ and $Pmo_{0.1}$. Each different shaped symbol represents one patient. $Poes_{0.1}$ and $Pmo_{0.1}$: pressure generated 100 ms after the onset of an occluded inspiratory effort measured at the oesophagus and mouth, respectively. □ : patient No. 1; ▼ : patient No. 2; ◆: patient No. 3; ▲: patient No. 4; ○: patient No. 5; ✱: patient No. 6; ●: patient No. 7; Δ: patient No. 8.

Table 2. – Ratio $Pmo_{0.1}$ to $Poes_{0.1}$, 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

Pt no.	Ratio $Pmo_{0.1}/Poes_{0.1}$	Cov %	EEPoes kPa	CoV %	Time delay ms	CoV %
1	0.86 (0.64–1.07)	19	+0.09 (-0.35–0.35)	332	120 (100–170)	17
2	0.98 (0.76–1.11)	12	+1.8 (1.3–2.4)	18	110 (80–140)	17
3	0.44 (0.29–0.50)	15	+0.73 (0.25–1.60)	68	180 (140–290)	27
4	1.00 (0.87–1.17)	10	+0.45 (0.0–0.85)	76	100 (60–120)	23
5	0.94 (0.75–1.13)	15	+0.73 (0.4–1.5)	55	140 (120–230)	25
6	0.67 (0.47–0.75)	14	+0.93 (0.3–1.1)	31	120 (80–140)	19
7	1.21 (0.81–1.52)	20	+0.15 (-0.3–0.2)	195	120 (80–150)	20
8	0.99 (0.88–1.16)	10	+0.75 (0.5–2.05)	62	145 (120–260)	32
Mean	0.89	14.4	+0.7	105	129	22.5
±SD	±0.24	±3.7	±0.54	±106	±25	±5.3

Data are presented as median and range in parenthesis. $Pmo_{0.1}$ and $Poes_{0.1}$: 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.

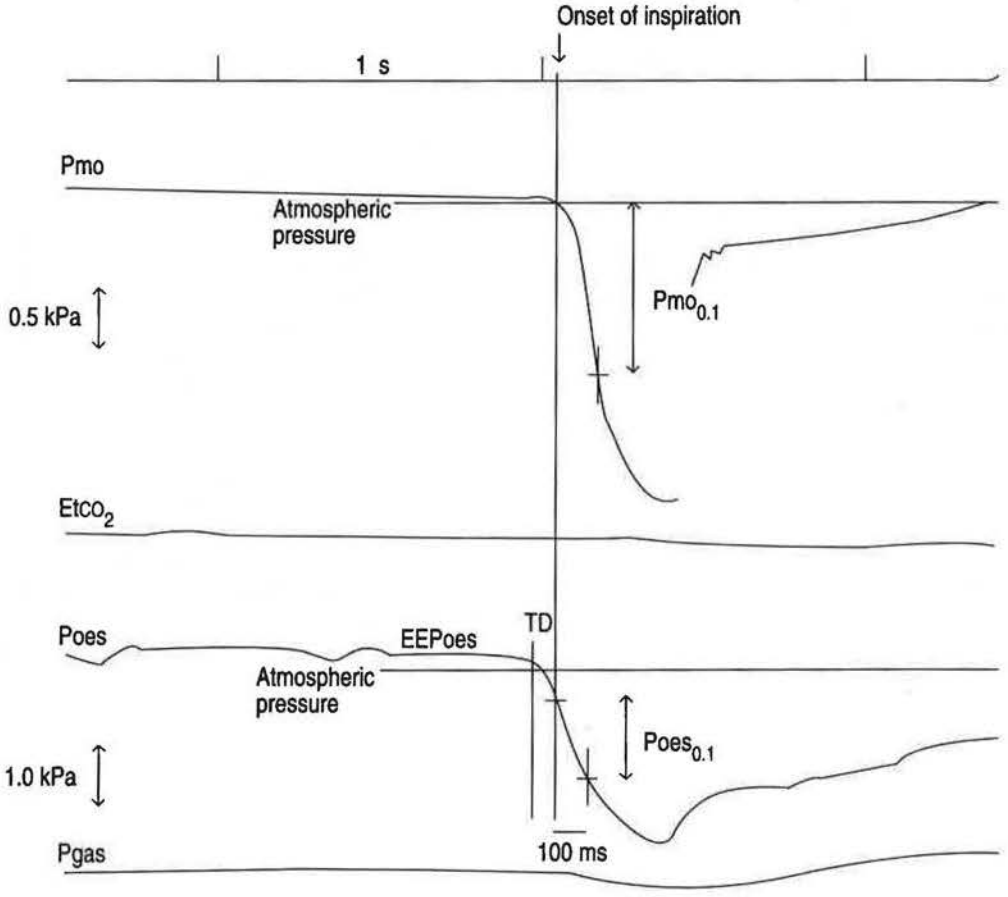

Fig. 2. – Pmo, $Etco_2$ and Poes showing end-expiratory Poes (EPPoes) and the time delay (TD) from the fall of Poes from EEPoes to the onset of "inspiration" (defined as starting when Pmo falls below atmospheric pressure). $Pmo_{0.1}$ and $Poes_{0.1}$ are also shown. Pmo: mouth pressure; Poes: oesophageal pressure; Pgas: gastric pressure; $Etco_2$: end-tidal carbon dioxide pressure.

Discussion

Our results confirm that there is a difference in $P_{0.1}$ 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 $Pmo_{0.1}$ and $Poes_{0.1}$ are modified by different and independent factors.

The finding that $Poes_{0.1}$ was less than $Pmo_{0.1}$ in 18 out of 61 measurements was surprising. There are two possible mechanisms to explain this. Firstly, $Pmo_{0.1}$ may be greater than $Poes_{0.1}$ if the glottis is closed and the patient exerts a negative pressure with pharyngeal or cheek muscles [15]. Secondly, Poes may not be representative of global, and hence driving, pleural pressure. MURCIANO *et al.* [2] found no difference in Poes 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 $Pmo_{0.1}$ and $Poes_{0.1}$ 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 $P_{0.1}$ measured in the oesophagus and trachea in patients with COPD, and concluded that the difference between $Pmo_{0.1}$ and $Poes_{0.1}$ could be attributed to the compliance of the upper airway. JAEGER [17] found that the distensibility of the upper airway ranged between 0.01–0.001 $l \cdot cmH_2O^{-1}$ in normal subjects, and proposed that, in COPD this could cause an underestimation of $Pmo_{0.1}$ 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 $Pmo_{0.1}$ and $Poes_{0.1}$ within a rebreathing run.

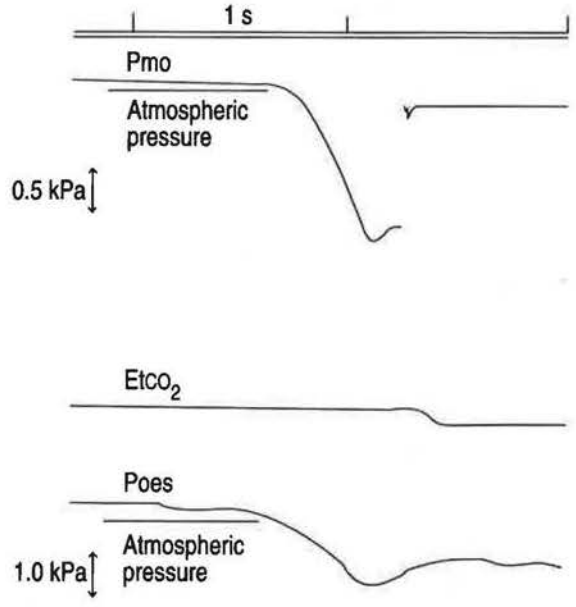

Fig. 3. – Recordings of $Poes_{0.1}$ and $Pmo_{0.1}$ showing that there is no distinct inflection in the Poes waveform, making it difficult to define the onset of inspiration from the oesophageal pressure trace alone. For abbreviations see legend to figure 2.

MARAZZINI *et al.* [3] suggested that $Poes_{0.1}$ was a better, and reasonable, measure of respiratory output in patients with intrinsic lung disease. Our data suggest that even this measurement has its problems. The variability in EEPoes suggests that active expiratory effort and/or intrinsic positive end-expiratory pressure (PEEP) varied during a rebreathing run. These changes in EEPoes may affect lung volume, thus, changing the longitudinal configuration of the inspiratory muscles, with the result that the measured pressure change in the mouth and the oesophagus is not constantly related to muscle tension and, therefore, respiratory centre output. For instance, if the end-expiratory volume increases, inspiratory muscle fibres will shorten, and the pressure change for a given muscle tension will be less, giving the illusion of reduced neural drive. In addition, the expiratory muscles affect inspiration indirectly, by acting as inspiratory agonists. For example, if the patient generates a large positive intrathoracic pressure during expiration, and then makes no inspiratory effort at all, Poes may fall to the level at relaxed end-expiration, giving a false appearance of active inspiratory effort.

The time delay (TD) in the fall of Poes from EEPoes to the onset of "inspiration" judged from Pmo also affects $P_{0.1}$ 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 Poes, which does not change linearly. This variability in TD means that $P_{0.1}$ was measured at different times after activation of the inspiratory muscles and, therefore, $P_{0.1}$ may change independently of the intensity of overall neural drive. Taking the point when Poes 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 $P_{0.1}$ in a clinical or experimental situation defeats the object of using $P_{0.1}$ 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 $Pmo_{0.1}$ and $Poes_{0.1}$ 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 $Pmo_{0.1}$ or $Poes_{0.1}$ reliably represent central respiratory drive in these patients during rebreathing.

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