

The pattern of resting breathing in patients with upper airway obstruction

J. Sanchis, J.L. Díez-Betoret, P. Casan, J. Milic-Emili*

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ABSTRACT: The flow-time curve of resting breathing was recorded in 14 patients (aged 36 ± 16 yrs) with mild to moderate symptoms of upper airway obstruction (UawO) and compared to that of 28 matched, healthy controls (HC) in order to characterize the breathing pattern of such patients. The inspiratory time over total time (T_i/T_{tot}) was higher in the patients (0.42; SD 0.04) than in HC (0.37; SD 0.04) ($p < 0.001$), and tidal volume (V_T) over T_i was lower in patients (0.37; SD 0.07 $l \cdot s^{-1}$) than in HC (0.43; SD 0.09 $l \cdot s^{-1}$) ($p < 0.01$). Inspiratory and expiratory peak flows at rest were also lower in the patients ($p < 0.001$). In these, the mean to peak flow ratio of inspiration (0.74; SD 0.07) was higher than in HC (0.66; SD 0.04) ($p < 0.0005$). This indicates a more rectangular wave of inspiration in the patients. All of these changes may be due to the increased inspiratory load. However, since the patients were breathing at rest with V_T and flows far below their values on the maximal flow volume loop, the changes can also be interpreted as adaptive rather than imposed by absolute mechanical limitations.

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Obstructive lesions of the upper airway, from carina to epiglottis, are classified as fixed or variable according to the dynamics of airflow limitation (AFL) [1]. A fixed lesion produces AFL during inspiration and expiration. When the lesion renders the airway more compliant the obstruction is variable and depends on the effect of changes in pressure on the airway wall. Its location determines the phase of breathing, inspiration or expiration, in which AFL occurs [1]. Variable extrathoracic lesions mainly affect inspiration, whilst variable intrathoracic lesions principally limit expiratory flow.

An obstructive lesion of the upper airway increases turbulent flow, thus markedly raising airway resistance as flow increases in a mechanically intact respiratory system. Upper airway obstruction (UawO) can be characterized by two physiological abnormalities: the inspiratory flows are markedly reduced and the peak expiratory flow (PEF) is disproportionately low relative to the forced expiratory volume in one second (FEV_1) [2]. Attention has therefore been focused on the following ratios: maximum mid-expiratory flow to maximum mid-inspiratory flow (FEF_{50}/FIF_{50}) [3]; forced expired volume in one second to the peak expiratory flow rate (FEV_1/PEF) [4]; FEV_1 to forced expired volume in 0.5 s ($FEV_1/FEV_{0.5}$) [5]; and maximal voluntary ventilation (MVV) to FEV_1 [6, 7].

Apart from these indices, the overall shape of the maximal flow-volume loop (MFVL) is in itself informative as indicated by MILLER and HYATT in 1969 [1, 2]. Extensive study has since been done on the MFVL of patients with UawO. However, little attention has been focused on the pattern of resting breathing in UawO. In the present study, we sought to obtain new information on the breathing strategies these patients use in the face of increases in upper airway flow resistance, by comparing the patients' resting breathing pattern with that of healthy controls.

Patients

The studies were performed on 14 patients (9 women) with extrathoracic UawO as confirmed by direct endoscopy and pulmonary function tests. The patients' anthropometric and clinical data, together with individual values for selected pulmonary function indices of UawO, are presented in table 1. All patients reached at least two of the index values used as criteria for extrathoracic UawO. In addition, the contour of the maximal flow-volume loop in patients with fixed narrowing showed nearly equal degrees of flattening of the inspiratory and expiratory loops, whereas in patients with lesions of variable narrowing the MFVL showed

Table 1. - Characteristics of the patients with upper airway obstruction

Patient No.	Sex	Age yr	Height cm	Cause of UawO	Type of UawO	Grade of dyspnoea*	Ventilatory/Function indices**				
							FIF ₅₀	FEF ₅₀ /FIF ₅₀	FEV ₁ /PEF	FEV ₁ /FEV _{0.5}	MVV/FEV ₁
1	F	34	157	Glottic stenosis, iatrogenic	Fixed	II	1.06	1.25	11.2	1.65	17.8
2	M	56	165	Supra-glottic carcinoma	Fixed	I	2.01	0.85	8.5	1.80	37.8
3	F	56	150	Left vocal cord paralysis, oedema	Fixed	IV	0.35	1.41	13.1	1.89	24.7
4	M	38	163	Carcinoma of larynx	Variable	I	1.86	1.81	11.8	1.69	13.9
5	M	28	175	Vocal cord paralysis, trauma	Variable	I	3.40	1.56	7.7	1.40	25.0
6	F	41	154	Vocal cord paralysis, goitre	Variable	I	2.69	1.50	8.3	1.36	21.3
7	F	48	149	Tracheal adenocarcinoma	Fixed	II	1.12	1.17	12.6	2.03	19.4
8	F	17	158	Tracheal stenosis, traumatic	Fixed	I	2.54	1.16	13.6	2.30	15.7
9	M	59	171	Tracheal compression, oesophageal carcinoma	Variable	I	1.56	2.61	9.5	-	15.2
10	F	23	153	Supraglottic carcinoma	Fixed	II	1.49	1.30	14.1	2.00	14.9
11	M	21	171	Hemilaryngectomy, thyroid carcinoma	Variable	II	2.42	1.76	12.1	1.70	16.5
12	F	21	152	Vocal cord paralysis, arytenoidectomy	Variable	III	1.36	1.70	10.1	1.70	12.3
13	F	14	160	Vocal cord paralysis tracheal stenosis	Fixed	II	1.39	1.04	11.7	1.91	12.7
14	F	39	160	Tracheal stenosis, iatrogenic	Fixed	II	1.50	1.30	13.8	2.20	11.6

*: according to MRC Classification [8]; **: from refs [5, 7, 9]; UawO: upper airway obstruction; FIF₅₀: maximum mid-inspiratory flow l·s⁻¹; FEF₅₀/FIF₅₀: ratio of maximum mid-expiratory flow to maximum mid-inspiratory flow; FEV₁/PEF: ratio of forced expired volume in one second to peak expiratory flow rate; FEV₁/FEV_{0.5}: ratio of FEV₁ to forced expired volume in 0.5 s; MVV/FEV₁: ratio of maximal voluntary ventilation to FEV₁.

mainly a flattening of the inspiratory loop. Patients reported no respiratory symptoms prior to development of their UawO. Only patient No. 5 had been a smoker.

The control group consisted of 28 healthy subjects (19 women), selected solely on the basis of similarity to the patients' ages, heights and weights, and to provide a similar male/female ratio. The mean values of physical characteristics and pulmonary function data of both groups can be seen in table 2. The study was approved by the hospital's Ethics Committee. Informed consent was obtained from patients and healthy volunteers.

Table 2. - Physical characteristics and pulmonary function data

	Controls (n=28)	UawO patients (n=14)
Sex	9M/19F	5M/9F
Age yr	33 (9)	36 (16)
Height cm	162 (6)	160 (9)
Weight kg	57 (8)	61 (13)
FVC l	3.8 (0.7)	3.4 (1.1)
FEV ₁ l	3.1 (0.6) *	2.3 (1.0)
FEV ₁ /FVC %	82 (7) *	67 (11)
FRC l	2.8 (0.6)	2.8 (0.7)
TLC l	5.3 (0.9)	5.0 (1.4)
RV/TLC %	27 (3) *	33 (7)
MVV l·min ⁻¹	126 (32) *	43 (20)
Raw _i hPa·l ⁻¹ ·s	1.8 (0.7) *	6.6 (5.4)
Raw _e hPa·l ⁻¹ ·s	1.9 (0.7) *	7.9 (6.7)
Pao ₂ kPa	-	12.1 (1.2)
Paco ₂ kPa	-	5.2 (0.7)

Values are means with sd in parentheses. *: p<0.005; M: male; F: female; FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; FRC: functional residual capacity; TLC: total lung capacity; RV: residual volume; MVV: maximum voluntary ventilation; Raw_i and Raw_e: inspiratory and expiratory airway resistance, respectively; Pao₂ and Paco₂: arterial oxygen and carbon dioxide tension, respectively; UawO: upper airway obstruction.

Methods

Using standard techniques [10], spirometry and 15s MVV were recorded with a Fleisch No. 3 pneumotachograph (Pulmonary System, Hewlett-Packard HP21072B, Palo Alto, Ca., USA) connected to a pressure transducer, analogue-to-digital converter (HP47310A) and desk-top computer (HP9825A) assembly. Apparatus deadspace was 130 ml. Functional residual capacity (FRC) was measured by helium-dilution (Mark V.P.K. Morgan, UK) and inspiratory and expiratory airway resistance (Raw_i, Raw_e) were determined with a body plethysmograph (Fenyves & Gut, Basel, Switzerland). All volumes were adjusted for body temperature, atmospheric pressure and saturation. Samples of arterial blood were drawn, in patients only, by puncture from the radial artery and immediately

analysed with a blood gas analyser (ABL 30 Radiometer, Copenhagen, Denmark).

Mouth occlusion pressure (P_{0.1}) was measured according to the technique of WHITELAW *et al.* [11] with a silent, hand-operated valve and a pressure transducer (Hewlett-Packard HP270) and amplifier (HP8805C) whose signal was displayed graphically by an X-Y recorder (HP07041A). The result reported for each subject is the mean value of the three best of ten recordings as judged by the technician.

Airflow at rest was measured at the mouth by means of the same equipment used for spirometry and MVV; with the computer suitably programmed to record the flow signal at 50 ms intervals, up to a period of 5 min per sample, at least twice for each subject, and then stored on floppy disks for later analysis. Volume was obtained by electronic integration of the flow signal. The various breathing pattern indices were estimated cycle-by-cycle and then averaged for each 5 min sample in each subject. Because of their smaller variability, mean values of the second sample were used for analysis. Minute ventilation (V_E), breathing frequency (f), tidal volume (V_{Ti}, V_{Te}), mean flows (V_{Ti}/T_i, V_{Te}/T_e), peak flows (V̇_{imax}, V̇_{emax}), inspiratory and expiratory times (T_i, T_e) and duty cycle (T_i/T_{tot}) were measured. If present, T_{tot} included the end-expiratory pause (eeP), *i.e.* a period with no flow at the end of expiration. Possible differences in the overall shape of the flow-time profile were assessed by measuring the ratio of the mean to peak flow in each phase of breathing ((V_{Ti}/T_i)/V̇_{imax} and (V_{Te}/T_e)/V̇_{emax}, respectively).

A frequency distribution analysis of data was performed by the Kolmogorov-Smirnov test for each variable. The test showed no significant difference from the Gaussian distribution for all variables, with the exception of eeP (p<0.032). Therefore, t-test comparisons of variables from UawO patients and healthy controls were carried out. A correlation analysis was performed with variables of the resting breathing and the MFVL in the patients. Statistical significance was accepted at p<0.05.

Results

Comparison of physical and pulmonary function data of patients and healthy controls (table 2) showed statistically significant differences for FEV₁, FEV₁ as percentage of forced vital capacity (FEV₁/FVC), residual volume as percentage of total lung capacity (RV/TLC), MVV, Raw_i and Raw_e. Thus, as a group, patients had a significant degree of AFL during forced expiration and inspiration. In the absence of previous lung disease, all these abnormalities of lung function can be attributed solely to UawO.

The means of the resting breathing pattern variables together with P_{0.1} of patients and controls are shown in table 3. P_{0.1} was significantly higher in the UawO patients. In contrast, their mean inspiratory flow was significantly lower due to lower V_T and longer T_i. This was associated with a significantly higher T_i/T_{tot} and a shorter end-expiratory pause in the UawO patients. In

fact, an $eeP > 0.2$ s was present in only two of the 14 UawO patients, whilst in the control group it was observed in seven of the 28 healthy volunteers. The $(V_T/T_i)/\dot{V}_{I\max}$ and $(V_T/T_E)/\dot{V}_{E\max}$ ratios were significantly higher in the UawO patients. This reflects the more rectangular shape of the patients' inspiratory and expiratory flow-time profiles as graphically illustrated by the comparison of the flow-time curve of two representative cases: a UawO patient and a healthy control (fig. 1).

Table 3. - Resting breathing pattern

	Controls		UawO patients
$P_{0.1}$ kPa	1.2 (0.5)	*	2.2 (1.4)
\dot{V}_E $l \cdot \text{min}^{-1}$	8.91 (1.7)		8.81 (1.6)
V_T l	0.62 (0.10)		0.57 (0.12)
f min^{-1}	14.8 (3.2)		15.8 (3.8)
T_I s	1.61 (0.40)		1.70 (0.39)
T_E s	2.65 (0.63)		2.37 (0.65)
T_I/T_{tot}	0.37 (0.04)	+	0.42 (0.04)
eeP s	0.26 (0.26)	+	0.05 (0.10)
V_T/T_i $l \cdot s^{-1}$	0.43 (0.09)	*	0.37 (0.07)
$\dot{V}_{I\max}$ $l \cdot s^{-1}$	0.66 (0.12)	++	0.50 (0.09)
V_{TE}/T_E $l \cdot s^{-1}$	0.27 (0.06)		0.26 (0.06)
$\dot{V}_{E\max}$ $l \cdot s^{-1}$	0.48 (0.12)	+	0.37 (0.08)
$V_{TI}/T_i)/\dot{V}_{I\max}$	0.66 (0.04)	++	0.74 (0.07)
$V_{TE}/T_E)/\dot{V}_{E\max}$	0.56 (0.06)	++	0.69 (0.07)

Values are means with SD in parentheses. *: $p < 0.01$; +: $p < 0.001$; ++: $p < 0.0005$; $P_{0.1}$: mouth occlusion pressure; \dot{V}_E : minute ventilation; V_T : tidal volume; f : breathing frequency; T_I : inspiratory time; T_E : expiratory time; T_I/T_{tot} : duty cycle; eeP : end-expiratory pause; V_T/T_i and V_{TE}/T_E : mean flows; $\dot{V}_{I\max}$ and $\dot{V}_{E\max}$: peak flows; $(V_T/T_i)/\dot{V}_{I\max}$ and $(V_{TE}/T_E)/\dot{V}_{E\max}$: ratio of mean to peak inspiratory and expiratory flow, respectively; UawO: upper airway obstruction.

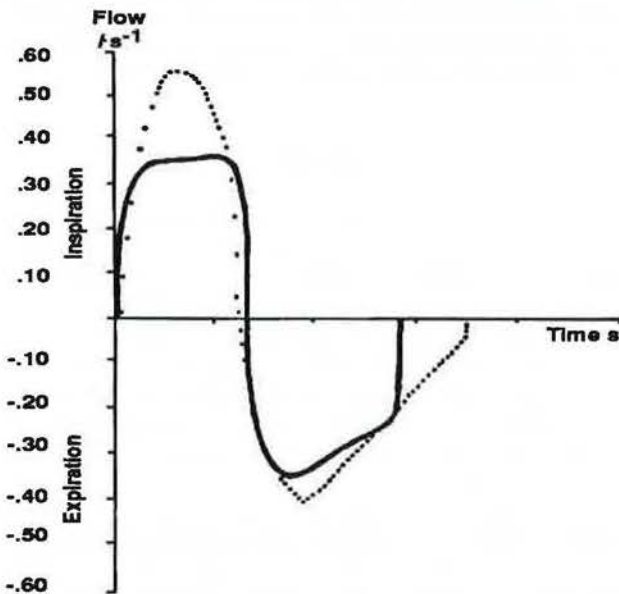


Fig. 1. - Mean flow/time curve (re-drawn) of a patient with UawO (continuous trace) superimposed on that of a control (dotted line), to stress differences in flow and shape.: healthy control; —: upper airway obstruction.

The correlation analyses showed significant degrees of association between T_I/T_{tot} and R_{awI} ($r = -0.66$) and R_{awE} ($r = 0.61$) in the UawO patients. In the analyses of variables of resting breathing and those of the MFVL, only the correlation between resting $(V_T/T_E)/\dot{V}_{E\max}$ and FIF_{50} ($r = 0.70$) was significant. The following correlations between resting breathing pattern variables were found to be significant: V_T/T_i and $\dot{V}_{I\max}$ ($r = 0.87$); V_T/T_i and $\dot{V}_{E\max}$ ($r = -0.74$); $\dot{V}_{I\max}$ and $\dot{V}_{E\max}$ ($r = -0.69$); and, finally, $(V_T/T_i)/\dot{V}_{I\max}$ and $(V_T/T_E)/\dot{V}_{E\max}$ ($r = 0.84$).

Discussion

The UawO patients of the present study exhibited the characteristic abnormalities in lung function previously reported (tables 1 and 2). Both inspiratory and expiratory R_{aw} were significantly increased. Arterial oxygen tension (P_{O_2}) and carbon dioxide tension (P_{CO_2}) were within normal limits, except in patient No. 3 in whom P_{O_2} was 9.4 kPa (71 mmHg), less than predicted, and P_{CO_2} was 6.4 kPa (48 mmHg). Judging from the dyspnoea reported by our patients and from their pulmonary function data, we can say that different degrees of obstruction were present in the group although there was a predominance of mild cases.

The use of noseclip, mouthpiece and a sizeable deadspace may increase \dot{V}_E , V_T , T_I and V_T/T_i , and decrease f , inducing a more regular breathing pattern [12, 13]. However, a direct recording of airflow is necessary when the objective is to analyse the flow-time profile of breathing. On the other hand, inductive plethysmography does not provide sufficiently accurate data on peak flow and is not devoid of some substantial sources of error [14, 15]. Nevertheless, any possible artefacts of breathing due to the system used for recording of flow at the mouth are not likely to explain the differences in breathing pattern observed in the present study. Our UawO patients showed a breathing pattern different from normal in that V_T/T_i and $\dot{V}_{I\max}$ were significantly lower while T_I/T_{tot} was significantly higher. The $(V_T/T_i)/\dot{V}_{I\max}$ and $(V_T/T_E)/\dot{V}_{E\max}$ ratios were also significantly higher, whereas the end-expiratory pause was practically nil. The low V_T/T_i was related to the increased inspiratory load caused by the increased inspiratory flow resistance (0.66 kPa· l^{-1} ·s in our patients), which was only partly compensated for by the increase in neuromuscular inspiratory drive as reflected in a significant increase in $P_{0.1}$ (table 3). The concomitant increase of T_I/T_{tot} compensated for the decrease in V_T/T_i to such an extent that minute ventilation was essentially the same in the UawO patients as in the normal controls. This increase in T_I/T_{tot} was mainly due to an increase in T_I , which might be attributable to the longer mechanical time constant of the respiratory system resulting from the increased flow resistance [16]. In fact, T_I/T_{tot} was the only variable showing a significant correlation ($r = 0.66$, $p < 0.01$) with plethysmographic airway resistance. The finding of a similar V_T/T_E in patients and HC can probably be explained in part by the shorter duration of the patients' end-expiratory pause, i.e. an increased expiratory flow

resistance will reduce the rate of lung emptying but V_T/T_E will remain unchanged, provided that the duration of expiration is sufficiently long [17]. A reduction in post-inspiratory activity of the inspiratory muscles and/or recruitment of expiratory muscle activity may also play a role in maintaining a fixed V_T/T_E in the face of increased flow resistance [17].

Since V_{imax} and V_{emax} were significantly lower in patients, both flow ratios, $(V_T/T_I)/V_{imax}$ and $(V_T/T_E)/V_{emax}$, were found to be higher in UawO ($p < 0.0005$) (table 3) and this finding indicates that the shape of the pneumotachogram will be more "rectangular" (fig. 1). Empirically, we can say that for constant flow (i.e. rectangular shape of the pneumotachogram) the value of these ratios should be 1. For a sinusoidal shape the ratios should be 0.64, and for a triangular pattern, 0.50. The rectangular shape provides more volume of air for similar phase time and peak flow. Therefore, the differences in shape of the flow-time profile of our patients with respect to the controls may, again, be interpreted as an adaptation to maintain \dot{V}_E .

Thus far, the changes of resting breathing in our patients have been attributed directly to the increased inspiratory load. An alternative explanation, however, is suggested by the paucity of correlation between variables of resting breathing and MFVL, which implies that the two flow recordings convey independent information. The flow limitation observed in the MFVL was not evident in resting breathing. For example, on average, V_T was 18% of FVC and V_{imax} reached only 28% of its value in the MFVL. Thus, one can speculate that changes in the resting pattern may represent an adaptive central response to minimize the increased turbulent flow characteristic of UawO.

The finding of a high T_I/T_{tot} is unusual in respiratory disease. BELLEMARE and GRASSINO [18] pointed out that an increase in T_I/T_{tot} brings the inspiratory muscles closer to their fatigue threshold. Thus, together with the low V_T/T_I , a high T_I/T_{tot} could be regarded as disadvantageous in the event of concurrent respiratory disease in UawO patients.

Information about changes in the resting breathing pattern due to long-standing increased flow resistance comes almost exclusively from observation of patients with chronic obstructive pulmonary disease (COPD) [19–22]. At rest, such patients tend to breathe with a significantly higher \dot{V}_E than healthy people. Patients attain this mainly by increasing f , thus shortening both T_I and T_E , whilst leaving T_I/T_{tot} unchanged [19, 21]. V_T has been found to be either normal or slightly higher [19, 20], whereas V_T/T_I has consistently been found to be high in COPD patients. Thus, it appears that in COPD patients \dot{V}_E , f , T_I/T_{tot} and V_T/T_I differ entirely from what we have observed in patients with UawO.

ZECHMAN *et al.* [23] studied the breathing pattern of healthy subjects breathing through resistance of increasing magnitude applied to inspiration, expiration or both. With inspiratory resistance there was a reduction of inspiratory flow and f , a notable increase of T_I and T_I/T_{tot} (from about 0.45 to 0.54, as one can estimate from figure 2 in their paper), a more rectangular

inspiration and almost no change in expiration. The resistance applied to the whole respiratory cycle altered both phases in terms of flow magnitude and profile, induced a marked reduction of f and decreased T_I/T_{tot} . With expiratory resistance the subjects increased their inspiratory flows and f and decreased T_I/T_{tot} . Inspiration tended to be more triangular and expiration more rectangular. While these changes are similar to those exhibited by patients with COPD, most of the characteristics exhibited by our UawO patients seem to fit better into the two previous situations: resistance applied to inspiration or to the whole respiratory cycle.

In summary, we conclude that increased airflow resistance in the extrathoracic airway induces abnormalities in the pattern of resting breathing, and that these abnormalities seem to be different from those of patients with generalized lung disease.

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Le type de respiration au repos chez les patients atteints d'obstruction des voies aériennes supérieures. J. Sanchis, J.L. Díez-Betoret, P. Casan, J. Milic-Emili.

RÉSUMÉ: Nous avons enregistré les courbes débit/temps pendant la respiration au repos chez 14 patients (âge 36 ± 16 ans) avec des symptômes légers à modérés d'obstruction des voies aériennes supérieures (UaWO), et les avons comparées à celles de 28 sujets contrôle bien portants (HC) afin de caractériser le type respiratoire de ces patients. Le rapport temps inspiratoire/temps total (T_i/T_{tot}) est plus élevé chez les patients ($0.42 \text{ SD } 0.04$) que chez les contrôles sains ($0.37 \text{ SD } 0.04$) ($p < 0.001$); le rapport volume courant (V_r) sur T_i est plus bas chez les patients ($0.37 \text{ SD } 0.07 \text{ l}\cdot\text{s}^{-1}$) que chez les contrôles ($0.43 \text{ SD } 0.09 \text{ l}\cdot\text{s}^{-1}$) ($p < 0.01$). Les débits de pointe inspiratoires et expiratoires au repos s'avèrent également abaissés chez les patients ($p < 0.001$). Chez ceux-ci, le rapport du débit moyen sur le débit de pointe à l'inspiration ($0.74 \text{ SD } 0.07$) est plus élevé que chez les sujets normaux ($0.66 \text{ SD } 0.04$) ($p < 0.0005$). Ceci indique une vague plus rectangulaire d'inspiration chez les patients. Toutes ces modifications pourraient être dues à une augmentation de la charge inspiratoire. Toutefois, puisque les patients respirent au repos avec des valeurs de V_r et de débit bien inférieures à leurs valeurs sur la boucle débit-volume maximal, les modifications peuvent également être interprétées comme étant une adaptation plutôt qu'une conséquence imposée des limitations mécaniques absolues.

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