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Expiratory flow limitation in awake sleep-disordered breathing subjects

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Expiratory flow limitation in awake sleep-disordered breathing subjects. G. Liistro, C. Veriter, M. Dury, G. Aubert, D.C. Stanescu. ©ERS Journals Ltd 1999.

ABSTRACT: Increased upper airways (UA) collapsibility has been implicated in the pathogeny of sleep-disordered breathing (SDB). An increased UA instability during expiration has recently been shown in healthy subjects. The present study assessed UA collapsibility in SDB patients by applying negative pressure during expiration.

Full-night polysomnography was performed in 16 subjects (all snorers) with a wide range of SDB, and in six healthy control subjects. Physical examination, spirometry, and maximal inspiratory and expiratory flow rates were within normal limits for all 22 subjects. Negative expiratory pressure (NEP) (-5 cmH_2O) was applied during quiet breathing in seated and supine position. Flow limitation (FL) during NEP was expressed as the percentage of tidal volume during which expiratory flow was less than or equal to the flow recorded during quiet breathing (%FL).

The mean desaturation index (DI) of the 16 subjects was 27.3±26.4 (±SD) and the average FL in supine position was 38.4±37.9%. A close correlation between %FL supine during wakefulness and DI during sleep ($r=0.84$, $p<0.001$) was found. All obstructive sleep apnoea subjects had >30%FL supine. There was no FL in the six control subjects.

In conclusion, negative expiratory pressure application during expiration appears to be a useful, noninvasive method for the evaluation of subjects with sleep-disordered breathing. Present results suggest that upper airway collapsibility can be detected in these subjects during wakefulness.

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In contrast to the trachea, pharyngeal structure is predominantly muscular. Its permeability depends essentially on the tone of the pharyngeal muscles. Upper airway (UA) collapsibility is increased during sleep in snorers and in patients with obstructive sleep apnoea syndrome (OSAS) resulting in flow limitation (FL), hypoventilation or apnoea.

Several methods to measure UA collapsibility have been reported previously [1, 2]. Authors have either used inspiratory loads or application of negative pressures at the mouth during inspiration. Large negative pressures were necessary to detect UA obstruction [1]. Indeed, UA muscle tone is higher during inspiration than expiration [3] and UA collapsibility is lower during inspiration. It has recently been shown that in healthy subjects the application of negative pressure at the mouth during muscular relaxation induces expiratory FL [4].

Therefore, this study was designed to assess UA collapsibility during expiration. The study utilizes a recently developed method of detecting intrathoracic FL in chronic obstructive pulmonary disease (COPD) patients, by applying negative expiratory pressure (NEP) [5–8]. This method has the advantages of being simple, rapid and, in contrast to previous methods, noninvasive. FL induced by NEP during wakefulness was related to O_2 saturation during sleep in patients with sleep-disordered breathing.

Methods

Subjects

Twenty-two subjects (two females), (all nonsmokers except three) were recruited from consecutive patients referred for snoring or suspicion of OSAS. A complete physical examination was followed by an ear, nose, throat (ENT) examination, which included anterior rhinoscopy, endonasal flexible endoscopy and both anterior and posterior semi-quantitative rhinomanometry. The other routine tests were plain chest radiograph and thyroid function tests. All subjects had standard spirometric measurements, maximal inspiratory and expiratory flow volume curves, carbon monoxide diffusing capacity ($D_{L,CO}$) and arterial blood gas measurements.

Polysomnographic studies

A full-night diagnostic polysomnography (PSG) was performed on each subject according to standard criteria as previously described [9]. A microphone was glued onto the patients' neck. Snoring was designated on the basis of the characteristic microphone trace during sleep. Snoring index (SI) was defined as the number of 30-s sleep epochs with at least one snore over total number of sleep epochs, $\times 100$. A movement arousal (MA) was defined as the

abrupt appearance of an alpha rhythm in the electroencephalogram (EEG) during a sleep epoch, accompanied by an increase in electromyogram (EMG) activity for at least 2 s. The movement arousal index (MAI) is the number of MA per hour of sleep. The desaturation index (DI) was the number of desaturations (≥4%) per hour of sleep. DI was used rather than the apnoea/hypopnoea index since both are related to abrupt reductions of oronasal flow signals [9]. OSAS was diagnosed when the DI was superior or equal to 15 [9].

Negative expiratory pressure

NEP was applied according to the method of KOULOURIS *et al.* [8]. The subjects breathed through a mouthpiece connected in series with a mouth pressure port, a Fleisch No. 3 pneumotachograph (Fleish, Lausanne, Switzerland) and a T-tube (fig. 1). One side of the T-tube was left open and the other side was connected to a vacuum cleaner (General Electric C-13; General Electric, Bridgeport, CT, USA). An electrical valve was placed between the T-tube (22mm diameter) and the vacuum cleaner. Closure time of the electrical valve was 0.025 s. Size of the tube and flow of the vacuum cleaner were adjusted to create a NEP of -5 cmH_2O at the subjects′ mouth. Mouth pressure was measured with a ±20 cmH_2O Celesco (Canoga Park, CA, USA) differential pressure transducer. Airflow (V′) was measured with the heated Fleisch pneumotachograph connected to a ±2 cmH_2O Validyne differential pressure transducer (Validyne Engineering Corporation, Northridge, CA, USA). Volume was obtained by electrical integration of the flow signal. The breathing assembly was characterized by the following pressure-flow relationship: $P=0.16\ V' + 0.24\ V'^2$, where P is pressure (cmH_2O) and V′ is flow ($L \cdot s^{-1}$). This equation is comparable to that of KOULOURIS *et al.* [5]. The signals were recorded on paper (Gould ES1000 electrostatic recorder; Gould) and simultaneously backed up on tape (TEAC R81 cassette recorder). A noseclip precluded nasal breathing. Measurements were performed in seated and supine positions in a random order. During the measurements care was taken to avoid any change in head position. When the subjects were seated, gaze was parallel to the floor, while in the supine position gaze was perpendicular to the floor. Subjects were asked to breathe quietly through the device and negative pressure was applied during expiration. The operator surveyed the tidal volume of the subject which was displayed on a large monitor. When lung volume reached end inspiration, the electrical valve connecting the subject with the negative pressure (produced by the vacuum cleaner) was opened. The valve was closed at end expiration. The detection of FL during expiration was performed according to the criteria of KOULOURIS *et al.* [8]. The flow-volume curve recorded during NEP was superimposed upon that recorded during quiet breathing immediately before. Expiratory flow was considered flow-limited when during NEP application flow rate was equal or inferior to the corresponding flow during quiet breathing (see fig. 2). FL was expressed as percentage of tidal volume during NEP application (% FL). Reported values of (%FL) are the average of five measurements. All the procedures, including pulmonary function tests and sleep studies, were performed within the same week.

The study was approved by the local Ethics Committee and all the subjects gave informed consent.

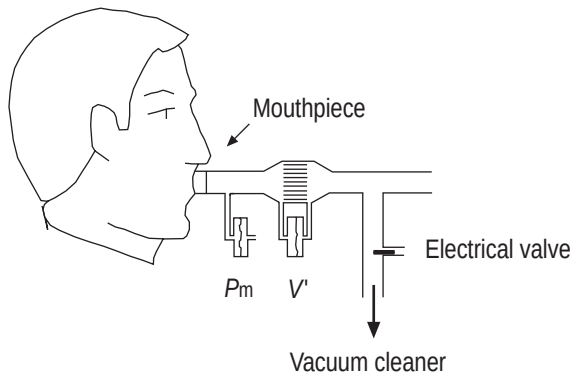

Fig. 1. – Schematic representation of the negative expiratory pressure device. *P*m: mouth pressure, *V'*: flow.

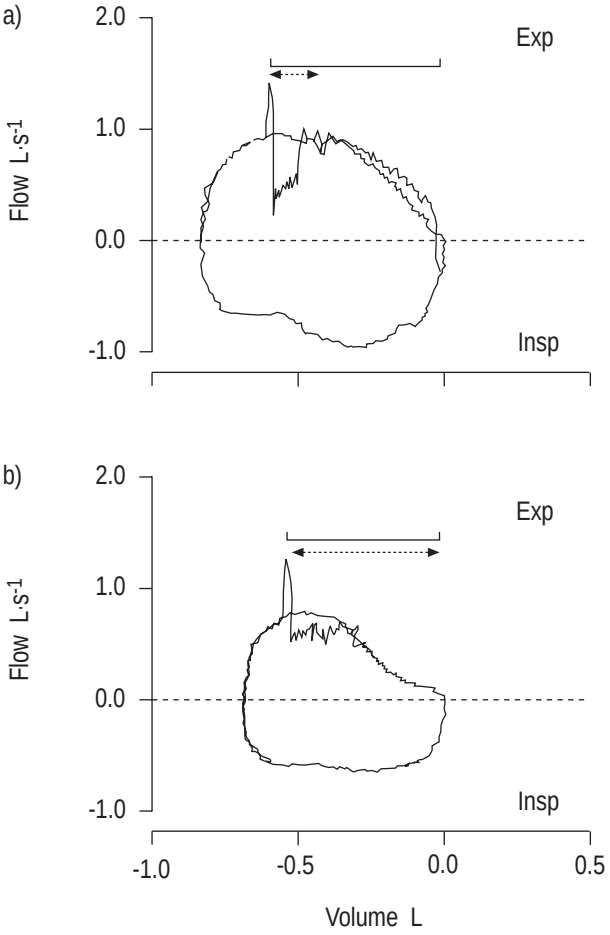

Fig. 2. – Superimposed flow/volume curves during quiet breathing and during negative expiratory pressure (NEP) in a subject (No. 15 in table 2) in: a) seated and b) supine position (%FL=93). The vertical arrows show the beginning and end of NEP application. The horizontal bar represents the tidal volume during which NEP was applied, with the dotted arrow representing the proportion of tidal volume during which flow was limited. The zero volume was arbitrarily taken as the end-expiratory lung volume of control breaths. Flow limitation (percentage of tideal volume during which expiratory flow was ≤ to the flow during quiet breathing) was present in both seated (30%) and supine position (93%). Exp: expiration; Insp: inspiration.

Statistical analysis

Standard statistical tests including linear regression and Student's t-test for paired data were used and a p-value <0.05 was considered to be statistically significant.

Results

Among the 22 subjects, six (mean age 50.6±6.2 yrs, body mass index 24.4±1.5 kg·m^{-2}, all males and non-smokers) had no sleep-disordered breathing (SDB) and were considered as healthy control subjects. They did not snore and their DI was <10. Their pulmonary function tests, as well as chest radiographs, physical and ENT examinations were within normal limits. Anthropometric data and the results of pulmonary function tests of the 16 subjects with SDB are listed in table 1. All subjects had spirometric data [10] and $D_{L,CO}$ (92.5±25.6% of predicted) [11] within normal limits. The maximal inspiratory and expiratory flow-volume curve, except in four subjects with a saw-tooth pattern, had a normal configuration during both inspiration and expiration. Arterial oxygen (11.2±1.4 kPa (83.9±10.7 mmHg)) and carbon dioxide (5.2±0.4 kPa (39.4±3.3 mmHg)) tensions at rest were within normal limits. Physical and ENT examinations as well as chest radiographs were also normal in all subjects.

Table 2 presents individual and mean (±SD) values of %FL seated and supine as well as some polysomnographic indices. Eight subjects had a DI ≥15 and were considered as OSAS [9]. All 16 subjects were snorers.

In the 16 subjects average %FL increased significantly when passing from seated to supine position (p=0.002 by Student's t-test for paired data). There was a significant correlation between %FL seated and supine (r=0.80, p< 0.001). OSAS patients had >30 %FL in supine position.

Table 1. – Anthropometric and pulmonary function test data for subjects with sleep-disordered breathing

Subject No.	Age yrs	Weight kg	BMI kg·m^{-2}	FEV1/VC % pred	VC % pred	F/V aspect
1	36	88	30.4	82	77	n
2	50	95	32.1	117	81	n
3	64	70	28.4	110	89	n
4	55	86	29.1	105	91	n
5	32	86	25.7	105	91	n
6	46	68	25.3	100	102	st
7	48	96	29.6	108	89	n
8	66	72	28.8	109	94	n
9	70	80	24.7	95	104	n
10	63	97	31.7	116	89	n
11	43	68	21.7	96	102	n
12	55	82	30.5	114	114	n
13	47	92	31.1	101	99	st
14	51	102	32.5	119	88	st
15	56	95	37.1	110	84	st
16	40	130	42.0	101	91	n
Mean±	51.4±	87.9±	30.0±	99.1±	92.7±	
SD	10.9	15.7	4.8	9.6	9.5	

BMI: body mass index; FEV1: forced expiratory volume in one second; VC: vital capacity; F/V: flow/volume aspect; n: normal; st: sawtooth pattern.

Table 2. – Flow limitation (FL) and polysomnographic indices

Subject No.	%FL seated	%FL supine	DI	MAI	TST min
1	27.7	81	31	32	286
2	0.0	0.0	2	4	436
3	0.0	0.0	5	20	368
4	0.0	8.8	6	2	414
5	0.0	0.0	6	14	243
6	0.0	25.0	7	12	310
7	0.0	0.0	7	4	346
8	0.0	0.0	14	9	386
9	18.6	18.0	14	15	306
10	20.4	46.3	21	30	349
11	56.5	93.0	28	32	414
12	12.2	34.0	31	30	331
13	0.0	41.9	44	35	436
14	0.0	79.8	57	82	418
15	54.3	92.9	79	62	362
16	43.2	94.0	85	56	444
Mean±	14.6±	38.4±	27.3±	27.5±	365.6±
SD	20.5	37.9	26.4	22.8	59.9

%FL: percentage of tidal volume during which expiratory flow was less than or equal to the flow recorded during quiet breathing; DI: desaturation index; MAI: movement arousal index; TST: total sleep time.

There was a close relationship between %FL supine and the desaturation index (r=0.84), p<0.001) (fig. 3). DI and %FL in seated position were also significantly related (r=0.65, p=0.007). Average tidal volume and average flow rate did not change significantly between seated and supine positions (p>0.05). In the six healthy control subjects there was no FL during NEP. Expiratory flow increased in all of them, in both seated and supine positions.

Figure 2 shows examples of expiratory FLs during NEP application in both seated (a) and supine (b) positions. Figure 4 presents a subject with FL occurring only in supine position and figure 5 shows the flow-volume curves of a patient without FL in either position.

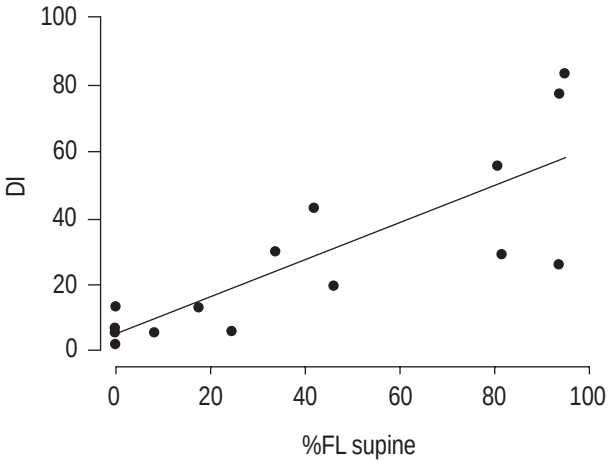

Fig. 3. – Relationship between percentage of tidal volume during which expiratory flow was less than or equal to the flow recorded during quiet breathing (%FL) in the supine position and desaturation index (DI) in the 16 subjects. The regression line is shown (r=0.84; p<0.001).

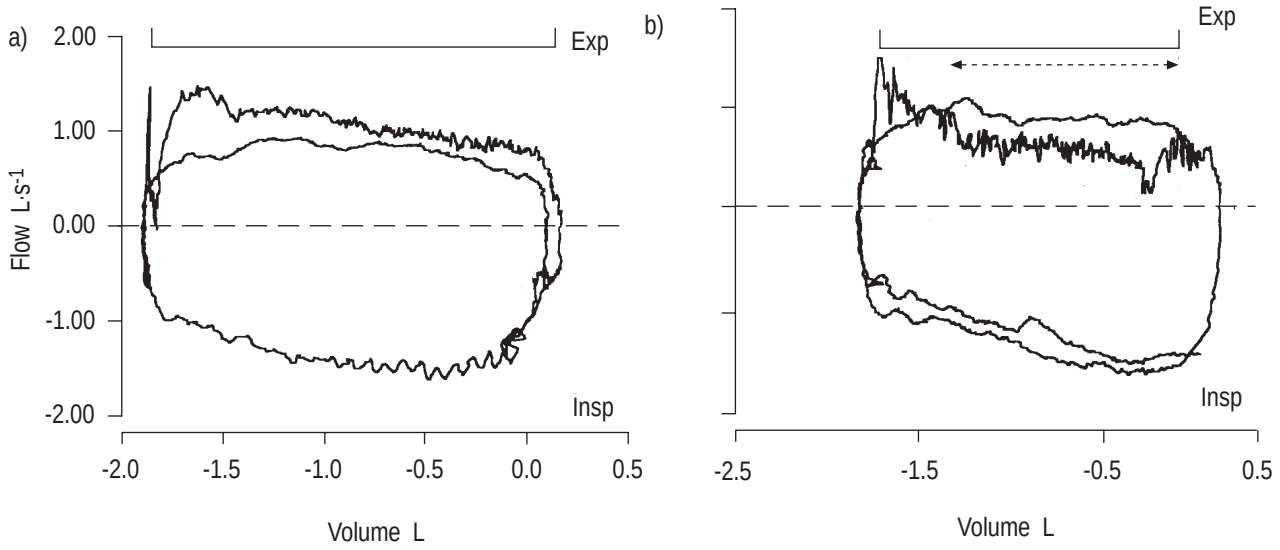

Fig. 4. – Flow/volume curves during quiet breathing and during negative expiratory pressure in a subject which presented flow limitation (FL) only in supine position (No. 14 in table 2) in: a) seated and b) supine position (%FL=85). The horizontal bar represents the tidal volume during which NEP was applied, with the dotted arrow representing the proportion of tidal volume during which flow was limited. The zero volume was arbitrarily taken as the end-expiratory lung volume of control breaths. Exp: expiration; Insp: inspiration.

Discussion

It was found in a group of awake subjects with SDB that expiratory FL during negative pressure application was significantly correlated with the DI recorded during sleep. In other words, subjects with a high collapsibility of UA, as shown by the application of NEP, narrowed these airways during sleep, resulting in apnoea and hypopnoea and as a consequence O_2 arterial desaturation. It was also observed that FL increased when passing from seated to supine positions.

The NEP technique has been previously validated for the detection of intrathoracic FL in patients with COPD [5, 6, 8]. Briefly, the authors reasoned that in these patients application of negative pressure at the airway opening should increase the expiratory driving pressure (*i.e.* the pressure gradient between alveoli and airway opening) if the patient is not flow limited and therefore it should enhance the expiratory flow. If the expiratory FL is already present, the application of negative pressure would not change the expiratory flow. To avoid confounding factors promoting FL, patients with OSAS or UA obstruction have been excluded from their studies. Since the hypothesis behind the current study was that NEP could detect an increased UA collapsibility, patients with SDB were selected and patients with intrathoracic airflow limitation were excluded. In subjects with a high DI during sleep, expiratory flow did not increase during NEP. It even decreased. Decrease of expiratory flow during application of negative pressure at the mouth was previously reported from this laboratory [12]. NEP at the mouth would change the positive transmural pressure existing in the extrathoracic airways during expiration into a negative one narrowing these airways and decreasing airflow. A decrease of cross sectional area during negative pressure application at the mouth was previously reported [13, 14]. In the six control subjects without any impairment of upper or lower airways, NEP induced an increase in the expiratory flow, with respect to control breathes, as a consequence of the increase in the pressure gradient between alveolar and airway opening. Similar results have been reported recently by TANTUCCI *et al.* [15] in 10 healthy subjects.

Aerodynamic theory and physical models predict that in a collapsible airway FL is facilitated when airflow resistance and airway wall compliance are increased and when airway cross-sectional area is decreased [16]. Several studies have shown that upper airway resistance is higher in both awake and asleep OSAS patients compared to normal subjects [17–19]. This is probably due to the smaller pharyngeal size of awake apnoeic patients [18, 20]. Upper airway collapsibility is also higher in awake OSAS patients than in normal subjects [1, 14]. As previously shown by SURATT *et al*. [1] awake OSAS patients developed UA obstruction when submitted to subatmospheric airway pressures ranging from -17– -40 cmH_2O. No obstruction occurred in healthy subjects. In normal sleeping subjects UA occlusion occurred on average at -13 cmH_2O [2] but failed to occur at pressure as low as -27 cmH_2O in another study [21]. These pressures were much more subatmospheric than the NEP used in the current study (-5 cmH_2O). However, in all these studies, large negative pressures were used which produced collapse of UA. In the current study narrowing but not collapse of UA was induced. Flow rate diminished (or did not increase) but did not reach zero. Furthermore, in contrast with previous studies, the method used is noninvasive; it does not require insertion of a pressure catheter in the UAs or an oesophageal balloon [1, 2].

Unlike previous studies, this study limited application of negative pressure to expiration. UA muscles are activated prior to the diaphragm [22], stiffening these airways to resist the negative transmural pressure that they are submitted to during inspiration. Conversely, during

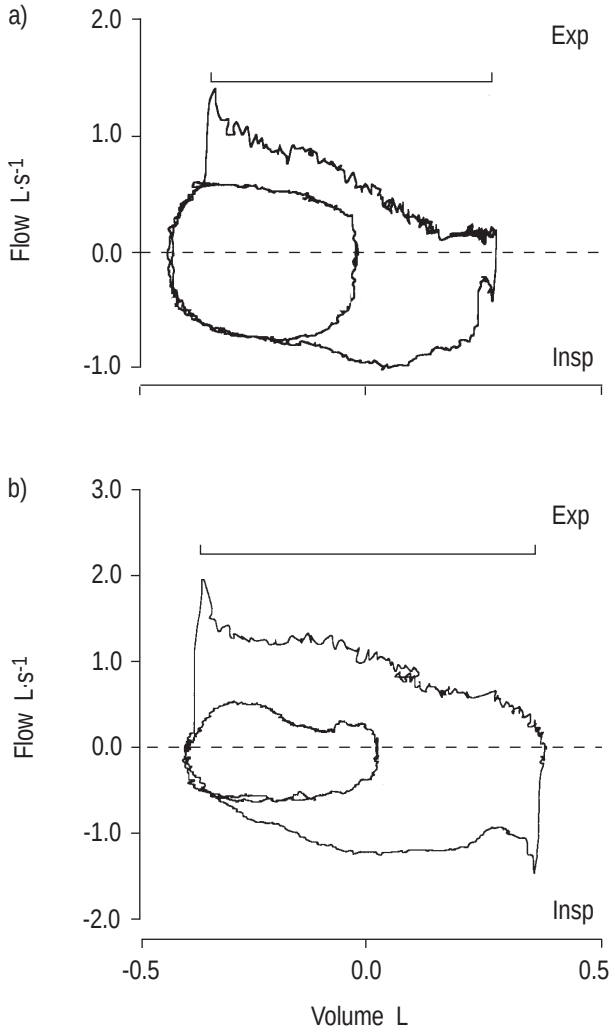

Fig. 5. – Flow/volume curves during quiet breathing and during negative expiratory pressure (NEP) application in one of the six normal subjects without flow limitation (FL) in: a) seated; and b) supine position. The horizontal bar represents the tidal volume during which NEP was applied. The zero volume was arbitrarily taken as the end-expiratory lung volume of control breaths. Exp: expiration; Insp: in-spiration.

expiration, UA muscles′ activity decreases, rendering these airways vulnerable to negative pressure. It has been shown previously that in relaxed supine healthy volunteers a negative pressure of only -2 cmH_2O was sufficient to induce FL when applied at the mouth during expiration [4]. When subjects contracted their UA muscles "to resist" to the applied pressure, there was no FL. Timing of the application of NEP during expiration is also important, because it can modulate the reflex activity of UA muscles. TANTUCCI *et al.* [15] confirming previous findings [23], showed that application of NEP in healthy seated subjects at the onset of expiration elicits no reflex response of the genioglossus. However, when NEP was applied at end expiration it induced an increase in genioglossus EMG activity.

The authors have also previously shown in healthy awake volunteers that UA "compliance" was higher during expiratory, than during inspiratory, efforts against a closed airway [13]. A higher expiratory than inspiratory UA compliance was reported by BROWN *et al.* [14] using the acoustic reflection technique. These authors also found that expiratory compliance of UA was higher in OSAS patients that in normal subjects. Recently, MORTIMORE and DOUGLAS [24] have shown that untreated OSAS patients present impaired palatal muscle EMG response to negative airway pressure application. This means that the compliance of UA is increased in OSAS patients but also that their UAs have an impaired defence against negative pressure application. Interestingly, nightly treatment by continuous positive airway pressure improved UA EMG response of these patients.

It has been found that a larger part of the tidal flow was flow limited in supine than in seated position. UA resistance is higher in supine than in seated position in both awake healthy subjects and OSAS patients [17]. This increase in resistance has been attributed to a passive movement of the tongue reducing UA calibre in supine position. Indeed, posture was shown in healthy subjects and OSAS patients to influence UA dimension measured by cephalometry [25] and acoustic reflection technique [26]. Functional residual capacity decreases when passing from seated to supine position. BROWN *et al.* [27] have shown in normal subjects that pharyngeal cross-sectional area decreases as lung volume decreases from total lung capacity to residual volume. However, FOUKE and STROHL [26] concluded that changes in UA cross-sectional area are independent of changes in lung volume.

In conclusion, application of negative pressure during expiration appears useful in the evaluation of patients suspected of sleep-disordered breathing. This method is simple, rapid and noninvasive. The results add weight to the hypothesis that upper airway abnormalities are involved in the genesis of obstructive sleep apnoea syndrome. Present findings suggest, as previously stated [1], that these abnormalities can be detected during wakefulness.

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