

Influence of lung volume in sleep apnoea

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ABSTRACT The influence of a constant increase in functional residual capacity on apnoea characteristics was studied in patients with the sleep apnoea syndrome. Pulmonary inflation was achieved by applying a continuous negative extrathoracic pressure into a Poncho type respirator. Nine patients slept in the Poncho for two consecutive nights, negative extrathoracic pressure being applied during the second night. There was no difference in the total sleep time, its composition within the different sleep stages, the apnoea and apnoea-hypopnoea indices, or the sleep time spent in apnoea between the two nights. The mean (SD) apnoea duration increased with negative extrathoracic pressure from 25.3 (2) to 30.5 (3) seconds ($p = 0.003$) and time spent in obstructive apnoea (percentage of apnoea time) from 56 (13) to 75 (8) ($p = 0.02$). The mixed apnoea time (%) decreased from 37 (7) to 21 (7) ($p = 0.02$). Despite the increase in apnoea duration, less time was spent below each oxygen saturation value during negative extrathoracic pressure. The results were similar for apnoeic episodes during non-REM (non-rapid eye movement) sleep, whereas no significant modifications were seen during REM sleep. It is concluded that the composition of apnoea time and resulting oxygen desaturation are influenced by lung volume.

Introduction

The pathophysiology of the sleep apnoea syndrome is multifactorial; it includes a sleep induced decrease in activity of upper airways muscles, an increase in upper airways collapsibility and resistance, and an increase in pharyngeal transmural inspiratory pressure. Recent reports have shown a reduction in the pharyngeal cross sectional area with decreasing lung volumes, especially below functional residual capacity (FRC).¹ In addition, oxygen desaturation after an episode of apnoea has been found to be volume dependent in normal awake subjects.^{2,3} This suggests that lung volumes could have an important role in the initiation of apnoea and in the resulting arterial desaturation. During sleep FRC is influenced by many factors, including position (especially important in obese patients), changes in muscle tone, intrathoracic blood redistribution, and repetitive small volume expirations during episodes of obstructive apnoea. Continuous positive airway pressure has been reported to be effective in sleep apnoea.⁴ The role of changes in FRC

that accompany it is, however, unknown. We studied the effects of pulmonary inflation on sleep apnoea and oxygen desaturation in nine patients with documented sleep apnoea syndrome.

Methods

SUBJECTS

Fifteen men with the sleep apnoea syndrome participated. The diagnosis of the sleep apnoea syndrome was based on typical symptoms (overweight, snoring, nocturnal choking and waking, morning headache, hypersomnia) and polysomnographic results (apnoea-hypopnoea index > 10). Only one subject was being treated for the sleep apnoea syndrome at the time of the study (medroxyprogesterone 90 mg/day).

TECHNIQUES

An electroencephalogram (EEG), electro-oculogram (EOG), and submental electromyogram (EMG) were used for sleep staging. Airflow was recorded at the nose and mouth by thermocouples mounted on nasal prongs. Abdominal and chest wall movements were recorded by an inductive plethysmograph vest (Respitrace, Respitrace Corporation, Ardsley, New York). The vest was calibrated by the least square

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Accepted 19 October 1988

method.⁵ A thin walled, 5 cm latex balloon was positioned in the middle third of the oesophagus to measure oesophageal pressure. Arterial oxygen saturation (Sao₂) was measured by a Biox II ear oximeter (measurements below 60% were included in the <60% interval because this is the lower limit of linearity of our oximeter). Recordings were made on a polygraph (Model 78D, Grass instruments, Quincy, Montana) at a paper speed of 10 mm/second. Sleep stage scoring and respiratory patterns were defined by standard criteria.^{6,7}

PROTOCOL

Pulmonary inflation was achieved by applying a constant negative extrathoracic pressure into a Poncho type respirator; this is physiologically equivalent to a tank respirator. All patients, who had previously had a diagnostic sleep study, were evaluated on two consecutive nights. The first night the patient slept in a Poncho type respirator (Emerson) without negative pressure (control night), and during the second night a constant vacuum induced negative extrathoracic pressure was applied (NEP night). A conventional Poncho type respirator was modified to prevent compression of the thorax not covered by the cage; this was achieved by putting hard plastic bands above the shoulders and the upper portion of the thorax. We used the usual Poncho sealing at the hips, arms, and base of the neck. In four very obese patients we used an extra large custom made cage.

Of the 15 patients studied on the control night, six had a total sleep time of less than four hours and were not retained for this study. The other nine subjects had at least four hours' sleep on both nights and their results were analysed.

The level of negative pressure to be applied during the night was determined while the patients were awake. The subject lay supine in the Poncho respirator, breathing into a 10 litre Collins water sealed spirometer with a carbon dioxide absorber. Then we determined for each subject the negative extrathoracic pressure required to achieve a 0.5 l increase in the end expiratory lung volume. During the negative extrathoracic pressure night this constant negative pressure was applied throughout the night and the pressure inside the Poncho was continuously recorded. The negative pressure was interrupted only briefly every 30 minutes and the Resptrace was switched to the DC mode to check that the degree of inflation remained stable. Because the subject's position changed during the night, only semiquantitative measurements could be made.

DATA COLLECTION AND STATISTICAL ANALYSIS

From each recording we looked at the sleep period time and total sleep time; the amount of total sleep

time spent in stage I-II, stage III-IV, and the REM stage; the apnoea index and apnoea-hypopnoea index; the apnoea time index (time in apnoea divided by total sleep time); and the mean apnoea duration. Nocturnal desaturation was quantified as the cumulative distribution of total sleep time spent below given Sao₂ values in the range 60-90%. As data were not normally distributed, values were compared by means of the Wilcoxon signed rank test.

We also looked at the relation between apnoea duration and apnoea induced desaturation: for each apnoeic event the maximal fall in Sao₂ during the apnoeic episode (Δ Sao₂) was plotted against the corresponding apnoea length. The resulting "desaturation curve" fitted a polynomial regression model and characterised the apnoea induced desaturation for each subject. To reduce the influence of the preapnoeic Sao₂ on the apnoea induced desaturation, we considered only apnoeic episodes in which the preceding Sao₂ was more than 90%.

Results

The anthropometric characteristics of the patients and results of pulmonary function tests (sitting position) are reported in table 1; the characteristics of the six patients not retained for the study were not different from the nine others. Predicted values were those of Grimby.⁸ Seven of the nine subjects weighed more than 115% of their ideal body weight.⁹ Expiratory reserve volume was decreased, the decrease being more severe as weight increased (data not shown).

A -5 to -9 cm H₂O pressure was required to achieve a 0.5 l increase in FRC when subjects were awake. The same negative pressure was applied and maintained throughout the night.

During the control night the mean (SEM) sleep period time was 6.2 (0.3) hours and the total sleep time 5.5 (0.2) hours. These values were not significantly different during the negative extrathoracic pressure

Table 1 Characteristics of the 15 patients and their lung function results* (mean (SEM), % predicted)

	Retained patients (n = 9)	Eliminated patients (n = 6)
Age (y)	52 (3)	55 (6)
Weight (% ideal value)	124 (5)	121 (6)
TLC (%)	110 (9)	107 (10)
FRC (%)	102 (10)	99 (8)
ERV (%)	63 (7)	66 (7)
RV (%)	125 (12)	122 (10)
FEV ₁ (%)	92 (4)	90 (5)

*Lung volumes are expressed as percentages of the ideal body weight values. There is no difference between the nine patients retained for the study and the six eliminated.

TLC—total lung capacity; FRC—functional residual capacity; ERV—expiratory reserve volume; RV—residual volume; FEV₁—forced expiratory volume in one second.

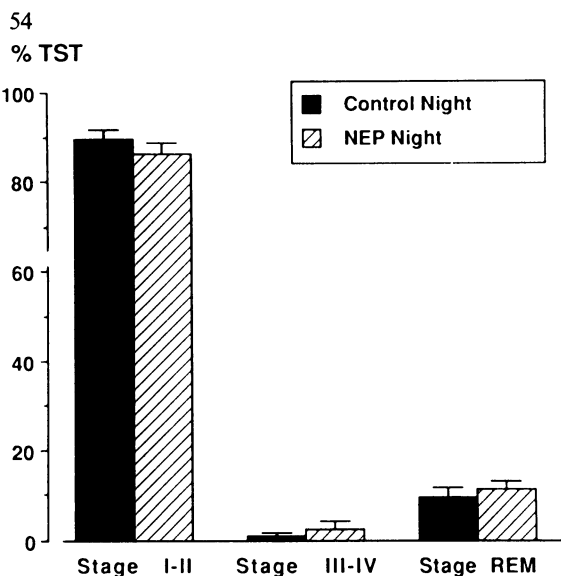


Fig 1 Composition (mean and SEM) of total sleep time (TST) within different sleep stages during control and negative extrathoracic pressure (NEP) nights for the nine subjects ($p > 0.05$).

night (sleep period time 6.2 (0.4) hours, total sleep time 5.9 (0.4) hours). Sleep stages I and II predominated in all patients, with little slow wave sleep (fig 1). There were no differences in total sleep time composition between control and negative extrathoracic pressure nights. There was no difference in the apnoea index or the apnoea-hypopnoea index between the first diagnostic study and the control study. From the control night to the negative extrathoracic pressure night the apnoea index fell from 46.9 (7.4) to 40.9 (8.1) and the apnoea-hypopnoea index from 64.5 (4.5) to 60.7 (5.6). These changes were not significant. The apnoea time index during the control night was 35.3% (7.7%), and it did not change significantly with negative extrathoracic pressure (36.0% (8.7%)).

There was no difference in the composition of the apnoea time between the diagnostic sleep study and the control night. Figure 2 shows that the time spent in

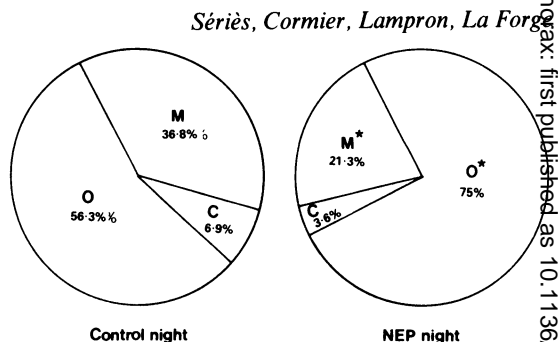


Fig 2 Mean composition of apnoea time spent as obstructive apnoea (O), mixed apnoea (M), and central apnoea (C) for all nine subjects. Negative extrathoracic pressure decreased mixed apnoea time and increased obstructive apnoea time * $p < 0.05$.

obstructive apnoea, expressed as a percentage of the total apnoea time, increased from 56.3 (12.6) during the control night to 75.0 (8.1) during the negative extrathoracic pressure night ($p = 0.02$), whereas the percentage of time spent in mixed apnoea decreased from 36.8 (10.8) to 21.3 (7.0) ($p = 0.02$). The percentage of central apnoea time decreased from 6.9 (4.0) to 3.6 (1.8) ($p = 0.054$). During non-REM sleep obstructive and mixed apnoeas showed a similar pattern as during total sleep time whereas the percentage of central apnoea time decreased significantly from 7.4 (4.0) to 3.9 (1.8) ($p = 0.03$). The composition of apnoea time for the REM stage was unchanged by negative extrathoracic pressure.

Negative extrathoracic pressure was associated with a significant increase in the duration of apnoea as whole and of obstructive apnoea both for the whole night and for stage I-II sleep (table 2). The lengthening of mixed apnoeic episodes was significant only during stage I-II. There were no significant changes in apnoea duration during REM sleep.

The cumulative distribution of total sleep time spent below a given Sao_2 in the range 60–90% for negative extrathoracic pressure nights and control nights is shown in figure 3. Less time was spent below each

Table 2 Effect of negative extrathoracic pressure (NEP) on mean (SEM) apnoea duration (seconds) for all apnoea and for each type of apnoea during the total sleep time and the different sleep stages

Night:	Total sleep time		Stage I-II		REM	
	Control	NEP	Control	NEP	Control	NEP
All apnoea	25.3 (2.3)	30.5 (2.8)*	23.4 (2.1)	26.5 (2.5)*	46.1 (4.9)	47.7 (4.8)
Obstructive apnoea	23.8 (2.6)	30.1 (2.9)*	21.9 (2.1)	26.2 (2.5)*	41.5 (7.6)	46.8 (5.3)
Mixed apnoea	23.6 (3.3)	30.5 (3.6)	22.6 (3.2)	29.2 (3.5)*	34.8 (7.7)	36.1 (9.5)
Central apnoea	13.9 (1.3)	11.5 (1.6)	13.9 (1.3)	11.5 (1.6)		

There were no central apnoeic episodes during REM sleep, and no apnoeic episodes during stage III-IV sleep.

* $p < 0.05$ for control v NEP.

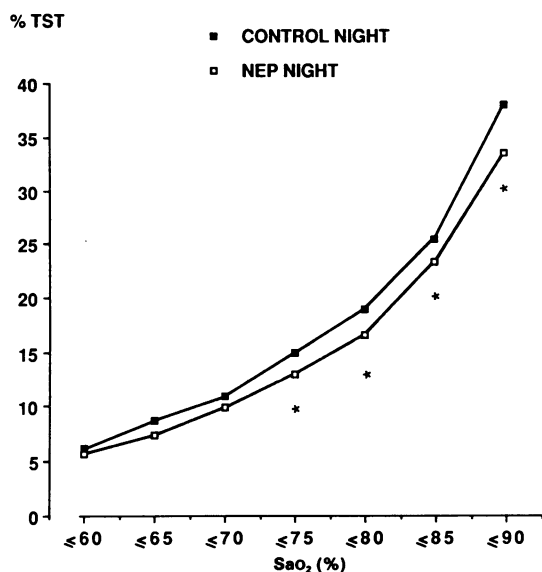


Fig 3 Mean cumulative distribution of total sleep time (TST) spent below a given arterial oxygen saturation (Sao_2) for all subjects. Negative extrathoracic pressure night values were significantly lower than control night values for Sao_2 values above 70%. * $p < 0.05$.

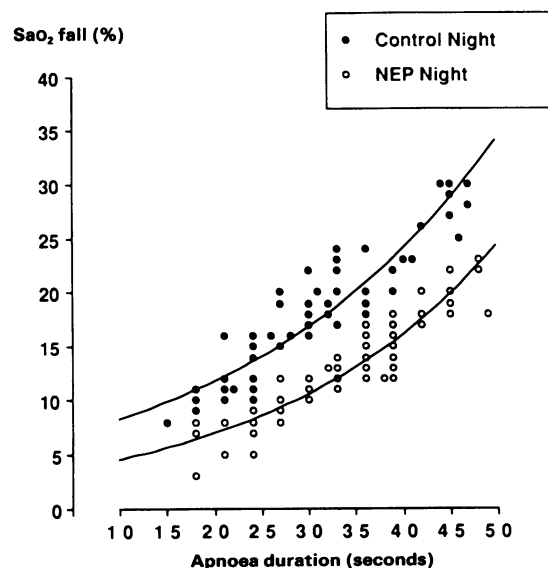


Fig 4 Influence of negative extrathoracic pressure (NEP) on the "desaturation curve" of obstructive apnoea in a typical subject. ● Obstructive apnoeic events during the control night; ○ obstructive apnoea during the negative extrathoracic pressure night. During the negative extrathoracic pressure night the desaturation curve was shifted to the right so that a similar apnoea duration resulted in a smaller fall in arterial oxygen saturation (Sao_2).

saturation value during negative extrathoracic pressure, the differences being significant for Sao_2 values greater than 70%. Baseline Sao_2 did not change with negative extrathoracic pressure. There was a similar improvement in oxygen saturation during stage I–II sleep, but the cumulative distribution remained unchanged during REM sleep.

As expected, there was a strong correlation between ΔSao_2 and apnoea duration in each patient, confirming the validity of the desaturation curve to characterise the individual relation between apnoea duration and Sao_2 fall (fig 4). There was a right shift in the "desaturation curve" with negative extrathoracic pressure in every patient—that is, for a given apnoea duration the Sao_2 fall was less with negative extrathoracic pressure. Thus despite lengthening of the apnoeic episodes apnoea induced desaturations were less during negative extrathoracic pressure nights than during control nights.

Discussion

The results of this study show that increases in lung volumes, within the range applied in this study, do not influence sleep pattern or the amount of sleep time spent in apnoea in patients with the sleep apnoea syndrome, although they do modify the distribution of apnoea types and the resulting oxygen desaturation. Our results are unlikely to be the consequences of our selection criteria, because the clinical and the sleep disordered breathing characteristics of the nine patients included in the study were similar to those of the six who were excluded. The limitation to movement that is usually observed when subjects lie in the Poncho apparatus (thoracic cage, plastic dorsal sheet) was probably responsible for the reduction in total sleep time in these six patients. For the other nine subjects there was no change in the characteristics of the apnoeic episodes between the first (diagnostic) study and the control night. The enforced supine posture did not modify the sleep pattern and we believe that our results are related to the specific effect of the negative extrathoracic pressure. A direct effect of the Poncho apparatus—for example, neck compression by the Poncho sealing—is unlikely, because this was over the lower part of the neck in front of the sternal notch. Any compression induced by negative extrathoracic pressure would have been applied over the trachea, below the area where obstructive apnoea originates.¹⁰

The consistency of the pulmonary inflation level was estimated every 30 minutes by obtaining the sum tracing of the RespiTrace used in the DC mode. When the patient slept in the Poncho, verification of the position of the thoracic and abdominal bands of the RespiTrace was not possible, so the nocturnal FRC

measurements are regarded as only semiquantitative. Even if the level of pulmonary inflation that was achieved during the night was not the same as during wakefulness the stability of the FRC tracing suggests that this level did not change throughout the night.

Our finding that negative extrathoracic pressure increases the time spent in obstructive apnoea and decreases the apnoea induced desaturation could be due to the effects of pulmonary volume on pharyngeal cross sectional area or the influence of the fall in Sao_2 on the stability of the respiratory control system, or to both mechanisms.

The increase in obstructive apnoea time with negative extrathoracic pressure was associated with a concomitant fall in mixed and central apnoea time, suggesting that central apnoea and obstructive apnoea may be different expressions of a single pathological event. During wakefulness upper airway patency must depend on lung volume—firstly, because the pharyngeal cross sectional area decreases at low lung volumes, especially in patients with obstructive sleep apnoea¹¹; and, secondly, because pharyngeal inspiratory resistance decreases with passively increasing FRC in normal subjects.¹² These results suggest that negative extrathoracic pressure was probably accompanied by an increase in upper airway patency. The greater lung volume dependence of the pharyngeal area in snorers with central apnoea than in non-apneic snorers¹³ suggests that the inhibition of respiratory drive that characterises central events could be the consequence of complete or partial collapse of the pharynx. The effect of continuous positive airway pressure on central apnoea support the hypothesis that the reflex cessation of breathing may originate from the upper airways.^{14,15} With nasal continuous positive airway pressure the relative contributions of change in upper airway pressure and change in lung volume cannot be distinguished; possibly the increase in FRC induced by negative extrathoracic pressure increased upper airway patency sufficiently to prevent central apnoea, but not enough to prevent obstructive sleep apnoea. This could explain why there was no reduction in apnoea index or apnoea time index and why we observed an increase in obstructive apnoea. A 0.5 litre increase in FRC is probably similar to the lung volume increase achieved with low levels of continuous positive airway pressure; thus the effectiveness of this range of continuous positive airway pressure in the treatment of obstructive sleep apnoea cannot be attributed to increase in FRC alone. This is in accordance with the results of previous studies, where the electromyographic activities of upper airway dilator muscles were reported to decrease with nasal continuous positive airway pressure during sleep,^{16,17} suggesting that the efficacy of continuous positive airway pressure is related to its

pneumatic splinting effect.

The composition of apnoea time did not change during REM sleep. This is not surprising as only mixed and central apnoea time decreased with negative extrathoracic pressure during stage I–II and almost all apnoeic events during REM sleep were obstructive in type.

A previous study showed a decrease in apnoea index and apnoea duration and an improvement in nocturnal oxygenation with expiratory positive airway pressure,¹⁸ and attributed the findings mainly to a change in FRC. Negative extrathoracic pressure did not, however, change apnoea frequency or the time spent in apnoea whereas expiratory positive airway pressure did. Although the increase in FRC achieved in our study may not be the same as with a 10 cm H_2O expiratory positive airway pressure, the main difference between negative extrathoracic pressure and expiratory positive airway pressure is the presence of positive expiratory upper airway pressure with the latter. The increase in expiratory resistance from the second to the first breath before an obstructive event¹⁹ suggests that the inspiratory phase does not entirely account for the onset of obstructive apnoeas. The effects of expiratory positive airway pressure could result, at least in part, in the prevention of the expiratory component of airway collapse.

Another explanation for our results with negative extrathoracic pressure could be an effect similar to that of oxygen therapy, as an increase in mean apnoea duration and in obstructive apnoea with a reduction of mixed and central apnoeas has been reported with oxygen therapy.²⁰ As with oxygen, negative extrathoracic pressure prevented the largest falls in Sao_2 during stage I–II sleep, thus possibly reducing the postapnoea hyperventilation and hypocapnia. Fluctuation in chemical stimuli during sleep and differences between inhibition of upper airway and inspiratory muscles during hypocapnia could affect upper airway patency and contribute to the obstructive apnoea.²¹

Baseline Sao_2 was not modified by negative extrathoracic pressure; the improvement in Sao_2 was related to the desaturation mechanisms during apnoea and not to a shift in the preapnoeic Sao_2 . An increased intrathoracic oxygen store at the beginning of an apnoeic episode and an improved \dot{V}_A/\dot{Q} distribution in dependent zones by negative extrathoracic pressure could explain the lesser desaturation with negative extrathoracic pressure.

As with oxygen therapy,²⁰ apnoea induced desaturation during REM sleep was not modified by negative extrathoracic pressure. Possibly the increase in FRC induced by negative extrathoracic pressure was not sufficient to prevent shunting during this sleep stage. The lack of improvement in Sao_2 with negative

extrathoracic pressure during REM sleep may account for the absence of significant changes in the characteristics of the apnoea during this sleep stage.

As with oxygen therapy, the duration of apnoea increased with negative extrathoracic pressure, whereas the rate and depth of the fall in SaO_2 was reduced. Thus the mechanisms underlying termination of apnoea must include factors other than hypoxaemia.^{22,23}

We conclude that lung volume has an important influence on the pathophysiology of apnoea, particularly the apnoea induced fall in SaO_2 and, possibly as a consequence, the apnoea time composition. Our results suggest that the therapeutic effect of low levels of continuous positive airway pressure are related more to change in upper airway pressure (inspiratory and expiratory) than to lung inflation.

This study was supported by the Fondation JD Bégin de l'Université Laval.

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