Effect of reduced expiratory pressure on pharyngeal size during nasal positive airway pressure in patients with sleep apnoea: evaluation by continuous computed tomography

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Abstract
Background **This study aimed to determine whether reducing the expiratory pressure during nasal positive airway pressure for reasons of comfort causes a substantial decrease in the upper airway calibre.**
Methods **Eight patients with obstructive sleep apnoea were studied. Continuous computed tomography (each run lasting 12 seconds) was used to measure minimum and maximum pharyngeal cross sectional areas at the velopharynx and the hypopharynx. Pharyngeal areas were measured while patients were awake and breathing without assistance, during the application of 12 cm H_2O continuous positive airway pressure, and during bi-level positive airway pressure with an inspiratory pressure of 12 cm H_2O and an expiratory pressure of 6 cm H_2O.**
Results **Nasal continuous positive airway pressure significantly increased the mean minimum and maximum upper airway areas at both the velopharynx and the hypopharynx compared with normal unassisted breathing. Bi-level positive airway pressure did not show a statistically significant increase in the minimum upper airway area at either level compared with normal unassisted breathing. The minimum areas of the velopharynx and hypopharynx were smaller with bi-level than continuous positive airways pressure in six of eight and eight of eight patients respectively but these were still greater than during unassisted breathing in seven of eight and six of eight patients respectively.**
Conclusions **Continuous positive airway pressure at 12 cm H_2O is more effective in splinting the pharynx open than bi-level positive airway pressure with an inspiratory positive airway pressure of 12 cm H_2O and an expiratory pressure of 6 cm H_2O in patients with obstructive sleep apnoea during wakefulness, suggesting an important role for expiratory positive airway pressure. The clinical importance of this finding needs to be evaluated during sleep**

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Nasal continuous positive airway pressure (CPAP) is an established treatment for obstructive sleep apnoea.[1][2] With pressures of 10 cm H_2O or higher, however, the resistance felt during expiration and the required tightness of the nose mask can be unpleasant for the patient and may therefore impair treatment compliance. To overcome these difficulties a more sophisticated technique, a bi-level positive airway pressure device (Bi-PAP; Respironics Inc, Monroeville, PA, USA) has been developed that allows separate adjustments of inspiratory and expiratory positive airway pressures.

Numerous studies have investigated the dimensions of the upper airways in awake subjects and discussed their importance with regard to sleep apnoea.[3-11] Two groups succeeded in obtaining computed tomograms during sleep and found that upper airways were narrower than during wakefulness.[12][13] In a recent review on the mode of action of nasal CPAP, Sullivan and Grunstein stated that 'all the evidence points to its action as a physical pressure splint as the dominant reason for its success'.[14] The results of a study using endoscopic observation and a recent study measuring pharyngeal volume by magnetic resonance imaging provide further evidence that nasal CPAP works mainly by enlarging the pharyngeal size and splinting the airway open.[15][16] It is not known, however, whether Bi-PAP is as efficient in dilating the upper airway as conventional CPAP or whether the greater comfort of lower expiratory pressures permits a substantial reduction in the upper airway calibre. We used computed tomography to determine the effect of CPAP and Bi-PAP on upper airway calibre in awake patients suffering from obstructive sleep apnoea.

Methods

SUBJECTS AND SLEEP STUDIES
Eight men (mean (SD) age 53 (6·7) years, mean body mass index 32 (5) kg/m^2) with a diagnosis of obstructive sleep apnoea took part in the study. Overnight polysomnography (mean (SD) apnoea/hypopnoea index 55 (10·3)) was performed between six and 12 months before the study in all patients. Oronasal flow was monitored with thermocouples and thoracoabdominal movement by inductance plethys-

mography (Respitrace, Respitrace, Ardsley, NY, USA). Sleep was monitored by recording the electroencephalogram (silver cup electrodes, F0 C0 P0 T4 T3), electromyogram (submental and nuchal), and electro-oculogram (four electrodes outside and above the outer canthi). Finger oxygen saturation was monitored with an Ohmeda Biox 3700 oxymeter. All signals were recorded on an 18 channel van Gogh polygraph. Sleep stage was determined by the criteria of Rechtschaffen and Kales.[17] Any cessation in airflow that lasted longer than 10 seconds was scored as an episode of apnoea. Obstructive apnoea was considered present when an episode of apnoea was associated with inductance plethysmography deflections indicating thoracoabdominal movement. A > 50% decrease in thoracoabdominal amplitude (shown on the Respitrace) for 10 seconds or longer in the presence of continued airflow was scored as hypopnoea.[18] Seven patients were having CPAP treatment at home and patient 8 was waiting for his CPAP ventilatory support system to be delivered. The mean (SD) CPAP value of the eight patients was 10·8 (2·8) cm H_2O.

Informed consent was obtained and the investigation was approved by the hospital authority.

POSITIVE AIRWAY PRESSURE DEVICE
A Bi-PAP S/T-D ventilatory support system (Respironics Inc, Monroeville, PA, USA) was used for CPAP and Bi-PAP. This device allows separate ajustment of inspiratory (IPAP) and expiratory (EPAP) positive airway pressure. In this study the pressure was set at 12 cm H_2O for CPAP. IPAP was set at 12 cm H_2O and EPAP at 6 cm H_2O during Bi-PAP application. The spontaneous mode was used for Bi-PAP. The pressures were calibrated by a water manometer. The patients used their own face masks (Respironics Inc) to ensure a good fit and comfort. Practice runs were performed immediately before computed tomography.

COMPUTED TOMOGRAPHY
A third generation scanner with continuous rotation capabilities (Somatom Plus, Siemens Company, Germany) was used. Computed tomography of the upper airways was performed with the head in a neutral, supine position and the subjects awake. Head position was maintained constant by a harness. A lateral view (topographic scout view) was taken to determine the scanning levels. Two parallel sections perpendicular to the posterior pharyngeal wall were selected, one at the level of the soft palate (velopharynx) and the other above the tip of the epiglottis (hypopharynx). The slice thickness was 1 mm, the tube current 150 mA. All computed tomography was performed during quiet tidal breathing without breathholding.[7 9] The patients were instructed to keep their mouth closed, not to move at any time during the examination, and not to swallow when the scans were being performed. Patients were reminded of these instructions before each scanning run.

The computed tomography computer was

always started at the end of an inspiration, determined by observation. The time gap between starting the computer and the actual acquisition of an image sequence was three seconds. During each run (image acquisition sequence), computed tomography projections (raw data) were continuously acquired for 12 seconds and included at least two full respiratory cycles.

Since the projections obtained over 0·7 seconds (corresponding to 0·7 seconds of a full rotation) were the minimum required to reconstruct an image, 23 overlapping 0·7 second images were reconstructed at intervals of 0·5 seconds from the raw data of a single sequence. Hard copies were taken at a window width of 600 HU and a level of + 40 HU.

The cross sectional areas of the upper airways were measured semiautomatically using experimental software designed for quantitative densitometric pulmonary studies.[19 20] A starting point inside the lumen of the upper airway was indicated manually (with the cursor) on the monitor. Including adjacent pixels of densities between − 100 and − 1024 HU, an automatic and precise tracing of the airway circumference (fig 1) and determination of the airway area was then performed by the computer. The accuracy of airway calibre determination by computed tomography had been verified in an earlier study.[21] If necessary, user interaction served to verify inclusion of only the functional air column behind the soft palate—that is, to exclude the non-functional airway between the tongue and the soft palate. In the lower hypopharyngeal airway, the area occupied by the tip of the epiglottis was included in the cross sectional measurements in cases where it became visible.

From each single computed tomography sequence (each of 23 images) the images with the minimum and maximum cross sectional area were used for comparisons.

PROTOCOL
In each patient a total of six computed tomography sequences were obtained during
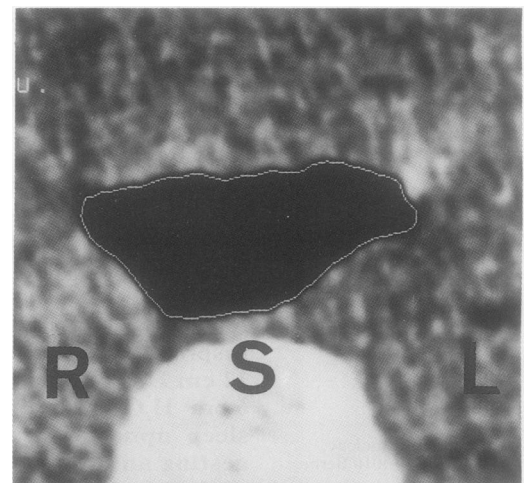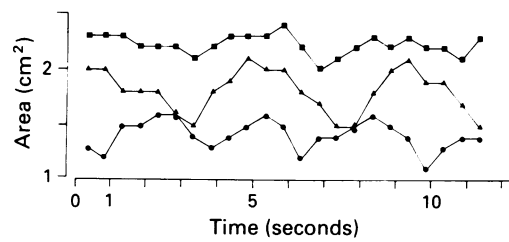

Figure 1 Computed tomogram of the velopharynx during bi-level positive airway pressure. The circumference of the airway is outlined by automatic electronic cursor (see Methods). R = right; L = left; S = spine.

Figure 2 Changes in the cross sectional area of the velopharynx in patient No 4 over three 12 second computed tomography sequences during spontaneous breathing (circles), constant positive airway pressure (CPAP) (squares) and bi-level positive airway pressure (Bi-PAP) (triangles).

Results

Figure 2 shows the effects of both CPAP and Bi-PAP on upper airway dimensions and their periodic variability in one patient. The tracings show the changes in cross sectional areas at the velopharyngeal level registered during three 12 second scanning sequences.

The effects of nasal CPAP and Bi-PAP on the minimum and maximum cross sectional areas of both velopharynx and the hypopharynx are shown in figures 3 and 4, and in table 1. Three findings appear noteworthy. Firstly, in line with previous studies a CPAP of 12 cm H_2O considerably and significantly increased the minimum and maximum cross sectional areas of both the velopharynx and the hypopharynx. Secondly, compared with the data obtained during unassisted breathing the effects of Bi-PAP were less consistent: only the increase of the maximum area at the velopharynx reached statistical significance. At the hypopharynx, however, three out of eight patients did not show any appreciable airway widening. Lastly, between the CPAP and Bi-PAP applications there was a conspicuous and highly significant difference in the mean minimal cross sectional area of the hypopharynx.

quiet tidal breathing. Three of the six sequences were obtained at the velopharynx and three at the hypopharynx. Twenty three images per sequence were obtained during each of the six 12 second periods of continuous scanning in each patient (6 × 23 images per patient).

Firstly, the three computed tomography sequences at the velopharynx were obtained. Sequence one was obtained while the patients wore the nose mask but were not being subjected to PAP. Sequence two was obtained during CPAP and sequence three during Bi-PAP via a nose mask.

Secondly, the three sequences at the hypopharynx were obtained in the same order.
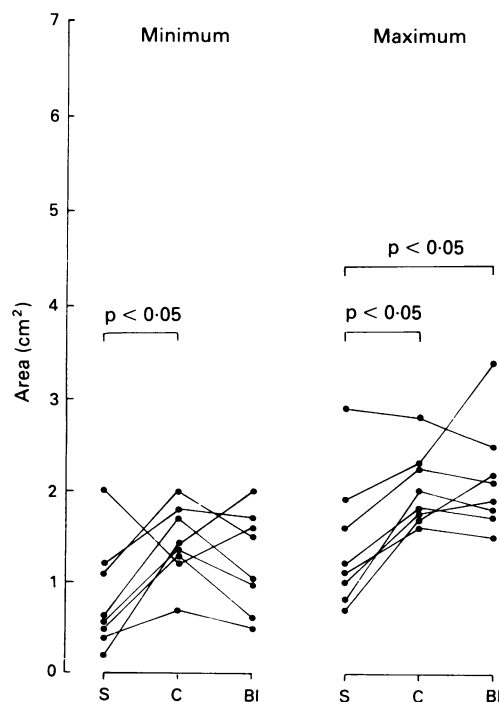
The patients were on CPAP or Bi-PAP respectively for 2 minutes before each scan with PAP.

The patients could not be blinded to the three procedures and therefore a fixed order of administration of no PAP, CPAP, and Bi-PAP was chosen.

STATISTICAL ANALYSIS
One way analysis of variance and Duncan's multiple range post hoc test were used to compare pharyngeal areas. The significance level was taken to be $p < 0.05$. Mean (SD) values are given.

Discussion

The most important finding of this study is that dilatation of the upper airway is reduced during Bi-PAP breathing at the chosen pressure settings, as reflected by the insignificant increases in the crucial minimum cross sectional areas at both the velopharynx and hypopharynx. The

*Figure 3 Individual minimum and maximum upper airway cross sectional areas of the velopharynx.
S = spontaneous breathing without positive airway pressure, C = constant positive airway pressure, BI = bi-level positive airway pressure. Only significant p values are shown.*
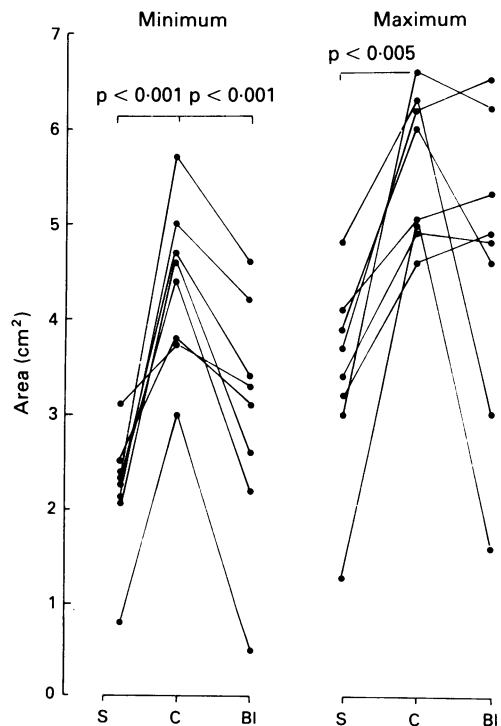

*Figure 4 Individual minimum and maximum upper airway cross sectional areas of the hypopharynx.
S = spontaneous breathing without positive airway pressure application, C = constant positive airway pressure, BI = bi-level positive airway pressure. Only significant p values are shown.*

Mean cross sectional upper airway areas (cm^2)

	Velopharynx						Hypopharynx					
	Spontaneous		CPAP		Bi-PAP		Spontaneous		CPAP		Bi-PAP	
	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
Mean	0·83	1·40	1·44	2·04	1·24	2·14	2·20	3·43	4·38	5·56	2·99	4·61
(SD)	(0·58)	(0·73)	(0·40)	(0·40)	(0·54)	(0·60)	(0·65)	(1·03)	(0·83)	(0·77)	(1·27)	(1·62)

CPAP = constant positive airway pressure; Bi-PAP = bi-level positive airway pressure.

comparative data obtained in the same patients during CPAP application, which are consistent with the results observed in previous studies,[7][8][22] confirm that the relative lack of effect of Bi-PAP is not a consequence of patient selection or of technical problems.

Several factors in the current study must be considered. Firstly, because ultrafast cine computed tomography was not available we were not able to monitor precisely the dimensional changes of the upper airways within a single respiratory cycle. Instead, a modern general purpose scanner was used with continuous rotation and scanning, typically at a rate of one rotation per scan. We chose 700 ms scans, and by reconstructing them every 500 ms obtained some temporal overlap. Hence, it is possible that some short-lasting volume changes of the pharynx have been missed. This disadvantage, however, is probably outweighed by the continuous data acquisition over a longer period of time. An additional technical problem pertains to the determination of the cross sectional areas of the pharynx. Since the drawing of airway circumferences and the calculation of cross sectional areas are by computer, a user-dependent bias can be excluded. Previous evaluation of the method used in this study is reassuring and our data compare favourably with those of others.[5][12][19-21]

Secondly, can data obtained during wakefulness be extrapolated to sleeping patients. Making measurements during sleep would be most accurate but this is difficult to achieve with today's technology[3-11] and thus only scanty computed tomography data during sleep are available.[12][13] Evidently, the effect of any PAP-application as therapy for sleep apnoea must eventually be ascertained by polysomnographical studies. There is, however, considerable evidence that the finding of a splinting effect of PAP-application during wakefulness has some predictive power to choose an adequate modality to treat patients with sleep apnoea.[14][16][23]

Finally, one might argue that the insufficient effect of Bi-PAP observed in this study was predictable as the average pressure over a respiratory cycle was lower (about 9 cm H_2O) than during CPAP (12 cm H_2O). Indeed, it is possible that by increasing the Bi-PAP to an average pressure of 12 cm H_2O, a significant effect on upper airway dimensions may be achieved. This study could not check this by a dose-response relation with Bi-PAP, but recent studies indicate that the problem is complex. Kuna *et al*[8] have shown an approximately linear relation between the CPAP level and upper airway calibre. On the assumption that the average pressure is the most relevant parameter, a more noticeable effect of Bi-PAP should have been detectable in the present study. The relatively small number of patients studied may be responsible for the fact that differences in upper airway size between Bi-PAP and both CPAP and no PAP were not clearly seen. However, by inference from a careful polysomnographical study it appears that the expiratory pressure is of considerable importance in that it may influence the effect of inspiratory pressure.[24]

It has been shown that patients with obstructive sleep apnoea have a smaller pharyngeal area[4][11][22] and that longstanding CPAP treatment increases the pharyngeal area during breathing without PAP compared with pre-treatment measurements.[25] Furthermore, it has been shown that pharyngeal transverse diameters are smaller in patients than in healthy subjects.[26] In this study, visual inspection
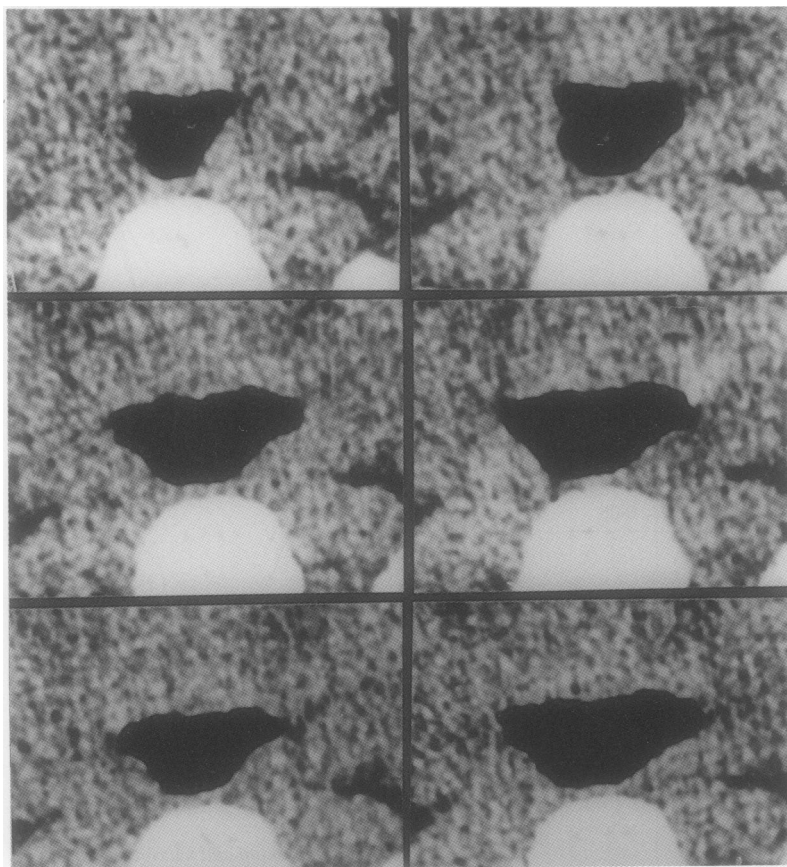

Figure 5 Computed tomograms showing minimum (left) and maximum (right) airway area at the velopharynx during spontaneous breathing without positive airway pressure application (top), with constant positive airway pressure (middle) and bi-level positive airway pressure (bottom) application. For orientation see figure 1.

of the computed tomograms showed clearly that the increase in pharyngeal area with CPAP or Bi-PAP was mainly the consequence of an increased transverse diameter in all subjects, illustrated in one patient in figure 5. Thus, CPAP or Bi-PAP seem to increase the size of the upper airway by restoring its physiological shape.

In conclusion, Bi-PAP with an inspiratory pressure of 12 cm H_2O an an expiratory pressure of 6 cm H_2O seems to be much less effective in splinting the upper airway open than a CPAP of 12 cm H_2O. This finding in awake patients with obstructive sleep apnoea is of physiological interest but further sleep studies are required to determine its clinical relevance.

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