Effects of posture on carbon dioxide responsiveness in patients with obstructive sleep apnoea

M Satoh, W Hida, T Chonan, S Okabe, H Miki, O Taguchi, Y Kikuchi, T Takishima

Abstract

Background—It is well known that upper airway resistance increases with postural change from a sitting to supine position in patients with obstructive sleep apnoea (OSA). It is not known, however, how the postural change affects the ventilatory and occlusion pressure response to hypercapnia in patients with OSA when awake.

Methods—The responses of minute ventilation (VE) and mouth pressure 0-1 seconds after the onset of occluded inspiration (P01.) to progressive hypercapnia (ΔVE/ΔPCO2, ΔP01./ΔPCO2) both in sitting and supine positions were measured in 20 patients with OSA. The ratio of the two (ΔVE/ΔP01.) was obtained as an index of breathing efficiency. The postural changes in response to carbon dioxide (CO2) after uvulopalatopharyngoplasty (UPPP) were also compared in seven patients with OSA.

Results—There were no significant changes in the resting values of end tidal PCO2, P01., or VE between the two positions. During CO2 rebreathing, ΔVE/ΔPCO2 did not differ between the two positions, but ΔP01./ΔPCO2 was significantly higher in the supine than in the sitting position (supine, mean 0.67 (SE 0.09) cm H2O/mm Hg; sitting, mean 0.57 (SE 0.08) cm H2O/mm Hg), and ΔVE/ΔP01. decreased significantly from the sitting to the supine position (sitting, 4.6 (0.4) l/min/cm H2O; supine, 3.9 (0.4) l/min/cm H2O). In seven patients with OSA who underwent UPPP, ΔVE/ΔP01. improved significantly in the supine position and postural change in ΔVE/ΔP01. was eliminated.

Conclusions—These results suggest that in patients with OSA the inspiratory drive in the supine position increases to maintain the same level of ventilation as in the sitting position, and that the postural change from sitting to supine reduces breathing efficiency. Load compensation mechanisms of patients with OSA appear to be intact while awake in response to the rise in upper airway resistance.

Patients with obstructive sleep apnoea (OSA) have higher upper airway resistance than normal subjects1 2 and show decreased pharyngeal size and an increase in upper airway resistance on postural change from sitting to supine positions, even while awake.13 5 Moreover, the ratio of the forced expiratory flow to the forced inspiratory flow at mid vital capacity as an index of upper airway obstruction4 increases in the supine position compared with the sitting position in these patients,1 which suggests that they may have greater resistive loading in the supine than in the sitting position. Rajagopal et al6 studied the response of ventilation and occlusion pressure to hypercapnia without and with the application of a flow resistive load in patients with OSA and found that the level of ability to compensate for the externally added inspiratory loads was impaired. We therefore hypothesise that the respiratory neuromuscular drive to hypercapnia in patients with OSA may not increase despite an increase of respiratory impedance in the supine position compared with the sitting position. It is not known, however, how postural change affects the ventilatory and occlusion pressure responses to hypercapnia in such patients while awake.

The purpose of this study was to examine postural effects on the respiratory response to hypercapnia and to compare these with postural changes in response to hypercapnia after uvulopalatopharyngoplasty (UPPP) in patients with OSA.

Methods

Subjects and Sleep Studies

The study was carried out in 20 patients (19 men, one woman) with OSA previously diagnosed by polysomnography according to the definitions proposed by Guilleminault and coworkers.6 All patients had a history of snoring and complained of excessive daytime sleepiness. Eight patients complained of morning headache. They were free of complications such as lung disease or heart failure, but the one female patient had rheumatoid arthritis. The anthropometric data, spirometry, blood gas measurements, haemoglobin concentrations, and polysomnographic data of the patients are shown in table 1.

Vital capacity (VC) and forced expiratory volume in one second (FEV1) were measured...
with a 13.5 l spirometer (Tatebe Seishudo Co, Tokyo, Japan), and arterial blood gas tensions and pH were measured with a pH/blood gas analyser (Model 213 Instrumentation Laboratories, Lexington, USA). Spirometry and sampling of arterial blood from the radial artery were performed in the sitting position. Overnight sleep studies were recorded in a quiet darkened room using standard polysomnographic techniques including recording of electroencephalograms (C3/A1; C4/A2), electro-oculograms, and submental electromyograms with surface electrodes to determine sleep stages.10 Air flow at the nose and mouth was recorded with two thermistors and respiratory effort was assessed with an inductive plethysmograph (Respiritrace; Ambulatory Monitoring Inc., Ardsley, New York, USA) at the level of the mid thorax and umbilicus. Oxygen saturation was measured continuously with a pulse oximeter (Biox 3700; Ohmeda, Boulder, Colorado, USA). All variables were reset of inspiration and expiration with an eight-channel thermal pen recorder (Model 360; NEC Sanei, Tokyo, Japan) and a data recorder (A-109; Sony, Tokyo, Japan).

Written informed consent was obtained from each subject before the start of the study, which was approved by the institution's committee on human research.

MEASUREMENTS OF PULMONARY AND UPPER AIRWAY FUNCTION

Resting values of breathing frequency (f), tidal volume (Vt) and minute ventilation (VE) were measured with the spirometer.

In 16 subjects forced inspiratory and expiratory flow-volume curves were measured with a direct pen writing recorder (OST-70D Chest, Tokyo, Japan).11 Three reproducible flow-volume curves were obtained in each patient and the highest values for both the forced expiratory and inspiratory flows at mid vital capacity (FEF25 and FIF25, respectively) were calculated. The ratio of FEF25 to FIF25 (FEF25/FIF25) was also adopted as an index of extrathoracic airway obstruction.4 Patients were coached to avoid neck flexion and extension and to perform maximal expiratory and inspiratory effort in the two postures.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45 (9-6)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>166 (5-6)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77 (13-0)</td>
</tr>
<tr>
<td>VC (% pred)</td>
<td>104 (14-6)</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>80 (6-4)</td>
</tr>
<tr>
<td>pH</td>
<td>7.40 (0-05)</td>
</tr>
<tr>
<td>Pao2 (mm Hg)</td>
<td>77-3 (9-1)</td>
</tr>
<tr>
<td>Paco2 (mm Hg)</td>
<td>39-1 (3-6)</td>
</tr>
<tr>
<td>Haemoglobin concentration (g/dl)</td>
<td>15-8 (2-0)</td>
</tr>
<tr>
<td>Apnoea index (episodes/hour)</td>
<td>56-2 (16-9)</td>
</tr>
<tr>
<td>Longest apnoea duration (s)</td>
<td>82-4 (31-4)</td>
</tr>
<tr>
<td>Lowest Sao2 during sleep (%)</td>
<td>56-6 (20-3)</td>
</tr>
</tbody>
</table>

VC—slow vital capacity; FEV1—forced expiratory volume in one second; FVC—forced vital capacity; Pao2—arterial oxygen pressure; Paco2—arterial carbon dioxide pressure.

CO2 RESPONSIVENESS AND BREATHING EFFICIENCY

Respiratory response to hyperoxic hypercapnia was measured by the technique of Read12 four times in each subject, twice while seated and twice while supine, using a circuit previously described.1314 The order of assumed postures was randomised. The subject wore a noseclip and breathed through a mouthpiece connected to a rebreathing circuit. A low dead space two way valve (Model 1900, Hans Rudolph, Kansas City, Missouri, USA) was attached to the mouthpiece. The inspiratory side of the two way valve was connected to a solenoid valve, three way tap, and the rebreathing bag which contained a constant amount (VC+1 litre) of 7% CO2 in O2. The expiratory side of the two way valve was connected to a Fleisch pneumotachograph (No 3), another three way tap, and the rebreathing bag. Air flow was measured with the pneumotachograph and a differential pressure transducer (Validyne MP45 ± 5 cm H2O; Validyne Corporation, Northridge, California, USA). Tidal volume was obtained by electrical integration of the expiratory flow signal and VE was derived from multiplying the accumulation of 10 seconds of tidal breathing by six. End tidal PCO2 and PO2 were continuously monitored at the mouthpiece with a mass spectrometer (WSMR-1400; Westron, Chiba, Japan). Mouth pressure was measured at the mouthpiece using a pressure transducer (Validyne MP45 ± 50 cm H2O). Mouth pressure 0-1 s after the onset of an occluded inspiration (P0.1) was measured with a system previously reported.1314 Occlusion of the solenoid valve was controlled manually by a logic circuit and the valve was occluded once every two to five breaths. Occlusion was induced during the preceding expiration to ensure that the airway was completely occluded at the onset of inspiration. The valve was automatically opened after the first 120 ms of occluded inspiration. The onset of inspiration and expiration was detected electronically by changes in mouth pressure. Circuit resistance was 0-9 cm H2O/l/s and linear to 3 l/s. Both responses of VE and P0.1 to the increase in PCO2 were analysed by linear regression.1214 In calculating the regression lines the values of VE, P0.1, and end tidal PCO2 were averaged every 30 seconds during rebreathing. We obtained the slope of the ventilatory response to hypercapnia (ΔVE/ΔPCO2), the slope of the occlusion pressure response (ΔP0.1/ΔPCO2) and the ratio (ΔVE/ΔPCO2) to ΔP0.1/ΔPCO2 (ΔVE/ΔP0.1). This ratio indicated the increase in ventilation obtained by a given increase in neuromuscular output and was defined as the breathing efficiency during hyperventilation.15 Moreover, we obtained VE and P0.1 at the PCO2 of 60 mm Hg from the regression line by interpolation. Mean values from two regression lines were accepted for individual data.

In the measurement of pulmonary function and ventilatory response to hypercapnia, patients were coached to avoid volume leaks at the mouthpiece and care was taken to keep
Postural effects on ventilatory drive in obstructive sleep apnoea

![Graph](image)

Figure 1 Mean (SE) effects of postural change on the responses of VE (ΔVE/ΔPCO₂, left) and P₁ (ΔP₁/ΔPCO₂, middle) to hypercapnia, and breathing efficiency (ΔVE/ΔP₁, right) in 20 patients. Open bars, sitting; hatched bars, supine.

Table 3 Mean (SE) results of maximal expiratory and inspiratory flow-volume curve in the sitting and supine positions in 16 patients

<table>
<thead>
<tr>
<th>Sitting</th>
<th>Supine</th>
<th>Significance of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (l)</td>
<td>4.14 (0.15)</td>
<td>4.12 (0.14)</td>
</tr>
<tr>
<td>FEF₆₀ (l/min)</td>
<td>3.79 (0.31)</td>
<td>3.67 (0.30)</td>
</tr>
<tr>
<td>P₁ (l/min)</td>
<td>4.30 (0.30)</td>
<td>3.90 (0.25)</td>
</tr>
<tr>
<td>FEF₆₀/FIF₀</td>
<td>0.88 (0.04)</td>
<td>0.94 (0.05)</td>
</tr>
</tbody>
</table>

FVC—forced vital capacity; FEF₆₀—forced expiratory flow at 50% of FVC; FIF₀—forced inspiratory flow at 50% of FVC; FEF₆₀/FIF₀—ratio of forced expiratory flow to forced inspiratory flow at mid vital capacity.

The head, neck, and trunk configuration as constant as possible between the two postures. For each study the height of the rebreathing circuit was adjusted to allow subjects to breathe through the mouthpiece without altering posture.

**STUDIES AFTER UPPP**

Seven patients who had complained of excessive daytime sleepiness, severe snoring, and morning headache, had severe episodes of apnoea and severe desaturation and underwent UPPP for treatment of OSA, were retested 2–6 months after surgery.

**STATISTICAL ANALYSIS**

Matched paired data within groups were compared by the Wilcoxon signed rank test. Values of p<0.05 were considered significant (two tailed test). Data are expressed as means (SE).

**Results**

Figure 1 shows the mean data of CO₂ responsiveness and breathing efficiency in sitting and supine positions in 20 patients. VE response to hypercapnia was similar in the two positions (sitting, mean 2.1 (SE 0.2) l/min/mm Hg; supine, 2.1 (SE 0.2) l/min/mm Hg), but the P₁ response to hypercapnia was significantly higher in the supine than in the sitting position (supine, 0.67 (0.09) cm H₂O/mm Hg; sitting, 0.57 (0.08) cm H₂O/mm Hg, p<0.05). Breathing efficiency (ΔVE/ΔP₁) decreased significantly from the sitting to the supine position (sitting, 4.6 (0.4) l/min/cm cm H₂O; supine, 3.9 (0.4) l/min/cm cm H₂O, p<0.01). As shown in fig 2, the values of VE at PCO₂ of 60 mm Hg were similar in the two positions (sitting, 36.0 (2.7) l/min; supine, 35.7 (2.7) l/min), but the value of P₁ at PCO₂ of 60 mm Hg was significantly higher in the supine than in the sitting position (supine, 9.5 (1.0) cm H₂O; sitting, 8.3 (0.9) cm H₂O, p<0.05).

There were no significant changes in VE, VT or f between the two positions, nor for the resting values of end tidal Pco₂ or P₁ (table 2). FEF₆₀ was also similar for the two positions but FIF₀ was smaller in the supine position. FEF₆₀/FIF₀ was significantly greater in the supine than in the sitting position (table 3).

In the seven patients who underwent UPPP the apnoea index decreased significantly from 56.4 (2.8) episodes/hour to 36.0 (7.9) episodes/hour (p<0.05) and the lowest Sao₂ increased from 50.6% to 63.6% (p<0.01). Following UPPP body weight decreased in five patients but increased in two; as a whole, however, there were no significant changes in body weight before and after UPPP (before UPPP, 75 (1.6) kg; after UPPP, 71 (1.4) kg).

Table 4 shows ventilatory and occlusion pressure responses to hypercapnia in the seven patients before and after UPPP, both in the sitting and supine positions. Before UPPP, ΔP₁/ΔPCO₂, P₁, at PCO₂ of 60 mm Hg, and FEF₆₀/FIF₀ in the supine position increased

![Graph](image)

Figure 2 Mean (SE) effects of postural change on minute ventilation (VE, left) and occlusion pressure (P₁, right) at an PCO₂ of 60 mm Hg in sitting and supine positions. Open bars, sitting; hatched bars, supine.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sitting (SE)</th>
<th>Supine (SE)</th>
<th>Significance of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>P₁ (cm H₂O)</td>
<td>5.0 (0.3)</td>
<td>6.0 (0.4)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>VE (l/min)</td>
<td>40 (2.5)</td>
<td>45 (3.0)</td>
<td>NS</td>
</tr>
<tr>
<td>VT (l)</td>
<td>0.65 (0.12)</td>
<td>0.62 (0.14)</td>
<td>NS</td>
</tr>
<tr>
<td>f (min⁻¹)</td>
<td>16 (3.1)</td>
<td>15 (3.1)</td>
<td>NS</td>
</tr>
<tr>
<td>F₁ (l/min)</td>
<td>2.4 (0.5)</td>
<td>2.5 (0.6)</td>
<td>NS</td>
</tr>
</tbody>
</table>

VE—minute ventilation; VT—tidal volume; f—breathing frequency; Pₑ₁—mouth pressure 0.1 s after the onset of occluded inspiration; NS—not significant.
Table 4 Mean (SE) hypercapnic responses and maximal expiratory and inspiratory flow-volume curves in sitting and supine positions before and after UPPP in seven patients with OSA

<table>
<thead>
<tr>
<th>Sitting</th>
<th>Before UPPP</th>
<th>After UPPP</th>
<th>p&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Supine</th>
<th>Before UPPP</th>
<th>After UPPP</th>
<th>p&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔVE/ΔPCO₂</td>
<td>2·3 (0·3)</td>
<td>2·6 (0·3)</td>
<td>NS</td>
<td>2·3 (0·4)</td>
<td>3·1 (0·3)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>ΔP₀₁/ΔPCO₂</td>
<td>0·53 (0·10)</td>
<td>0·61 (0·08)</td>
<td>NS</td>
<td>0·71 (0·17*)</td>
<td>0·64 (0·06)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>ΔVE/ΔP₀₁</td>
<td>4·6 (0·6)</td>
<td>4·6 (0·6)</td>
<td>NS</td>
<td>3·8 (0·4*)</td>
<td>4·9 (0·4)</td>
<td>&lt;0·05</td>
<td></td>
</tr>
<tr>
<td>FEF&lt;sub&gt;25&lt;/sub&gt;/FEF&lt;sub&gt;50&lt;/sub&gt;</td>
<td>37·7 (4·4)</td>
<td>40·5 (2·0)</td>
<td>NS</td>
<td>39·2 (4·9)</td>
<td>45·9 (3·2)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>P₀₁ at 60 mm Hg</td>
<td>7·5 (1·1)</td>
<td>8·7 (0·9)</td>
<td>NS</td>
<td>10·1 (1·3*)</td>
<td>9·1 (0·8)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>FEF&lt;sub&gt;50&lt;/sub&gt; (0/min)</td>
<td>4·38 (0·42)</td>
<td>4·46 (0·52)</td>
<td>NS</td>
<td>4·22 (0·45)</td>
<td>4·20 (0·46)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>FIF&lt;sub&gt;25&lt;/sub&gt; (0/min)</td>
<td>4·90 (0·36)</td>
<td>5·17 (0·29)</td>
<td>NS</td>
<td>4·36 (0·27*)</td>
<td>4·82 (0·34)</td>
<td>&lt;0·05</td>
<td></td>
</tr>
<tr>
<td>FEF&lt;sub&gt;50&lt;/sub&gt;/FIF&lt;sub&gt;25&lt;/sub&gt;</td>
<td>0·88 (0·05)</td>
<td>0·86 (0·09)</td>
<td>NS</td>
<td>0·96 (0·06*)</td>
<td>0·81 (0·08)</td>
<td>&lt;0·05</td>
<td></td>
</tr>
</tbody>
</table>

UPPP—uvulopalatopharyngoplasty; ΔVE/ΔPCO₂—slope of ventilatory response to hypercapnia; ΔP₀₁/ΔPCO₂—slope of occlusion pressure response to hypercapnia; ΔVE/ΔP₀₁—ratio of increase in P₀₁ to ΔP₀₂/ΔPCO₂.

<sup>p<0·05</sup> (significance between sitting and supine before or after UPPP).
<sup>1</sup>Comparison before and after UPPP (significance between sitting and supine before or after UPPP).

significantly, and ΔVE/ΔP₀₁ and FIF<sub>50</sub> in the supine position decreased significantly compared with the corresponding values in the sitting position. These findings were consistent with data obtained from all patients (figs 1, 2, and table 3). There were no differences in any parameters before and after UPPP in the sitting position. The differences in the supine position before UPPP were eliminated after surgery. Furthermore, after UPPP ΔVE/ΔP₀₁ and FIF<sub>50</sub> in the supine position increased significantly, and the supine FEF<sub>50</sub>/FIF<sub>25</sub> fell significantly compared with the corresponding value in the supine position before UPPP.

Discussion
The study showed that the VE response to hypercapnia was unaffected by posture but that the P₀₁ response to hypercapnia was greater in the supine than in the sitting position in patients with OSA. Furthermore, the breathing efficiency (ΔVE/ΔP₀₁) was less when supine than when sitting. Following UPPP there was no change in the ventilatory drive and efficiency parameters while sitting, but the breathing efficiency improved in the supine position.

There are several explanations for the increased P₀₁ responses to hypercapnia in the supine position despite the lack of the positional effect on the VE response to hypercapnia. Firstly, as the postural change from sitting to supine decreases functional residual capacity (FRC), this causes an increase in the resting length of the diaphragm<sup>14</sup> and a shift in its force-length relationship to a more favourable position with an increase in its contractile efficiency.<sup>17</sup> Furthermore, Xie et al<sup>18</sup> showed that VE and diaphragmatic EMG activity responses to hypercapnia were not affected by posture. The EMG activity of the scalene muscle, however, increased to overcome the gravitational load of the thoracic cage when moving from the supine to the sitting position. Lopata et al<sup>19</sup> also showed that although diaphragmatic EMG was not affected by posture at high ventilatory rates during hypercapnia, increases in the expiratory abdominal muscle activity were observed, particularly in the upright position. These two studies suggest that the respiratory control system appears to adjust the neuromuscular output to maintain the same ventilatory output between the two postures. The augmented P₀₁ response to hypercapnia found in our study may be explained by a similar adjustment of neuromuscular drive during the change in FRC associated with postural change.

Although we did not measure FRC, we could estimate changes in FRC with posture spirometrically with the assumption that residual volume was independent of posture.<sup>4</sup> In our study the decrease in FRC was a maximum of 0·20–1·01 (mean (SE) 0·41 (0·26) litres) from the sitting to the supine position, which was within the range reported in normal subjects.<sup>10,20–22</sup> It is therefore unlikely that change in FRC causes the increase in P₀₁ response to hypercapnia observed in the supine position in patients with OSA.

Although we did not directly measure upper airway resistance, it has been reported that patients with OSA have higher values than normal subjects<sup>1,2</sup> and show decreased pharyngeal size and an increase in upper airway resistance on postural change, even when awake.<sup>1,3–5</sup> We found an increase in FEF<sub>50</sub>/FIF<sub>25</sub> in the supine position which may mean that patients with OSA have greater upper airway resistance when supine. An increased P₀₁ response to hypercapnia in the supine position in patients with OSA therefore suggests an ability to compensate for the increase in upper airway resistance. This is supported by the fact that after UPPP both VE and P₀₁ responses to hypercapnia were less affected by posture as has been reported in previous studies on normal subjects.<sup>10,20–22</sup>

The elimination of postural effects on the breathing efficiency after UPPP is probably caused by a disappearance of the load compensation mechanisms associated with a decrease in upper airway resistance in the supine position following surgery. This decrease would be supported by a fall in supine FEF<sub>50</sub>/FIF<sub>25</sub> together with an increase in FIF<sub>50</sub>. We therefore suggest that the load compensation mechanisms for the increase in upper airway resistance in patients with OSA after UPPP are present at least while they are awake.

It is not clear whether compensation for an
increase in the internal loads operates equally during sleep as the measurements were all made while the subjects were awake. During sleep the upper airway muscles become more hypotonic and the airway becomes narrower both in normal subjects and in patients with OSA.\textsuperscript{23,24} Greater activation of inspiratory muscles is therefore required to maintain ventilation, but this may not occur as the load compensation ability of respiratory muscles is less during sleep than when awake.\textsuperscript{25-27} Moreover, increased activity of the inspiratory muscles without recruitment of upper airway dilating muscles could worsen upper airway obstruction. Further studies are needed to elucidate the actual load compensation of both upper airway and inspiratory muscles in response to positionally induced mass loading of the upper airway, especially during sleep.

We would like to thank Mr G Crittenden for his help in preparation of the manuscript and Drs N Iwase and C Miura for their technical assistance.

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