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Breath-holding Time in Normal Subjects, Snorers, and Sleep Apnea Patients*

Varsha Taskar, MD; Nigel Clayton, HNC; Mark Atkins, HNC, BSc; Zubair Shaheen, MD; Patricia Stone, MB, ChB; Ashley Woodcock, MD, FCCP

Background: The onset of irregular inspiratory muscle activity has been observed toward the breakpoint of the breath-holding maneuver. We wondered if this was similar to the increased respiratory effort with paradoxical breathing seen during the resolution of an apnea in obstructive sleep apnea syndrome (OSAS).

Study objective: To compare the breakpoint of breath holding in normal subjects, OSAS patients, and snorers.

Methods: Thirty normal subjects, 30 patients with OSAS, and 16 snorers performed serial breath-holding maneuvers at functional residual capacity (FRC) under standardized pretest conditions using the rebreathing method of Read.

Results: Intergroup comparisons were carried out by analysis of variance with post hoc Tukey’s Highest Significant Difference tests. Basal end-tidal carbon dioxide (EtCO2) was significantly higher in OSAS than in normal subjects and snorers. Basal breath-holding time (BHT) was shorter in OSAS as compared with that in normal subjects and snorers (p<0.05). The maximal EtCO2 level attained was higher in OSAS as compared with normal subjects (p<0.05) and snorers (p=0.052). The maximal BHT in OSAS was shorter than in normal subjects (p<0.05) but not in snorers. The slope of BHT/EtCO2 differed significantly in OSAS compared with normal subjects and snorers (p<0.05). No significant correlation was found between slope BHT/EtCO2 and age or body mass index using multiple regression analysis. The FRC of OSAS patients and snorers were similar (p=0.792).

Conclusion: We conclude that BHT and slope of BHT/EtCO2 are different in OSAS subjects as opposed to those in normal subjects and snorers. (Chest 1995; 107:959-62)

BHT=breath-holding time; BMI=body mass index; CPAP=constant positive airway pressure; EtCO2=end-tidal CO2; FRC=functional residual capacity; OSAS=obstructive sleep apnea syndrome

Key words: breath holding; respiratory paradox; sleep apnea;

Materials and Methods

Clinical Data

We studied 30 normal subjects, 30 patients with OSAS (mean apnea index, 46.3; SD, 8.3), and 16 snorers (apnea index <5) from the Sleep Clinic at Wythenshawe Hospital, North West Lung Center, United Kingdom. Normal subjects were recruited from the staff members after ruling out respiratory symptoms or oral questioning. All snorers and patients with OSA had overnight polysomnography. All OSAS patients were established on constant positive airway pressure (CPAP) for a median time of 11 months (range, 1 to 38 months) and had normal daytime blood gas values at the time of the study. The CPAP was used for a median of 5.25 h per night (range, 2 to 7 h per night). With this, the OSAS patients had a median arousal index of 10 arousals per hour (range, 3 to 28 arousals per hour). All subjects underwent serial breath-hold measurements at functional residual capacity (FRC) with steadily increasing concentrations of end tidal CO2 (EtCO2), with the rebreathing method of Read.7,8 This method was preferred since the rate of rise of PaCO2 is steady and predictable after the first 20 s of rebreathing, with the PaCO2 remaining independent of lung volume. All measurements were made at the same time of the day.

Respiratory Data

The rebreathing circuit was set up as in Figure 1. Respiratory movements and flow at the airway opening were monitored us-
ing chest and abdomen surface monitors (DENSAD pneumograph DMS-100, DENSAD Ltd, United Kingdom) and a pneumotachograph (Fleisch, Erich Jaeger, Germany), respectively. These were documented on a multichannel recorder (Model No RS 3600, Gould Medical Ltd, Coventry, United Kingdom). The EtCO₂ was recorded with a capnograph (Multicap CNO-103, Datex Instrumentation Corp, Finland). After priming the system with 100% oxygen and calibrating the capnograph, surface apnea monitors, and the pneumotachograph, the patients were connected to the circuit with the nose clip in place. The procedure was explained, and the patients were allowed a settling period of 30 s. The EtCO₂ recorded at this instant was termed as the basal EtCO₂. A change in the EtCO₂ of 1% corresponded to 7.6 mm Hg starting from a pretest level of 0%=0.0 mm Hg. The basal breath-holding maneuver was then performed by giving all patients the identical instruction: “Hold your breath at the end of a normal breath and keep holding it for as long as you can.” At the end of the breath-holding maneuver, the patients remained connected to the circuit and continued to rebreathe. The breath-holding maneuvers were repeated at each 1% increase in EtCO₂ up to the maximal tolerated level or 10% if this was achieved. Tolerance was defined as the maximal discomfort in the form of suffocation, bursting headache, or lightheadedness experienced by the patient and necessitating disconnection from the rebreathing circuit. The EtCO₂ concentration prior to termination of the test was considered the “maximal EtCO₂” and the corresponding BHT was recorded as the “maximal BHT.” One trial run was discarded, and the second set of readings was considered. The BHT was calculated as the period of zero flow recorded on the moving paper recorder. Throughout the test, the inspired oxygen in the breathing circuit was kept greater than 60% to avoid hypoxia. Breath holding with swallowing interference as well as breath holding in which chest and abdominal movements were recorded throughout were discarded.

Each subject had at least three values of BHT at successive EtCO₂ concentrations which were plotted, and the individual slope of BHT/EtCO₂ was derived for each patient.

Statistical Analysis
The values are expressed as mean ± SD. Intergroup comparisons of basal and maximal EtCO₂ and BHT and the slope of their relationship were carried out using simple factorial analysis of variance with post hoc comparison by Tukey’s Highest Significant Difference test. Univariate regression analysis was used to determine the correlation between slope of BHT/EtCO₂ and body mass index (BMI) and age. Statistical significance was considered at a probability of less than 0.05. The analysis was carried out with a statistical software program SPSS version 5 (Statistical Package for Social Sciences, SPSS, Chicago, IL).

RESULTS
In our group of 76 subjects, 30 had OSAS (mean apnea index, 46.3 ± 8.3) and 16 were nonapneic snorers. Their mean age, sex distribution, and BMI are described in Table 1. All patients had normal lung function tests and normal daytime blood gases at the time of the study. The subgroups, therefore, differed only in terms of their BMI and apnea index.

As shown in Table 2, OSAS patients had a significantly higher basal EtCO₂ compared with that of normal subjects and snorers. The basal BHT (seconds) was significantly shorter in OSAS compared with normal subjects and snorers. The maximal EtCO₂ that OSAS subjects could tolerate was significantly higher than in normal subjects but marginally higher than in snorers (p=0.052). The maximal BHT in OSAS subjects was significantly lower than in normal subjects. It was also lower in OSAS subjects as compared with snorers, but the difference did not achieve statistical significance. The proportion of subjects who tolerated an EtCO₂ of more than 8% was significantly greater in OSAS subjects (20 of 30) compared with snorers (8 of 16) and normal subjects (9 of 30 [p=0.018, χ² test]).

The slope of the relationship between BHT and EtCO₂ in OSAS was significantly different from that in normal subjects and snorers. There was no relationship between the slope of BHT/EtCO₂ and age (r=0.3), sex (r=0.1), and BMI (r=0.2) in OSAS subjects and similarly in snorers (age [r=0.3], sex [r=0.4], BMI [r=0.2]) and normal subjects (age [r=0.2], sex [r=0.2], BMI [r=0.1]). Lung function overall was within normal limits and in particular (FRC) values.

![Diagram](https://example.com/diagram.png)
in OSAS patients (2,834 ± 829.5 mL) and snorers (2,920 ± 586.5 mL) were comparable (p=0.792).

**DISCUSSION**

This study shows that OSAS patients have a different relationship between BHT and EtCO2 as compared with normal subjects and snorers. The basal BHT is shorter with a higher basal EtCO2, and the slope BHT/EtCO2 is steeper. The steeper slope could be caused by a curvilinear relationship between BHT/EtCO2 combined with a shift to the right due to the higher basal EtCO2. Respiratory drive may be related to BMI. A previous study showed that BHT was shorter in obese subjects compared with normal subjects, though this was not specifically associated with EtCO2. Miyamura et al11 studied the slope of the hypercapnic ventilatory response and found it to be lower in subjects with a high BMI compared with that of the normal subjects. However, in this study, differences in BHT seen in sleep apnea could not be attributed to obesity or to an abnormality of FRC.

The determinants of a maximal voluntary breath hold are initial lung volume, prior oxygenation, and prior PaCO2. By flushing our rebreathing circuit with 100% oxygen prior to the test, we ensured that hypoxemia or variation in rates of fall of oxygen saturation did not affect the BHT. During the test, the subject’s psychological willpower and endurance influence the duration of the breath holding. The breakpoint of breath holding is preceded by the onset of respiratory movements. These irregular contractions of the inspiratory muscles reduce the unpleasant sensation in the lower thorax and abdomen that occurs progressively through a breath-holding period. Campbell et al13 showed that complete muscle paralysis with curare caused prolongation of the BHT in the absence of the unpleasant sensation of breath holding and concluded that inspiratory muscle activity was the final common pathway determining the breakpoint. The onset of electrical activity during a breath holding period is closely related to the alveolar PaCO2.14

In this study, all patients with OSAS had PaCO2 of less than 45 mm Hg. However in OSAS, after settling on the breathing circuit, the basal EtCO2 was higher than normal subjects or snorers (Table 2). In addition, OSAS patients tolerated breath holding at a higher maximal EtCO2. This may indicate a greater tolerance of inspiratory loading inevitably seen with this experimental setup, perhaps suggesting diminished ventilatory response to CO2.

Another possibility for the shorter BHTs in OSAS and the absence of any difference between snorers and normal subjects can be derived from the continuum hypothesis of sleep-disordered breathing.1516 Accordingly, normal subjects, snorers—which would include a diverse group of symptomatic individuals with and without an increased upper airway resistance (not assessed in the present study), and OSAS patients have a progressive increase in the severity of symptoms associated with a reduction of BHT.

All OSAS patients were already established on nasal CPAP. A previous study on the effect of nasal CPAP on daytime hypercapnic ventilatory response17 showed that the slope of the ventilatory response remains essentially unchanged in the absence of daytime hypercapnia. One mechanism for the depressed ventilatory response to CO2 in OSAS could be sleep fragmentation, since a night of total sleep deprivation produces a reversible decrease in the hypercapnic ventilatory response in normal human volunteers.18 However, in the present study, patients were not sleep-deprived, being already maintained on nasal CPAP and corroborated by their arousal index. A further study would be needed to establish whether breath holding is changed by institution of CPAP therapy.

**Table 1—Characteristics of the Subjects***

<table>
<thead>
<tr>
<th></th>
<th>Normal Subjects</th>
<th>Snorers</th>
<th>OSAS Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>30</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Age, yr</td>
<td>47.4 ± 10.2†</td>
<td>47.0 ± 10.5†</td>
<td>50.3 ± 10.6†</td>
</tr>
<tr>
<td>M to F ratio</td>
<td>26.4</td>
<td>13.3</td>
<td>28.2</td>
</tr>
<tr>
<td>BMI</td>
<td>23.8 (3.3)‡</td>
<td>26.6 (3.8)‡</td>
<td>33.9 (5.5)§</td>
</tr>
<tr>
<td>Apnea index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRC, L</td>
<td>2.9 (0.58)§</td>
<td>2.6 (0.83)§</td>
<td></td>
</tr>
</tbody>
</table>

*Values are expressed as mean ± SD.
†The BMI in OSAS was greater than the BMI in the other two groups (p<0.001).
‡The FRC values in OSAS patients and snorers were comparable (p=0.792).
§The FRC values in OSAS patients and snorers were comparable (p=0.792).

**Table 2—Measured Variables in Normal Subjects, OSAS Patients, and Snorers***

<table>
<thead>
<tr>
<th></th>
<th>Normals</th>
<th>Snorers</th>
<th>OSAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal BHT, s</td>
<td>36.2 ± 12.0</td>
<td>33.6 ± 21.7</td>
<td>20.6 ± 11.9</td>
</tr>
<tr>
<td>Basal EtCO2, %</td>
<td>5.8 ± 0.6</td>
<td>6.0 ± 0.5</td>
<td>6.7 ± 1.2</td>
</tr>
<tr>
<td>Maximal BHT, s</td>
<td>18.4 ± 7.0</td>
<td>16.4 ± 10.5</td>
<td>13.2 ± 6.1</td>
</tr>
<tr>
<td>Maximal EtCO2</td>
<td>7.5 ± 0.7</td>
<td>7.7 ± 1.0</td>
<td>8.3 ± 0.9</td>
</tr>
<tr>
<td>Slope (BHT/EtCO2)</td>
<td>-12.5 ± 4.8</td>
<td>-11.9 ± 10.2</td>
<td>-6.5 ± 5.1</td>
</tr>
<tr>
<td>Subjects with EtCO2&gt;8%</td>
<td>9 of 30</td>
<td>8 of 16</td>
<td>20 of 30**</td>
</tr>
</tbody>
</table>

*Values are mean ± SD.
†Probability value less than 0.05 compared with normal subjects and snorers.
‡Probability value less than 0.05 compared with normal subjects and snorers.
§Probability value less than 0.05 compared with normal subjects (p=0.052 compared with snorers).
¶Probability value less than 0.05 compared with normal subjects (p=NS compared with snorers).
**The χ² test (p=0.018 compared with normal subjects and snorers).
Recent evidence has suggested that increased ventilatory effort may be the stimulus to arousal from sleep. The different threshold for perception of breathing discomfort from the respiratory muscles may explain the variability in the length of apneas prior to arousal in different patients. A further study of the breath-holding response is needed within a large group of patients with OSAS to investigate whether there is any link between the tolerance of respiratory discomfort during a breath-holding maneuver and the length of time to arousal during apnea in patients with OSAS.

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