Heavy snoring with upper airway resistance syndrome may induce intrinsic positive end-expiratory pressure

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Lofaso, Frédéric, Anne Marie Lorino, Redouane Fodil, Marie Pia D’Ortho, Daniel Isabey, Hubert Lorino, Françoise Goldberg, and Alain Harf. Heavy snoring with upper airway resistance syndrome may induce intrinsic positive end-expiratory pressure. J. Appl. Physiol. 85(3): 860–866, 1998.—We studied eight heavy snorers with upper airway resistance syndrome to investigate potential effects of sleep on expiratory airflow and lung resistance, intrinsic positive end-expiratory pressure, hyperinflation, and elastic inspiratory work of breathing (WOB). Wakefulness and non-rapid-eye-movement sleep with high- and with low-resistance inspiratory effort (H-RIE and L-RIE, respectively) were compared. No differences in breathing pattern were seen across the three conditions. In contrast, we found increases in expiratory airflow and lung resistance during H-RIE compared with L-RIE and wakefulness (56 ± 24, 16 ± 4, and 11 ± 4 cmH2O·l−1·s−1, respectively), with attendant increases in intrinsic positive end-expiratory pressure (5.4 ± 1.8, 1.4 ± 0.5, and 1.3 ± 1.3 cmH2O, respectively) and elastic WOB (6.1 ± 2.2, 3.7 ± 1.2, and 3.4 ± 0.7 J·min−1, respectively). The increase in WOB during H-RIE is partly caused by the effects of dynamic pulmonary hyperinflation produced by the increased expiratory resistance. Contrary to the Starling model, a multiple-element compliance model that takes into account the heterogeneity of the pharynx may explain flow limitation during expiration.

In patients with snoring and obstructive hypopnea, partial collapse of upper airways occurs during inspiration. It has been suggested that this can be explained by the Starling resistor theory (26, 28), which predicts that the flow increases with negative intraluminal driving pressure only up to a critical value. Above this critical value, greater collapse occurs and there is no further increase in flow despite a greater inspiratory effort. The occurrence during sleep of labored inspiratory effort is generally ascribed to this phenomenon, which is called flow limitation (11, 27). Expiratory resistance has received much less attention. On the one hand, the expiratory resistance of the upper airways is generally assumed to be normal in the absence of negative intraluminal pressure. On the other hand, studies relating to obstructive sleep apnea syndrome (OSAS) and heavy snorers (13, 23, 29) have found an increase in upper airway expiratory resistance not explained by the Starling resistor theory.

Studies in chronic obstructive pulmonary disease (COPD) patients have demonstrated that expiratory narrowing of the airway facilitates dynamic pulmonary hyperinflation, which is characterized by the persistence of a positive elastic recoil of the respiratory system at the end of expiration (22). Hyperinflation is usually assessed by measuring intrinsic positive end-expiratory pressure (PEEPi), defined as the difference between end-expiratory alveolar pressure and atmospheric pressure (Patm). The most important clinical consequence of PEEPi is an increase in the patient’s energy cost of breathing because of the fact that the inspiratory muscles must counterbalance the positive alveolar pressure before inspiratory flow can occur (22); this imposes an extra load on the inspiratory muscles.

We hypothesized that, if the largest component of the increased inspiratory work of breathing (WOB) during sleep and snoring, compared with wakefulness or sleep without snoring, is resistive, an important part is caused by the occurrence of dynamic pulmonary hyperinflation. We therefore investigated whether labored breathing during sleep in snorers was associated with large increases in expiratory airflow and lung resistance during expiration, in end-expiratory lung volume (EELV), and in PEEPi. Because an increase in PEEPi can increase the elastic work of breathing (elWOB), we also compared the resistive WOB and inspiratory elWOB during normal and labored breathing.

METHODS

Entry criteria. All subjects included were patients with suspected upper airway resistance syndrome and were taken from a group of heavy snorers who complained of daytime tiredness and/or daytime sleepiness (7). Two polysomnographic evaluations were required for the diagnosis of upper airway resistance syndrome (7).

A home polysomnography study was done first to identify a subgroup of snorers who had abnormal sleep fragmentation (arousal index >10/h), according to the reference value for our laboratory (12), but did not have OSAS or periodic leg movements to explain this finding. This polysomnography included electroencephalography (C4-A1, C3-A2), electrooculography, chin electromyography, electromyography of the tibialis anterior muscle of both legs, thermistor oronasal airflow assessment, rib cage movements (Multi-Parameter Analysis recorder 2/Medilog 9200; Oxford Medical Instrument, Abingdon, UK), and arterial pulse oximetry (Nellcor BS; Nellcor, Hayward, CA). During this home polysomnography, according to the clinical criteria commonly used for thermistor signals, an abnormal breathing event during sleep was defined as either a complete cessation of airflow lasting at least 10 s (apnea) or a reduction in the oronasal airflow lasting at least 10 s and accompanied with hypopnea (a drop of at least 3% in arterial O2 saturation vs. baseline; see Ref. 16). OSAS was ruled out on the basis of an apnea-hypopnea index value of <5/h of sleep.
Table 1. Characteristics of 8 snorers with upper airway resistance syndrome

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age, yr</th>
<th>BMI, kg/m²</th>
<th>Per Hour of Sleep</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Al</td>
<td>AHI</td>
</tr>
<tr>
<td>1</td>
<td>48</td>
<td>26</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>28</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>44</td>
<td>25</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>27</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
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<td>7</td>
<td>43</td>
<td>26</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>51</td>
<td>26</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Means ± SD</td>
<td>48 ± 8</td>
<td>26 ± 2</td>
<td>0 ± 0</td>
<td>3 ± 2</td>
</tr>
</tbody>
</table>

Values are those measured except for means ± SD (n = 8 subjects). BMI, body mass index; Al, apnea index; AHI, apnea-hypopnea index; ARI, arousal index; SaO₂, arterial oxygen saturation; PaO₂, arterial PO₂; PaCO₂, arterial PCO₂; TLC, total lung capacity; VC, vital capacity; FEV₁, forced expiratory volume in 1 s; %pred, %predicted value (predicted values were those of the European Community (19)).
statistical difference test. The level of significance was set at \( P = 0.05 \).

**RESULTS**

During 1996, we studied 422 snorers who underwent home polysomnography. Among these patients, 35 met our criteria for further polysomnographic investigation, including respiratory effort evaluation by Pes measurement and quantitative assessment of ventilation by a pneumotachometer. Of these 35, 12 agreed to undergo the second polysomnography study. Eight of the 12 persons studied displayed sustained labored inspiratory effort during >10% of the total sleep time; these persons were the eight subjects in this study.

Physical, respiratory, and home polysomnography characteristics of the eight patients studied are listed in Table 1. No patients had evidence of airway or lung disease according to European Community reference values (19).

Ventilatory patterns, dynamic lung compliance, inspiratory and expiratory airway and lung resistances, PEEPi, and WOB observed in each condition are listed in Table 2. Figure 1 shows typical signals observed in a representative patient. Figure 2 illustrates changes in resistive pressure and flow in the same patient during each condition, thus giving an index of the changes in inspiratory and expiratory airway and lung resistances that occurred across the three conditions. There were no differences in breathing pattern across the three conditions, but, as expected, total inspiratory WOB increased during H-RIE. Interestingly, during H-RIE, expiratory airway and lung resistance was increased to the same extent as inspiratory airway and lung resistance. Because PEEP was also increased during H-RIE, the increase in WOB was due not only to an increase in

<table>
<thead>
<tr>
<th></th>
<th>Wake</th>
<th>Lab_</th>
<th>Lab_</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT, ml</td>
<td>515±92</td>
<td>511±92</td>
<td>500±100</td>
<td>NS</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>14±3</td>
<td>15±3</td>
<td>15±4</td>
<td>NS</td>
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<tr>
<td>Ti/Ttot, %</td>
<td>41±6</td>
<td>40±5</td>
<td>40±5</td>
<td>NS</td>
</tr>
<tr>
<td>Esophageal pressure swing, cmH2O</td>
<td>9±2</td>
<td>11±4</td>
<td>28±7</td>
<td>††</td>
</tr>
<tr>
<td>Dynamic lung compliance, ml/cmH2O</td>
<td>134±71</td>
<td>128±56</td>
<td>130±57</td>
<td>NS</td>
</tr>
<tr>
<td>Mean inspiratory airway and lung resistance, cmH2O·l(^{-1})·s(^{-1})</td>
<td>11±4</td>
<td>16±5</td>
<td>63±27</td>
<td>*††</td>
</tr>
<tr>
<td>Mean expiratory airway and lung resistance, cmH2O·l(^{-1})·s(^{-1})</td>
<td>11±4</td>
<td>16±4</td>
<td>56±24</td>
<td>*††</td>
</tr>
<tr>
<td>Inspiratory airway and lung resistance at 200 ml/s, cmH2O·l(^{-1})·s(^{-1})</td>
<td>10±4</td>
<td>15±5</td>
<td>64±22</td>
<td>*††</td>
</tr>
<tr>
<td>Expiratory airway and lung resistance at 200 ml/s, cmH2O·l(^{-1})·s(^{-1})</td>
<td>11±3</td>
<td>16±3</td>
<td>45±14</td>
<td>*††</td>
</tr>
<tr>
<td>PEEPi, cmH2O</td>
<td>1.3±1.3</td>
<td>1.4±0.5</td>
<td>5.4±1.8</td>
<td>††</td>
</tr>
<tr>
<td>Total WOB, J/min</td>
<td>6.7±1.4</td>
<td>6.8±2.1</td>
<td>15.4±2.1</td>
<td>††</td>
</tr>
<tr>
<td>Resistive WOB, J/min</td>
<td>3.4±1.3</td>
<td>3.1±1.8</td>
<td>9.3±3.5</td>
<td>††</td>
</tr>
<tr>
<td>Elastic WOB, J/min</td>
<td>3.4±0.7</td>
<td>3.7±1.2</td>
<td>6.1±2.2</td>
<td>††</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 8 subjects. Wake, wakefulness period; Lab\_\_ \_ Lab\_+, non-rapid-eye-movement sleep period without and with laborious breathing; PEEPi, intrinsic positive end-expiratory pressure; Ti/Ttot, inspiratory time-to-total cycle time; VT, tidal volume; WOB, work of breathing; NS, not significant. * \( P < 0.05 \) Wake vs. Lab\_\_; † \( P < 0.05 \) Wake vs. Lab\_+; †† \( P < 0.05 \) Lab\_\_ vs. Lab\_+. 

Fig. 1. Tracing obtained in a representative patient during wakefulness (Wake, A), non-rapid-eye-movement (non-REM) sleep with low-resistance inspiratory effort (L-RIE, B) and non-REM sleep with high-resistance inspiratory effort (H-RIE, C). Top to bottom: EEG, electroencephalography; Flow, respiratory flow; Pes, esophageal pressure; and cross-sectional areas of rib cage (RC) and abdomen (Ab). In Pes, zero pressure corresponded to atmospheric pressure. Note that L-RIE was associated with a paradoxical decrease in cross-sectional area of RC during inspiration and with a high level of intrinsic positive end-expiratory pressure (PEEP; 9 cmH2O).
resistive work, but also to an increase in the eWOB (see Table 2 and Fig. 1).

Analysis of the periods in which abnormal Pes swings abruptly returned to normal as a result of arousal showed significant decreases both in EELV (of 74 ± 29 ml) and in PEEPi (1.9 ± 1.3 after the arousal vs. 6.3 ± 1.7 cmH$_2$O before the arousal). An example of these changes is given in Fig. 3, top. Figure 3, bottom, depicts changes in resistive pressure and flow during an arousal, thus providing an indication of changes in inspiratory and expiratory airway and lung resistances produced by arousal.

DISCUSSION

Previous studies have demonstrated that narrowing of the upper airway in OSAS in snorers and normal subjects can occur not only during inspiration but also during expiration (13, 15, 23, 24, 29). For example, it has been clearly demonstrated in OSAS that expiratory resistance is already increased during the breath preceding the initial occluded inspiratory effort of occlusive apnea (23). In addition, this increase in expiratory resistance may induce intermittent interruptions and/or a prolongation of expiration (24). More recently, it has also been demonstrated that expiratory flow limitation can occur during sleep in snorers, and that, consequently, upper airway obstruction can be present even during expiration (29). Our data corroborate these observations and demonstrate that the increase in expiratory resistance is of similar magnitude as the increase in inspiratory resistance. Because intraluminal pressure is positive during expiration, models that use collapsible tubes do not explain this increase in expiratory resistance. Instead, the effect of gravity on upper airway structures (2), together with relaxation of pharyngeal dilator muscles, such as the tensor palatini and the genioglossus (21), may promote local upper airway narrowing during expiration. We recently developed a model that consists of a series of successive individualized mass-spring components, each of which has its own compliance on the basis of local differences in anatomic and physiologic properties across pharyngeal regions. When we applied gravity and Bernouilli’s law to this model, we observed a flow limitation during inspiration associated with segmental narrowing of the upper airway (6). We also tested this model during expiration and observed that, contrary to the Starling resistor model, it may induce an expiratory-flow-limitation phenomenon (see APPENDIX). Expiratory-flow limitation has been recently observed in snorers in whom the pressure drop in the upper airway was directly detected by the measurement of supraglottic pressure (29). This method is more appropriate than ours for detecting expiratory-flow limitation and/or increase in expiratory resistance. However, this method cannot detect the dynamic pulmonary hyperinflation resulting from the increased expiratory resistance and its repercussion on inspiratory WOB. The best way to test these phenomena during expiration and to validate the multiple-element compliance model is probably to record Pes and supraglottic pressure simultaneously at different sites along the upper airway. Unfortunately, this study has not yet been performed.

Because gravity facilitates upper airway narrowing (2), body position is an important determinant of upper airway caliber. It is likely that the upper airway is narrower in the supine position than in the lateral position. Consequently, the supine position adopted in our study is probably the position most likely to allow detection of differences across conditions.

Combined lung and upper airway resistances were used in the present study. Previous studies demonstrated that most of the increase in airway resistance occurring during sleep and snoring was caused by an increase in upper airway resistance (27–29). Therefore, we are confident that our findings reflect changes in resistance to air flow in the upper airway.

Conditions that increase expiratory resistance and/or shorten expiratory time may promote dynamic hyperinflation, i.e., cause the EELV to rise above the relaxation volume (30). This leads to a positive elastic recoil of the
respiratory system at the end of expiration. The inspiratory muscles begin to contract before the start of inspiratory flow in an effort to counteract the elastic recoil pressure of the total respiratory system (22). This elastic recoil pressure shared by the inspiratory muscles corresponds to the PEEPi, measured as the amplitude of the negative deflection of Pes between the onset of inspiratory effort and the onset of inspiratory flow (22). This additional inspiratory WOB markedly increases the elWOB (22). In our study, total WOB increased more than twofold in the H-RIE situation compared with the L-RIE situation (Table 2), reaching a level (>10 J/min) at which diaphragmatic electromyography suggested excessive loading (4). About one-third of this increase was caused by the increase in elWOB resulting from the dynamic pulmonary hyperinflation produced by the increased expiratory resistance, whereas the remaining two-thirds were caused by the increase in inspiratory resistive WOB induced by the increase in inspiratory airway and lung resistance (see Table 2).

In addition to this increase in expiratory resistance, other mechanical factors may have contributed to the PEEPi increase. The PEEPi increase may have been caused in part by inspiratory muscle activity in response to upper airway narrowing (18). Although no clinical expiratory activity was detectable in our patients, this possibility cannot be ruled out, because we did not perform objective assessments of expiratory muscle activity such as electromyography or gastric pressure measurements. Because EELV is generally lower than the functional residual capacity (FRC) when PEEPi is induced solely by an increase in expiratory resistance (22), we analyzed the concomitant changes in PEEPi and in EELV.

As expected, we observed an abrupt decrease in EELV when inspiratory effort and PEEPi returned to normal after an arousal. However, this decrease in EELV was smaller than the one previously observed in COPD (22). This difference may be caused in part by
the lower lung compliance of our patients compared with COPD patients. Another explanation may involve the effects of arousal on FRC. In previous studies involving careful measurement of FRC in normal subjects, FRC clearly decreased during sleep (1, 8). This phenomenon was ascribed to loss of postural tone of inspiratory muscles (17). By contrast, we observed an EELV decrease of \(-100\) ml when H-RIE abruptly returned to normal after an arousal. This suggests that the marked reduction in EELV that can be expected to occur with a reduction in PEEPi was partly counterbalanced, in our patients, by an increase in FRC caused by the sleep disruption induced by the awakening. Assuming normal respiratory system compliance, a 4-cmH\(_2\)O decrease in PEEPi would result in an EELV decrease of \(-400\) ml. The EELV decrease in our study was only \(-100\) ml; this result suggests that the FRC increase caused by sleep disruption was \(-300\) ml. Interestingly, a similar magnitude of change in FRC was observed from Wake to sleep in normal subjects (1, 8). However, abrupt arousal may not represent resting Wake baseline condition. Nevertheless, because FRC increases are commonly observed during awakening in normal subjects, the EELV decrease in our patients during awakening strongly suggests that pulmonary hyperinflation occurred during sleep and H-RIE.

Morrell et al. (15) used a method similar to that used in our study to calculate airway and lung resistance in normal nonsnoring subjects during Wake and sleep. They observed, from Wake to sleep, a nonsignificant increase in expiratory resistance of \(-150\%\). A similar increase was observed in our patients when we compared Wake and periods of sleep with L-RIE. Morrell et al. did not evaluate PEEPi, but our results obtained during L-RIE suggest that this parameter was probably \(-2\) cmH\(_2\)O. However, we found a sixfold increase in mean expiratory resistance during sleep with H-RIE compared with Wake (see Table 2). This also explains the differences in lung volume changes from sleep to Wake between normal subjects and snorers.

When no expiratory activity is present, alveolar expiratory pressure can be mathematically described by a single exponential time function, which equals PEEPi at the end of expiration and can be expressed as (5, 10)

\[
\text{PEEPi} = \left(\frac{V_T}{C}\right) e^{-\frac{T_e}{RC}}
\]

where \(T_e\) is the expiratory time, and \(R\), \(C\), and \(RC\) are the resistance, compliance, and time constant of the respiratory system, respectively.

Tuxen and Lane (30) validated this mathematical model in mechanically ventilated patients with severe airflow obstruction and also found clear evidence that the risk of dynamic hyperventilation was greater when the volume delivered by the ventilator (\(V_T\)) was increased and the \(T_e\) reduced. The fact that \(V_T\) and \(T_e\) did not vary across the different conditions in our study suggests that the increase in PEEPi resulted entirely from an increase in the time constant of the respiratory system, which was perhaps mainly caused by an increase in expiratory resistance (Table 2).

In conclusion, our data corroborate previous observations that upper airway narrowing during sleep can persist during expiration (13, 15, 23, 24, 29). In addition, our study demonstrates that the increase in WOB during H-RIE compared with L-RIE is partly caused by the effects of dynamic pulmonary hyperinflation produced by the increased expiratory resistance. A model different from the Starling resistor model of upper airway narrowing is needed to explain the increase in expiratory resistance during sleep and snoring. A two-element compliance model, which takes into account the anatomic and physiological heterogeneities of the pharynx, is therefore proposed to explain the occurrence of flow limitation.
APPENDIX

The single-element compliance model, often referred to as the Starling resistor, predicts an expiratory flow-pressure relationship typical of a nonlinear resistive behavior resulting from the simultaneous increases in cross-sectional area and expiratory flow with increasing expiratory pressure (Pexp). Therefore, this model fails in describing the expiratory-flow alteration observed during the patient’s expiratory effort.

The two-element compliance model proposed by Fodil et al. (6) is represented in Fig. A1A. This model consists of 1) an upstream element which represents the oropharyngeal segment and is submitted to an upstream pressure equal to the supraglottic Pexp, and 2) a downstream element which represents the nasopharyngeal segment and is submitted to a downstream pressure equal to the Patm. The model represented in Fig. A1A is characterized, at the beginning of expiration, by an initial cross-sectional area of the oropharyngeal segment (A1) smaller than the initial cross-sectional area of the nasopharyngeal segment (A2). This difference between A1 and A2 is in accordance with the assumption of a narrowing of the oropharyngeal segment induced by the flow structure coupling that occurred during the preceding inspiration. The Fodil model of Fig. A1A predicts 1) the occurrence of expiratory-flow limitation (Fig. A1B), which can explain the plateau observed for the flow signal during the first part of expiration, and 2) the progressive narrowing of the oropharyngeal segment and the unchanged caliber of the nasopharyngeal segment during expiration (Fig. A1C). Flow limitation, which is specific for expiration, results from the coupling that occurs between expiratory flow and each of the pharyngeal segments. The oropharyngeal segment, which is the site of flow acceleration as Pexp increases, progressively narrows as a result of the decrease in its internal lateral pressure, whereas the nasopharyngeal segment, which is submitted to an internal pressure close to Patm, keeps a roughly constant cross-sectional area.

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