Airway obstruction during exercise and isocapnic hyperventilation in asthmatic subjects

Oscar E. Suman, Kenneth C. Beck, Mark A. Babcock, David F. Pegelow, and William G. Reddan

We compared pulmonary mechanics measured during long-term exercise (LTX = 20 min) with long-term isocapnic hyperventilation (LTIH = 20 min) in the same asthmatic individuals (n = 6). Peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV1) decreased during LTX (−19.7 and −22.0%, respectively) and during LTIH (−6.66 and 10.9%, respectively). In contrast, inspiratory pulmonary resistance (Ri) was elevated during LTX (57.6%) but not during LTIH (9.62%). As expected, airflow function deteriorated post-LTX and post-LTIH (FEV1 = −30.2 and −21.2%; Ri = 111.8 and 86.5%, respectively). We conclude that the degree of airway obstruction observed during LTIH is of a greater magnitude than that observed during LTX. Both modes of hypoxia induced similar levels of airflow obstruction in the posthyperpnea period. However, the greater airway obstruction during LTX suggests that a different process may be responsible for the changes in airway function during and after the two modes of hypopnea. This finding raises questions about the equivalency of LTIH and LTX in the study of exercise-induced asthma.

In Exercise-Induced Asthma (EIA) a transient airway obstruction occurs 5–15 min after the cessation of exercise (2, 6, 20, 31). Voluntary hyperventilation and exercise are often used interchangeably to induce airway obstruction in asthmatic subjects (16, 20). Two studies have shown that airway obstruction also develops during exercise of 20 min or longer duration (4, 32). On the other hand, airway obstruction does not seem to occur during isocapnic hyperventilation of <12-min duration (6, 16, 31). To date there has been no direct comparison of changes in airway function during exercise and hyperventilation in asthmatic subjects other than the limited study (3 asthmatic subjects) of Stirling and colleagues (31). In this study, a decrease in pulmonary resistance in asthmatic individuals was reported during both exercise and isocapnic hyperventilation of ∼12-min duration.

To directly compare the changes in airway function during exercise and voluntary hyperventilation, we measured pulmonary responses to both modes of hypopnea in the same asthmatic individuals while attempting to match minute ventilation (VE). We quantified events occurring during as well as after hypopnea. We hypothesized that similar changes in airway function (i.e., presence or absence of airway obstruction) would occur during both types of hypopnea.

METHODS

Individuals (n = 6 men) with a clinical history of EIA and a positive exercise challenge test, indicated by a reduction in forced expiratory volume in 1 s (FEV1) >10% of the baseline value postexercise, were included. Subjects regularly used an inhaled β2-adrenergic agonist and/or oral theophylline. None of the participants utilized oral steroids or inhaled corticosteroids in their medication regimen. Informed consent was obtained from each individual before participation. This study was approved by the Human Subjects Committee Review Board at the University of Wisconsin-Madison.

Pulmonary function and the maximal exercise test. Vital capacity, FEV1, and inspiratory capacity were determined by using a Collins 13.5-liter water-sealed spirometer (Warren E. Collins, Braintree, MA). Functional residual capacity (FRC) was determined in a Collins body plethysmograph. Total lung capacity (TLC) was determined as the sum of FRC and inspiratory capacity. Pulmonary function tests were performed after antiasthmatic medications were withheld for at least 12 h.

Immediately after pulmonary function tests, a progressive exercise test was performed on a treadmill to determine each subject’s exercise capacity. Each participant started by walking at 4.0 miles/h (mph) and 0% grade for 3 min as a warm-up. The speed was then increased to 6.0 mph. Every 3 min the speed of the treadmill was increased by 1 mph until the running cadence was satisfactory to the participant. (Note that 1 subject remained at a speed of 4.0 mph throughout his progressive exercise test, but his treadmill incline level was progressively increased.) From this point the treadmill was maintained at a constant speed, and grade was increased by 2% until a maximal volitional effort was achieved. Maximal oxygen consumption (VO2max) was calculated by using open-circuit expired-gas analysis, as previously described (26). Measurements of expired gas, inspiratory capacity, end-expiratory lung volume (EELV), and inspiratory and expiratory flow rate were made during the last minute of each exercise stage.

Evaluation of pulmonary mechanics. The breathing circuit used to obtain spirometry, ventilation, and pulmonary mechanics data consisted of a Hans Rudolph two-way nonbreathing valve (model 2700, Hans Rudolph, Kansas City, MO). Matched Hans Rudolph pneumotachographs (model 3813) were used to measure inspired and expired flows. End-tidal gases were sampled at the mouthpiece and ana-
lyzed by a Perkin-Elmer mass spectrometer (model 1100). Signals were relayed at 75 Hz through an analog-to-digital board (Scientific Solutions Labmaster PGH) to a personal computer, where data were kept in files for later analysis. Inspired and expired volumes were calculated by integration of the flow signals. A Validyne transducer (model MP 45–871 Validyne, Northridge, CA; ± 300 cmH2O) connected to polyethylene tubing (PE-200) measured mouth pressure. Esophageal pressure (Pes) was measured with a 10-cm latex balloon, positioned 8–10 cm above the gastroesophageal junction, connected by polyethylene tubing (PE-200) to a Validyne transducer (model MP 45–871, ±200 cmH2O). Transpulmonary pressure (Ptp) was obtained by computer subtraction of mouth pressure from Pes. Inspiratory pulmonary resistance (R(I)) was calculated at the volume corresponding to peak inspiratory flow (PIF). The resistive pressure was determined by subtraction of the elastic pressure drop caused by the volume at peak flow from the Pes at peak flow. The resistive pressure was then divided by PIF to determine inspiratory pulmonary resistance. In other words

$$R_{I} = \frac{[Ptp(PIF) - Ptp(EELV)] - \nu/Cl}{PIF}$$

where Ptp(PIF) is Ptp measured at PIF, Ptp(EELV) is Ptp measured at EELV, \(\nu\) is volume above EELV at PIF, and Cl is dynamic compliance for each breath (14). By using the mean flow-volume and pressure-volume (F-V and P-V, respectively) loops plotted for each individual at rest, during exercise, and during recovery, ventilatory volume variables and ventilatory timing variables were measured to obtain an estimation of the ventilatory work. This method is described in detail by Otis (25). Flow and pressure signals were verified to be in phase up to 12 Hz.

Esophageal temperature was measured as an index of body core temperature. A nasopharyngeal temperature sensor (Mon-a-therm, size 9-Fr, Mallinckrodt Medical, St. Louis, MO) was inserted through the nares into the esophagus. The position of the temperature probe was 30–35 cm from the nares. The temperature was read from a Mon-a-therm digital display box (model 6500, Mallinckrodt Medical). This system gives a temperature reading that is updated every 4 s. The temperature of the expired air was obtained with similar equipment by using a probe placed at the expired port of the breathing valve. This corresponded to a distance of 5–10 cm from the mouth.

EELV was measured by having individuals perform inspiratory capacity maneuvers during each collection period. To verify that TLC was attained during each inspiratory capacity maneuver, we confirmed that a peak negative Pes similar to that obtained during the inspiratory capacity maneuver at rest was attained. An index of the difficulty of breathing or dyspnea was also obtained at each collection period by having the subject select a number on the Borg rate scale of perceived exertion (10-point category ratio) (21).

Long-term exercise (LTX) session. Subjects were asked to return within 1 wk for LTX at 70%–85% of their personal VO2max. The duration of exercise was 20 min. To ensure that a return within 1 wk for LTX at 70%–85% of their personal VO2max.

The session involved 20 min with ventilation equal to or higher than the exercise Ve obtained near the end of the LTX session. Participants withheld their antiasthmatic medication for at least 12 h before each session (the same as for the LTX session). Measurements were made and analyzed as in the LTX session: breathing circuit, Pts, Ptp, pulmonary resistance, work of breathing, temperature, EELV, rate of perceived exertion, and spirometry. Subjects were asked to match their averaged Pes-Vt loop obtained during LTX while matching respiratory rate by using a metronome. Their real-time P-V loop was displayed on a storage oscilloscope (Tektronix 5113A, Beaverton, OR) where the averaged Pes-Vt loop from the previous LTX session was displayed and superimposed on the screen. The subject was instructed to match the superimposed loop. In addition, a metronome signaled the desired breathing frequency (inspiration and expiration) and ratio of inspiratory time to total breath time (T(I)/T(T)). This arrangement allowed us to match Vt, frequency, T(I)/T(T), Ptp excision, and duration of LTIH. Before the start of LTIH, resting levels of end-tidal PCO2 (PetCO2) were obtained; this level was maintained during LTIH by adding CO2 to the inspired gas.

Data analysis. Statistical comparisons within and between the LTX or LTIH sessions were made by using repeated-measures ANOVA followed by paired t-tests. All data are shown as means ± SE unless otherwise noted. All statistical tests of significance were set at a P < 0.05 level.

RESULTS

Maximal exercise test session. Subject characteristics are shown in Table 1. Baseline pulmonary function showed that all subjects were within the normal range of predicted values for TLC, vital capacity, and FRC (Table 2). Two subjects had a reduced FEV1 (<80% predicted), and one of them had a lower than predicted FEV1-to-FVC ratio, indicating a mild airflow limitation. None of the subjects had an increased FRC (gas trapping).

LTX session. During the LTX session all subjects showed changes during recovery consistent with EIA, i.e., a fall in both FEV1 and peak expiratory flow (PEF) > 10% of the preexercise value. The mean PEF fell 24.2% from the baseline value of 8.7 l/s at rest. FEV1 decreased by 30.2%, whereas mean Rl increased by 111.77%. All preexercise-to-postexercise comparisons were significantly different (P < 0.05) (Figs. 1–3).

To detect changes in airway function during LTX, comparisons between values at 2 (early stage) vs. 20 min (late stage) of exercise were made for PEF, FEV1, and Rl. PEF and FEV1 decreased significantly at the late stages of LTX by −19.7 and −22.0%, respectively (Figs. 1 and 2), whereas Rl showed a significant increase of 57.6% (Fig. 3).

Table 3 displays the ventilatory responses during LTX and LTIH. Ve was relatively constant, ranging
from 74.0 to 86 l/min as O2 consumption was maintained between 73.0 and 80.0% of (mean = 76.0%) during LTX. The exercise Vt also remained fairly constant throughout exercise (2.2–2.5 liters), whereas breathing frequency increased from 31.0 breaths/min at minute 2 to 40 breaths/min at minutes 15 and 20. EELV (expressed as %TLC) remained at its preexercise level of 44% (3.1 liters) early in exercise but by minute 20 had increased significantly to 57% of TLC (4.0 liters). EELV tended to be elevated postexercise when compared with rest (54% of TLC, P = 0.06). End-inspiratory lung volume (EILV) increased significantly from 78% of TLC during early exercise to 89% of TLC at 20 min of exercise. The work of breathing ranged from 181.0 J/min at 2 min to 349.0 J/min at minute 20 (P = 0.02).

LTIH session. Changes in PEF, FEV1, and Rl pre-LTIH to post-LTIH were −18.5, −21.2, and 86.5%, respectively, indicating similar levels of bronchospasm to those obtained during LTX (Figs. 1–3).

Comparisons between the onset of LTIH (minute 2) and later stages of LTIH (minute 20) showed that PEF (−6.67%) and FEV1 (−10.9%) decreased significantly but that Rl (9.62%) remained unchanged during the later stages of LTIH.

Table 3 displays the ventilatory responses during LTIH. In contrast to during exercise (during which Ve had a tendency to slowly increase) subjects maintained constant target levels of Ve during LTIH, ranging from 93.0 to 97.0 l/min. Petco2 was maintained at resting levels (4.6%–4.7%). Vt also remained constant throughout LTIH (2.6–2.7 liters). Breathing frequency increased to the constant value of 38.0 breaths/min at minute 2 and was constant throughout LTIH. EELV remained at 44% of TLC (3.1 liters) during minute 2 of mimicking, but by minute 20 reached a level to 50% of TLC (3.5 liters). EELV was not increased post-LTIH when compared with rest. EILV increased from 64.0% of TLC at rest to 83.0% of TLC during early LTIH and increased further to 92.0% of TLC at 20 min of LTIH. The work of breathing ranged from 307.0 J/min at minute 2 to 394.0 J/min at minute 20.

LTX session compared with LTIH session (Table 3). The percent changes in PEF, FEV1, and Rl at 4 min after hyperpnea compared with prehyperpnea were not significantly different between LTX and LTIH (Figs. 1–3). However, the percent changes between minutes 2 and 20 of hyperpnea were different between sessions, indicating that a more intense bronchospasm developed during LTX compared with LTIH.

Ve was higher at the initial stages of LTIH, but, by minute 5 of both challenges, this difference was no longer statistically significant between sessions at comparative time points. This reflects the target levels of ventilation presented to the subjects, who attempted to match Ve obtained at later stages of LTX. Vt was similar at all time points during LTIH compared with LTX. Ti/TT (0.46 ± 0.01 during both LTX and LTIH) and EELV were similar during both sessions. Relative humidity (45 ± 3% for LTX vs. 45 ± 2% for LTIH) and room temperature were also similar during both sessions.

DISCUSSION

This study measured and directly compared pulmonary mechanics in the same asthmatic individuals during LTX and LTIH matched for ventilation. Previous studies that investigated pulmonary responses during isocapnic hyperventilation and exercise cannot

Table 2. Pulmonary function tests

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>TLC, liters</th>
<th>IC, liters</th>
<th>FRC, liters</th>
<th>%Pred FRC*</th>
<th>VC, liters</th>
<th>FEV1/FVC Ratio</th>
<th>FEV1, l/s</th>
<th>%Pred FEV1*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.71</td>
<td>3.21</td>
<td>3.55</td>
<td>104</td>
<td>5.06</td>
<td>0.82</td>
<td>3.64</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>7.32</td>
<td>3.62</td>
<td>3.70</td>
<td>106</td>
<td>5.69</td>
<td>0.78</td>
<td>4.42</td>
<td>99</td>
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<td>3</td>
<td>7.06</td>
<td>3.89</td>
<td>3.17</td>
<td>87</td>
<td>5.19</td>
<td>0.75</td>
<td>3.93</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>7.25</td>
<td>3.92</td>
<td>3.33</td>
<td>91</td>
<td>5.22</td>
<td>0.65</td>
<td>3.37</td>
<td>73</td>
</tr>
<tr>
<td>5</td>
<td>6.61</td>
<td>3.46</td>
<td>3.15</td>
<td>95</td>
<td>5.47</td>
<td>0.77</td>
<td>4.22</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td>7.14</td>
<td>4.02</td>
<td>3.13</td>
<td>85</td>
<td>5.08</td>
<td>0.81</td>
<td>4.37</td>
<td>128</td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>7.02 ± 0.1</td>
<td>3.69 ± 0.13</td>
<td>3.34 ± 0.1</td>
<td>95 ± 3.6</td>
<td>5.29 ± 0.1</td>
<td>0.76 ± 0.02</td>
<td>3.99 ± 0.17</td>
<td>92.2</td>
</tr>
</tbody>
</table>

TLC, total lung capacity; IC, inspiratory capacity; FRC, functional residual capacity; Pred, predicted; VC, vital capacity; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity. All pulmonary function tests were performed while subjects were on their antiasthma medications. Predicted values are from Ref. 24.
be used to directly compare the two modes of challenge. Blackie and colleagues (6) measured \( \text{FEV}_1 \) in five asthmatic subjects during 16 min of isocapnic hyperventilation and reported no change in \( \text{FEV}_1 \). Although their results are consistent with our data obtained during the first 4 min of LTIH, they did not report data during exercise. Stirling et al. (31) measured pulmonary resistance in three asthmatic subjects during exercise and isocapnic hyperventilation, but their calculations of expiratory pulmonary resistance could have been significantly affected by dynamic compression of the airway. We expanded on both studies by directly measuring inspiratory resistance and spirometry throughout LTX and LTIH. \( R_{\text{LI}} \) is an effort-independent parameter and is unaffected by dynamic compression of the airway (32). In addition, we conducted statistical analyses within and between both sessions for the full 20-min duration.}

**Limitations.** During LTIH we attempted to replicate several key respiratory parameters found during LTX: \( \text{VT} \), respiratory frequency, \( \text{VE} \), and \( \text{Pes} \) swings. Our results indicate that an individual's breathing frequency, \( \text{PET}_{\text{CO}_2} \), \( \text{EELV} \), \( \text{VT} \), and \( \text{Ti/Tt} \) were matched but that \( \text{VE} \) values in the early stages of exercise were not matched. Although \( \text{VE} \) tended to be higher throughout the LTIH session, this difference was not statistically significant in later stages of hyperventilation.}

Because it is known that the level of \( \text{VE} \) is associated with the severity of \( \text{EIA} \) (2, 20), our higher absolute level of \( \text{VE} \) during LTIH should have produced a more severe airway obstruction. However, all indexes of airway obstruction showed comparable changes at 4 min post-LTX and 4 min post-LTIH. The difficulty in matching ventilatory parameters during LTX and LTIH has been...
reported in a study by Aaron and colleagues (1) in which subjects tended to overbreathe even though careful attempts were made to control Ve, respiratory rate, Vt, and EELV. Our results followed a similar pattern. However, because we were interested in investigating EIA during LTIH, having subjects exceed their target ventilation assured us that the absence of airway obstruction was not caused by insufficient ventilation. In addition, the nonrebreathing diaphragms prevented blow-by gases from flowing across the expiration port of the breathing valve during LTIH.

Potential mechanisms. Our results imply that different factors could have contributed to the maintenance of airway patency during LTIH compared with LTX. These potential factors include level of ventilation, breathing pattern, body core temperature, airway temperature, water content of expired air, cardiac output, plasma catecholamines, or locally released mediators.

The level of ventilation and water content of the expired air are thought to have the greatest influence on respiratory heat loss (20) because respiratory heat loss is thought to be directly related to the severity of airway obstruction in EIA (8). Our estimated mean respiratory heat loss (1.44 kcal/min) during LTIH was similar to that reported by Deal and colleagues (10), whose subjects experienced slightly greater bronchoconstriction, not less. Similarly, because room air relative humidity was similar in the two trials, the airway global water losses should have been similar or greater during LTIH because of the higher Ve achieved.

An increased Vt could be associated with the bronchodilation observed during hyperpnea (6, 18, 19, 23, 31) caused by a reflex inhibition of bronchomotor tone via slowly adapting pulmonary stretch receptors (19, 30) or direct mechanical stretch of airway smooth muscle (14). Then tendency to higher Vt observed during LTIH compared with LTX in our study may thus have inhibited airway obstruction during LTIH until Vt returned to resting levels in the recovery period. This explanation and our data seem to fit well with the concept of lung inflation modulating airway smooth muscle contraction (15, 33). During LTX, EELV continued to increase progressively above rest (>44% of TLC). The EELV achieved was similar during LTX and LTIH (89 and 92% of TLC, respectively); this EELV value was similar to those previously reported for LTX (32). One consequence of breathing at such high lung volumes is increasing the work of breathing. The mean total work of breathing that our asthmatic subjects achieved during LTX and LTIH was higher compared with the level of total ventilatory work achieved by normal subjects (125 J/min) working at a higher %V˙O2max (85%) and level of ventilation (120 l/min) (1).

One interpretation of our breathing pattern results is that, early in LTX, airway patency is maintained (less airway obstruction) because of a higher Vt compared with baseline. However, Vt continued to progressively decrease (5 of 6 participants) during LTX concomitantly with the appearance of airway obstruction. Maintaining Vt during LTIH could possibly have prevented airway obstruction. In the recovery period Vt decreased (approaching baseline values), and bronchoconstriction developed after both challenges.

### Table 3. Mean ventilatory response to LTX and LTIH

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>2 min</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>20 min</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>%Vo2max (%)</td>
<td>8 ± 0.3</td>
<td>73 ± 5</td>
<td>74 ± 4</td>
<td>80 ± 2</td>
<td>75 ± 4</td>
<td>76 ± 2</td>
<td>NA</td>
</tr>
<tr>
<td>PETCO2, mmHg</td>
<td>4.5 ± 0.3</td>
<td>4.6 ± 0.3</td>
<td>4.7 ± 0.3</td>
<td>4.6 ± 0.3</td>
<td>4.6 ± 0.3</td>
<td>4.6 ± 0.3</td>
<td>NA</td>
</tr>
<tr>
<td>V˙E, l/min</td>
<td>16 ± 2</td>
<td>74 ± 6</td>
<td>76 ± 5</td>
<td>86 ± 7</td>
<td>82 ± 7</td>
<td>84 ± 7</td>
<td>35 ± 4*</td>
</tr>
<tr>
<td>VT, liters</td>
<td>19 ± 2</td>
<td>93 ± 4</td>
<td>96 ± 6</td>
<td>97 ± 6</td>
<td>94 ± 5</td>
<td>94 ± 4</td>
<td>26 ± 1</td>
</tr>
<tr>
<td>EELV, %TLC</td>
<td>1.1 ± 0.13</td>
<td>2.4 ± 0.22</td>
<td>2.5 ± 0.22</td>
<td>2.4 ± 0.24</td>
<td>2.2 ± 0.27</td>
<td>2.3 ± 0.28</td>
<td>2.0 ± 0.25*</td>
</tr>
<tr>
<td>EILV, %TLC</td>
<td>1.3 ± 0.1</td>
<td>2.6 ± 0.21</td>
<td>2.7 ± 0.22</td>
<td>2.7 ± 0.23</td>
<td>2.7 ± 0.22</td>
<td>2.7 ± 0.3</td>
<td>1.5 ± 0.1</td>
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<tr>
<td>f, breaths/min</td>
<td>15 ± 1</td>
<td>31 ± 3</td>
<td>32 ± 3</td>
<td>37 ± 4</td>
<td>40 ± 4</td>
<td>39 ± 5†</td>
<td>17 ± 1</td>
</tr>
<tr>
<td>V˙E, l/min</td>
<td>15 ± 2</td>
<td>39 ± 4</td>
<td>38 ± 4</td>
<td>37 ± 4</td>
<td>37 ± 4</td>
<td>37 ± 4</td>
<td>17 ± 2</td>
</tr>
<tr>
<td>EELV, %TLC</td>
<td>44 ± 4</td>
<td>43 ± 2</td>
<td>50 ± 3</td>
<td>51 ± 4</td>
<td>52 ± 4</td>
<td>57 ± 4†</td>
<td>54 ± 2</td>
</tr>
<tr>
<td>EILV, %TLC</td>
<td>45 ± 5</td>
<td>44 ± 5</td>
<td>46 ± 4</td>
<td>51 ± 4</td>
<td>50 ± 5</td>
<td>50 ± 4</td>
<td>50 ± 4</td>
</tr>
<tr>
<td>WV, J/min</td>
<td>63 ± 4</td>
<td>78 ± 2</td>
<td>85 ± 3</td>
<td>85 ± 3</td>
<td>85 ± 3</td>
<td>89 ± 2†</td>
<td>79 ± 4‡</td>
</tr>
<tr>
<td>V˙E, l/min</td>
<td>64 ± 5</td>
<td>83 ± 2</td>
<td>85 ± 3</td>
<td>92 ± 2</td>
<td>89 ± 2</td>
<td>92 ± 1‡</td>
<td>73 ± 5‡</td>
</tr>
<tr>
<td>V˙E, l/min</td>
<td>17 ± 3</td>
<td>181 ± 315</td>
<td>192 ± 38</td>
<td>290 ± 63</td>
<td>330 ± 70</td>
<td>349 ± 73†</td>
<td>75 ± 21‡</td>
</tr>
<tr>
<td>V˙E, l/min</td>
<td>12 ± 1</td>
<td>307 ± 396</td>
<td>321 ± 38</td>
<td>362 ± 25</td>
<td>362 ± 61</td>
<td>394 ± 31</td>
<td>55 ± 11‡</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 subjects. LTX, long-term exercise; LTIH, long-term isocapnic hyperventilation; Post, after exercise. PETCO2, end-tidal PCO2; TLC, total lung capacity; Ve, minute ventilation; Vt, tidal volume; f, breathing frequency; EELV, end-expiratory lung volume; EILV, end-inspiratory lung volume; WV, work of breathing. *Statistically significant (within) pre-LTX vs. postexercise comparisons. P < 0.05. †Statistically significant (within) 2- vs. 20-min comparisons, P < 0.05. ‡Statistically significant pre-LTX to post-LTX %change vs. pre-LTIH vs. post-LTIH %change comparisons, P < 0.05. §Statistically different time point during LTX vs. respective time point during LTIH comparison, P < 0.05.
Table 4. Mean temperature response to LTX and LTIH

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>2 min</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>20 min</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>( T_{\text{E}} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>LTX</td>
<td>28.8 ± 0.3</td>
<td>30.0 ± 0.1</td>
<td>30.2 ± 0.2</td>
<td>30.3 ± 0.2</td>
<td>30.3 ± 0.2</td>
<td>30.4 ± 0.2</td>
<td>29.2 ± 0.2</td>
</tr>
<tr>
<td>LTIH</td>
<td>28.4 ± 0.3</td>
<td>29.3 ± 0.3</td>
<td>29.1 ± 0.3</td>
<td>29.1 ± 0.2</td>
<td>29.1 ± 0.1</td>
<td>29.0 ± 0.2</td>
<td>28.6 ± 0.2</td>
</tr>
<tr>
<td>( T_{\text{es}} )</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>LTX</td>
<td>35.8 ± 0.3</td>
<td>36.1 ± 0.4</td>
<td>36.3 ± 0.4</td>
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<td>36.8 ± 0.5</td>
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<td>35.3 ± 1.0</td>
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<tr>
<td>LTIH</td>
<td>36.4 ± 0.0</td>
<td>35.7 ± 0.3</td>
<td>35.6 ± 0.3</td>
<td>35.5 ± 0.3</td>
<td>35.6 ± 0.3</td>
<td>35.6 ± 0.3</td>
<td>36.1 ± 0.1</td>
</tr>
</tbody>
</table>

Values are means ± SE. \( T_{\text{E}} \), expiratory temperature; \( T_{\text{es}} \), esophageal temperature.
explain EIA. A description of pulmonary mechanics and analysis of breathing pattern during exercise or hyper-ventilation can provide a better understanding of EIA pathophysiology. In view of the differences in airway function encountered during both bouts of hyperpnea, when mechanisms of EIA are being investigated, it is imperative that exercise be utilized as the specific mode of hyperpnea. Further investigation is needed on the role of exercise and isocapnic hyperventilation used interchangeably to induce and study airway obstruction in individuals with EIA.

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