Effects of Weight Loss on Peak Flow Variability, Airways Obstruction, and Lung Volumes in Obese Patients With Asthma*

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Study objectives: To clarify the pathophysiologic features of the relation between asthma and obesity, we measured the effects of weight reduction on peak expiratory flow (PEF) variability and airways obstruction, compared to simultaneous changes in lung volumes and ventilatory mechanics in obese patients with stable asthma.

Methods: Fourteen obese asthma patients (11 women and 3 men; aged 25 to 62 years) were studied before and after a very-low-calorie-diet period of 8 weeks. PEF variability was determined as diurnal and day-to-day variations. FEV₁, and maximal expiratory flow values were measured with a flow-volume spirometer. Lung volumes, airways resistance (Raw), and specific airways conductance were measured using a constant-volume body plethysmograph. Minute ventilation was monitored in patients in supine and standing positions.

Results: As patients decreased their body mass index (SD) from 37.2 (3.7) to 32.1(4.2) kg/m² (p < 0.001), diurnal PEF variation declined from 5.5% (2.4) to 4.5% (1.5) (p = 0.01), and day-to-day variation declined from 5.3% (2.6) to 3.1% (1.3) (p < 0.005). The mean morning PEF, FEV₁, and FVC increased after weight loss (p = 0.001, p < 0.005, and p < 0.05, respectively). Flow rate at the middle part of FVC (FEF₂₅–₇₅) increased even when related to lung volumes (FEF₂₅–₇₅/FVC; p < 0.05). Functional residual capacity and expiratory reserve volume were significantly higher after weight loss (p < 0.05 and p < 0.005, respectively). A significant reduction in Raw was found (p < 0.01). Resting minute ventilation decreased after weight loss (p = 0.01).

Conclusion: Weight loss reduces airways obstruction as well as PEF variability in obese patients with asthma. The results suggest that obese patients benefit from weight loss by improved pulmonary mechanics and a better control of airways obstruction.

Key words: airways obstruction; asthma; obesity; peak expiratory flow variation; pulmonary function; weight loss

Abbreviations: AFV = area under the expiratory flow volume curve; BHR = bronchial hyperresponsiveness; BMI = body mass index; DLCO = diffusing capacity of the lung for carbon monoxide; ERV = expiratory reserve volume; FEF₂₅–₇₅ = flow rate at the middle part of FVC; FRC = functional residual capacity; NS = not statistically significant; PD₁₅ = provocative dose causing a 15% fall in FEV₁; PEF = peak expiratory flow; Raw = airways resistance; RR = respiratory rate; RV = residual volume; SGaw = airways conductance; TLC = total lung capacity; TLC-B = TLC measured using body plethysmograph; TLC-He = TLC measured using the single-breath helium dilution method; VAS = visual analogue scale; V̇e = minute ventilation; VLCD = very-low-calorie-diet; Vt = tidal volume

The prevalence of asthma and obesity has been increasing worldwide in recent years.¹² Several studies have reported the association between body mass index (BMI) and asthma prevalence.³–⁶ Whether asthma patients gain weight as a result of activity limitations or whether obesity increases the risk of developing asthma is uncertain.⁷ Luder et al⁸ studied the relationship between asthma symptoms and overweight in children. They found that a higher BMI was associated with more severe asthma symptoms. In adult obese asthmatics, improvement in asthma severity after weight loss has been reported.⁹,¹⁰

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It could be assumed that impairment in pulmonary mechanics related to obesity, such as reduction in lung volumes, increased airways resistance (Raw), and impairments in small airways function, may contribute to an increase in asthma severity. Although there is evidence that weight loss may improve lung function and oxygenation in obesity, very little is known about the effects of weight loss on the severity of asthma in terms of variability of airways obstruction.

To clarify pathophysiologic features of the relation between asthma and obesity, we measured the effects of weight loss on peak expiratory flow (PEF) variability and airways obstruction, compared to simultaneous changes in lung volumes and ventilatory mechanics in obese patients with stable asthma.

**Materials and Methods**

Fourteen patients (11 women and 3 men; aged 25 to 62 years) with a clinical diagnosis of asthma and moderate to morbid obesity BMI (range, 32.5 to 42.5 kg/m²) were recruited for the study. Characteristics of the patients and antiasthmatic medications are presented in Table 1. Prior to our study, all patients participated as a control group in another study. Their spirometric and serial PEF values were carefully followed up every 2 months for 1 year before starting in our study. Because they were control patients, they underwent no interventions other than education concerning asthma and allergy. Medical therapy included regular use of inhaled corticosteroids in all 14 patients, sustained-release theophylline compounds in 2 patients, and regular long-acting inhaled β₂-agonists in 3 patients. All patients were nonsmokers or ex-smokers who had stopped smoking for ≥2 years (Table 1). Patients gave informed consent to participate in the study, which was approved by the Ethical Committee of the Department of Pulmonary Medicine of Helsinki University Hospital.

### Study Protocol

All patients participated in a weight reduction program starting with a very-low-calorie-diet (VLCD) period of 8 weeks. The VLCD preparation used was Nutrillett (Nycomed Pharma AS; Oslo, Norway). The daily dose gives 1,760 kJ/d, and contains daily allowances of all essential nutrients. The principles of this weight reduction program are described by Pekkarinen et al.13

Before weight loss and after the VLCD period, PEF measurements for 2 weeks, pulmonary function tests (see below), and arterial blood gas analyses were evaluated. The symptoms (i.e., dyspnea and cough) were recorded on a 100-mm visual analogue scale (VAS), where 0 mm represented best possible and 100 mm represented worst possible. The use of rescue medication was recorded. Patients had been advised not to change their antiasthmatic treatment other than short-acting β₂-agonists during the study if the stability of asthma was clinically acceptable. Patients with allergy to pollen were studied out of season. The dose and timing of long-acting β₂-agonists and sustained-release theophylline compounds were identical at study visits before and after weight loss. Patients did not consume any caffeinated beverages or short-acting bronchodilators for 4 h before pulmonary function tests.

### Pulmonary Function and Arterial Blood Gas Measurements

Flow-volume spirometry was performed using a rolling seal spirometer (CPI 220; Cardio Pulmonary Instruments; Houston, TX) connected to a microcomputer system (Medikro 202; Medikro Oy; Kuopio, Finland) according to European recommendations. The results from the envelope curve of at least three superimposed forced expiratory flow-volume curves were recorded. FEV₁, FVC, flow rate at the middle part of FVC (FEF₂₅₋₇₅), and area under the expiratory flow volume curve (AFV) were determined with the patient in the sitting position. Vital capacity (VC), total lung capacity (TLC), residual volume (RV), functional residual capacity (FRC), Raw, and specific airways conductance (SGaw) were measured using a constant-volume body plethysmograph (Bodyscreen; Erich Jaeger; Wurzburg, Germany) during tidal breathing timed with a metronome (30/min). The mean value of 3 to 5 determinations was recorded for analysis. A single-bowel diffusing capacity test (Master Lab; Erich Jaeger) was used for measuring diffusing...
capacity of the lung for carbon monoxide (DLCO). TLC was also measured using the single-breath helium dilution method (TLC-He). The value of nonventilated lung compartment was calculated as the TLC measured using body plethysmograph (TLC-B) minus the TLC-He.

Minute ventilation (V\(\text{e}\)), tidal volume (V\(\text{t}\)), and respiratory rate (RR) were continuously monitored and recorded over a 30-s interval in patients in supine and standing positions. A face mask (Rudolph series 7910; Hans Rudolph; Kansas City, MO) was tightly attached and connected to an automatic gas exchange analyzer with a mixing chamber (Ergo-Oxyscreen; Erich Jaeger). The mask and the valve system had a dead space of 185 mL. The mean values of 10 consecutive measurements of 30 s in both body positions were calculated for further analyses.

Arterial blood samples for blood gas analysis were taken from a brachial artery after a rest of 10 min with the patients in supine position.

Histamine Challenge

A rapid dosimetric method with controlled tidal breathing was used for histamine challenge of the airways. Patients with an FEV\(_1\) of \(\geq 70\%\) predicted were excluded from histamine provocation testing. If FEV\(_1\) decreased from the baseline by \(\geq 15\%\) after any dose, further administration of histamine was discontinued. The provocative dose causing a 15% fall in FEV\(_1\) (PD\(_{15}\)) was calculated from logarithmically transformed histamine doses.

PEF Variability

The highest of three measurements of PEF by mini-Wright peak flowmeter was recorded by the patients themselves every morning and evening during 14 successive days before and after the weight loss period. If patients were receiving bronchodilator, PEF values were measured before its use. PEF variability was expressed in three ways: as the diurnal PEF variation (highest PEF – lowest PEF/mean value of the two, \(\times 100\%\)), the mean difference between the highest and lowest morning PEF values measured over a follow-up period of 14 days, and the day-to-day PEF variation (SD percent mean morning PEF).

Statistical Analysis

Pulmonary function data are expressed as mean (SD). PD\(_{15}\) values were analyzed after log\(_{10}\) conversion. Wilcoxon signed-rank test was used in statistical comparisons of lung function variables between baseline and after treatment. The relations between two variables were calculated with Spearman’s correlation test. A p value < 0.05 was considered to indicate statistical significance.

RESULTS

The effects of weight reduction on BMI and symptom scores as well as use of rescue medication are shown in Table 2. The mean weight loss was 13.7 kg (range, 8 to 18 kg). The mean BMI decreased by 5.1 kg/m\(^2\) (range, 3.0 to 7.4 kg/m\(^2\)). Symptoms were recorded on a VAS scale from 0 to 100 mm. A significant reduction in dyspnea was demonstrated; the change in cough score was not statistically significant (NS). The use of rescue sympathomimetics was < 1 dose per day at baseline, and it did not change by the end of the weight reduction period.

A significant improvement in the mean morning and evening PEF values with weight loss was found. The difference between the daily highest and lowest PEF did not change. Before weight loss, it was 24 L/min (range, 10 to 59 L/min), and after weight loss, it was 20 L/min (range, 8 to 41 L/min). Diurnal PEF variation declined from 5.5% (2.4) to 4.5% (1.5) (p = 0.01). PEF indexes over a follow-up period of 14 days are presented in Table 2. Calculated from the serial morning PEF values over 2 weeks, the mean difference between the highest and lowest morning PEF values fell by 38% with weight reduction (Table 2). Day-to-day PEF variation decreased from 5.3% (2.6) to 3.1% (1.3) (p < 0.005). Individual changes in diurnal and day-to-day PEF variations are shown in Figure 1.

Seven patients met the inclusion criteria for the histamine challenge test. The mean PD\(_{15}\) was 0.20 mg (range, 0.015 to 1.6 mg) before weight loss and 0.30 mg (range, 0.043 to 1.6 mg) after weight loss. The change was NS.

Pulmonary function data are shown in Table 3. The mean FEV\(_1\) was low before weight loss (77% of
predicted; range, 50 to 105%), while the mean FVC was within normal range (93% of predicted; range, 71 to 114%). Weight reduction induced a significant increase in FEV1 (percent predicted; p < 0.01) and FVC (percent predicted; p < 0.05). Also, AFV increased with weight loss (p < 0.005). FEV1/FVC ratio did not change. Flow rates at low lung volumes (FEF25–75) were slightly reduced and showed a significant rise after weight loss (percent predicted; p = 0.01) also when related to FVC (FEF25–75/FVC percent; p < 0.05; Table 3). DLCO was within normal range in all patients before and after weight loss. The mean baseline DLCO was 102.5% of predicted (range, 84 to 121% of predicted).

The mean values of FRC, VC, and TLC were within normal range before weight loss, but still a significant increase in lung volumes was demonstrated with weight reduction. RV or RV/TLC did not change. The most significant improvement in lung volumes was the increase in expiratory reserve volume (ERV) from 0.43 L (0.22) to 0.72 L (0.50). The rise in ERV also mainly accounts for the increase in FRC, because RV did not change. TLC-He and TLC-B are presented in Table 3. Nonventilated gas compartment (TLC-B - TLC-He) was 0.43 L before and 0.61 L after weight loss; the change was NS. The mean Raw was high before weight loss (329% predicted; range, 161 to 579% predicted; Table 3). In response to weight reduction, Raw decreased toward the normal level (p < 0.05), but the mean value was still after weight reduction 252% of predicted (range, 67 to 473% predicted). The change in BMI expressed as a percent baseline value correlated with the increase in SGaw (1/Raw; r = 0.59; p < 0.05).

The mean baseline arterial oxygen tension (PaO2 = 11.4 [0.9] kPa) and the mean carbon dioxide tension (PaCO2 = 5.2 [0.3] kPa) were within normal range. Weight loss did not alter the values. The effects of weight loss on VE are shown in Table 4. VE measured in patients in supine and standing positions fell after weight loss by 16% (p < 0.01) and by 14% (p = 0.01), respectively. VT also showed slight decrease (p = 0.07 supine; p < 0.05 standing) while RR did not change.

**Discussion**

The results of our study indicate improved pulmonary function after weight reduction in obese patients with asthma, suggesting that these patients benefit from even modest weight loss. The increase in FEV1 with no change in FEV1/FVC ratio may rather reflect improvement in lung volumes, a well-known effect of weight loss in obesity, than decrease in airways obstruction. However, increased FEF25–75 even when related to volume (FEF25–75/FVC) may suggest a relief in peripheral airways obstruction. Furthermore, increased FVC and VC may indicate improvement in small airways obstruction. However, the decrease in PEF variability after weight loss found in the present study refers to an attenuated variability of bronchial obstruction in larger airways. Also the decline in Raw may reflect the decrease in airways obstruction more in large than in small airways.

In obesity, increased volumes after weight loss, especially ERV or FRC, have been reported in several studies. RV usually remains unchanged. In chronic asthma, RV and FRC can be elevated because of hyperinflation. In obese asthmatics, weight reduction and a decrease in asthma severity with lessened hyperinflation may change FRC values to opposite directions. The results of the present study demonstrated a significant increase in

**FIGURE 1.** The individual changes in (top, a) diurnal and (bottom, b) day-to-day PEF variations before and after weight loss in obese patients with asthma (n = 14). The bars present the mean values. The p values refer to Wilcoxon signed rank test.
the mean FRC after weight reduction, although the individual changes in FRC varied within a wide range. The increase in ERV was more constant. In this respect, changes in ERV may better than FRC reflect the effects of obesity or weight loss on lung volumes in this study.

Mechanisms how higher lung volumes affect pulmonary mechanics and work of breathing in asthma are not clear. Based on previous data concerning pulmonary function in asthma or obesity, several mechanisms could be postulated. Firstly, increase in FRC may contribute to a decrease in Raw that further reduces work of breathing.\(^{19}\) Secondly, in acute asthma with bronchoconstriction, a certain degree of hyperinflation with increased FRC may decrease work of breathing.\(^{20}\) It could be hypothesized that in this respect, low FRC could be unfavorable in obese asthmatics. Thirdly, low FRC with further decrease in FRC in supine position and concomitant increase in Raw may worsen nocturnal airways obstruction and increase diurnal variation of obstruction in asthma.\(^{21}\)

Both obesity and asthma can cause an excessive small airway closure and increase in gas trapping.\(^{11,12,22}\) Of parameters that reflect small airways obstruction, our data showed reduced FEF\(_{25-75}\) that increased after weight loss as well as FEF\(_{25-75}/\text{FVC}\). Also, an increase in FVC and VC may reflect decreased small airway obstruction. However, only slight, if any, gas trapping was observed based on our TLC-B\(_2\) TLC-He data.

Rapid shallow breathing pattern with low \(V_t\) has been reported in morbid obesity.\(^{11}\) However, our data showed higher \(V_e\) and \(V_t\) before than after weight loss. Tobin et al\(^{23}\) have suggested that symptomatic patients with chronic asthma may display increased \(V_e\) in association with an elevated respiratory center drive. They have reported increased \(V_t\) in patients with asthma while breathing frequency may be normal. Our findings are in keeping with this, suggesting that tendency to increase \(V_t\) in asthma patients may counteract the effects of obesity on breathing pattern.

There are increasing data available on the relation between obesity and bronchial hyperresponsiveness (BHR). It has been postulated that the lower \(V_t\) of obese patients results in less tidal stretching of

### Table 4—The Effects of Weight Loss on \(V_e\), \(V_t\), and RR Measured with Patients in Supine and Standing Positions\(^*\)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before Weight Loss</th>
<th>After Weight Loss</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(V_e), L/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>8.6 (1.5)</td>
<td>7.2 (1.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Standing</td>
<td>11.1 (4.1)</td>
<td>9.6 (3.8)</td>
<td>=0.01</td>
</tr>
<tr>
<td>(V_t), L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>0.53 (0.1)</td>
<td>0.47 (0.1)</td>
<td>=0.07</td>
</tr>
<tr>
<td>Standing</td>
<td>0.74 (0.3)</td>
<td>0.64 (0.2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>(RR), breaths/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>16 (2)</td>
<td>15 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>Standing</td>
<td>15 (3)</td>
<td>15 (3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

\(^*\)Data are presented as mean (SD).
airways smooth muscle and could promote airway narrowing and possibly airway hyperreactivity.24 Kaplan and Montana25 have studied exercise-induced bronchospas in obese nonasthmatic children. They demonstrated that the frequency and degree of exercise-induced bronchospas was higher in obese children. Huang and colleagues26 have studied the relation between BMI and BHR in adolescents in Taiwan. They found that BMI was a significant predictor of BHR in teenage girls but not in boys. If obesity is associated with an increased risk of BHR, one would expect a decrease in bronchial responsiveness with weight loss. FEF<sub>25–75</sub>/FVC ratio has been reported to be associated with airways responsiveness.27 The results of the present study showed increase in FEF<sub>25–75</sub>/FVC, which may indicate decreased BHR after weight loss. In this study, the small number of patients tested may partly explain why we did not find a significant change in BHR measured using a histamine challenge test.

To our knowledge, there are no previous studies concerning the effects of weight loss on PEF variability in obese asthma patients. The results of the present study indicated that PEF variability decreased with weight loss. The mechanism is not clear, but the increase in PEF values could partly explain the reduction in diurnal variation, assuming parallel changes in morning and evening PEF values. However, the increase in PEF values may not explain the decline in day-to-day PEF variation reported herein. Our data showed that the difference between highest and lowest morning PEF values decreased with weight reduction. An interesting finding was that the lowest morning PEF values increased significantly while the highest morning PEF remained unchanged. The mechanisms of how weight loss affects PEF variation remain unclear. The decrease in airways obstruction and improved ventilatory mechanics after weight loss may contribute to a better control of airways obstruction.

It is also possible that there are other mechanisms linking weight loss to the decrease in bronchial obstruction and hyperreactivity. Earlier studies have reported changes in serum leptin levels after weight loss.28 According to preliminary results, leptin may have proinflammatory effects in the airways and may affect bronchial reactivity.29 Gene polymorphism may alter adrenergic receptor responsiveness both in asthma and obesity.30 Altered adrenoceptor function could be another common pathway between obesity and asthma. Further studies concerning effects of weight loss on responsiveness of β<sub>2</sub>-adrenoceptors in lungs would be of interest.

The results of our study suggest that obese asthmatics benefit from weight loss as all obese patients do in terms of increased lung volumes and improved ventilatory mechanics. Our results also indicate decreased airways obstruction as well as lower PEF variability after weight loss, suggesting that obesity may increase the degree and variability of airways obstruction in asthmatics. Yet, further studies with larger patient groups will be necessary to clarify the relationship between obesity and asthma.

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