Comparison of helium dilution and plethysmographic lung volumes in pregnant women


ABSTRACT: The multibreath helium equilibration method is the technique recommended for routine measurement of static lung volumes in normal subjects. However, pregnancy could be an exception to this general rule, due to airway closure during the second half of gestation. The aim of this study was to compare the measurements of lung volumes by plethysmography and helium dilution during pregnancy.

Twenty three healthy women were studied at 12, 24 and 36 weeks of pregnancy, and 4 months postpartum. Total lung capacity (TLC), functional residual capacity (FRC) and residual volume (RV) were measured by multibreath helium equilibration (TLCHe, FRCHe and RVHe) and by plethysmography (TLCbox, FRCbox and RVbox).

Only at 36 weeks were there differences between the two methods. RVbox was significantly larger than RVHe (1.01±0.18 vs 0.77±0.21 L; p<0.001). FRCbox was larger than FRCHe (1.95±0.32 vs 1.60±0.32 L; p<0.001) and TLCbox was larger than TLCHe (4.83±0.52 vs 4.45±0.51 L; p<0.05). The 95% limits of agreement for differences between lung volumes measured by the two techniques (helium dilution - plethysmography) at 36 weeks were: -0.42 to -0.06 L for RV; -0.54 to -0.17 L for FRC; and -0.66 to -0.11 L for TLC.

We conclude that using the multibreath helium equilibration method to measure lung volumes in at-term pregnant women results in underestimation of functional residual capacity and total lung capacity.

Measurement of static lung volumes provides information about the mechanical properties of the ventilatory apparatus that may be of considerable importance in understanding the pathophysiological changes in patients with lung disease [1, 2]. Various procedures can be used to measure static lung volumes [2]. The two most widely used are multibreath helium equilibration and body plethysmography [1, 2]. Classically, it is accepted that in normal individuals and in patients with interstitial lung disease, these two techniques produce equivalent mean values [2–4], whereas the helium dilution method underestimates the absolute lung volumes in patients with obstructive lung disease to an extent that depends on the severity of airway obstruction [2, 3–5]. Pregnancy could be an exception to this general principle. It is well known that, when supine, some healthy pregnant women have hypoxaemia and an increase in the alveolar-arterial oxygen gradient [6–12]. These alterations have been attributed to airway closure during normal tidal breathing [13]. The existence of lung areas which communicate poorly with the central airways in pregnant women might result in a significant underestimation of true lung volumes measured by helium dilution as compared to plethysmography.

To examine this possibility, we have measured lung volumes by multibreath helium equilibration and plethysmography in normal pregnant women both during gestation and again postpartum.

Subjects and methods

Subjects

Twenty three healthy pregnant women without previous history of cardiovascular or respiratory diseases were studied. The subjects were aged 29±3 yrs (mean±SD), 159±4 cm in height and 58±7 kg in weight when non-pregnant. They were judged to be healthy by history, physical examination, electrocardiogram, basal spirometry, complete blood cell count and automated serum chemistry panel. All of the women had uncomplicated singleton pregnancies. Seventeen had no previous pregnancies, four had one, one had two, and one had three. Eleven of the women smoked. All volunteers were taking iron and/or vitamin supplements only.

Informed consent was obtained from all subjects, and the protocol was approved by the institutional Ethics Committee.
Methods

Study sessions were planned for weeks 12, 24 and 36 of pregnancy, and 4 months after childbirth for measurement in the nonpregnant state. Investigations commenced at the same time in the morning and in baseline conditions. Subjects were asked not to eat in the 4 h before the study. After a few minutes of adaptation to the mouthpiece, pulmonary function studies were started, with the subject seated in an upright position.

Spirometry was obtained by means of a pneumotachograph, and static lung volumes were measured both by body plethysmography and multibreath helium equilibration. In all subjects, pulmonary function tests were carried out by the same technician. The automated equipment (MasterLab 3.2; Jaeger, Würtzburg, Germany) used for all determinations was checked periodically following the European Respiratory Society guidelines [14]. Room temperature and barometric pressure were recorded twice daily with mean values of 22°C and 94.6 ± 1.3 kPa (mean ± SD), respectively.

After spirometry, lung volumes were determined using a constant-volume body plethysmograph. Thoracic gas volume (TGV) at the level of functional residual capacity (FRCbox) was measured while the subjects made gentle breathing movements against the shutter at a rate of <1 L·s⁻¹. Corrections for not occluding the airway at a representative end-expiratory lung volume were made to obtain FRCbox [14]. Inspiratory capacity (IC) and expiratory reserve volume (ERV) were measured during the same manoeuvre from which FRC was determined. FRCbox was reported as the mean of three or more measurements which differed by less than 5% from the mean. Total lung capacity (TLCbox) was calculated by adding the mean FRCbox to the largest IC derived from a TGV which was within 5% of the mean. Similarly, residual volume (RVbox) was determined by subtracting the ERV from FRCbox. Airway resistance (Raw) was computed from pressure and flow measurements breathing warm, moist air fulfilling body temperature, atmospheric pressure and saturation with water vapour (BTPS) conditions [15]. The frequency of panting was 2 Hz [14].

Thirty minutes after plethysmography, lung volumes were measured using the multibreath helium dilution method, while the subjects were sitting in the body plethysmograph. The closed circuit was filled with a mixture of 10% He, 35% O₂ and the rest N₂. A helium heat conductivity analyser was employed. Oxygen was added to replenish the air taken up during rebreathing, and the CO₂ produced was removed by an in-line soda lime absorber. The helium equilibration was assumed to be complete when the concentration changed by less than 0.02% in 30 s [14]. The rebreathing started from the resting end-expiratory position and lasted 5–7 min. At the end of rebreathing, a number of IC and ERV manoeuvres were performed to calculate total lung capacity (TLChe = FRChे - ERV). Lung volumes by helium dilution were the mean of duplicate measurements.

Statistical analysis

The results are expressed as mean and standard deviation (SD). Statistical analysis was performed with BMDP (Classic release 7.0 (Statistical Solutions Ltd, Cork, Ireland). All data were analysed using an analysis of variance (ANOVA) for repeated measures. Post-hoc multiple comparisons were performed using the Bonferroni correction. Simple effects within each factor (lung volumes by plethysmography and helium dilution in each trimester) were analysed. A p-value of less than 0.05 was accepted as the minimum level of statistical significance [16]. Agreement between pairs of measurements (plethysmographic vs helium dilution) were analysed according to the methods described by Bland and Altman [17].

Results

Dynamic and static lung volumes and airway resistance for each trimester of pregnancy and after delivery are shown in table 1. No significant changes in forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), FEV₁/FVC ratio or Raw were observed during pregnancy or postpartum. RV was significantly less at 36 than at 12 and 24 weeks and after delivery. FRC decreased progressively during pregnancy, the difference reaching statistical significance by week 24. An increase was noted after delivery. TLC was significantly greater at postpartum and at 12 and 24 weeks than at the end of pregnancy.

Table 1. – Lung function during pregnancy and statistical significance of the differences in value between the trimesters of pregnancy and between the plethysmographic and helium dilution methods of measurement

<table>
<thead>
<tr>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC L</td>
<td>3.45±0.43</td>
<td>3.58±0.32</td>
<td>3.50±0.37</td>
</tr>
<tr>
<td>FEV₁ L</td>
<td>3.19±0.38</td>
<td>3.17±0.28</td>
<td>3.08±0.33</td>
</tr>
<tr>
<td>FEV₁/FVC%</td>
<td>89±4</td>
<td>88±4</td>
<td>88±4</td>
</tr>
<tr>
<td>Raw kPa·L⁻¹·s⁻¹</td>
<td>0.26±0.09</td>
<td>0.24±0.08</td>
<td>0.26±0.10</td>
</tr>
<tr>
<td>RVbox L</td>
<td>1.27±0.24</td>
<td>1.25±0.21</td>
<td>1.01±0.18</td>
</tr>
<tr>
<td>RVite L</td>
<td>1.21±0.24</td>
<td>1.14±0.21</td>
<td>0.77±0.21</td>
</tr>
<tr>
<td>FRChे L</td>
<td>2.43±0.37</td>
<td>2.40±0.35</td>
<td>1.60±0.32</td>
</tr>
<tr>
<td>TLCbox L</td>
<td>5.01±0.57</td>
<td>5.12±0.39*</td>
<td>4.83±0.52</td>
</tr>
<tr>
<td>TLCHe L</td>
<td>4.94±0.59</td>
<td>4.99±0.40</td>
<td>4.45±0.51</td>
</tr>
</tbody>
</table>

FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; Raw: airway resistance; RVbox: plethysmographic residual volume; RVite: helium dilution residual volume; FRCbox: plethysmographic functional residual capacity; FRChे: helium dilution functional residual capacity; TLCbox: plethysmographic total lung capacity; TLCHe: helium dilution total lung capacity. Values are presented as mean±SD (n=23); *: p<0.05 vs postpartum; #: p<0.05 vs week 12; †: p<0.05 vs week 24; ‡: p<0.05 vs helium dilution method; ‴: p<0.001 vs helium dilution method.
Table 2. – Differences between lung volumes measured by helium equilibration and plethysmography during pregnancy

<table>
<thead>
<tr>
<th>Week</th>
<th>RV</th>
<th>FRC</th>
<th>TLC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Week 12</td>
<td>-0.07 (-0.21, 0.08)</td>
<td>-0.10 (-0.21, 0.02)</td>
<td>-0.07 (-0.19, 0.05)</td>
</tr>
<tr>
<td>Week 24</td>
<td>-0.12 (-0.30, 0.07)</td>
<td>-0.08 (-0.24, 0.07)</td>
<td>-0.13 (-0.26, 0.01)</td>
</tr>
<tr>
<td>Week 36</td>
<td>-0.24 (-0.42, -0.06)</td>
<td>-0.36 (-0.54, -0.17)</td>
<td>-0.38 (-0.56, -0.11)</td>
</tr>
<tr>
<td>Postpartum</td>
<td>-0.13 (-0.76, 0.50)</td>
<td>-0.09 (-0.33, 0.15)</td>
<td>-0.09 (-0.29, 0.10)</td>
</tr>
</tbody>
</table>

Values are presented as mean difference (helium equilibration minus plethysmography) and 95% limits of agreement in parenthesis. RV: residual volume; FRC: functional residual capacity; TLC: total lung capacity.

Discussion

The results of the present study demonstrate that static lung volumes measured by helium dilution are lower than those measured by plethysmography during the third trimester of pregnancy.

As reported by others [18–20], we have not observed changes in dynamic lung volumes during pregnancy. The present results describing the evolution of static lung volumes are similar to previous reports [21–25]. We found a 27% decrease in FRCbox between postpartum and 36 weeks, which is similar to the decrements of 9.5 to 25% reported by other authors [7, 18, 21]. The fall in FRC at the end of pregnancy has been explained by the shift to the right of the chest wall pressure-volume curve [22]. Although some authors [24, 25] have reported that RV remains unchanged during pregnancy, others [7, 11, 18, 21] have found a 7–22% decrease of RV starting from the second half of gestation. We observed a 26% decrease in RVbox between week 36 of pregnancy and postpartum. In the present subjects, TLCbox was slightly (5%) diminished at term. This is in agreement with previous investigations that found minor changes of TLC in both directions [21]. The increase of the transverse diameter of the thorax, together with the unimpaired diaphragmatic function, causes the IC to increase in the second half of gestation [11]. The increase of IC is sufficient to compensate for the decrease of FRC, thus maintaining a constant TLC.

The comparison of lung volumes measured by plethysmography and helium dilution shows large differences at the end of pregnancy, principally in FRC and TLC. In some circumstances, the plethysmographic method induces errors in the measurement of lung volumes. In patients with high airway resistance, plethysmography may overestimate lung volume. In these subjects, the flow resulting from the motion of upper airway walls during panting may be responsible for a substantial pressure difference between mouth and alveoli [4, 26]. In the present subjects, no changes in airway resistance were noted during pregnancy (table 1). Moreover, the...
plethysmographic measurements were performed at a rate of <1 L·s⁻¹ to minimize the overestimation of lung volume [27, 28]. Plethysmography may also overestimate thoracic gas volume in infants due to high compliance of extrathoracic airways [29], but this is not the case in adults [30].

The differences between the two methods could be attributed to an underestimation of lung volumes by the multibreath helium equilibration method. Airway closure at the end of pregnancy is well documented. In the last month of pregnancy, 50% of women show airway closure during normal ventilation [6]. Some authors [9, 10] have reported a slight increase in closing volume during pregnancy, which was attributed to an increase in lung water or to a change in the elastic properties of the lungs [10]. However, these studies failed to detect significant changes in lung volumes during pregnancy. In other studies [6, 7, 31, 32], no change in closing capacity was found throughout pregnancy, but the difference between closing capacity and FRC decreased as a consequence of a reduction in FRC. These changes may also explain airway closure during normal ventilation in the third trimester of pregnancy. Indirect evidence in support of premature airway closure during pregnancy is provided by measurements of oesophageal and gastric pressures [19], which are more positive in the third trimester of pregnancy than in postpartum. The resulting decrease in transpulmonary pressure could explain peripheral airway collapse.

Despite the absence of airway obstruction in the present subjects, the existence of poorly or nonventilated airspaces could induce an underestimation of lung volumes measured by helium dilution. Even in erect subjects, an increased airway closure (FRC and RV differences >150 mL at week 36) must induce hypoxaemia due to shunt, because the slight physiological hyperventilation of pregnancy would not undo the venous admixture in very poorly-ventilated or closed compartments [32, 33]. Other possible mechanisms to explain the difference between the two techniques are a change in transpulmonary pressure gradient [34], or changes in the pressure-volume characteristics of the lung [35].

In conclusion, it appears that the multibreath helium equilibration method underestimates lung volumes in healthy subjects, an increased airway closure (FRC and RV differences >150 mL at week 36) must induce hypoxaemia due to shunt, because the slight physiological hyperventilation of pregnancy would not undo the venous admixture in very poorly-ventilated or closed compartments [32, 33]. Other possible mechanisms to explain the difference between the two techniques are a change in transpulmonary pressure gradient [34], or changes in the pressure-volume characteristics of the lung [35].

References


