Density dependence of respiratory input impedance re-evaluated with a head generator minimizing upper airway shunt

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ABSTRACT: Total respiratory impedance was assessed from 4 to 30 Hz in ten normal subjects breathing air and a helium-oxygen gas mixture using two methods of applying pressure oscillations at the airway opening: 1) the conventional method where pressure is varied at the mouth; 2) the method recently developed by Peslin et al. (J Appl Physiol, 1985, 59, 1790-1795) in which pressure is varied both at the mouth and around the head to minimize transmural pressure across upper airway walls, and the corresponding artifact. When breathing air slightly lower resistances (p < 0.05) and considerably higher inertances (p < 0.001) were found using the head generator. Breathing helium-oxygen reduced respiratory resistance and its frequency dependence, as well as respiratory inertance very significantly (p < 0.001), with minor differences between the changes seen with the two methods. In contrast, the changes in respiratory compliance were small, and not in the same direction, when pressure was varied at the mouth and around the head. It is concluded that the accuracy of the conventional method may be sufficient for diagnostic purposes in subjects without gross mechanical abnormalities, i.e. for early detection of mechanical abnormalities.

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Total respiratory impedance measurements by forced oscillations, as first described by DuBois et al. [1], are theoretically sensitive to a number of lung and chest wall mechanical abnormalities. Thanks to microcomputers, they are now easy to implement and, in contrast to spirometric investigations, they do not require active co-operation from the subject. This makes them a potentially useful tool for field studies, in particular for early detection of airway abnormalities. Indeed, previous investigations have revealed that both total respiratory resistance (Rrs) and reactance (Xrs), derived from impedance measurements, could be modified in smokers and/or in relation to professional exposure [2-7]. A particularly interesting observation in some studies has been the occurrence of a decreased Rrs with increasing frequency [2-3], a finding which could be interpreted in terms of parallel inhomogeneities in the lung according to the models of Otis et al. [8] or Mead [9]. However, these changes were usually small, and it was suggested that the sensitivity of the method to peripheral abnormalities could be much enhanced if the measurements were made after washing the airways with a lighter gas mixture than air, thereby decreasing the contribution of central airways to total respiratory impedance [10, 11]. Using that approach Bhansali et al. [10] observed a greater negative frequency dependence of Rrs after histamine infusion when breathing 80%He-20%O2 than when breathing air. Brochard et al. [12] also showed recently that both the frequency dependence of Rrs and its change when breathing He-O2 were better related to smoking history and occupational exposure than were parameters derived from spirometric measurements. Their results, however, were at variance with those of Bhansali et al. [10] since they observed that the negative frequency dependence of Rrs was less in He-O2 than in air in exposed subjects.

On the other hand, it has recently been demonstrated that the negative frequency dependence of Rrs, as well as other impedance parameters, could be seriously misestimated when using the conventional forced oscillation technique, with pressure variations applied at the mouth [13, 14]. This is due to the shunt impedance of upper airway walls Zuaw (mouth, pharynx, larynx), which are mechanically in parallel with the total respiratory system. The error varies between subjects according to the ratio of Zuaw to respiratory system impedance (Zrs) and is not properly eliminated by supporting the cheeks firmly with both hands [13], which only doubles Zuaw [15]. It has been shown to be particularly large in obstructive patients [13, 14], and is expected to vary when the subject's own impedance varies. It is,
therefore, not only a cause for misestimating respiratory impedance parameters, including the frequency dependence of $R_{rs}$, but also their changes when breathing a lighter gas mixture. It has also been shown that the error could be almost completely eliminated by applying the input pressure around the head, rather than just at the mouth, so as to minimize transmural pressure across upper airway walls [14]. In this study we took advantage of this new method to re-evaluate the influence of breathing a lighter gas mixture on respiratory impedance in healthy subjects. Data were also obtained with the conventional set-up, for comparison.

Methods

The study was conducted in ten asymptomatic subjects (six males) from the staff of the laboratory. In each subject respiratory impedance was measured from 4-30 Hz by applying pseudorandom pressure variations either at the mouth or simultaneously at the mouth and around the head by using a head pressure generator as previously described [14]. The pressure signal was the sum of the harmonics of 2 Hz from 4-30 Hz. The amplitude and phase of the fourteen components were designed to improve the signal/noise ratio at the mouth and to reduce the peak to peak/rms ratio of the signal [16]. The input pressure then had a coloured spectrum with greater amplitudes for low frequencies at which the noise of spontaneous breathing is more important.

Conventional set-up

Pressure variations at the mouth were obtained with a 90 W loudspeaker driven by a computer and mounted in the wall of a wooden chamber. The latter was connected to a bag-in-box system containing air or the He-0$_2$ mixture (fig. 1). The subject breathed the gas from the bag through a heated pneumotachograph. A 0.02 l/s$^{-1}$ bias flow prevented rebreathing. The measurements were started after a wash-in period of one minute and were performed whilst the subject supported his cheeks firmly with both hands.

Head generator method

The basic experimental set-up was almost identical to that previously described [14]. The subject was seated inside a wooden frame, used to support the head generator (fig. 1), and wore a neck collar. The latter was made of a flat ring-shaped rubber bag filled with small glass beads connected to a vacuum-line. The head generator was made of an Altuglas cylinder, the top of which was equipped with a 90 W loudspeaker. The subject breathed through a heated pneumotachograph, also placed within the cylinder. Before helium measurements were taken the air in the head generator was flushed with a continuous flow of 80%He-20%O$_2$ until the helium concentration, as recorded with a thermoconductivity analyser, was steady. Due to leaks around the neck, helium concentration in the cylinder did not reach 80%, but was on average 69% (range 64-77%). A small flow of He-0$_2$ was continued throughout the measuring period to keep the concentration constant.

In both instances, mouth pressure ($P_m$) was measured with a Celesco transducer (±2 hPa) and mouth flow ($V_m$) with a Fleisch No. 2 pneumotachograph connected to a similar pressure transducer. The latter had a common mode rejection ratio of 66 dB at 30 Hz. The frequency responses of the two pressure channels were matched within 1% of amplitude and 2° of phase up to 30 Hz. The influence of the gas mixture on the frequency response was studied and found to be negligible when using short connecting tubes. The time constant of the Fleisch pneumotachograph, which is a function of kinematic viscosity and varies with the gas mixture, was assessed by reference to a gas capacitance [17]. As expected, it was found to be much smaller with 80%He-20%O$_2$ than with air (0.58 ms vs 2.2 ms). It was corrected for, using an analogue computer. Gain factors were measured using a slanted fluid manometer for $P_m$ and a 3 l syringe for $V_m$. The pressure-flow ratio of the
pneumotachograph was found to increase by 10% with 80% He:20% O2.

Pressure and flow signals were passed through band-pass filters (1–30 Hz) and digitized on-line at a rate of 128 Hz by an Apple IIe system. Results from six to eight 16 s periods were averaged for each measurement. The relationship between flow and pressure signals was analysed as described by MICHAELSON et al. [4], except that the fast Fourier transforms were made on blocks of 256 points with 50% of overlapping between blocks. Hence estimates of cross-spectra and autospectra for each 16 s period were made from the average of 15 blocks of 2 s each. Results of a particular frequency were discarded when the respective value of coherence function was lower than 0.95.

Measurements by the two methods, with air and with an 80% He:20% O2 gas mixture, were made in succession with the subject seated in exactly the same posture. The order of administration of the two gas mixtures was randomized and was the same for both methods.

Impedance curves, averaged from 6–8 measuring periods in each condition, were characterized by the following indices: the total respiratory resistance (R), compliance (C) and inertance (I), the resonant frequency (fn) and the change in respiratory resistance with increasing frequency (L/RjL/f). R, C and I were computed by fitting the values of measured impedance to those of a linear resistance-inertance-compliance (RIC) model. The fit was obtained by minimizing the mean relative distance between subject's and model impedance in the Rrs-Xrs plane. \( \Delta R/\Delta f \) was computed as the relative change of Rrs from 8–12 Hz to 26–30 Hz and expressed in \% Hz\(^{-1}\). All statistical comparisons were made using the t-test for paired data.

**Results**

For both air and He–O\(_2\) differences were seen between the average impedance curves obtained with the head generator and with the standard generator (fig. 2) and between the derived parameters (table 1). Compared with the data obtained with the head generator, resistance values differed little in air but tended to be systematically lower in He–O2, with the conventional method at the largest frequencies. Much larger differences were seen for the reactance values, which were significantly lower with the conventional method at most frequencies, and increased less with increasing frequency; as a consequence, resonant frequencies were much larger with the conventional method, particularly in He–O2 (p < 0.001). When the curves were interpreted with the RIC model (table 1), these differences in reactance resulted in 50% lower inertance values (p < 0.001) in both air and He–O2 with the conventional method, and slightly lower compliances in He–O2 (p < 0.01). Resistance values differed little with the two methods but \( \Delta R/\Delta f \) was significantly lower with the conventional method.

On average, breathing helium-oxygen significantly

![Graph](image-url)
Table 1. - Parameters derived from impedance curves obtained in air and in \textit{He-}O\textsubscript{2} with the head generator and with the conventional generator.

<table>
<thead>
<tr>
<th>gas mixture</th>
<th>generator</th>
<th>R ( \text{kPa} \cdot \text{s}^{-1} \cdot \text{Hz}^{-1} )</th>
<th>( \Delta R/\Delta f ) ( % \text{Hz}^{-1} )</th>
<th>I ( \text{kPa} \cdot \text{s}^2 )</th>
<th>C ( \text{ml} \cdot \text{kPa}^{-1} )</th>
<th>( f_r ) Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>Head</td>
<td>2.39±0.46</td>
<td>1.00±0.47</td>
<td>1.97±0.28</td>
<td>26.6±5.8</td>
<td>7.1±0.4</td>
</tr>
<tr>
<td></td>
<td>Standard</td>
<td>2.48±0.50</td>
<td>0.56±0.31</td>
<td>0.97±0.34</td>
<td>28.6±6.9</td>
<td>9.8±0.4</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.05</td>
<td></td>
<td>&lt;0.02</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>He-O\textsubscript{2}</td>
<td>Head</td>
<td>1.96±0.36</td>
<td>0.45±0.44</td>
<td>0.69±0.09</td>
<td>29.5±5.9</td>
<td>11.4±1.2</td>
</tr>
<tr>
<td></td>
<td>Standard</td>
<td>1.82±0.40</td>
<td>-0.58±0.21</td>
<td>0.34±0.07</td>
<td>24.5±5.1</td>
<td>18.1±3.0</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.007</td>
<td>&lt;0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>p(He-O\textsubscript{2} air)</td>
<td>Head</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Standard</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ±1 SD in ten subjects. Statistical significance of the comparisons by t-test for paired data; NS: not significant; R, I, C: respiratory system resistance, inertance and compliance; \( f_r \): resonant frequency at which \( X_{rs}=0 \); \( \Delta R/\Delta f \): percent change in resistance from 8–12 Hz to 26–30 Hz.

Reduced total respiratory resistance (\( p<0.001 \)), and the changes were significantly less with the head generator than with the conventional method (helium/air ratio = 0.82 ± 0.07 vs 0.72 ± 0.05; \( p<0.01 \)); the changes were significantly, although not tightly correlated (fig. 3). Reducing gas density also significantly decreased \( \Delta R/\Delta f \); the changes in slope observed with the two methods were significantly correlated (fig. 3), but were less with the head generator than with the conventional method (\( -0.55±0.28\% \text{ Hz}^{-1} \) vs \( -1.14±0.42\% \text{ Hz}^{-1} \); \( p<0.01 \)). As expected, the lighter gas mixture considerably reduced total respiratory inertance (\( p<0.001 \)), the absolute changes being much larger with the head generator than with the conventional method, but the relative changes being almost identical (helium/air ratio = 0.36 ± 0.05 with
Discussion

The main differences between the impedance curves obtained when pressure was varied at the mouth and around the head are in agreement with those previously reported during air breathing [14]. Contrary to observations in obstructive patients [13], the upper airway artefact does not much influence the estimation of total respiratory resistance in normal subjects. The slightly larger values of resistance seen with the conventional method (table 1, p < 0.05) as previously reported [13], are unlikely to be due to that artefact, but are more likely to represent a small degree of upper airway compression when the cheeks are firmly supported. Indeed, the difference disappears when the cheeks are not supported [13].

On average, respiratory resistance increased by 1%/Hz when measured with the head plethysmograph, and slightly less (p < 0.02) with the conventional method. These results are somewhat different from those in a previous study, where the upper airway artefact was measured with a small plethysmograph placed around the head and corrected for [13]. Then, AR/AF was significantly larger with the conventional method than when the artefact was eliminated. We have no explanation for this difference between the two series, but one must keep in mind that AR/AF varies greatly among individuals and is very sensitive to small technical details. On the other hand, as previously reported [14], reactance curves were substantially different when pressure was varied at the mouth rather than around the head. The upper airway artefact was responsible for an increased resonant frequency (p < 0.001) and an underestimation of inertance by a factor of two. The values of inertance obtained with the conventional method are in agreement with previous observations in the same conditions [3, 6].

The main motivation for measuring respiratory impedance in He-O₂ is to decrease central airway impedance, so that the method becomes more sensitive to mechanical abnormalities in the peripheral lung [10, 11]. A significant decrease in total respiratory resistance was indeed found with the conventional method [10-12, 17]; the changes ranged from 10% [10] to 39% [11], and our data with the same method are within that range (27%). The changes seen with the head generator were slightly but significantly less (~18%). This was certainly due in part, but probably not entirely, to the lower helium concentration (69% instead of 80%). Assuming, as a first approximation, that total respiratory resistance is the sum of a component directly proportional to gas density (central airways, Rc), and of a component completely independent of density (peripheral airways and tissues), and neglecting the slight change in gas viscosity, it is possible to estimate Rc from the change in resistance and the ratio of gas densities (Rrs₂ - Rrs₁ = Rc (p₂/p₁ - 1)). Rc was estimated to represent about 32 and 40% of total resistance from the data obtained with the head generator and the conventional method, respectively. This computation takes into account the actual densities of the two gas mixtures, and suggests that the change in resistance is slightly overestimated with the conventional method.

Another consequence of helium breathing was to decrease AR/AF. This was not found in normal subjects by BHANSALI et al. [10] who used a limited frequency range (4-12 Hz), but was reported by LANDSER et al. [17] and by BROCHARD et al. [12]. The latter authors suggested that the decrease in AR/AF when breathing He-O₂ was a sensitive index, and was much less in smokers and in subjects exposed to respiratory irritants. This study showed that the changes in AR/AF are overestimated by the conventional method (p < 0.01). As the influence of the upper airway artefact on AR/AF is larger in obstructive patients [13, 14], it is expected that the error on the changes induced by He-O₂ will also be more important in subjects with an increased impedance. However, it is not for use in obviously abnormal subjects, but for early detection of mechanical abnormalities, that this index has been recommended [12]. The correlation between the changes observed with the two methods in this study (fig. 3) rather suggests that the upper airway artefact will not impair the detection of a clearly abnormal pattern.

The last obvious effect of He-O₂ was, as expected, a reduction of total respiratory inertance. The latter has been shown to be located for a small part in the tissues [18], which undergo little acceleration, and for about 90% in the airways. Hence, total inertance is expected to decrease almost in proportion with gas density. In the present study this was very nearly so with the conventional method, although the absolute values of inertance were largely underestimated: the helium/air ratio was of 0.37 for an expected value of 0.40 (based on a density ratio of 0.33 and a ratio of 9 between airway and tissue components: expected 1₁₀₂/₁₈ = (1 + ab)/(1 + b) with a the density ratio and b the ratio of airway and tissue inertance in air). On the other hand, the changes seen with the head plethysmograph were somewhat larger than predicted (helium/air ratio of 0.36 for a predicted value of 0.30 with a density ratio of 0.44). They were even in excess of the changes expected if all of the inertance was located in the airways. This surprising finding cannot be explained on the basis of a simple RIC model, as it would imply a negative tissue inertance. However, it may be mimicked with a more complicated model featuring alveolar gas compressibility and two tissular pathways in parallel [18]. It could, therefore, reflect mechanical non-homogeneity of the respiratory system.

Finally, breathing He-O₂ was also responsible for some systematic changes in the apparent component
of the respiratory system. Whilst gas physical properties cannot influence tissue elasticity, a decreased density is likely to change gas distribution in the lung, particularly at such high frequencies, and consequently to modify its effective compliance. Indeed, dynamic lung compliance was already found to be larger in helium than in air at frequencies of 1–1.5 Hz [19]; this mechanism could account for the slightly larger values seen in He–O₂ with the head generator. The changes in the opposite direction observed with the conventional method are difficult to explain on physiological grounds, and are more likely to be related to the upper airway artefact.

To summarize our observations with the head generator, breathing a lighter gas mixture decreased total respiratory resistance and its frequency dependence, reduced respiratory inductance more than expected from the change in gas density, and slightly increased total respiratory compliance. Using the conventional method, reactance values were largely different due to the upper airway artefact. However the changes induced by breathing He–O₂ were, except for compliance, qualitatively similar to those obtained with the head generator. In particular, the changes in resistance and its frequency dependence seen with the two methods were significantly correlated. We conclude that although the effect of gas density cannot be precisely assessed with the conventional method, its accuracy may still be sufficient for diagnostic purposes.

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References


RÉSUMÉ: L'impédance respiratoire totale a été déterminée chez dix sujets normaux respirant de l'air ainsi qu'un mélange d’oxygène et d’hélium, entre 4 et 30 Hz, en utilisant deux méthodes pour appliquer les oscillations de pression à l’ouverture des voies aériennes: 1) la méthode conventionnelle où la pression varie à travers la bouche; 2) la méthode récemment développée par Peslin et collaborateurs (J Appl Physiol, 1985, 59, 1790–1795) où la variation de pression est appliquée à la fois à la bouche et autour de la tête, de façon à minimiser la pression transmurole au travers des parois des voies aériennes supérieurs ainsi que l'artefact correspondant. Lorsqu'on respire de l'air, l'utilisation du générateur cephalique entraîne des résistances légèrement diminuées (p < 0.05) et des instabilités considérablement augmentées (p < 0.001). Le fait de respirer un mélange hélium-oxygène réduit de façon très significative (p < 0.001) la résistance respiratoire et sa dépendance à l'égard de la fréquence, tout autant que l'impédance respiratoire, avec des différences minimes dans les modifications observées avec les deux méthodes. Par contre, les modifications de la compliance respiratoire sont faibles et n'apparaissent pas dans la même direction lorsqu'on fait varier la pression à la bouche ou autour de la tête. On peut cependant que la précision de la méthode conventionnelle peut être suffisante dans un but diagnostique chez les sujets sans grosses anomalies mécaniques; elle permet donc la détection précoces des anomalies mécaniques.