Respiratory resistance by the forced oscillation technique in asthmatic children and cystic fibrosis patients

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ABSTRACT: Measurement of the total resistance of the respiratory system (Rrs) is an attractive alternative to measurement of forced expiratory volume in one second (FEV1) in young children because it requires minimal co-operation. The purpose of this study was to assess the ability of the forced oscillation technique (FOT) to detect airway obstruction in asthmatic children and in patients with cystic fibrosis (CF).

Spirometry and Rrs were recorded in 45 asthmatic children (32 males and 13 females) and in 45 patients with CF (28 males and 17 females). Rrs was measured at 10 Hz with the Siregnost FD5 (Siemens, Germany).

The asthmatic children were slightly younger than the patients with CF (10±3 vs 14±7 yrs), and had milder airway obstruction (FEV1 80±19 vs 66±27% of predicted). Rrs was significantly higher in the asthmatic children (6.6±1.7 cmH2O·L-1·s) than in the patients with CF (4.8±1.4 cmH2O·L-1·s). A normal FEV1 (±mean -2SD) was associated with a normal Rrs (±mean +2SD) in 17 of the 45 asthmatic children and in 13 of the 45 CF patients. By contrast, a low FEV1 (mean -2SD) was associated with an increased Rrs (mean +2SD) in 21 of the 45 asthmatic children, but in only 3 of the 45 CF patients. Thus, FEV1 and Rrs yielded concordant information in asthmatic children much more often (38 out of 45) than in CF patients (16 out of 45) (p<0.001). In CF, Rrs failed to detect even severe airways obstruction. These findings might be accounted for by the inability of Rrs to reflect peripheral obstruction.

We conclude that total respiratory resistance is suitable to assess airways obstruction in asthmatic children but not in cystic fibrosis patients.


Measurement of forced expiratory volume in one second (FEV1) is considered to be the basic test for the assessment of airway obstruction. However, it requires comprehension and co-operation from the subject. Usually, it cannot be performed by young children, less than 6 yrs of age. Measurement of total resistance of the respiratory system (Rrs) with the forced oscillation technique (FOT) is a particularly attractive tool, especially in young children, since it requires minimal co-operation.

In two previously published studies, Rrs has been found to have a large interindividual variability and wider normal limits than FEV1 [2, 3]. More recently, predicted values with a much lower dispersion [4] have been described using a simple system, which provides a continuous display of Rrs and allows immediate detection of artefacts, such as swallowing or leaks at the mouth. This suggests that the clinical value of this technique could be substantially improved.

In the present study, we therefore aimed to assess the ability of the Rrs, using a simple technique, to detect airway obstruction in patients with cystic fibrosis (CF) and bronchial asthma, the most frequent chronic pulmonary diseases of childhood.

Materials and methods

Forty five asthmatic children (32 males and 13 females) and 45 CF patients (28 males and 17 females), without associated bronchial asthma or allergic bronchopulmonary aspergillosis, were studied.

Rrs was measured with the FOT at 10 Hz, using the Siregnost FD5 (Siemens, Erlangen, Germany). Details of the procedure have been reported previously [5]. Briefly, respiratory resistance can be computed from measurements both of impedance and phase angle, referred to as Rez, or a simplified approach measuring impedance and an approximation of phase angle, called Rrs. Both indices were computed in this study.

The child was seated, breathing quietly, with the cheeks and chin supported. Resistance was measured over the entire respiratory cycle, and the Rrs reported is the mean of three consecutive Rrs values, each recorded over 2.5 s. Rrs was always recorded before forced expiration to preclude any effect of the latter manoeuvre on resistance measurements. Forced vital capacity (FVC) and FEV1 were determined with an automated 8 L water-sealed spirometer (Eagle 1; W.E. Collins, Boston, MA, USA) [6], using standard techniques [7]. Predicted values for


Rs and spirometric indices were obtained in our laboratory, using the same technique and apparatus as in the present study [4]. In 10 CF patients more than 18 yrs of age, reference values for spirometry were from Dickman et al. [8]. Both Rs and FEV1 were expressed as absolute values and as SD scores, e.g. multiples of the standard deviation away from the mean. Rs and FEV1 were considered within normal limits when both values were within mean±2SD, and outside normal limits when these limits were exceeded.

In 20 of the 45 asthmatic children, with reversible airways obstruction (FEV1 increase of ≥20%), Rs and FEV1 were also measured before and 20 min after inhaled salbutamol (two puffs of 100 µg each). To assess the reversibility of airflow obstruction, we considered, like most authors, that a 20% improvement in FEV1 is beyond the variability of this index, and reflects a significant change. For Rs, we considered as significant those changes exceeding twice the average intraindividual coefficient of variability (CV) of these 20 asthmatic children.

A Fisher's exact test was used to compare the concordance of the Rs and FEV1 in asthmatic and CF patients. Physical data and FEV1 and Rs values were compared with the Mann-Whitney test. A paired t-test assessed changes in FEV1 and Rs after bronchodilation. A p-value of less than 0.05 was considered significant.

### Results

Physical data and average values of FEV1 and Rs are presented in table 1. Height, which is the single most important determinant both of Rs and FEV1, was comparable in the two groups, but asthmatic children were slightly younger than CF patients (p<0.05). If we discard 10 patients with CF older than 18 yrs, then age in the two groups (asthmatics: n=45, age 10±3 yrs; CF patients: n=35, age 11±4 yrs; p>0.05) as well as height (asthmatics: 139±15 cm; CF patients: 137±19 cm) become comparable.

Rs was 4.8±1.4 cmH2O·L⁻¹·s and Rs of 4.9±1.9 cmH2O·L⁻¹·s (r=0.97; p<0.001) in CF patients. Corresponding values in children with bronchial asthma were 6.6±1.7 and 7.0±2.2 cmH2O·L⁻¹·s (r=0.91; p<0.001). Since comparable results were obtained for Rs and Rs, only the results of the former index were presented, and referred to as Rs.

### Table 1. – Physical data, FEV1 and Rs values in asthmatic and cystic fibrosis patients

<table>
<thead>
<tr>
<th></th>
<th>Bronchial asthma (n=45)</th>
<th>Cystic fibrosis (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs</td>
<td>10±3</td>
<td>14±7*</td>
</tr>
<tr>
<td>Height cm</td>
<td>139±15</td>
<td>144±22</td>
</tr>
<tr>
<td>FEV1 L</td>
<td>1.69±0.67</td>
<td>1.48±0.62</td>
</tr>
<tr>
<td>% pred</td>
<td>80±19</td>
<td>66±27**</td>
</tr>
<tr>
<td>Rs cmH2O·L⁻¹·s</td>
<td>6.6±1.7</td>
<td>4.8±1.4</td>
</tr>
<tr>
<td>% pred</td>
<td>131±32</td>
<td>101±18***</td>
</tr>
</tbody>
</table>

Values are presented as mean±sd. FEV1: forced expiratory volume in one second; Rs: total resistance of the respiratory system. *: p<0.05; **: p<0.01; ***: p<0.001, compared to asthmatic children.

Rs was significantly higher (p<0.001) in the children with bronchial asthma (6.6±1.7 cmH2O·L⁻¹·s) than in the patients with CF (4.8±1.4 cmH2O·L⁻¹·s). The latter had a lower FEV1 (66±27 vs 80±19% predicted, respectively; p<0.01).

Both FEV1 and Rs were within normal limits in 17 of the 45 asthmatic children and in 13 of the 45 CF patients. A low FEV1 was associated with an increased Rs, in 21 of the 45 asthmatic children, but in only 3 of the 45 CF patients (fig. 1). Thus, FEV1 and Rs yielded concordant information (fig. 1, quadrants A and D) much more often in asthmatic children (38 out of 45) than in CF patients (16 out of 45), and this difference was highly significant (p<0.001). If the 10 CF patients more than 18 yrs of age are omitted, a similar conclusion is reached. Concordant information was observed in 38 of the 45 asthmatic children but in only 14 of the
35 CF patients (p<0.001). In CF patients, Rs failed to detect even severe airway obstruction, as assessed by FEV1. Inhalation of salbutamol by 20 asthmatic children (15 males and 5 females; (mean±sd) age 10±3 yrs; height 138±13 cm) increased FEV1 from 65 to 85% pred (p<0.001) and decreased Rs from 155 to 99% pred (p<0.001) (fig. 2). The average intraindividual CV of Rs for the group of asthmatic children as a whole was 6.9%. Significant changes in Rs, i.e. two times the CV, were recorded in each patient after bronchodilatation. In fact, in all but one child, these changes exceeded five times the intraindividual CV.

**Discussion**

In the present study, it was found that in bronchial asthma measurement of FEV1 and Rs provided concordant information, i.e. either of these tests could be used to demonstrate the functional abnormality. However, in CF Rs values failed to identify most of the patients with an abnormal FEV1. In order to define the comparative merits of two or more tests, the appropriateness of the reference values is of utmost importance. Since some of the CF patients studied were older than the children from whom we derived reference values [4], their FEV1 values were compared with those of Dickman et al. [8] for adults. The reason for this choice is that at 18 yrs of age our reference values in children [4] and the reference values of Dickman et al. [8] are very similar. However, the latter values are somewhat higher than those of Crapo et al. [9] used in the USA [10], or Quanjer et al. [11] in Europe. When using these latter two equations, there was, however, little change in the sd scores of the present patients. In CF patients more than 18 yrs of age, our own reference values for Rs [4] were used. With the same apparatus as used in the present study, Gimeno et al. [12] found that in adults Rs is related only to height and does not change with age.

When compared to more sophisticated systems providing access to additional parameters of respiratory mechanics, the simple technique used in the present study has a practical advantage probably derived from the lower dispersion of normal values: most asthmatic children with a low FEV1 also had an increased Rs (fig. 1a). This is in contrast to results of Konno et al. [13], who found that only 2 out of 13 Rs values fell outside the normal range in asthmatic children with an abnormal FEV1. Cogswell [14] reported that asthmatic children "may have values of Rs several times greater than the expected mean". However, almost half of these values were within their normal limits in a group of asthmatic children, most of whom had grossly abnormal spirometry [13]. More recently, in agreement with our data, Buhr et al. [15] found, in children (5–8 yrs of age) with asthma, that the diagnostic values of forced oscillations, spirometry and plethysmography (for measuring airway resistance) were similar.

In bronchial asthma, it is considered that there is an involvement both of large and small airways [16]. Our results are in keeping with this view; both FEV1 and Rs provided concordant information (fig. 1). Furthermore, inhalation of a sympathicomimetic bronchodilator induced a change both in FEV1 and Rs (fig. 3), suggesting a decrease in the obstruction both of large and small airways. The decrease of Rs was larger than that of FEV1 emphasizing the sensitivity of this index to changes in the large airways. Following salbutamol, all children decreased their Rs beyond the average intraindividual CV, suggesting that Rs may be used to assess reversibility of airway obstruction not only in a group of patients [17–20], but also in a given individual [13].

Due to the diversity of techniques of measurement and sometimes to a lack of detailed spirometric data, results on Rs measurements in CF are rather difficult to compare. Among 44 children with CF, 24 of whom were too young to perform spirometry, Cogswell [14] observed an increase in Rs (measured at 5 Hz) in only five patients. In 46 children, Landau and Phelan [21] concluded that the FOT (at 4 Hz) was without significant relationship to the clinical score and was poorly correlated with other functional tests. In 13 patients with abnormal FEV1 and/or maximal flow at 50% forced vital capacity (Vmax,50), Solymar et al. [22] found a low discriminatory power of Rs (measured at 2, 4 and 12 Hz). In a recent abstract, Hellincks et al. [23] reported that with the FOT (between 4 and 24 Hz) both Rs and airways resistance (Raw) were within normal limits in 20 children (mean age 12 yrs) with a moderate decrease in FEV1. In keeping with the present data, previous studies suggest that Rs is of limited value in this disease.

The discrepancy between Rs and FEV1 in CF is not actually surprising. Indeed, peripheral airway obstruction is an early and prominent feature of this disease [24–26]. Therefore, Rs, reflecting essentially the caliber of large airways, would not be affected by a distal, peripheral airway obstruction. The latter would instead be reflected by a decrease in FEV1.

Some authors [27, 28] using a forcing function containing multiple frequencies have claimed, from the behaviour of the frequency dependence of resistance, the possibility of partitioning resistance into a central and peripheral component. These attempts, as emphasized by Peslin
et al. [29] are based on a model proposed by Mead [30]. However, if the model proposed by Mead [30] is not an accurate reflection of the behaviour of the lung, partitioning of resistance into its two components is not warranted. Furthermore, upper airway wall motion is responsible for large errors in the estimation of frequency dependence of resistance, especially so in patients, and Peslin et al. [29] have suggested the use of a head plethysmograph to correct for these errors. The method, thus, becomes cumbersome and expensive. On the basis of electrical models of the lung, it might be predicted that peripheral obstruction would be poorly explored by the use of a single and relatively high frequency (10 Hz). Rs measurements at lower frequencies (2 Hz) could prove to be more sensitive but are often inaccurate in children, as harmonics of a high respiratory rate will interfere with the Rs measurements.

An increase in upper airway compliance in CF was proposed by some authors [31–33]. If this was the case, it would magnify the frequency dependence of Rs. However, in a recent investigation, we found no difference in upper airway distensibility between patients with CF and healthy controls [34].

From the practical point of view, our results and data from other recent studies suggest that, in asthmatic children, either total respiratory resistance or forced expiratory volume in one second can assess airway obstruction and its reversibility. However, this is not true in cystic fibrosis. Indeed, in this latter disease forced expiratory volume in one second, but not total resistance of the respiratory system, should be used to demonstrate airway obstruction.

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References

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