How to express the reversibility of bronchial obstruction?

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Since the original description of the "épreuve de bronchodilatation par aérosols adrénergiques" [1], testing the reversibility of bronchial obstruction has become one of the most common measurements in the pulmonary function laboratory. It is performed for clinical assessments as well as for fundamental investigations. However there are still many questions and controversies on the technical aspects of the tests, the type of analysis and the clinical relevance of the results.

One of the most common ways of expressing the bronchodilating response is to quantify the change in forced expiratory volume in one second (FEV₁) as a percentage of the basal obstruction (prebronchodilator or initial FEV₁). In recent years, this mode of analysis has been challenged as reviewed by Messier and Racineux [2] for the following reasons: 1) this expression implies that the variation is related to the initial value, which has been shown to be false for FEV₁; 2) it gives an unjustified advantage to low initial values; and 3) it is affected by the error related to the tendency of any result to regress towards the mean. Most of these criticisms also apply to the index recommended by the Societas Europaea P/ysiologica Clinicae Respiratoriae (SEPCR) in 1983 [3] where the change in FEV₁ is expressed as a percentage of the mean between the initial and the final values of FEV₁.

A number of studies [4-7] have supported these criticisms through the analysis of the bronchodilator response of patients with asthma and chronic obstructive pulmonary disease (COPD).

For several years, there has been a tendency to substitute this index of bronchodilation (change in FEV₁ as a percentage of the initial FEV₁) with another expression of bronchodilation: the change in FEV₁ as a percentage of the predicted value of FEV₁, Eliasson and Degraff [4], in a large review of published data, and Messier and co-workers [2, 5] have shown that this index could be used to distinguish between patients with asthma and those with COPD and that it was not significantly correlated to initial FEV₁. However, one must keep in mind the possibility that, at least in some patient groups, there may be a real negative correlation between response and baseline spirometry.

In this issue of the Journal, Dompeling et al. [8] have reassessed the problem of expressing the bronchodilator response. They have followed a cohort of nearly 200 patients over two years and evaluated the bronchodilator response every six months. The analysis was performed by looking for a relationship between the index of reversibility and the prebronchodilator FEV₁, firstly at each period (equivalent to a cross-sectional study), but also by examining the responses of each subject along the six evaluations (longitudinal study); once more the improvement of FEV₁, expressed as % of initial value was shown to be highly dependent on the prebronchodilator value, both in the COPD patients and in the asthmatics. However, the disappointing observation was that the improvement of FEV₁, expressed as % of predicted value, was also dependent on the prebronchodilator value; this was especially marked in the patients with COPD for whom this index was nearly as dependent on the initial FEV₁ as the conventional method (% of initial value). The reasons for this discrepancy are not clear: among the differences with previous studies, one can note that the bronchodilator challenge consisted of the combination of salbutamol and ipratropium bromide, both at a higher dosage than usual for bronchodilator challenges; the assessment of bronchodilation was also performed one hour after the administration of the bronchodilators, a strategy which, for practical reasons, is difficult to recommend in the routine of lung function laboratories. On the other hand, the large number of subjects studied by Dompeling et al. [8] may have been a determinant factor in bringing to light the relationship between the change in FEV₁, expressed as % of predicted value, and the initial FEV₁.

Of the numerous indices that have been analysed by Dompeling et al. [8], the ratio of the change in FEV₁ to the difference between the predicted value and the initial value was found: 1) to have one of the best reproducibilities; and 2) to be independent of the initial FEV₁. This finding may explain some of the differences in results between this study and previous ones regarding the index "% of predicted FEV₁". Table 1 shows a theoretical computation of different indices of bronchodilation for different initial FEV₁ values; considering a constant value for the proposed index "% of predicted minus initial FEV₁", the index "% of predicted FEV₁" shows little variation, whereas, the index "% of initial FEV₁" varies considerably.
Table 1. - Theoretical computation of different indices of bronchodilation for different initial FEV₁ values

<table>
<thead>
<tr>
<th>Change in FEV₁ as % pred - initial</th>
<th>50</th>
<th>60</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>% pred</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>% initial</td>
<td>15</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>% initial</td>
<td>30</td>
<td>20</td>
<td>13</td>
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For a constant value of index "% of predicted minus initial FEV₁," the index "% of predicted FEV₁" decreases as the initial FEV₁ increases, however, with much less variation than the index "% of initial FEV₁." FEV₁: forced expiratory volume in one second; pred: predicted.

Therefore, the absence of statistical correlation between the change in FEV₁ as % of predicted FEV₁ and the value of the initial FEV₁ may be ascribed to statistical problems (type II or beta error), whereas, the change in FEV₁ as % of initial FEV₁, is so strongly dependent on the initial FEV₁, that it appears clearly even in a small number of subjects. The study of Dompeling et al. [8] demonstrates that this index "% of predicted minus initial FEV₁," can be used both to evaluate and to follow-up patients in terms of reversibility of obstruction.

It can be predicted that a number of further studies will be performed on the assessment of reversibility of bronchial obstruction: it can also be predicted that no single solution will be found for this difficult problem and that the question to be answered (test for drug trial in asthma [9], follow-up of COPD patients...) will be a determinant factor in selecting the most useful index. Among the basic recommendations, it has to be stressed that it is important to control as many of the possible variables that affect bronchodilator response, such as the type and dose of the bronchodilator used, method and quality of delivery, bronchodilator use before the test, time of day, subject performance etc. Considering the number of bronchodilator tests performed daily in Europe, and the miracles accomplished by computers, it can be suggested, if it is considered that this problem is worth solving, that the European Respiratory Society might organize a large data base, which could help to reach a consensus on how to assess reversibility.

References