Editorial

Forced expiratory volume in one second and bronchodilator response in chronic obstructive pulmonary disease – a needless ritual?

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Forced expiratory volume in one second (FEV1) was described by Tiffeneau and Pinelli, working in Paris in 1947, and in 1951 by Gaensler in the USA.[1-2] Maximal voluntary ventilation (MVV) had previously been described, and reduced MVV in individuals suffering from lung dissease had been correlated with the degree of dyspnea. Tiffenau and Gaensler observed that the pertinent portion of the forced expiration maneuver was the initial part since, in the MVV maneuver, the length of each expiration was typically less than one second. Gaensler correlated MVV with various forced expiratory volumes and found the best correlation to be with FEV_1.[2]

Since FEV_1 is a highly reproducible parameter that correlates with chronic obstructive pulmonary disease (COPD) prognosis, it has, in recent decades, come to be considered the most relevant functional data to be obtained in tests of pulmonary function.[3]

In a study based on the coefficient of variation of diverse functional parameters, including data obtained through plethysmography, Light et al. concluded that FEV1 was still the most important functional parameter in the evaluation of bronchodilator response.[4]

In 1988, Guyatt et al. demonstrated that one-third of all COPD patients responded to a bronchodilator in the pulmonary function laboratory, whereas two-thirds responded in multiple spirometric tests, and that there was no correlation between acute and long-term bronchodilator response.[5] Recent studies have confirmed these findings, including response to the same class of bronchodilators, among them the long-acting bronchodilators.[6-8] In all of these studies, FEV_1 was used to evaluate the response.

In the last 25 years, various studies have demonstrated that exercise tolerance, as measured using a walk test, improves after bronchodilator use. Surprisingly, no correlation has been found between increased distance walked and variations in FEV_1.[9] Studies conducted in the 1980s demonstrated that improved exercise tolerance after bronchodilator use correlated better with changes in slow vital capacity (SVC) than with changes in FEV_1.[9]

In the 1990s, it became clear that, in patients with COPD, dyspnea upon exertion correlated better with air trapping, which is accentuated during exercise.[10] The realization that significant improvement in symptoms, exercise tolerance and quality of life could occur when there was little variation in FEV_1 resulted in a search for better methods of evaluation. Studies conducted in recent years clearly demonstrate that the symptomatic benefit in COPD patients is attributable to a pharmacological reduction in lung volume.[9,11-12]

In COPD, increased end-expiratory volume is reflected as a drop in inspiratory capacity (IC). Therefore, increases in IC after bronchodilator use are associated with better exercise tolerance.[9-12]

The study conducted by Tavares et al.[13] and presented in this issue of the journal shows that 90% of patients with COPD responded in one or more functional parameters after bronchodilator use, although FEV_1 detected only 31% of the responses. Forced vital capacity (FVC) was the parameter that varied most frequently, followed by residual volume, specific airway conductance and SVC.

Various findings explain the poor predictive value of FEV_1 for improved exercise tolerance and reduced dyspnea. The FEV_1 parameter does not provide information regarding the degree of limitation in expiratory flow, as seen in the expiratory flow-volume curve, or regarding the degree of air trapping. All of these parameters are relevant in relation to the dyspnea and limited exercise tolerance seen in COPD, and each can vary greatly for a given value of FEV_1.[14]

The functional response to a bronchodilator can be classified as either a response in flow or a response in volume. In COPD, volume responses are generally observed more frequently in patients presenting a greater degree of obstruction, which, ironically, preserves the efficacy of bronchodilators in many advanced cases of the disease.[15]

The value of FEV_1 can be a parameter either of flow response or of volume response. In many patients, variations in FEV_1 after bronchodilator use simply reflect recruitment of lung volume, i.e. the FEV_1/FVC ratio does not change, demonstrating reduced air trapping caused by the concomitant increase in FVC. In the Tavares et al. study,[13] the significantly higher rate of response in SVC and FVC by patients in the group that presented significantly elevated FEV1 is evidence of such volume recruitment.

As recognized by the authors, the use of multiple tests aimed at detection of a single abnormality can lead to false-positive results. However, analyzing bronchodilator response in various parameters can express different physiological phenomena. A reduction in air trapping, with the consequent reduction in thoracic gas volume, introduces some difficulties in the interpretation of airway resistance and airway conductance. A reduction in lung volume resulting from bronchodilator use causes an increase in airway resistance, which is reduced through the use of medication. Therefore, it is not surprising that tests of airway resistance present low sensitivity. In addition, adjusting increases in airway conductance for lung volume, which would express airway dilation under isovolumic conditions, appears interesting. However, the 50% increase in relation to baseline values, held as significant, could be less so because many patients with airflow obstruction present baseline values below 0.05 L/cmH_2O/s. Therefore, small absolute variations, within the error of measurement, can result in considerable percentage variations.

In the study, the post-bronchodilator variations adopted for SVC, FVC and IC correlated with relevant improvement in exercise tolerance.(9) No such cutoff point was established for RV, although the criterion adopted (20% increase over predicted) seems reasonable.[16]

In several recent studies, it was demonstrated that long-acting bronchodilators reduce air trapping, minimize dyspnea and improve quality of life for individuals with COPD.[17-19] Compared to salmeterol, formoterol results in a more rapid reduction in air trapping in COPD patients, which explains the fact that many such patients prefer formoterol.[19]

Despite the fact that, in COPD, bronchodilators can increase exercise tolerance by reducing air trapping, not all patients respond. In addition, a lack of response to a certain class of drugs does not preclude the possibility of a response to a different category of bronchodilator. The limited exercise tolerance seen in COPD is multifactorial (including diverse factors other than ventilatory limitation).[20]

The role of FEV1 in predicting the long-term response of a COPD patient to a bronchodilator is limited. However, there have been few studies utilizing lung volumes, including the measurement of RV and IC, to that end. If positive, such studies could establish a relevant, previously unknown, role for pulmonary function tests in COPD patients and could allow physicians to prescribe, with greater confidence and no longer in an empirical fashion, medications that are, in some cases, quite costly.

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