Guidelines on standardized challenge testing for airway hyperresponsiveness

To the Editor:

I am very satisfied, as I am sure many other "lung doctors" all over Europe are, with the guidelines on lung function testing recently published in the European Respiratory Journal [1]. I am particularly interested in the section concerning airway responsiveness and am convinced this will help to standardize methods and facilitate comparison of the results of various studies.

Nevertheless, I am seriously worried about the statement in item 3.2.4. (page 63) of the Guidelines: "The challenge is stopped.... when there is a 20% reduction in FEV\textsubscript{1}, or a doubling (100% increase) in sRaw".

The authors refer to the previous SEPCR guidelines [2, 3], in which a 40% increase in specific airways resistance (sRaw) is considered a positive response to bronchial challenge [2]. In the recommendations edited by QUANJER [3] the variance coefficient of specific airways conductance (sGaw) (reciprocal of sRaw), according to literature data, is 14-39%. What is the reason behind accepting a doubling of specific airway resistance as the positive result of the test? Moreover, a 20% reduction in forced expiratory volume in one second (FEV\textsubscript{1}) is certainly not comparable with 100% increase in sRaw.

It seems even dangerous to recommend achieving a 100% increase of airway resistance during bronchial challenge. Pourquoi done?

References


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Consequently, the use of sRaw rather than Raw increases the sensitivity [7, 8] and, thus, the safety of the test; it also eliminates any error in the measurement of alveolar pressure by the plethysmographic technique [9]. The 100% change in sRaw is also appropriate in terms of signal to noise ratio. It is far beyond the 95% confidence interval of repeated measurements. Reproducibility is almost invariably reported as the coefficient of variation, which may not be appropriate, as in lung function tests the scatter is not usually proportional to the mean [10]. Reported variabilities range between 3-7.5% [7, 9, 11], which is remarkably low. Assuming a normal distribution, a change in sRaw in excess of 15% would indicate a significant change. This leaves a healthy margin between signal and noise, without risk.

Therefore, the PC\textsubscript{10}sRaw is a suitable index of sensitivity to inhaled bronchoconstrictors in man. The level of bronchoconstriction achieved does not reflect excessive airway narrowing [12] and can, therefore, be regarded as absolutely safe if the measurements have been standardized [10] and the usual safety precautions have been taken [1].

References

Models for analysis of longitudinal data

To the Editor:

In his editorial comment on the paper by Sherrill et al. [1] Ware [2] discusses the use of efficient statistical models for longitudinal data, and how improved efficiency and validity results from proper model specification.

He fails to point out, however, that these models are a special case of a more general class of "multilevel" models, which explicitly take account of hierarchically structured data. In longitudinal repeated measures designs we have a basic two-level hierarchy, where measurement occasions are nested within subjects. In fact, however, the paper by Sherrill et al. [1] analyses data which come from a three-level hierarchy, since individuals are further nested within households. Since the Sherrill et al. [1] model ignores this third level, it is incomplete and is potentially invalid if there is a sizeable between-household variation in respiratory symptoms.

General models for hierarchically structured data have been studied by a number of authors, not mentioned by Ware [2], and general purpose software packages are widely available. In particular, the model studied by Sherrill et al. [1] together with the extension to incorporate between-household variation as well as general continuous time autoregressive structures can be fitted using one of these packages, ML3 [3].

This package has been successfully used to describe the development of maximum oxygen consumption in young athletes [4]. The hierarchical model was used to assess the effects of training by separating this effect from those of normal growth and development.

References


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From the author:

The comments of Goldstein and colleagues provide a useful addition to the discussion of the paper by Sherrill et al. [1]. Those working to develop methods for the analysis of longitudinal data have tended to ignore other types of clustering in the data, in part because within-subject correlation tends to be much larger than correlation from other types of clustering. For example, intrafamily correlation of pulmonary function measurements will be much smaller than within-subject correlation. Nevertheless, it would be helpful to have the capacity to explore these issues empirically. In the past, efforts to do so have been handicapped by the limitations of available software. Perhaps the next generation of software, including ML3, will be more flexible.

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