Assessment of Bronchodilator Responsiveness after Methacholine-Induced Bronchoconstriction

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Spirometry is the only objective clinical tool available to physicians in the outpatient setting. Patient history is often unreliable and physical examinations are normal when the child doesn’t show symptoms. For that reason, spirometry is currently considered essential for asthma diagnosis, severity stratification, and monitoring asthma control in children ≥5 years. Bronchodilator responsiveness (BDR), which is an improvement of forced expiratory volume in 1 second after inhalation of β2-agonists, has traditionally been the definition of asthma and has recently been reported to reflect biomarkers of eosinophilic inflammation, bronchial hyperreactivity, and airway remodeling. BDR has also been regarded as a good predictor of response to therapy, a marker for long-term prognosis, and an important component in defining asthma phenotypes.

Since BDR is usually measured by changes in airflow before and after administration of β2-agonists, it is influenced by the baseline airway tone. If the airways at baseline were fully dilated by asthma treatment, airflow would barely increase. Moreover, asthmatic children usually show prebronchodilator spirometry within the normal range, regardless of their symptom-based severity of asthma control. Consequently, impaired β-adrenergic responsiveness, which plays a role in the pathogenesis of asthma, is rarely evident, especially when the children are taking controller medications.

In 1999, Hancox et al. first introduced the ‘challenge-rescue’ technique to assess BDR. They measured BDR after bronchoconstriction induced by methacholine, because β2-receptor responsiveness was easier to demonstrate under conditions of increased bronchomotor tone. The challenge-rescue model has been widely used because it has consistently provided evidence of bronchodilator tolerance, whereas previous studies of stable asthma have not. Moreover, it has obvious clinical relevance; asthmatics usually take β-agonists to relieve symptoms caused by bronchoconstriction.

Despite the usefulness of this approach, some problems exist in terms of data interpretation. BDR to salbutamol is confounded by spontaneous recovery from the bronchoconstricting effects of methacholine. Although spontaneous recovery for 15 minutes after bronchoconstriction is rare, other factors that facilitate recovery from bronchoconstriction may be displayed as an enhanced responsiveness to bronchodilators. On the other hand, geometric factors, such as airway mucus plugging and mucosal edema, might not be discerned from bronchodilator tolerance. Therefore, care must be taken when analyzing BDR data obtained from the challenge-rescue technique.

In the present issue of Allergy, Asthma, & Immunology Research, Bauer et al. assessed BDR using the challenge-rescue technique and evaluated the clinical factors that may affect BDR in children with mild to moderate asthma. Though the interpretation of the data is complicated, the results provide interesting information. Asthmatic patients with atopy and/or eosinophilia displayed higher BDR as compared with that of non-atopic and/or non-eosinophilic patients, which provides indirect evidence that BDR may be a marker for inflammation. While admitting that bronchoconstriction induced by methacholine may not exactly reflect clinical exacerbation of asthma, the results raise the possibility that more frequent or severe asthma attacks would occur in non-atopic and/or non-eosinophilic children with asthma. Another interesting finding is that no apparent differences were observed among the medication subgroups. Since inhaled long-acting β2 adrenergic agonists or corticosteroids were discontinued seven days prior to testing in...
this study, it is likely that tolerance to β-agonists would no longer be a concern when medications are withheld for more than seven days.

Assessment of BDR following induced bronchoconstriction may be a useful tool for evaluating impaired β-adrenergic responsiveness, which plays a key role in the pathogenesis of asthma. Further studies are needed to extend the application of BDR assessment to determine management options in asthmatic patients.

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