

Assessment of bronchial hyperresponsiveness in preschool children: methodological issues

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Bronchial responsiveness is difficult to assess reliably in young children due to the lack of techniques suited for testing of lung function in this age group. Spirometry and measurement of peak expiratory flow depend on the active cooperation of the subject and rarely produce reliable results in young children, and the techniques used for studying lung function in infants are not suited beyond infancy and usually require sedation. Methods suitable for routine testing of lung function in young children should not depend on the child's active cooperation or the use of sedatives. Furthermore, the practical execution of measurements should be readily accepted by the young child. Clearly, such demands limit the number of techniques which may be considered for the use in young children.

Furthermore, the practical execution and interpretation of measurements of bronchial responsiveness in young children deserves particular attention. When performing bronchial challenge tests using non-specific bronchoconstrictor agents, such as histamine and methacholine, the method used for delivery of aerosol may be more critical than previously recognized.

When inhaling a nebulized bronchoconstrictor by means of a facemask, infants will inhale undiluted aerosol. Beyond infancy the mass of inhaled bronchoconstrictor agent is largely independent of the size of the children (1), and consequently young children receive a larger dose relative to body size than do older children. With present procedures it is not possible to quantify the amount of inhaled aerosol nor to administer the aerosol according to the size of the child. This may question the appropriateness of comparing bronchial responsiveness in children of different age, and restricts the conclusions which may be drawn from longitudinal studies of

bronchial responsiveness (2). The relevance of measuring bronchial responsiveness for clinical and epidemiological purposes depends on the reliability of the outcome of the challenge test. Progress in this field requires the introduction of techniques meeting the demands dictated by the distinctive physiological and psychological features of young children.

Techniques for measuring respiratory function in young children

A number of techniques allow measurement of respiratory function in awake young children during normal tidal breathing, requiring only the passive cooperation of the child. One such technique is the transcutaneous measurement of oxygen (tcPO_2), which in a number of studies has been found to reliably reflect the response to inhaled histamine and methacholine. TcPO_2 measurements reflect only indirectly airway function during bronchial challenge. However, studies in schoolchildren have documented a close covariation between the decline of tcPO_2 and the increasing airflow limitation during bronchial challenge (3–5). The estimate of bronchial responsiveness obtained by tcPO_2 has been found to be as repeatable as the estimate obtained by measurements of FEV_1 (6). Pulse-oximetry may be considered as a simple and cheap alternative, however it seems less reliable than tcPO_2 (4). A practical drawback of tcPO_2 measurements is that an equilibration period lasting 15–20 minutes is required after the transcutaneous electrode has been attached to the child's skin before stable measurements can be obtained.

The forced oscillation technique (FOT) meets the demands for use in young children and reflects the mechanical properties of the respiratory system by

measuring the respiratory resistance and respiratory reactance. In schoolchildren, FOT has been found to be as sensitive as measurements of airway resistance (Raw) and FEV₁ in detecting the response to inhaled bronchoconstrictor agents (7, 8). FOT has been applied successfully in young children in a number of studies (9), though other investigators have found the FOT to be unreliable in this age group (5).

The interrupter technique (Rint), which measures respiratory resistance, has proved useful for measuring respiratory function in young children (10) and for detecting the response to inhaled methacholine (11).

Comparative techniques in young awake children

We have recently applied the above-mentioned techniques in a number of studies in young children in order to evaluate their applicability and ability to reflect changes in airway function. During methacholine challenge, measurements were compared to simultaneous measurements of the specific airway resistance (sRaw) and FEV₁ in 4- to 6-year-old asthmatics (12). We found that all of the techniques reliably reflected the increasing bronchoconstriction induced by inhalation of methacholine. A newly developed variant of the FOT, the impulse oscillation technique, was used, and measurements of respiratory reactance by this technique proved to be as sensitive as sRaw in detecting airway obstruction. The sensitivity of tcPO₂ was intermediate, whereas the sensitivity of Rint was somewhat lower, but comparable to the sensitivity of FEV₁.

In a study in 2- to 4-year-old asthmatics we found that the above conclusions regarding the performance of the techniques also applied to measurements in very young children (13). The issue of the sensitivity of the techniques is of importance mainly with respect to the dose of bronchoconstrictor required to induce a measurable bronchomotor response; however, a very low sensitivity may require the use of high doses, which are likely to adversely affect the compliance of young children.

Recently, we studied the repeatability of methacholine challenge in 2- to 4-year-old asthmatics and found that the estimate of bronchial responsiveness obtained on separate days proved to be repeatable.

Measurements by means of tcPO₂, sRaw and respiratory reactance were highly repeatable, within one doubling dose of methacholine, whereas measurements of Rint and respiratory resistance by the oscillation technique were less repeatable. At present, several techniques seem to hold promise for the use in young children. More studies are required to determine the potentials of the individual techniques.

Choice of bronchoconstrictor stimulus and interpretation of the response

The method used for testing of bronchial responsiveness in young children should be considered also. Challenge tests using inhaled histamine or methacholine have gained widespread use. In young children methacholine may be preferable, while having a longer duration of action and fewer side effects. The relatively long duration of action makes the timing between inhalation and subsequent measurements less critical.

The method used for delivery of the bronchoconstrictor agent has a major impact on the dose delivered to the child. Inhalation of nebulized methacholine by means of a facemask do not allow quantitative estimation of the inhaled dose. Moreover, beyond infancy the inspiratory flow rate of the child will exceed the output from the nebulizer and the aerosol becomes diluted by entrainment of air. Once this occurs the mass of the inhaled bronchoconstrictor agent will be independent of the size of the child and, consequently, young children will receive a larger dose relative to body size. This complicates the comparison of bronchial responsiveness in children of different size and also the comparison of repeated tests in individual children e.g. years apart.

Dosimetry has been claimed to be more accurate, while allowing a quantitative estimate of the amount of inhaled aerosol. Commonly, a number of full vital capacity inspirations are performed, each followed by 5–10 seconds of breath-holding, and the aerosol is delivered during the inspiratory phase only. However, young children are rarely able to perform the above procedures correctly. Furthermore, we have noticed that during inhalation challenge in young children, respiratory rate may increase significantly, and sometimes the timing of the delivery of aerosol and the child's inspiration becomes de-synchronized. Consequently, quantitation of the inhaled dose becomes uncertain. None of the presently used methods for administering aerosol are ideal for use in young children, and methods meeting the special requirements for use in young children should be developed. Alternative methods, such as exercise testing and inhalation of cold dry air, have not yet been investigated in young children.

Conclusion

Techniques suitable for measurement of respiratory function in young children have been introduced during recent years. Such techniques may be applied for objective assessment of bronchial responsiveness, and encouraging results have been obtained by several techniques. The forced oscillation technique, the interrupter technique and transcutaneous mea-

surements of oxygen have been found to provide a reliable estimate of the changes in airway function during bronchial challenge in children too young to perform measurements with standard lung function tests.

The methods presently used for delivery of bronchoconstrictor agents, such as methacholine, should be improved, taking into consideration the psychological and physiological characteristics of young children.

References

1. COLLIS GG, COLE CH, LESOUF PN. Dilution of nebulised aerosols by air entrainment in children. *Lancet* 1990; 336: 341-3.
2. LE SOUEF PN. Can measurements of airway responsiveness be standardized in children? *Eur Respir J* 1993; 6: 1085-7.
3. HOLMGREN D, ENGSTROM I, BJURE J, SIXT R, ÅBERG N. Respiratory resistance and transcutaneous PO₂ during histamine provocation in children with bronchial asthma. *Pediatr Pulmonol* 1993; 15: 168-74.
4. WILSON NM, PHAGOO SB, SILVERMAN M. Use of transcutaneous oxygen tension, arterial oxygen saturation, and respiratory resistance to assess the response to inhaled methacholine in asthmatic children and normal adults. *Thorax* 1991; 46: 433-7.
5. WILSON NM, BRIDGE P, PHAGOO SB, SILVERMAN M. The measurement of methacholine responsiveness in 5 year old children: three methods compared. *Eur Respir J* 1995; 8: 364-70.
6. PHAGOO SB, WILSON NM, SILVERMAN M. Repeatability of methacholine challenge in asthmatic children measured by change in transcutaneous oxygen tension. *Thorax* 1992; 47: 804-8.
7. BUHR W, JORRES R, BERDEL D, LANDSER FJ. Correspondence between forced oscillation and body plethysmography during bronchoprovocation with carbachol in children. *Pediatr Pulmonol* 1990; 8: 280-8.
8. DUIVERMAN EJ, NEIJENS HJ, VAN DER SNEE VAN SMAALEN M, KERREBIJN KF. Comparison of forced oscillometry and forced expirations for measuring dose-related responses to inhaled methacholine in asthmatic children. *Bull Eur Physiopathol Respir* 1986; 22: 433-6.
9. DUIVERMAN EJ, NEIJENS HJ, VAN STRIK R, VAN DER SNEE VAN SMAALEN M, KERREBIJN KF. Bronchial responsiveness in asthmatic children aged 3 to 8 years measured by forced pseudo-random noise oscillometry. *Bull Eur Physiopathol Respir* 1986; 22: 27-33.
10. CARTER ER, STECENKO AA, POLLOCK BH, JAEGER MJ. Evaluation of the interrupter technique for the use of assessing airway obstruction in children. *Pediatr Pulmonol* 1994; 17: 211-7.
11. CHOWIENCZYK PJ, LAWSON CP, LANE S, et al. A flow interruption device for measurement of airway resistance. *Eur Respir J* 1991; 4: 623-8.
12. BISGAARD H, KLUG B. Lung function measurement in awake young children. *Eur Respir J* 1995; 8: 2067-75.
13. KLUG B, BISGAARD H. Measurement of lung function in awake 2-4 year old asthmatic children, during methacholine challenge and acute asthma. *Pediatr Pulmonol* 1996; 21: 290-300.