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INVITED REVIEW

Lung Function Tests in Preschool Children

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Abstract

The measurement of lung function by spirometry is routinely used to monitor and adequately treat children with asthma. The assessment and evaluation of lung function in children aged 3–5 years has been neglected for a long time because of the difficulty to perform forced expiratory maneuvers. However, the use of techniques such as the interrupter technique and the forced oscillation technique, which only require passive collaboration and where the only request to the child is to breathe at tidal volume, has overcome this limitation. Other techniques such as the measurement of specific airway resistance by plethysmography or the measurement of the lung clearance index using the multiple-breath washout might be helpful in this regard, although these techniques are less standardized in preschool children.

KEYWORDS: Preschool, interrupter, forced oscillations, specific airway resistance, washout

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INTRODUCTION

The measurement of lung function in preschool children has been considered difficult and impossible for many years because of the limited cooperation and the difficulty in performing forced maneuvers. This limitation has been overcome in infants and children younger than 2 years of age with the use of sedation, but this requires long run times and highly trained personnel; thus, the routine use of infant lung function tests are difficult to be performed.

For preschool children (aged 2–5 years), several non-invasive techniques that require only minimal collaboration, such as breathing at tidal volume and not requiring sedation, were developed. The American Thoracic Society/European Respiratory Society (ATS/ERS) Working Group on Infant and Young Children Pulmonary Function Testing published the international recommendations for measuring lung function in preschool children in 2007 [1]. The objective of these recommendations was to standardize the techniques used in different laboratories to allow comparisons among centers. The same group has recently published a workshop report on the clinical applications of these techniques in preschool children [2].

Recently, many studies have shown the possible clinical applications of such techniques for preschoolers. In particular, we would like to focus on two different techniques that can be used in clinical practice, such as the interrupter technique and the forced oscillation technique. For both techniques, normal values measured in large populations of healthy children as well as cut-off values for the bronchodilator response are available. Preschoolers can also undergo other techniques such as the measurement of specific airway resistance by plethysmography or the lung clearance index using the multiple-breath washout (MBW); however, these techniques are less standardized in preschool children and difficult to use in routine clinical practice.

THE INTERRUPTER TECHNIQUE

The measurement of respiratory resistance through the interrupter technique (Rint) was reported for the first time in 1927 and then improved over the 1970–1980 period. In the last years, this technique has been routinely used in several centers of pediatric respiratory medicine. The principle of the technique is that during a sudden interruption of flow at tidal breathing, alveolar pressure and mouth pressure would rapidly equilibrate, thus allowing alveolar pressure to be estimated by measuring mouth pressure. Resistance can then be calculated as the ratio between the change in mouth pressure and flow measured immediately before (classical technique) or after ("opening" technique) the interruption.

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Rint is therefore a measure of the resistance of the respiratory system (airway, lung, and rib cage). Because of the viscoelastic properties of the respiratory system, Rint will approach pure airway resistance if pressure is measured at the beginning of the interruption (classical technique), whereas it will estimate the resistance of the entire respiratory system if pressure is measured at the end of the interruption ("opening" technique).

As stated in the ATS/ERS recommendations [1], the interrupter technique should be performed with the child sitting with a neutral position of the head and the cheeks supported; the child should be wearing a nose clip and breathe quietly through a mouthpiece with an antibacterial filter. In addition, the valve should close in less than 10 ms, and each interruption should not last more than 100 ms (so that the child is not actively breathing during the interruption); the interruption should be triggered by a flow that corresponds to the peak expiratory flow; 10 measurements should be recorded to obtain at least five acceptable measurements; and the median of the technically acceptable measurements should be reported [1].

The interrupter technique is highly feasible in preschool children, with values ranging from 81% to 98% both in the outpatient setting and in field studies such as those conducted in kindergartens [3]. The intra-measurement coefficient of variation (CV) is around 12% in healthy children and also in those with wheezing or cystic fibrosis (CF) [2]. The inter-measurement coefficient of repeatability (CR) in the short term (two times the standard deviation of the difference between the two measurements) was reported to be ranging between 0.17 and 0.28 kPa·L^{-1}·s in healthy children [1] and also in those with recurrent wheezing [2]. A similar value of long-term CR was observed in healthy children [1], whereas the results are less consistent in children who have respiratory symptoms [2]. Various reference equations have been published about the interrupter technique in both preschoolers and school-age children [1-4]; data from various centers for the classic technique have been recently unified, thereby obtaining a single international reference equation [5].

In clinical practice, children with wheezing or asthma have been shown to have baseline Rint higher than healthy children [4,6], and the same has been shown for children with CF [7]. However, for the clinical use of Rint, it is also very important to assess the possible bronchodilator response (BDR). There are many published data on the measurement of BDR using Rint [2]. A recent study showed that a decrease in Rint >0.25 kPa·L^{-1}·s (which corresponds to a change >1.25 expressed in Z-score) can discriminate children with respiratory symptoms at the time of the test with a sensitivity of 80% and a specificity of 82% [8]. The data reported in the literature show that BDR measured with Rint is able to discriminate children with recurrent wheezing from healthy children with a sensitivity that varies from 24% to 76% and a specificity from 70% to 92% [2].

THE FORCED OSCILLATION TECHNIQUE

The forced oscillation technique (FOT) is a simple, noninvasive technique, which is performed during tidal breathing and can therefore be easily used in preschool children. A pressure wave is applied to the mouth, causing changes in flow and pressure that can be measured by obtaining the value of impedance of the respiratory system (Zrs) broken down into its two components of resistance (Rrs) and reactance (Xrs). Rrs corresponds to the frictional losses of the respiratory system, whereas Xrs is given by the elasticity and the inert properties of the respiratory system [1]. A range of frequencies can be used at the same time; thus, the dependence of the respiratory system by the various frequencies through an analysis model that takes into account the complexity of the signal can be studied [1]. Zrs measured at 6–8 Hz is thought to reflect the mechanic properties of total airways, whereas lower frequencies reflect the lung tissue component of the respiratory system and higher frequencies reflect the upper airways [1,2].

The measurement conditions of FOT in preschoolers according to the international recommendations [1] are similar to those of Rint as far as the position of the child and mode of breathing are concerned. The forcing signal should include frequencies between 4 and 8 Hz, and each acquisition is expected to last between 8 and 16 s. The average between 3 and 5 measurements should be reported, and the coefficient of variability (CV) (defined as the ratio between the standard deviation and the average) should be calculated for each frequency and used as an index of reliability of the measurements [1].

Forced oscillation technique has good feasibility in preschool children, which varies between 79% and 95% [2]. For the inter-measurement repeatability, many studies report a short-term CR between 1.1 and 2.6 hPa·L^{-1}·s for Rrs, which corresponds to a relative change of 12%–30%, and between 1.2 and 2.0 hPa·L^{-1}·s for Xrs [2]. Similar values are reported for the long-term CR [2].

In the literature, several reference equations for FOT, both for preschool children and older children, have been reported [1,2,9,10]. Data are also available on BDR [1], and many studies suggest that a decrease in Rrs of 20%–40% compared with baseline should be considered as a positive response to bronchodilators. A recent study conducted on healthy Italian preschool children suggested to use a cut-off that corresponds to a change in the Z-score of –1.88 for Rrs8 and 2.48 for Xrs8 [9].

Forced oscillation technique has been used in many studies in children with asthma, with a sensitivity of 90% and a specificity of 53% to discriminate healthy children from children with a possible diagnosis of asthma [2]. FOT also looks promising in identifying children with abnormal lung function; for example, those diagnosed with chronic lung disease related to prematurity [11]. Children with CF also show higher values of Rrs and lower Xrs [12]. FOT also seems to be able to identify, in preschool children with CF, the response to treatment after a respiratory exacerbation [13], although this needs further assessment.

SPECIFIC AIRWAY RESISTANCE

The measurement of specific airway resistance (sRaw) through the plethysmographic technique is also performed at tidal breathing without the need to breathe against a closed valve, unlike that in conventional plethysmography. sRaw is the product of airway resistance by the thoracic gas volume (TGV) and is calculated by measuring the change in plethysmographic volume (ΔVbox) and the change in airflow (ΔV′) using the following formula: sRaw=(ΔVbox/ΔV′)–(Pamb–PH_2O), where Pamb represents the ambient pressure and PH_2O is the water vapor pressure at 37°C. The electronic thermal compensation takes into account the possible changes in humidity and temperature of the gas during the respiratory cycle and obviates the need for the panting maneuver.

Bisgaard and Nielsen [14] have reviewed the technical aspects of the measurement of sRaw in preschool children. The child seated in the body plethysmograph has to breathe at a respiratory rate of 30–45 breaths per minute. sRaw is obtained from the median of five technically acceptable cycles [14]. However, there is still no consensus on measurement conditions, methods, or outcome measures [2]; this impairs the comparison of results among centers.

The measurement of sRaw is easily applicable in young children (feasibility 57% in 2-year-old children) and is also repeatable (short-term CR 0.17–0.22 kPa/s, with similar values for long-term CR) [14]. Reference values are also available for this technique [14], and an attempt to create a single equation for white European children was made [15], although the lack of standardization made this process difficult. There are also data on BDR; a reduction was observed from baseline sRaw of 25% having a sensitivity of 66% and a specificity of 81% in discriminating between asthmatic and healthy preschool children [14]. Furthermore, sRaw has also been used in epidemiological studies [14]. In conclusion, plethysmograpic sRaw has a high clinical potential in preschool children, and there is an urgent need for methodological guidelines [15].

MULTIPLE-BREATH INERT GAS WASHOUT

The method of MBW is used to establish the homogeneity of ventilation in the lungs and for the measurement of functional residual capacity (FRC), typically using the washout of nitrogen with 100% oxygen. MBW can be performed in preschoolers because it only requires passive cooperation and breathing at tidal volume. For the measurement of MBW, other non-resident inert gases such as helium, argon, or sulfur hexafluoride (SF_6) can also be used, although some of them are not universally available [2]. MBW allows the identification of several indices representative of ventilation inhomogeneity. One of the most commonly used is the lung clearance index (LCI), which represents the number of lung volumes (expressed as FRCs) required to complete the washout period [1]. The analysis of the normalized concentration of the slope of phase III of the washout curve is a more complicated method. Although a recent ERS/ATS statement has reported the standard operating procedure for MBW [16], several technical details still need to be agreed on as far as preschool children are concerned, and a standardization project on MBW in preschoolers is currently being conducted.

According to the current recommendations for preschoolers [1], MBW should be performed while the child is sitting and breathing at tidal volume through a mouthpiece or mask closely fitted to his/her face. If using an inert gas, a sufficiently long washout period is required, and the washout should continue until the gas concentration at the end of the current volume has reached levels lower than 1/40 of the initial concentration over a period of more than three consecutive breaths. The average value of LCI between two washouts where FRCs differ by less than 10% should be reported as the final result [1].

The feasibility of measuring LCI is good in preschool children (between 75% and 84%) [2]. LCI seems to be independent of age and growth in healthy subjects [1] and has been used successfully for clinical purposes such as monitoring children with CF and asthma. This index is a sensitive tool and is very useful in documenting damage of the small airways such as the one that occurs in chronic lung diseases such as CF and bronchiolitis obliterans [1,2]. A 2005 study of Aurora et al. [17] reported that MBW was more sensitive than spirometry and plethysmography in detecting abnormal lung function in preschool children with CF. However, a very recent CF Foundation workshop report [18] concluded that the data to support the use of LCI or MBW parameters in the routine clinical management of patients with CF are currently insufficient.

In conclusion, Rint, FOT, sRaw, and MBW are easily feasible and reproducible in preschoolers. Given their role in identifying changes in airway caliber, these are potentially very useful tools in the clinical assessment of a child with respiratory disease. Further studies assessing the clinical short-term and long-term utility of these techniques in preschool children are urgently needed.

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